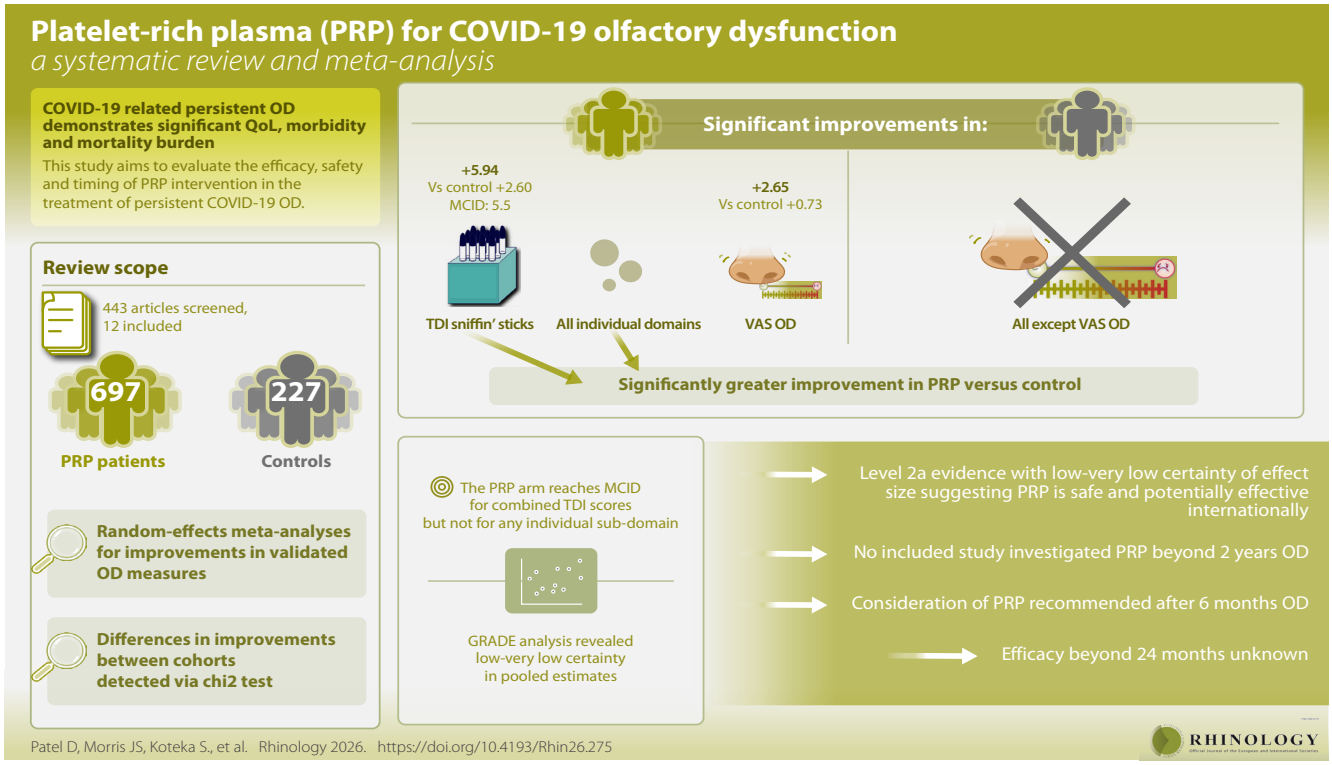
Platelet-rich plasma for COVID-19 olfactory dysfunction: a systematic review and meta-analysis

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Abstract

Introduction: COVID-19 related persistent OD internationally demonstrates significant quality-of-life, morbidity and mortality burden. We aim to evaluate the efficacy, safety and timing of PRP intervention in the treatment of persistent COVID-19 OD.

Methods: Systematic searches were performed to generate random-effects meta-analyses for improvements in validated OD measures. Differences in improvements between cohorts were detected via chi2 test.

Results: 443 articles screened with 12 inclusions; PRP patients (n=697), controls (n=227). Meta-analyses demonstrated significant improvements in PRP for TDI Sniffin' Sticks, all individual domains, and VAS OD; controls demonstrate significant improvements in all except VAS OD. There was a significantly greater improvement between PRP versus control for combined TDI Sniffin' Sticks (PRP: +5.94, control: +2.60), and all individual sub-domains. The PRP arm reaches MCID for combined TDI scores but not for any individual sub-domain. GRADE analysis reveals low-very low certainty in pooled estimates.

Conclusions: Level 2a evidence with low-very low certainty of effect size suggesting PRP is safe and potentially effective internationally. No included study investigated PRP beyond 2 years OD. Thus, we recommend considering PRP after 6 months of OD. Efficacy beyond 24 months remains unknown. Limitations include combining randomised and non-randomised trials, limited placebo injections across meta-analysed control cohorts (n=2), and PRP protocol variance.

Key words: platelet-rich plasma, olfaction disorders, olfactory impairment, smell dysfunction, COVID-19

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Introduction

Olfactory dysfunction (OD) is associated with significant morbidity and mortality [1–3], exceeding that observed in loss of other sensory modalities such as sight or hearing [4]. Morbidity encompasses cognitive decline [5]; malnutrition [6]; and mental health issues linked to reduced enjoyment of food [7] and anxiety surrounding body odour or halitosis [8]. Severe OD is associated with three-fold increased mortality in elderly populations [9], potentially due to inability to detect harmful gases, smoke or malodorous foods [10]. Coronavirus disease 2019 (COVID-19) can cause persistent OD, defined as lasting over six months [11], in 5% of cases, thus representing a significant global health burden.

Established therapeutic options for persistent COVID-19 OD largely consist of olfactory training (OT) [12]. Other less established options, such as Omega-3 [13], intranasal Vitamin A [14,15], intranasal corticosteroids [16,17], intranasal sodium citrate [18] and palmitoylethanolamide with luteolin [19] exist; however, despite the significant disease burden, unfortunately both efficacy and proportion of patients who show benefit from current therapies remain limited [20].

Platelet-rich plasma (PRP) is an autologous blood product which contains supraphysiologic concentrations of growth factors. PRP usage is well-established in other clinical fields including treatment of carpal tunnel syndrome [21–23] or traumatic peripheral nerve injury [24,25]. SARS-CoV-2 penetrates the olfactory neuroepithelium via the ACE2 and TMPRSS2-presenting sustentacular cells, causing disruption of the epithelial microenvironment, whilst the basal stem cell reservoir is largely preserved. This facilitates spontaneous recovery in most patients, whilst some display persistent OD relating to sustained local inflammation, impaired regeneration, or aberrant reinnervation [26–28]. PRP could improve persistent COVID-19 OD by regulating the inflammatory response in the microenvironment and promoting peripheral nerve regeneration via growth factor mediated axonal regrowth and angiogenesis [29,30]. PRP has historically shown mixed efficacy in systematic reviews [31,32], however, four large-scale randomised controlled trials (RCTs) or prospective controlled studies have been published in the past two years [33–36], warranting a critical and contemporaneous update to the literature.

We aim to evaluate the efficacy, safety and timing of PRP intervention in the treatment of persistent COVID-19 OD.

Materials and methods

Registration and systematic searches

This study was prospectively registered with PROSPERO on 09/08/2025 (CRD: 420251070286). Expert librarian support was sought to conduct systematic searches of Medline, Embase, Cochrane Library and Google Scholar on 02/07/2025 using search concepts relating only to olfactory dysfunction and platelet-rich plasma to ensure maximal sensitivity; for further rationale and full details of search terms please see File S1. Study titles and abstract records were independently screened using Rayyan [37] by two independent blinded reviewers (DP & SK) according to the PICOS framework and disputes settled by a third blinded reviewer (JSM). Included abstracts then underwent independent full-text review for confirmation that they met these criteria. For further methodological validity and assurance, as advised by the expert librarian, included full-text reports underwent further backwards citation searching. All records identified from backwards citation searching underwent manual full-text report screening according to the PICOS framework. The search was not updated since 02/07/2025.

The PICOS criteria for this systematic review were: Population: all patients with post-viral OD primarily related to COVID-19, Intervention: PRP injection, Comparison: a control population who did not receive PRP, Outcome: changes in validated measures of olfactory function, Study Design: full-text primary human studies reported in English including randomised trials, cohort studies, case-control studies, case series and individual case studies; for full PICOS criteria please see Table S1. Studies without a control cohort were not excluded. Topical PRP administration was excluded as it would be unlikely to deliver platelets into the subepithelial space, driving growth factor release which is postulated to be responsible for OD recovery (29,30). Data, including demographics and changes in olfactory function in both the intervention and control cohorts were extracted using a standardised template prior to analysis. Where changes were not reported, the values at baseline and follow up were extracted instead. Where visual analogue scales were used to quantify the degree of olfactory dysfunction, these were standardised across studies to a 0-10 scale with 0 representing the worst olfactory dysfunction and 10 representing normal olfaction. The length of follow up was defined using the time of administration of the first PRP dose as the start point. The methodology and results of this systematic review are presented in accordance with the PRISMA guidelines [38].

Statistical analysis

Where changes in olfactory function were not directly reported, they were calculated as the absolute difference in the mean between baseline and follow up. The standard deviation therein was imputed using the standard deviations in these values and a correlation coefficient of 0.5 according to the method developed by Follmann 1992 [39] and Abrams 2005 [40] and outlined in the Cochrane Handbook section 6.5.2.8 [41]. Where spread was instead reported as the range in values, this was approximated to 4xSD using the "rule of 4s" method [42]. The olfactory scores of each cohort were assumed to follow a normal distribution and

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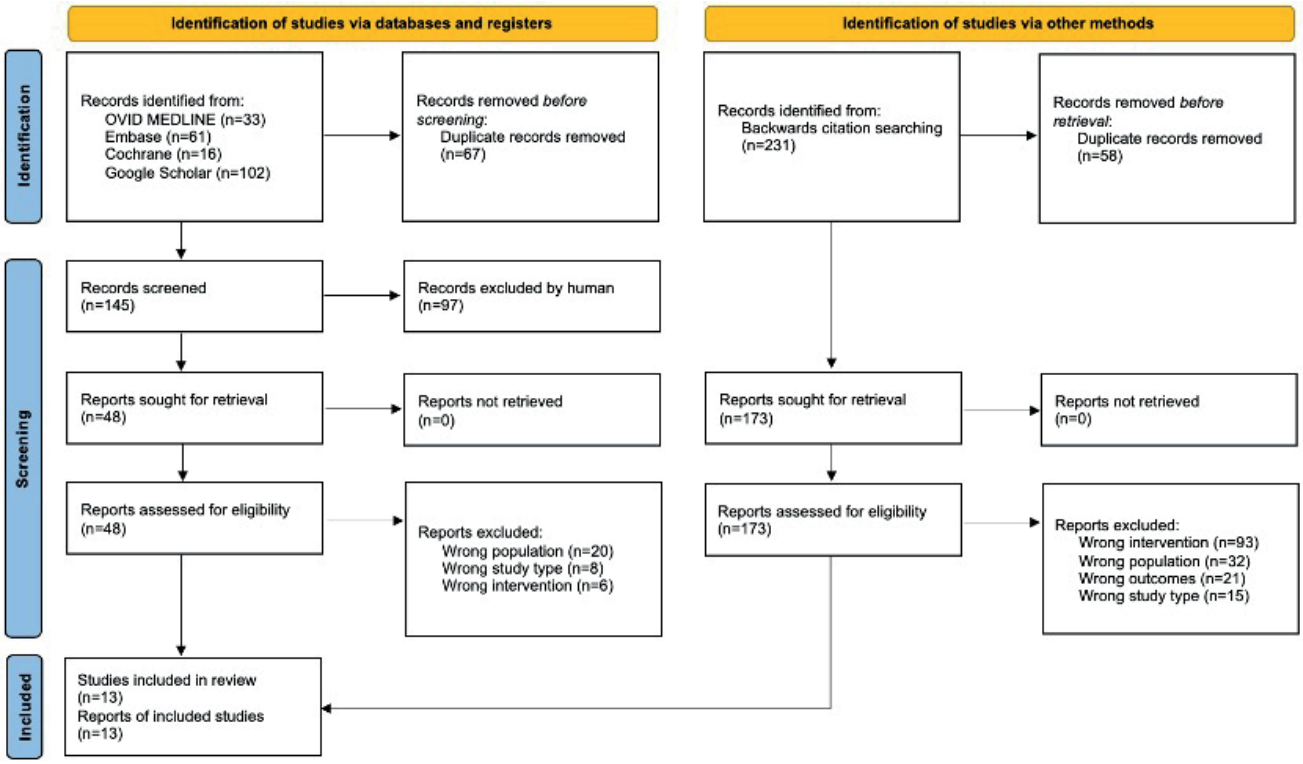


Figure 1. PRISMA flowchart outlining the study selection process.

transformed into the format: mean ± standard error to facilitate meta-analysis. Where data availability allowed, the random-effect meta-analysis model [43–45] was used to generate restricted maximum-likelihood estimates (REMLs) for the overall change in each measure of olfactory function in both the intervention and control cohorts. Significant differences between these groups with regards to each outcome metric were detected using the Q statistic. The individual estimates contributing to the intervention and control cohort estimates were assessed for between-study heterogeneity using the Cochran's Q statistic with a threshold for significance of α=0.05.

Risk of bias

The risk of bias in the included studies was assessed to Cochrane methodology using RoB 2 and ROBINS-I tools [46] for randomised and non-randomised studies of interventions respectively, and the robvis tool [46] was used to represent data. The risk of publication bias in the pooled estimates was assessed via funnel plots [47] and the Egger's regression-based test [48] against the t-distribution. Certainty in evidence was assessed using GRADEpro GDT [49]. All statistical analyses were conducted by JSM using STATA SE v18.0 [50].

Results

Demographics of included patients

Systematic searches coupled with backwards citation searching yielded 443 articles, of which 12 met the PICOS criteria (for full details of screening process, Figure 1). These included 924 patients (697 treated with PRP and 227 controls) followed up for a weighted mean of 3.01 months across a median study duration of 274 days (IQR: 212-730). Our analyses included 4 multi-centre studies, 2 conducted in Belgium [36,51] and 2 in the USA [35,52], as well as 8 single-centre studies, 4 conducted in Egypt [33,34,53,54], 2 in Belgium [55,56], and 1 in each of Portugal [57] and Turkey [58]. Ethnicity was only reported by 2 American studies [35,52] contributing 145 patients (14.4%). Of these, the PRP patients comprised 58.8% Caucasians, 5.9% African-Americans and 23.5% Hispanics compared to their control cohorts which comprised 67.9% Caucasians, 3.5% African-Americans and 17.9% Hispanics.

The weighted mean age of PRP patients was 45.3 years (pooled SD 12.5) compared to 42.1 years (pooled SD 11.2) in control patients. The weighted mean sex ratio was 35.6% male in PRP patients and 37.4% in controls. The weighted mean duration of olfactory dysfunction prior to treatment was 19.5 months (pooled SD 7.0) for the PRP cohorts and 11.2 months (pooled SD 3.9) in controls, although this was only reported in 7 [35,36,51,52,55–57,59] and 3 [35,52,55] included studies, respectively. Comorbidities were variably reported. The proportion of total participants contributed by the papers reporting rates of comorbidities were 69.7% for hypertension [36,51,52,57], 71.0% for diabetes mellitus [35,36,51,52,59], 72.3% for smoking [33,35,36,51] and 67.5% for asthma [36,51,52]. Comorbidities reported by PRP and control cohorts respectively were 13.5% and 7.8% for hypertension, 6.0% and 1.7%

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Table 1. Details of protocols for PRP and control cohorts across included studies.

Reference	Treatment cohort		Control cohort
	PRP administration	Additional therapies	
de Sousa et al. 2023	Single injection given.	Nil concurrently; prior failed OT (required) and varying adjuvant therapy including topical nasal corticosteroids/ vitamin A/vitamin B complex/vitamin E.	No control cohort.
ELNaeem et al. 2025	Three injections given, one month interval.	Nil concurrently.	OT.
El Naga et al. 2022	Three injections given, three-week interval.	Nil concurrently; prior failed 3 month OT + topical corticosteroids + omega-3, vitamin B12 + zinc.	OT, topical corticosteroids, Omega-3, Vitamin B12 and zinc.
Elsheikh et al. 2024	Three injections given, interval not specified.	Nil concurrently; prior failed medical treatment (unspecified)	Placebo: saline injection.
Evman et al. 2023	Single injection given.	Nil concurrently; prior failed 1 month OT + nasal steroids + nasal D-panthenol + nasal vitamin A	OT, nasal steroids and nasal D-panthenol/Vitamin A combination spray.
Fieux et al. 2025	Three injections given, two-week interval.	Concurrent OT; some had prior oral/topical steroids.	OT. 6 of 16 controls received placebo saline injection.
Lechien et al. 2023	Single injection given.	Concurrent OT; some had prior OT, nasal/oral corticosteroids, Zinc, vitamin A, vitamin B12, alpha-lipoic acid or Omega-3.	No control cohort.
Lechien et al. 2024	Single injection given.	Concurrent OT.	No control cohort.
Lechien et al. 2025	Single injection given.	Concurrent OT; some had prior OT, nasal/oral corticosteroids, Zinc, vitamin A, vitamin B12, or alpha-lipoic acid.	OT.
Sadek et al. 2023	Single injection given.	Nil concurrently.	No control cohort.
Steffens et al. 2022	Single injection given.	Nil concurrently.	OT.
Yan et al. 2023	Three injections given, two-week interval.	Nil concurrently; prior failed 3 month OT + topical budesonide irrigations.	Placebo: saline injection.

for diabetes mellitus, 7.1% and 19.5% for smoking, and 5.0% and 9.7% for asthma. Methods of diagnosing SARS-CoV-2 infection ranged from positive PCR [51–55,57,58], clinician evaluation [53], self-reported status [34,36], or not stated [33,35,56].

PRP and control protocols

Significant variation existed in PRP and control cohort protocols, including spin speed in revolutions per minute (rpm), number of spins, mode of PRP delivery, number of PRP doses including intervals between doses, and control cohort treatment (Table 1). Seven papers [33,36,51,53,54,56,57] gave details for local anaesthetic usage prior to PRP administration, 5 of whom [33,36,51,53,56] used xylocaine and xylometazoline chlorhydrate. For more expanded details of PRP protocols, alongside inclusion and exclusion criteria (Table S2).

Adverse events following PRP

Adverse events were not discussed in 4 included papers [34,35,53,54]. Of the 8 [33,36,51,52,55–58] that formally assessed for adverse events, 4 [52,55–57] demonstrated no notable adverse events in either cohort. Vasovagal episodes were reported in a total of 15 cases (2.5% of 604 PRP patients across these 8 studies) and 35 cases of epistaxis (5.8% of PRP patients), only 1 of which was described as persistent. Beyond this, there were no cases of grade 2-5 adverse events [60].

Reported olfactory outcomes

Changes in olfaction following PRP were quantified using a butanol threshold test in 2 papers [53,58], neither of which detected significant improvements; 0.83 (95%CI: 0.27-1.39) using 7 increasing concentrations of butanol reflecting the Connecticut Chemosensory Clinical Research Center (CCCRC) test protocol at 1 month follow up [58]; and 0.60 (95%CI: -0.13–1.33) using 10 increasing concentrations of butanol at 3 months follow up [53]; $p>0.05$ for both. The former also showed no significant improvements in olfaction for the 13 control patients: 0.08 (95%CI: -0.56-0.72, $p=0.81$).

The Olfactory Disorders Questionnaire (ODQ) was utilised in 2 papers [36,51], both of which demonstrated significant improvements following PRP: -10.30 (95%CI: -14.72– -5.88) after 2 months [51] and -4.40 (95%CI: -6.27– -2.53) after 3 months [36]. The latter demonstrated no significant improvements at 3-month follow up for controls: -0.80 (95%CI: -6.23–4.63, $p=0.77$).

The University of Pennsylvania Smell Identification Test (UPSIT)

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Table 2. Summary of findings table for meta-analysis and the certainty of evidence as assessed using GRADEpro GDT.

Outcome	Certainty assessment						№ of patients		REML for Improvement Change (95% CI)		Certainty
	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	PRP	Controls	PRP	Controls	
TDI Combined	5	2 RCTs 3 non-randomised studies	not serious	not serious	not serious	not serious	568	150	5.94 (4.95 – 6.92)	2.60 (0.99 – 4.20)	⊕⊕OO Low
TDI-T	5	2 RCTs 3 non-randomised studies	not serious	not serious	not serious	not serious	558	124	2.08 (1.68 – 2.47)	0.89 (-0.22 – 1.99)	⊕⊕OO Low
TDI-D	4	2 RCTs 2 non-randomised studies	not serious	not serious	not serious	not serious	538	124	2.60 (1.93 – 3.27)	1.21 (0.50 – 1.93)	⊕⊕OO Low
TDI-I	4	2 RCTs 2 non-randomised studies	not serious	not serious	not serious	not serious	538	124	2.15 (1.70 – 2.59)	1.16 (0.38 – 1.95)	⊕⊕OO Low
VAS OD	4	2 RCTs 2 non-randomised studies	not serious	serious	not serious	not serious	70	58	2.65 (1.19 – 4.11)	0.73 (-0.04 – 1.51)	⊕OOO Very low

was used in 1 paper [35], which showed significant improvements in olfaction following PRP (8.90, 95%CI: 6.25–11.55, p<0.00001) at 12-months follow up but no significant changes when PRP was not administered (1.30, 95%CI: -9.48–12.08, p=0.81).

Meta-analysis of olfactory outcomes

Data availability was sufficient to allow meta-analysis of responses to the overall combined threshold, discrimination and identification (TDI) Sniffin' Sticks assessment and individual components therein alongside the 0-10 visual analogue scale for subjective severity of olfactory dysfunction (VAS OD). Two papers were excluded from meta-analysis as they were deemed to be at critical [56] and serious risk of bias [53], respectively.

The change in the overall TDI result following PRP was assessed in 5 papers [33,36,51,52,55] producing a pooled estimate of 5.94 (95%CI: 4.95–6.92, p<0.00001). The improvements reported by individual studies did not exhibit significant between-study heterogeneity (Q(4)=4.59, p=0.33). This showed significant advantages compared to control cohorts (Q(1)=12.08, p<0.00001) which nonetheless exhibited significant improvements (2.60, 95%CI: 0.99–4.20, p<0.005) across a homogeneous group of studies [33,36,52,55] (Q(3)=1.45, p=0.69), of which one (52) received a placebo injection (Figure 2). The differences in TDI score can be attributed to significant differences between PRP and controls in all three components; threshold [33,36,51,52,57], discrimination [33,36,51,52] and identification [33,36,51,52] (Q(1)=3.94, p=0.047, Q(1)=7.75, p=0.01 and Q(1)=4.60, p=0.03, respectively).

PRP patients exhibited improvements in threshold [33,36,51,52,55] (2.08, 95%CI: 1.68–2.47, p<0.00001); discrimination [33,36,51,52] (2.60, 95%CI: 1.93–3.27, p<0.00001); and identification [33,36,51,52] (2.15, 95%CI: 1.70–2.59, p<0.00001) components. There was no significant difference between-study heterogeneity in the PRP cohorts of any of the three components (Q(4)=5.09, p=0.28, Q(3)=5.23, p=0.16, Q(3)=5.47, p=0.14, respectively). Controls demonstrated no significant changes in TDI threshold [33,36,52] (0.89, 95%CI: -0.22–1.99, p=0.12). However, controls demonstrated significant but smaller changes TDI discrimination (1.21, 95%CI: 0.50–1.93, p<0.001) [33,36,52] and TDI identification [33,36,52] (1.16, 95%CI: 0.38–1.95, p<0.005) [38,42]. These control cohorts demonstrated no significant between-study heterogeneity in threshold (Q(2)=4.45, p=0.11), discrimination (Q(2)=3.39, p=0.18), or identification components (Q(2)=1.54, p=0.46), respectively; additionally, only one cohort [52] within these received a placebo injection (Figures 3, 4 and 5).

Meta-analysis produced a pooled estimate for the change in VAS OD following PRP of +2.65/10 (95%CI: 1.19–4.11, p<0.0005) across 4 papers [35,52,54,57]. This was a significantly better improvement compared to controls (Q(1) = 5.16, p=0.02), which did not show any significant improvement after 2.5-12 months follow up (35,52,54): +0.73/10 (95%CI: -0.04–1.51, p=0.06). The PRP cohort suffered from significant between-study heterogeneity (Q(3) = 13.58, p<0.00001), whilst the control cohorts of included studies were consistent with regards to changes in VAS OD (Q(2) = 2.11, p=0.35), of which two [35,52] received placebo injections (Figure 6).

Risk of bias assessment certainty of evidence

Four papers underwent RoB 2 analysis for randomised trials, of which 1 [52] was deemed to be low risk of bias, and 3 [33,54,58] were

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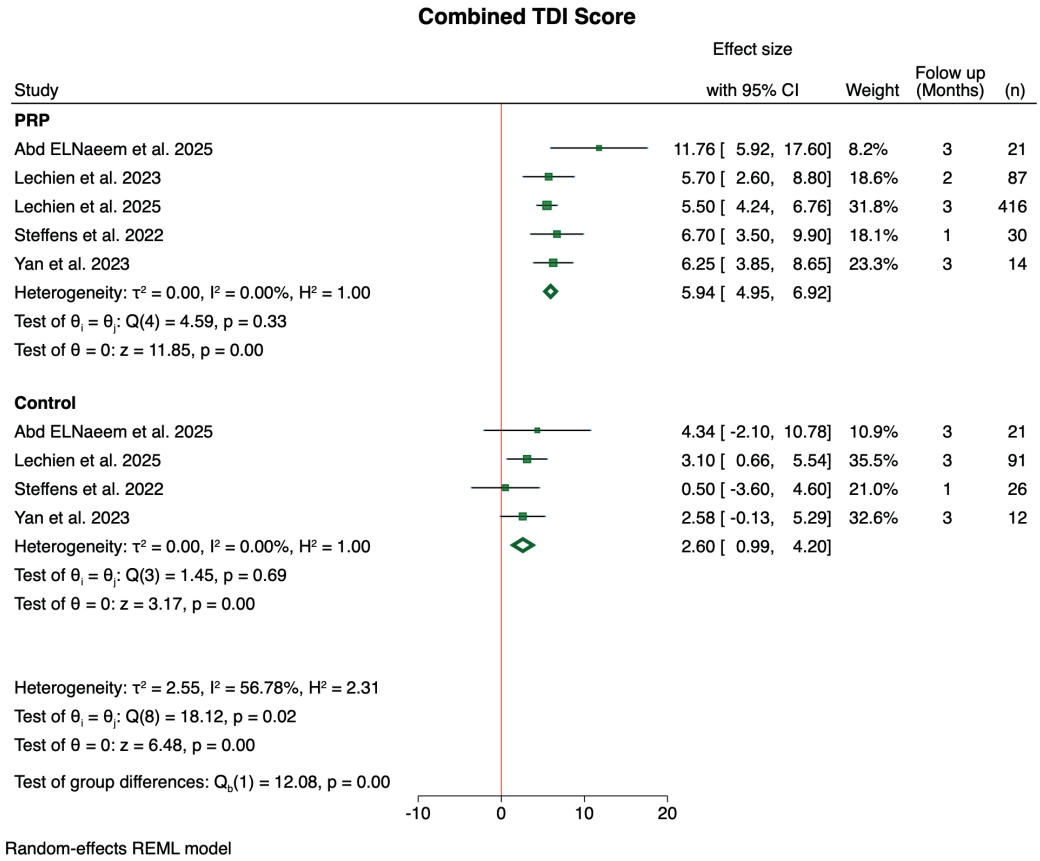


Figure 2. Forest plot summarizing the meta-analysis of change in overall TDI score amongst the PRP and control cohorts.

deemed to have some concerns (Figure 7). In all 3 cases where some concerns were noted, it was due to the absence of a placebo in the control group, meaning that participants could have been unblinded to their assignment to intervention.

Eight papers underwent ROBINS-I analysis for non-randomised trials, of which 5 [34–36,55,57] were deemed to have low risk of bias and 1 deemed to have moderate risk [51] due to missing data secondary to adherence and loss to follow-up (Figure 7). One paper was deemed to be at serious risk of bias [53] as reported statistical significance did not correlate with provided data, and was therefore removed from meta-analysis. Another paper was deemed to be at critical risk of bias at preliminary judgement [56] as the study design was a description of technique, with a sample size of 1 and thus, made no attempt to control for confounders (for this reason, it was deemed inappropriate to assess domains 2-6 of ROBINS-I for this paper as per the ROBINS-I algorithm).

Although the Egger's test is not valid for application in meta-analyses of fewer than 10 studies [61], it demonstrated no significant skew in funnel plots for the change in total TDI, TDI-Threshold, TDI-Discrimination, TDI-Identification or VAS OD (p values of 0.172, 0.428, 0.157, 0.357 and 0.344, respectively). The type-I error rate of Egger's test may also be artificially increased by virtue of the significant between-study heterogeneity of the PRP cohort in our analysis of VAS OD [61,62]. Visual inspection of funnel plots corroborated the conclusion of negligible publication bias for all funnel plots (Figure 9). However, this conclusion is dubious given the paucity of published studies that could be included in the funnel plots (n_x=4-5).

The certainty in the pooled estimates generated by meta-analysis was low (⊕⊕OO) for TDI score and associated sub-domains and very low (⊕OOO) for VAS OD. Certainty of evidence suffered as a result of including non-randomised studies alongside RCTs and due to between-study heterogeneity (or "inconsistency") in the case of VAS OD (Table 2).

Discussion

Through inclusion of both randomised and non-randomised trials, we present Level 2a [63] evidence with low to very low certainty of effect size, which cautiously supports PRP usage as a safe and potentially efficacious therapy for persistent COVID OD, with a minimal clinical risk profile. PRP demonstrates improvements across international cohorts despite known cultural variability of psychophysical olfaction tests [64], suggesting potential generalisability of findings. It is paramount to emphasise

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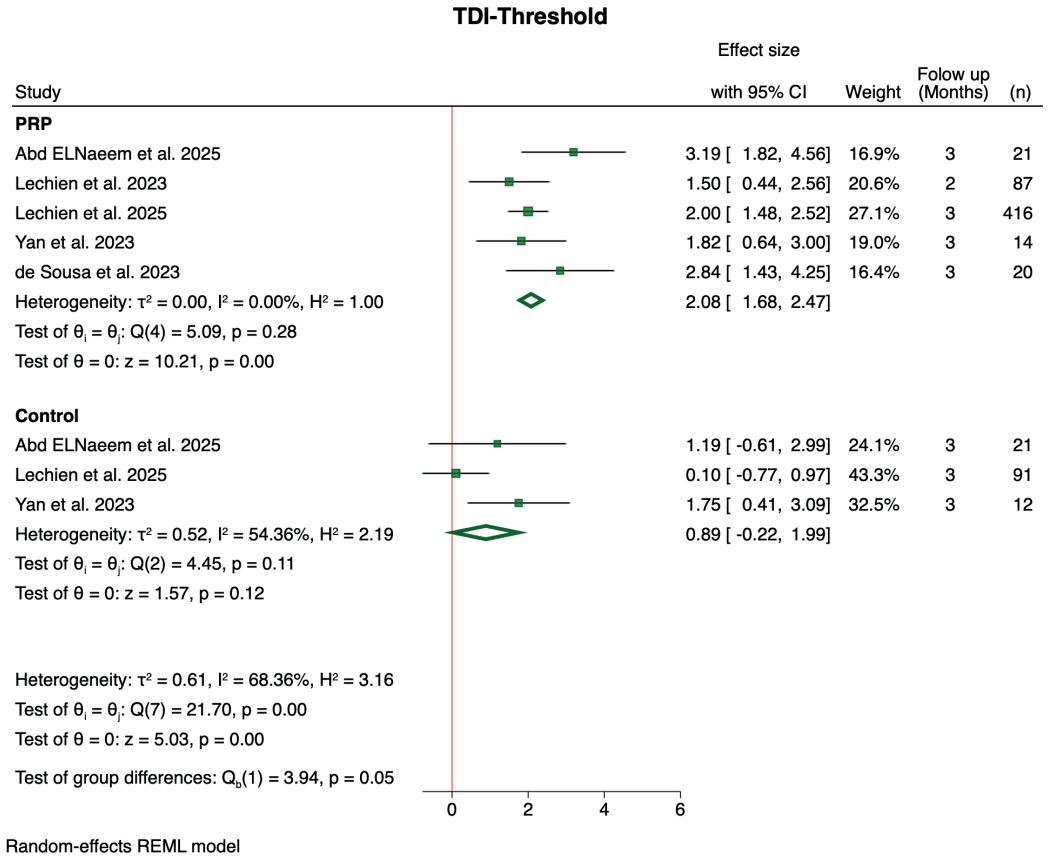


Figure 3. Forest plot summarizing the meta-analysis of change in TDI-Threshold score amongst the PRP and control cohorts.

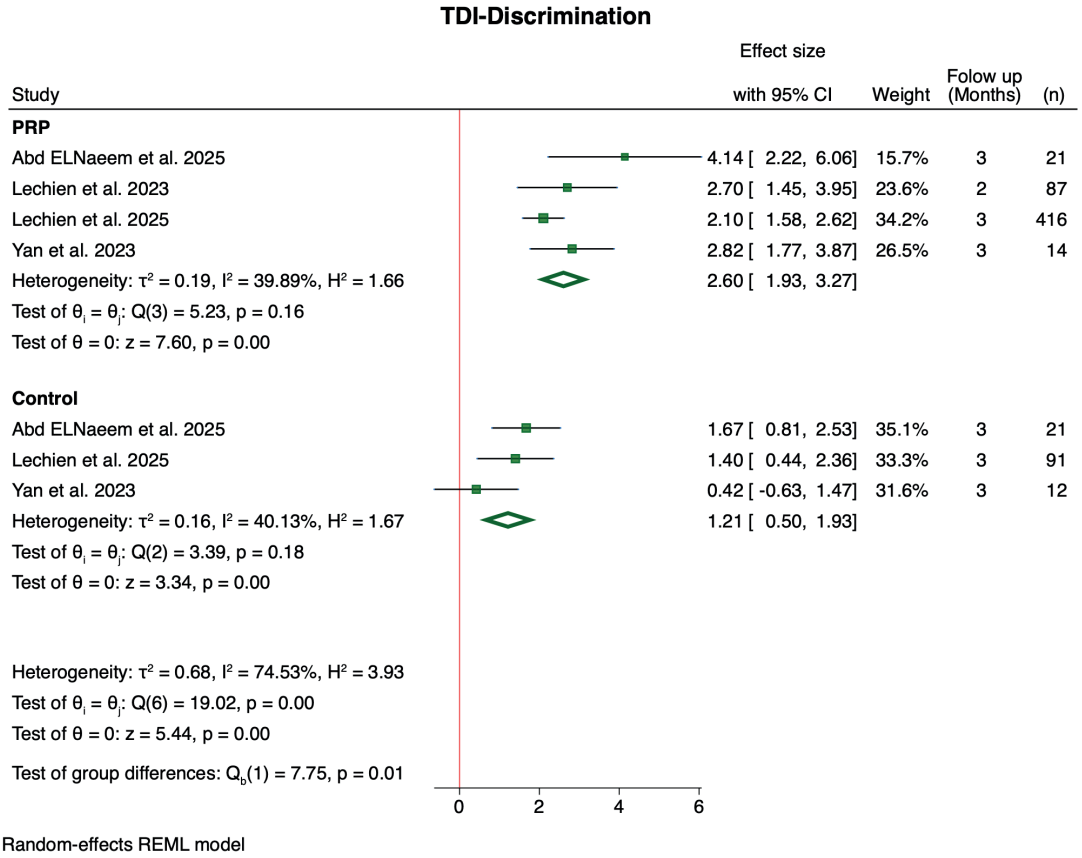


Figure 4. Forest plot summarizing the meta-analysis of change in TDI-Discrimination score amongst the PRP and control cohorts.

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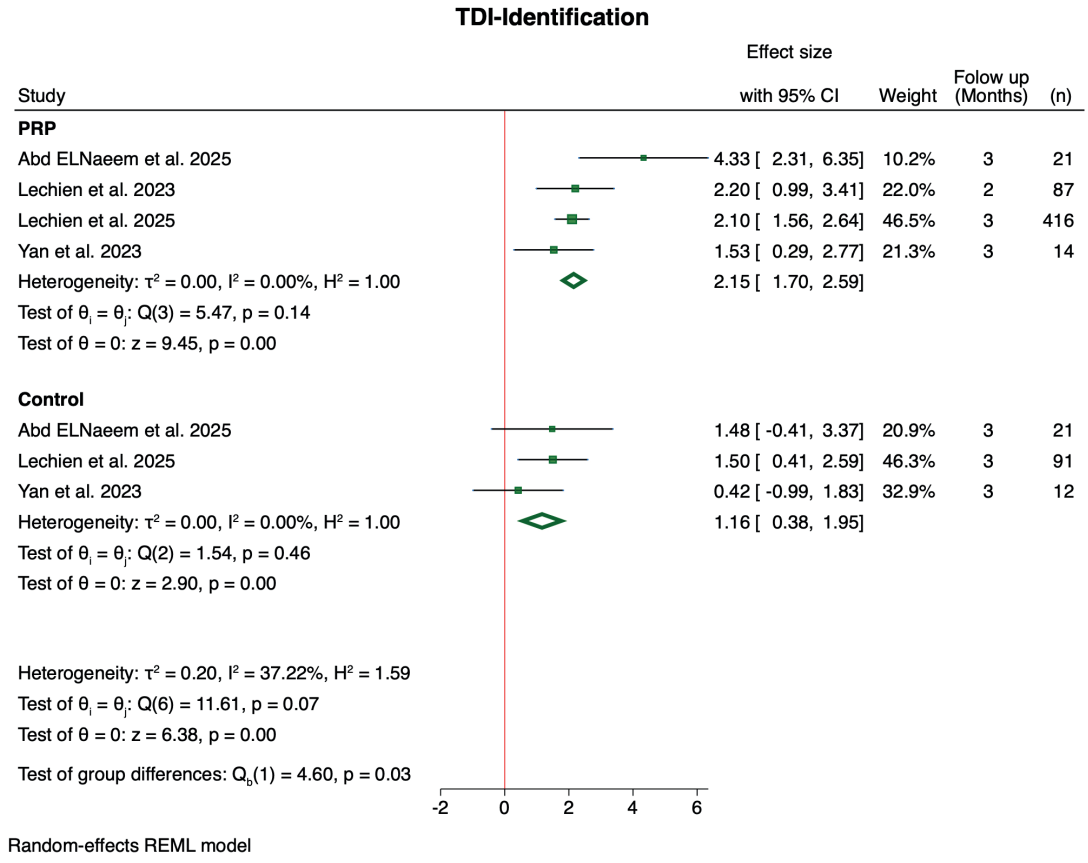


Figure 5. Forest plot summarizing the meta-analysis of change in TDI-Identification score amongst the PRP and control cohorts.

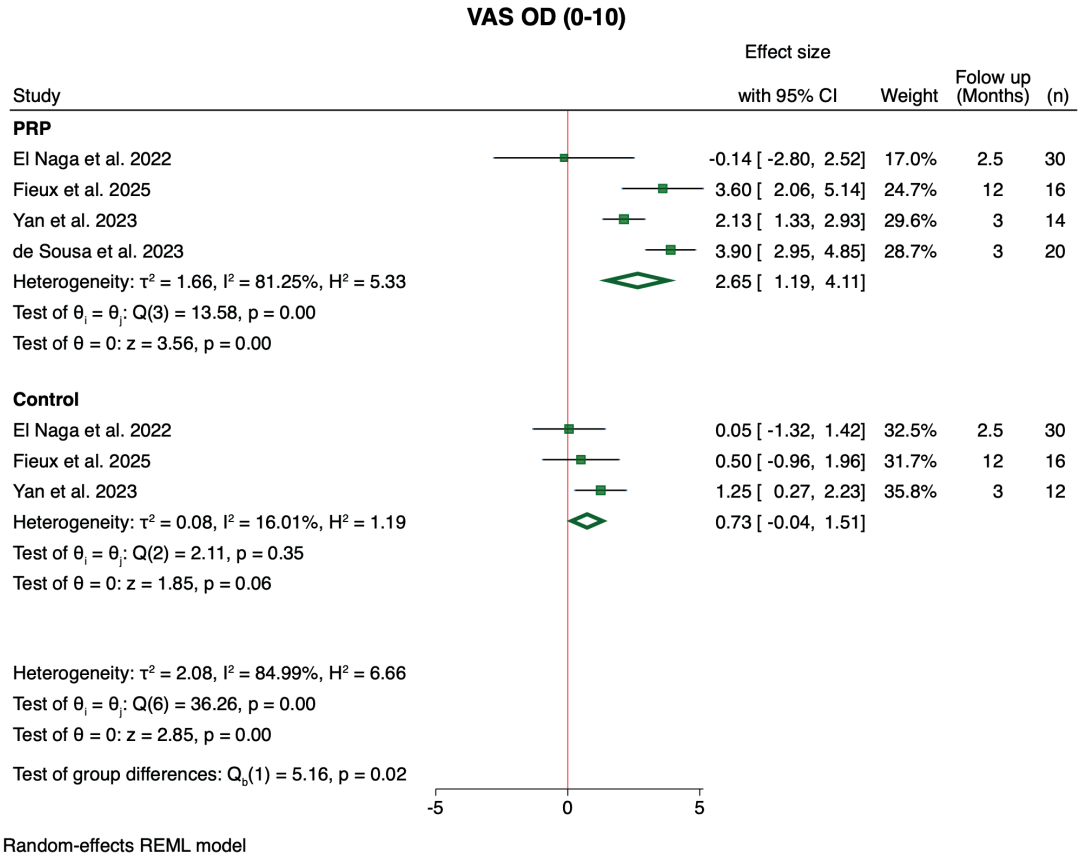
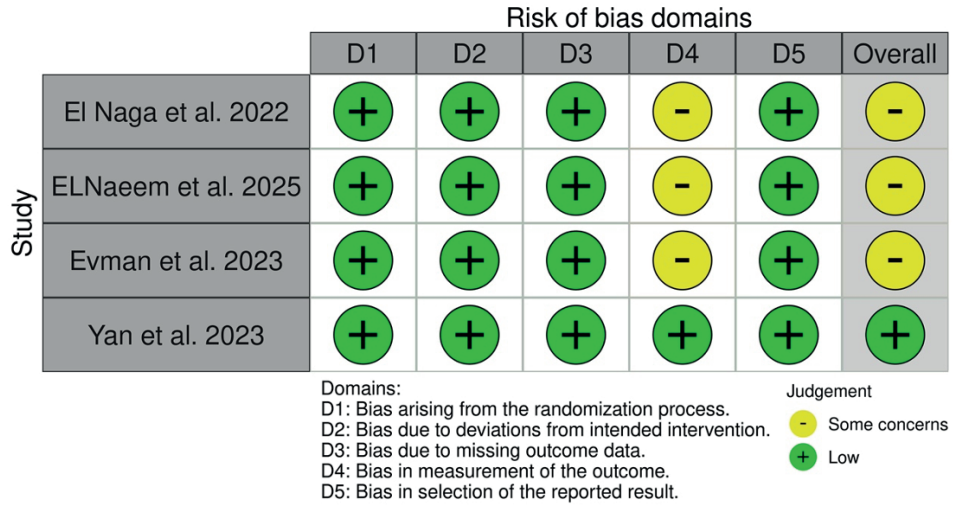


Figure 6. Forest plot summarizing the meta-analysis of change in VAS OD amongst the PRP and control cohorts.

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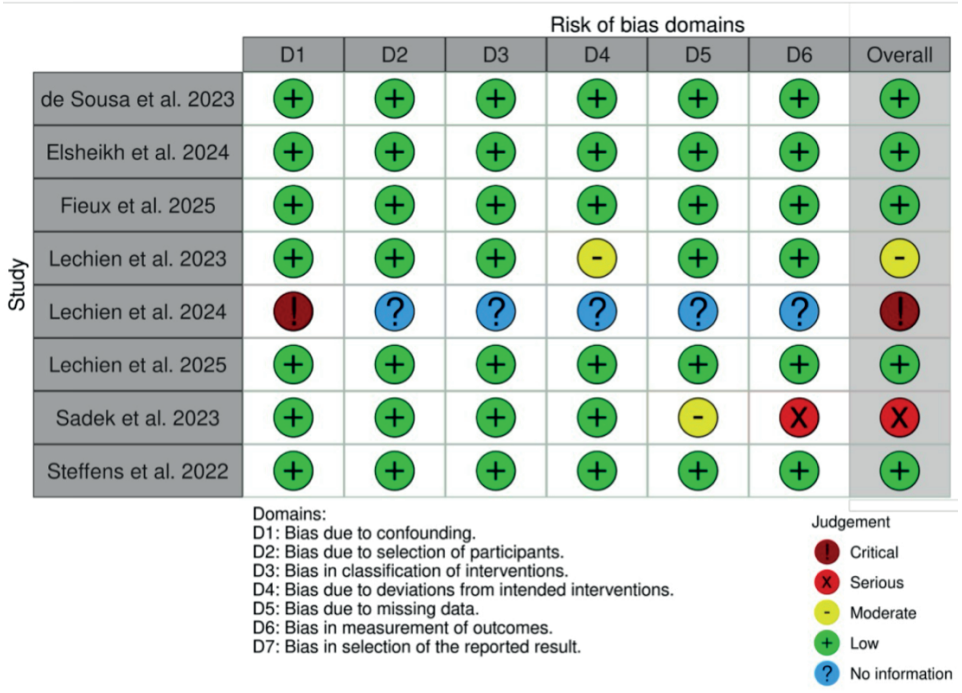


Figure 7. Risk of Bias using RoB 2 for randomised trials and ROBINS-I for non-randomised trials.

two key limitations, amongst others, which restrict both internal and external validity. Firstly, only two [35,52] of seven [33,35,36,51,52,54,57] control cohorts within our meta-analyses received placebo injections, thereby unblinding participants to their assignment to intervention. This can lead to participants significantly overstating improvements in olfaction, which has a significant subjective component. Secondly, marked variations exist within PRP protocols, with only one [52] study measuring platelet levels, creating significant unknown variance within treatment cohorts. The following discussion should be framed within the context of these, and other specified limitations, which are expanded upon within the limitations section.

PRP could be a suitable salvage intervention following trials of first-line therapies such as OT [12,65], given that the weighted mean duration of persistent OD for overall and combined TDI PRP cohorts was 19.4 months (range: 8.9 [52]-21.6 [36] months); and [12,65]19.7 months, respectively, largely due to the high participant number from Lechien et al. [36]. No included trials had a mean COVID-19 OD duration above 2 years, thus, PRP usage above this point was not evaluated in this review, however, PRP has been demonstrated to show significant improvements in TDI Sniffin' Sticks exceeding MCID in both post-traumatic OD (mean OD duration: 4.6 years) [66], and, more promisingly, postviral OD unrelated to COVID-19 (mean OD duration: 8.7

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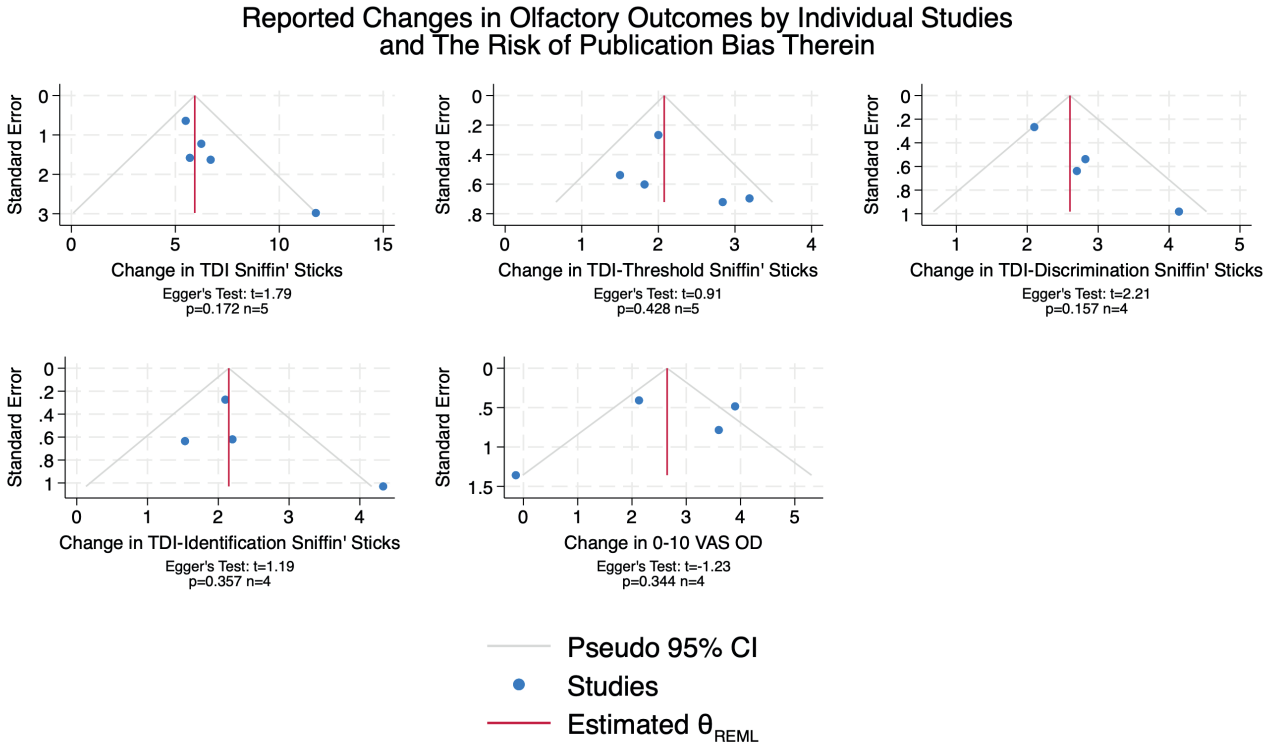


Figure 8. Funnel plots demonstrating the risk of publication bias in reported olfactory outcomes amongst studies included in meta-analysis. Results of the Egger's test are provided for each outcome.

years) [66,67]. This could give hope for PRP usage beyond 2 years, but, given that persistent COVID-19 OD natural recovery lessens after 2 years [68], it remains unclear whether this benefit will be similarly demonstrated in long-term COVID-19 cohorts.

Sniffin' Sticks, specifically, represents the gold-standard test of olfaction validated for assessment of threshold, discrimination and identification domains [69,70]. Importantly, the pooled TDI scores across PRP cohorts (+5.94), but not controls (+2.60), exceeded the minimum clinically important difference (MCID) of 5.5 [71], however, there is low certainty about the magnitude of our pooled estimates. This could suggest that some PRP patients may potentially self-report an improvement in their sense of smell where controls do not, despite both results reaching statistical significance, implying PRP may represent a clinically meaningful therapy for persistent COVID-19 OD. However, this should be interpreted with caution, given that with no individual domain within PRP cohorts reached the MCID of 2.5, 3 and 3 [71], respectively. Additionally, given that TDI controls [33,36,52,55] who received OT [33,36,55] or placebo saline injection [52], demonstrated a degree of significant natural improvement (+2.60), potentially enhanced by OT, the relative benefit of PRP administration should be interpreted with regard to the difference between PRP and control cohorts. The TDI gain achieved through PRP, compared to control, could be better conceptualised by subtracting the control arm from the PRP arm, creating a more realistic relative improvement of +3.34. Controls for Yan et al. [52] were the only cohort in our meta-analysis who did not receive OT during the study duration, but they did receive 3 months minimum of OT prior to recruitment. Only patients with objective OD between 6 to 12 months were included in the Yan et al. trial, due to the inverse relationship between duration of OD and recovery prognosis [72]. Thus, their control cohort may have regardless benefitted from an element of natural recovery [68].

Improvements in discrimination and identification scores reached significance in controls, but not threshold (0.89, p=0.12). Threshold, particularly, measures the peripheral, or end-organ component of olfaction [73], without relying on cerebral interpretation, and therefore does not demonstrate the cognitive age-related variability displayed by identification and discrimination tests [73,74]. Given that no individual domain reached MCID within PRP cohorts, the mechanism of action for PRP remains unclear. However, we can hypothesise that significant differences demonstrated in the threshold component may support biological mechanisms postulating that PRP acts upon the peripheral olfactory neuroepithelium by promoting peripheral nerve regrowth and reducing inflammation [29,30]. This mechanism is supported by animal models, in which PRP ac-

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celerated functional recovery and increased olfactory epithelial thickness, with reduced epithelial damage in an anosmia-induced murine model [75], and platelet-derived factors VEGF and PDGF enhanced regeneration of primary olfactory neurons following murine bulbectomy [76]. This could additionally suggest that improvements in OD following OT may be preferentially driven by neural plasticity and improvements in higher-order olfactory processing [77,78], whereas PRP acts more peripherally [29,30]. Existing literature similarly demonstrates that OT shows improvements in discrimination and identification components, but not threshold [79].

Improvements in VAS OD reached significance in PRP, but not control cohorts, however, our meta-analysis for VAS OD, a powerful and important measure of patient self-perception of smell, which more closely relates to quality of life [80], suffered from significant between-study heterogeneity for PRP cohorts, resulting in very low certainty of effect sizes. The low or very low certainty of our pooled estimates reflects the unavailability of sufficient volume of RCTs to conduct meta-analysis of outcomes from RCTs only. Thus, there is an urgent need for further RCTs to improve certainty regarding magnitude of effect size.

Our review exists alongside several [31,32,81–86] other reviews investigating the usage of PRP for OD. Some reviews [81,84] are broader in scope by investigating post-viral OD combined with other etiologies, such as post-traumatic. Others do not provide similar granularity to ours through TDI sub-domain meta-analysis [82,83,85,86], or they group of different psychophysical and subjective olfactory scores for meta-analysis [83–86]. Unfortunately, between study-heterogeneity is common across many papers [83–86] due to the aforementioned paucity of high-quality primary studies, resulting in similarly low or very low GRADE findings [83]. The marginal value of our review lies in investigating OD primarily related to COVID-19 and providing homogenous meta-analyses on TDI alongside individual sub-domains. Interestingly, despite the clear ongoing international interest motivating this and other reviews, the lack of sufficient primary studies suggests that real-world PRP adoption remains largely limited. Therefore, much of the evidence base surrounding PRP currently arises from review papers, instead of clinical trials, and the volume of this evidence base should not necessarily be mistaken for strength of underlying evidence. Further research should focus on RCTs, instead of additional review and synthesis. Developing international consensus on PRP protocols, including preparation, centrifugation, number of injections, administration intervals, delivery technique, alongside measurement of platelet levels within PRP may facilitate this.

Regardless, our findings cautiously suggest that PRP may represent a superior therapeutic option available versus alternatives for persistent COVID-19 OD, with only minor adverse effects reported, although widespread clinical uptake may be limited by cost and availability, as PRP can be significantly more expensive compared to OT [12,65]. Given this, we would initially recommend trials of cheaper and less invasive treatments such OT [12] coupled with intranasal or oral options such as Omega-3 [13], Vitamin A [14,15], corticosteroids [16,17], sodium citrate [18], or palmitoylethanolamide with luteolin for the initial 6 months of OD, to support natural recovery. After 6 months, given the favourable safety profile, and potentially clinically significant benefit that some patients may receive, we would advocate trialling PRP, despite a lack of standardised protocols. Long-term efficacy of PRP beyond 24 months remains unclear, given the lack of studies specifically investigating PRP for COVID-19 OD beyond this point.

Finally, significant improvements shown by our control cohorts in combined TDI, discrimination and identification domains within the overall mean 19.4 months OD in our review supports existing literature suggesting that persistent COVID OD undergoes natural recovery within the first 24 months [68]. Our results potentially imply PRP promotes or accelerates this inherent process through the release of additional growth factors. Alternative research interventions looking at persistent COVID OD beyond 24 months remain few in numbers, and thus all must be cautiously interpreted, but, they could provide an important solution for patients afflicted with severe anosmia from the initial waves of the pandemic after cessation of natural recovery. Functional septorhinoplasty (fSRP) has been investigated as an alternative research recovery hypothesis by potentially increasing activity-dependent recovery in dormant olfactory neurones [87]. Existing literature demonstrates that increased olfactory sensory stimulation increases adult newborn olfactory neuronal cell survival [88] and the number of newborn neurons in the adult olfactory bulb [89], whereas unilateral olfactory sensory deprivation causes the opposite effect, with a 25% reduction in the volume of the ipsilateral olfactory bulb after the corresponding naris is closed [90] through apoptotic cell death [91–94]. The hypothesis is that fSRP increases olfactory nasal airflow and thus could potentially promote activity-dependent recovery in dormant olfactory neurones [87]. However, the results of this trial must be interpreted with extreme caution, as this is a single non-randomised study with a very small sample of 12 fSRP patients, all of whom had pre-existing structural nasal deficits. Therefore, it is exceedingly likely that these patients had combined conductive and sensorineural OD, making it impossible to separate smell improvement from fixing any underlying conductive issues through fSRP from true olfactory neuronal recovery [87]. Additionally, the status of the olfactory cleft could represent an unexamined modifier of PRP response, as opacification implies a conductive contribution unlikely to respond

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to a regenerative therapy, yet may also reflect the persistent local inflammation that PRP is postulated to modulate. No study to date formally investigates cleft status with relation to PRP. Pendolino et al. reinforce that natural recovery lessens after 24 months of persistent COVID-19 OD, as their control arm did not show significant natural recovery [87]. There is insufficient evidence to recommend any invasive therapy for persistent COVID-19 OD beyond 24 months. Therefore, given the demonstrated natural recovery timelines, we would recommend restricting trials of invasive research interventions such as fSRP only after 24 months of persistent COVID OD.

Limitations

A paucity of RCTs prevented us from restricting meta-analyses to RCT-only to provide Level 1a [63] recommendations. Our GRADE analysis very significantly limits our certainty in the magnitude of our pooled estimates, and suggests further RCTs are very likely to change the magnitude of observed effect sizes, strongly justifying further RCTs in the future. One study [35] included a minority of patients with post-viral OD unrelated to COVID-19, but was included as more than 80% of the cohort had COVID-19 OD. This combines populations with potentially biologically distinct mechanisms, introducing heterogeneity. Whilst our results support the efficacy of PRP in Western cohorts, developing nations are less represented in the included studies. Therefore, further studies are required in order to validate PRP as a treatment for persistent COVID-19 OD in cohorts from South and East Asia, the Pacific , South America and Sub-Saharan Africa. Variation in the enrolment criteria such as length of OD, method of defining OD severity, prior treatment, or method of confirmation of SARS-CoV-2 infection limits the validity of head-to-head comparisons between studies and may have contributed to between-study heterogeneity in olfactory outcomes. This could be enhanced by lack of assessment of olfactory cleft status by all studies, potentially causing differing proportions of patients with conductive deficits across cohorts.

Some control groups received current standard-of-care while others received placebo only which limits the validity of our pooled estimates for changes in olfactory outcomes amongst control cohorts; differences in olfactory outcomes between PRP and control cohorts may be overstated in RCTs which did not administer placebo to their control arms due to participants being unblinded to their assignment to intervention. However, this does not affect the conclusion that PRP cohorts demonstrated statistically significant improvements in VAS OD, TDI scores and each of its 3 components.

Variation in PRP protocols between intervention groups, relating to preparation methods, centrifugation protocols, number of injections received, administration intervals, injection techniques and absence of measured platelet levels in all but one [52] study limits the internal validity of our pooled estimates, by introducing significant between-study heterogeneity. Only four [36,51,55,57] of six [33,36,51,52,55,57] overall studies in our TDI/sub-domain and two [35,52] of four [35,52,54,57] studies in our VAS OD meta-analyses, respectively, shared the same PRP treatment protocol relating to number and timing of injections. These above factors additionally limits our external validity, restricting our ability to provide recommendations on which protocol generates clinically important improvements in olfaction. Whilst pooled estimates for the mean change in VAS OD and TDI scores both exceeded the MCID, this does not inform clinicians of the response rate of patients where the benefit exceeds MCID. Without participant-level data, this cannot be deduced from the included studies, limiting our real-world utility. Validity of our pooled estimate for change in VAS OD in PRP cohorts may be compromised by significant between-study heterogeneity. Two papers were deemed to be at critical [56] and serious [53] risk of bias respectively; as such, they were excluded from meta-analyses to limit bias in our estimates for pooled effect size. Their findings were nonetheless discussed in the manuscript as they met the PICOS criteria for this systematic review.

Recommendations

There is an urgent need for large-scale, multicentre, methodologically-rigorous, placebo-controlled RCTs which utilise olfactory tests assessing all 3 domains of olfaction, especially threshold. Future RCTs should incorporate longer follow-up periods, ideally over 12 months, to assess long-term benefits of PRP treatment. Consensus should also be reached on optimal protocols for PRP, including preparation, centrifugation protocols, number of injections received, administration intervals and injection techniques in order to promote maximal efficacy. Platelet levels in PRP should be measured to facilitate standardisation and inform dosing. Olfactory cleft status should be documented in future PRP studies during pre-injection endoscopic cleft assessment. Preceding duration of OD should always be stated and all patients should have a minimum of 6 months of symptoms prior to treatment with PRP as most patients demonstrate natural resolution of COVID-19 OD within this timeframe [95]. PRP efficacy after 24 months of persistent COVID-19 OD remains unclear, given that no trials to date have investigated PRP after this point. Invasive trial interventions should only be considered after 24 months of persistent OD [87].

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Author contributions

DP, JSM, SK, VA and PA were involved in the acquisition, analysis and interpretation of data; in the drafts and revisions during the writing process and in the final approval of the article before submission to Rhinology. They are all accountable for all aspects of this work in ensuring that any questions related to the accuracy or integrity of any part of this work are appropriately investigated and resolved. Systematic screening and data extraction were conducted in parallel by DP and SK. All statistical analyses were conducted by JSM. All figures were produced by JSM.

Conflict of interest

The authors have no conflicts of interest to declare.

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References

1. Wilson RS, Yu L, Bennett DA. Odor identification and mortality in old age. Chem Senses. 2011;36(1):63-67.
2. Gopinath B, Sue CM, Kifley A, Mitchell P. The association between olfactory impairment and total mortality in older adults. J Gerontol A Biol Sci Med Sci. 2012;67(2):204-209.
3. Oleszkiewicz A, Croy I, Hummel T. The impact of olfactory loss on quality of life: a 2025 review. Chem Senses. 2025;50:bjaf023.
4. Schubert CR, Fischer ME, Pinto AA, et al. Sensory impairments and risk of mortality in older adults. J Gerontol A Biol Sci Med Sci. 2017;72(5):710-715.
5. Dintica CS, Marseglia A, Rizzuto D, et al. Impaired olfaction is associated with cognitive decline and neurodegeneration in the brain. Neurology. 2019;92(7):e700-e709.
6. Fluitman KS, Hesp AC, Kaihatu RF, et al. Poor taste and smell are associated with poor appetite, macronutrient intake, and dietary quality but not with undernutrition in older adults. J Nutr. 2021;151(3):605-614.
7. Liu DT, Prem B, Sharma G, Kaiser J, Besser G, Mueller CA. Depression symptoms and olfactory-related quality of life. Laryngoscope. 2022;132(9):1829-1834.
8. Croy I, Nordin S, Hummel T. Olfactory disorders and quality of life: an updated review. Chem Senses. 2014;39(3):185-194.
9. Devanand DP, Lee S, Manly J, et al. Olfactory identification deficits and increased mortality in the community. Ann Neurol. 2015;78(3):401-411.
10. Van Regemorter V, Hummel T, Rosenzweig F, Mouraux A, Rombaux P, Huart C. Mechanisms linking olfactory impairment and risk of mortality. Front Neurosci. 2020;14:140.
11. Boscolo-Rizzo P, Polesel J, Vaira LA. Smell and taste dysfunction after COVID-19. BMJ. 2022;378:o1653.
12. Patel ZM, Wise SK, DelGaudio JM. Randomized controlled trial demonstrating cost-effective method of olfactory training in clinical practice: essential oils at uncontrolled concentration. Laryngoscope Investig Otolaryngol. 2017;2(2):53-56.
13. Lerner DK, Garvey KL, Arrighi-Allisan A, et al. Omega-3 fatty acid supplementation for the treatment of persistent COVID-related olfactory dysfunction. Am J Rhinol Allergy. 2023;37(5):531-540.
14. Hummel T, Whitcroft KL, Rueter G, Haehner A. Intranasal vitamin A is beneficial in post-infectious olfactory loss. Eur Arch Otorhinolaryngol. 2017;274(7):2819-2825.
15. Reden J, Lill K, Zahnert T, Haehner A, Hummel T. Olfactory function in patients with postinfectious and posttraumatic smell disorders before and after treatment with vitamin A: a double-blind, placebo-controlled, randomized clinical trial. Laryngoscope. 2012;122(9):1906-1909.
16. Vaira LA, Hopkins C, Petrocelli M, et al. Efficacy of corticosteroid therapy in the treatment of long-lasting olfactory disorders in COVID-19 patients. Rhinology. 2021;59(1):21-25.
17. Nguyen TP, Patel ZM. Budesonide irrigation with olfactory training improves outcomes compared with olfactory training alone in patients with olfactory loss. Int Forum Allergy Rhinol. 2018;8(9):977-981.
18. Garcia ECD, Rosa LR, dos Santos ACR, Ishimatsu GKA, Lopes NMD, Fornazieri MA. Investigating the efficacy of melatonin, topical sodium citrate, and multivitamin with zinc as a potential treatment for postinfectious loss of smell. Braz J Otorhinolaryngol. 2024;90(6):101496.
19. Gellrich J, Czaplewski L, Haehner A, Hummel T. Palmitoylethanolamide and luteolin for postinfectious olfactory disorders: how clinically meaningful is its effect? ORL J Otorhinolaryngol Relat Spec. 2024;86(3-4):118-123.
20. Kim S, Finlay JB, Ko T, Goldstein BJ. Long-term olfactory loss post-COVID-19: pathobiology and potential therapeutic strategies. World J Otorhinolaryngol Head Neck Surg. 2024;10(2):148-155.
21. Jiang J, Xing F, Luo R, Liu M. Effectiveness of platelet-rich plasma for patients with carpal tunnel syndrome: a systematic review and meta-analysis of current evidence in randomized controlled trials. Front Pharmacol. 2022;13:834213.
22. Hong P, Zheng Y, Rai S, et al. Efficacy and safety of platelet-rich plasma in the treatment of carpal tunnel syndrome: a network meta-analysis of different injection treatments. Front Pharmacol. 2022;13:906075.
23. Wu YT, Ho TY, Chou YC, et al. Six-month efficacy of platelet-rich plasma for carpal tunnel syndrome: a prospective randomized, single-blind controlled trial. Sci Rep. 2017;7(1):94.
24. Dou XY, An M. Advances in the application of platelet-rich plasma in peripheral nerve injuries. Anesthesiol Perioper Sci. 2025;3(2):19.
25. Sánchez M, Garate A, Delgado D, Padilla S. Platelet-rich plasma, an adjuvant biological therapy to assist peripheral nerve repair. Neural Regen Res. 2017;12(1):47-52.
26. Laurendon T, Radulesco T, Mugnier J, et al. Bilateral transient olfactory bulb edema during COVID-19-related anosmia. Neurology. 2020;95(5):224-225.
27. Moran DT, Jafek BW, Eller PM, Rowley JC. Ultrastructural histopathology of human olfactory dysfunction. Microsc Res Tech. 1992;23(2):103-110.
28. Santos Guedes de Sá K, Silva J, Bayarri-Olmos R, et al. A causal link between autoantibodies and neurological symptoms in long COVID. Cell. 2026;189(11):3214-3235.e37.
29. Wang S, Liu X, Wang Y. Evaluation of platelet-rich plasma therapy for peripheral nerve regeneration: a critical review of literature. Front Bioeng Biotechnol. 2022;10:808248.
30. Wang S, Liu Z, Wang J, Cheng L, Hu J, Tang J. Platelet-rich plasma (PRP) in nerve repair. Regen Ther. 2024;27:244-250.
31. Al Aaraj M, Boorinie M, Salfity L, Eweiss A. The use of platelet-rich plasma in COVID-19 induced olfactory dysfunction: systematic review. Indian J Otolaryngol Head Neck Surg. 2023;75(4):3093-3097.
32. Alrajhi B, Alrodiman OA, Alhuzali AF, Alrashed H, Alrodiman YA, Alim B. Platelet-rich plasma for the treatment of COVID-19 related olfactory dysfunction: a systematic review. Rhinology. 2023;61(6):498-507.
33. Abd ELNaeem MM, Saleh EM, Hassani AA, Abdelhameed N, Sholkamy AG. Outcomes of platelet-rich plasma versus olfactory training in post COVID-19 smell disorders: a comparative study. Egypt J Neck Surg Otorhinolaryngol. 2025;11(2):43-51.
34. Elsheikh E, Tantawy AE, Monaider RH, Moustafa D, Elgandy MI. Effect of plasma rich protein use in post-COVID-19 anosmic patients. Zagazig Univ Med J. 2024;30(1.6):2910-2920.
35. Fieux M, Castro BR, Jang SS, Yan CH, Patel ZM. Long-term outcomes of PRP injections for post-viral olfactory loss: a prospective cohort study. Int Forum Allergy Rhinol. 2025;15(4):420-427.
36. Lechien JR, Saussez S. Platelet-rich plasma

Corrected Proof

for treating COVID-19-related anosmia, hyposmia, and parosmia: a controlled longitudinal study. Otolaryngol Head Neck Surg. 2025;172(4):1450-1458.
37. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Syst Rev. 2016;5(1):210.
38. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
39. Follmann D, Elliott P, Suh I, Cutler J. Variance imputation for overviews of clinical trials with continuous response. J Clin Epidemiol. 1992;45(7):769-773.
40. Abrams KR, Gillies CL, Lambert PC. Meta-analysis of heterogeneously reported trials assessing change from baseline. Stat Med. 2005;24(24):3823-3844.
41. Higgins JPT, Thomas J, Chandler J, et al., editors. Cochrane handbook for systematic reviews of interventions. 2nd ed. Chichester (UK): John Wiley & Sons; 2019.
42. Scheaffer RL, Mendenhall W, Ott L. Elementary survey sampling. Belmont (CA): Duxbury Press; 1990.
43. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177-188.
44. Hedges LV. A random effects model for effect sizes. Psychol Bull. 1983;93(2):388-395.
45. Raudenbush SW. Analyzing effect sizes: random-effects models. In: Cooper H, Hedges LV, Valentine JC, editors. The handbook of research synthesis and meta-analysis. 2nd ed. New York (NY): Russell Sage Foundation; 2009. p. 295-315.
46. Risk of bias tools [Internet]. [cited 2026 Mar 8]. Available from: https://sites.google.com/site/riskofbiastool/welcome
47. Light RJ, Pillemer DB. Summing up: the science of reviewing research. Cambridge (MA): Harvard University Press; 1984.
48. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-634.
49. Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. The GRADE Working Group; 2013.
50. StataCorp. Stata statistical software. College Station (TX): StataCorp LLC; 2023.
51. Lechien JR, Le Bon SD, Saussez S. Platelet-rich plasma injection in the olfactory clefts of COVID-19 patients with long-term olfactory dysfunction. Eur Arch Otorhinolaryngol. 2023;280(5):2351-2358.
52. Yan CH, Jang SS, Lin HC, et al. Use of platelet-rich plasma for COVID-19-related olfactory loss: a randomized controlled trial. Int Forum Allergy Rhinol. 2023;13(6):989-997.
53. Sadek AA, Gomaa MA, Abohashima OG, Mohammed AAB. Role of platelet-rich plasma in the treatment of post COVID-19 olfactory dysfunction. Minia J Med Res. 2023;34(4):123-132.
54. Abo El Naga HA, El Zaiat RS, Hamdan AM. The potential therapeutic effect of platelet-rich plasma in the treatment of post-COVID-19 parosmia. Egypt J Otolaryngol. 2022;38(1):130.
55. Steffens Y, Le Bon SD, Lechien J, et al. Effectiveness and safety of PRP on persistent olfactory dysfunction related to COVID-19. Eur Arch Otorhinolaryngol. 2022;279(12):5951-5953.
56. Lechien JR, Saussez S. Injection of platelet rich plasma in the olfactory cleft for COVID-19 patients with persistent olfactory dysfunction: description of the technique. Ear Nose Throat J. 2024;103(1 suppl):115S-119S.
57. de Sousa FA, Machado A de S, Costa JR, et al. Use of platelet rich plasma in persistent olfactory dysfunction after COVID-19: a prospective study. Rev Port Otorrinolaringol Cir Cabeça Pescoço. 2023;61(4):345-354.
58. Evman MD, Cetin ZE. Effectiveness of platelet-rich plasma on post-COVID chronic olfactory dysfunction. Rev Assoc Med Bras. 2023;69(11):e20230666.
59. Duffy A, Naimi B, Garvey E, et al. Topical platelet-rich plasma as a possible treatment for olfactory dysfunction—a randomized controlled trial. Int Forum Allergy Rhinol. 2024;14(9):1455-1464.
60. Common Terminology Criteria for Adverse Events (CTCAE) v6.0 (MedDRA 28.0) [Internet]. 2025 [cited 2026 Mar 8]. Available from: https://dctd.cancer.gov/research/ctep-trials/for-sites/adverse-events/ctcae-v6.pdf
61. Huedo-Medina TB, Sánchez-Meca J, Marín-Martínez F, Botella J. Assessing heterogeneity in meta-analysis: Q statistic or I2 index? Psychol Methods. 2006;11(2):193-206.
62. Terrin N, Schmid CH, Lau J, Olkin I. Adjusting for publication bias in the presence of heterogeneity. Stat Med. 2003;22(13):2113-2126.
63. Phillips B, Ball C, Sackett D, et al. Oxford Centre for Evidence-Based Medicine: levels of evidence (March 2009). Oxford: University of Oxford; 2009.
64. Doty RL, Newhouse MP, Azzalina JD. Internal consistency and short-term test-retest reliability of the University of Pennsylvania Smell Identification Test. Chem Senses. 1985;10(3):297-300.
65. Magruder ML, Caughey S, Gordon AM, Capotosto S, Rodeo SA. Trends in utilization, demographics, and costs of platelet-rich plasma injections: a ten-year nationwide investigation. Phys Sportsmed. 2024;52(1):89-97.
66. Lechien JR. Platelet-rich plasma for post-traumatic olfactory dysfunction: preliminary report of 33 patients. Otolaryngol Head Neck Surg. 2025;173(5):1297-1301.
67. Lechien JR, Saussez S. Effectiveness of platelet-rich plasma in long-lasting post-viral olfactory dysfunction: a case-series. Eur Arch Otorhinolaryngol. 2024;281(11):5841-5846.
68. Dias M, Shaida Z, Haloob N, Hopkins C. Recovery rates and long-term olfactory dysfunction following COVID-19 infection. World J Otorhinolaryngol Head Neck Surg. 2024;10(2):121-128.
69. Hummel T, Whitcroft KL, Andrews P, et al. Position paper on olfactory dysfunction. Rhinol Suppl. 2017;54(Suppl 26):1-30.
70. Whitcroft KL, Cuevas M, Haehner A, Hummel T. Patterns of olfactory impairment reflect underlying disease etiology. Laryngoscope. 2017;127(2):291-295.
71. Gudziol V, Lötsch J, Haehner A, Zahnert T, Hummel T. Clinical significance of results from olfactory testing. Laryngoscope. 2006;116(10):1858-1863.
72. London B, Nabet B, Fisher AR, White B, Sammel MD, Doty RL. Predictors of prognosis in patients with olfactory disturbance. Ann Neurol. 2008;63(2):159-166.
73. Gellrich J, Sparing-Paschke LM, Hummel T, Schriever VA. The influence of cognitive parameters on olfactory assessment in healthy children and adolescents. Chem Senses. 2021;46:bjaa072.
74. Gellrich J, Sparing-Paschke LM, Thieme T, et al. Normative data for olfactory threshold and odor identification in children and adolescents. Int J Pediatr Otorhinolaryngol. 2019;123:5-9.
75. Yasak AG, Yigit O, Araz Server E, Durna Dastan S, Gul M. The effectiveness of platelet-rich plasma in an anosmia-induced mice model. Laryngoscope. 2018;128(5):E157-E162.
76. Beecher K, Hafner LM, Ekberg J, St John JA, Chehrehasa F. Combined VEGF/PDGF improves olfactory regeneration after unilateral bulbectomy in mice. Neural Regen Res. 2018;13(10):1820-1826.
77. Han P, Musch M, Abolmaali N, Hummel T. Improved odor identification ability and increased regional gray matter volume after olfactory training in patients with idiopathic olfactory loss. Iperception. 2021;12(2):20416695211005812.
78. Sorokowska A, Drechsler E, Karwowski M, Hummel T. Effects of olfactory training: a meta-analysis. Rhinology. 2017;55(1):17-26.
79. Pekala K, Chandra RK, Turner JH. Efficacy of olfactory training in patients with olfactory loss: a systematic review and meta-analysis. Int Forum Allergy Rhinol. 2016;6(3):299-307.
80. Liu ZF, Yang JY, Gu JW, et al. [Analysis of factors influencing quality of life in patients with olfaction disorders]. Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2025;60(1):22-27. Chinese.
81. Moffa A, Nardelli D, Giorgi L, et al. Platelet-rich plasma for patients with olfactory dysfunction: myth or reality? A systematic review. J Clin Med. 2024;13(3):782.
82. Maniaci A, Lavalle S, Masiello E, et al. Platelet-rich plasma (PRP) in the treatment of long COVID olfactory disorders: a comprehensive review. Biomedicines. 2024;12(4):808.
83. Albazee E, Alajmi SA, Alkandari AM, et al. Platelet-rich plasma for COVID-19-related olfactory dysfunction: a systematic review and meta-analysis of randomized controlled trials. Cureus. 2025;17(10):e94386.

Corrected Proof

84. Kim DH, Stybayeva G, Hwang SH. Short-term efficacy of platelet-rich plasma in the treatment of persistent olfactory dysfunction: systematic review and meta-analysis. Eur Arch Otorhinolaryngol. 2025;282(1):37-46.
85. Jafar AB, Almeida G, Al Mousawi F, Rendon ED, Luong AU. Efficacy of platelet-rich plasma versus placebo for improvement in olfactory function in adults with olfactory dysfunction: a systematic review and meta-analysis. Laryngoscope Investig Otolaryngol. 2025;10(6):e70317.
86. Bae AY, Kim DH, Hwang SH. Efficacy of platelet-rich plasma in the treatment of persistent olfactory impairment after COVID-19: a systematic review and meta-analysis. J Rhinol. 2024;31(1):1-7.
87. Pendolino AL, Scarpa B, Andrews PJ. The effectiveness of functional septorhinoplasty in improving COVID-19-related olfactory dysfunction. Facial Plast Surg. 2026;42(1):17-27.
88. Lledo PM, Saghatelyan A. Integrating new neurons into the adult olfactory bulb: joining the network, life-death decisions, and the effects of sensory experience. Trends Neurosci. 2005;28(5):248-254.
89. Rochefort C, Gheusi G, Vincent JD, Lledo PM. Enriched odor exposure increases the number of newborn neurons in the adult olfactory bulb and improves odor memory. J Neurosci. 2002;22(7):2679-2689.
90. Brunjes PC. Unilateral naris closure and olfactory system development. Brain Res Brain Res Rev. 1994;19(1):146-160.
91. Fiske BK, Brunjes PC. Cell death in the developing and sensory-deprived rat olfactory bulb. J Comp Neurol. 2001;431(3):311-319.
92. Mandairon N, Jourdan F, Didier A. Deprivation of sensory inputs to the olfactory bulb up-regulates cell death and proliferation in the subventricular zone of adult mice. Neuroscience. 2003;119(2):507-516.
93. Petreanu L, Alvarez-Buylla A. Maturation and death of adult-born olfactory bulb granule neurons: role of olfaction. J Neurosci. 2002;22(14):6106-6113.
94. Najbauer J, Yan XX, Leon M. Internucleosomal DNA fragmentation during deprived and non-deprived olfactory development. Brain Res. 2002;926(1-2):118-125.
95. Khan AM, Lee J, Rammaha T, et al. Natural trajectory of recovery of COVID-19 associated olfactory loss. Am J Otolaryngol. 2022;43(5):103572.

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SUPPLEMENTARY MATERIAL

Table S1. PICOS inclusion and exclusion criteria for study selection.

Domain	Inclusion Criteria	Exclusion Criteria
Population	Clinical study conducted on human populations with olfactory dysfunction primarily related to COVID-19 regardless of age, gender, or ethnicity	Populations with COVID-19 without relation to olfactory dysfunction
Intervention	Patients treated with Platelet-Rich Plasma injections for post-viral OD primarily related to COVID-19, regardless of method of preparation or number of injections.	Populations treated with PRP for indications outside of COVID-19 OD PRP administered by any route other than injections (e.g. topical/surface dressing/PRP-impregnated packing)
Comparison	A non-exposed control group including alternative treatment or placebo	Control groups which included administration of PRP
Outcome	1. Validated psychophysical Olfaction scoring systems including but not limited to "Sniffin' Sticks" (TDI), UPSIT, or CCCRC. 2. Health-related QoL measured by validated disease-specific scoring systems such as ODQ. 3. Disease severity and extent through validated objective and subjective symptom scores such as VAS. 4. Short-term, medium-term and long-term reported adverse events and length of follow-up. 5. Epidemiological data surrounding populations in which PRP was administered including but not limited to demographics, previous treatment and length of olfactory dysfunction. 6. Description of PRP administration protocols including but not limited to preparation, amount, timing and duration.	Studies where no outcome measures are directly related to efficacy of PRP on olfactory or clinical outcomes in patients with COVID-19.
Study Design	Full-text primary studies written in English or with full-text English translation available	Case reports, abstracts, reviews. Studies without full-text English translation. Animal studies.

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Table S2. PRP protocols, inclusion and exclusion criteria for all included papers.

Reference	PRP protocol				Inclusion criteria	Exclusion criteria
	Blood draw	PRP preparation	Local anaesthesia	PRP administration		
de Sousa et al. 2023	Venous blood taken into three different 3.5ml tubes containing 3.2% sodium citrate.	. Centrifugation at 4000 rpm for 10 minutes. 2. PRP samples drawn into two separate 1ml syringes, only 0.9ml extracted into both.	Lidocaine given with prilocaine and phenylephrine hydrochloride soaked cotton pledgets placed at inferior meatus and predicted injection site under endoscopic visualisation for over 10 minutes.	1. Single-site injection performed along the superior nasal septum posterior to the head of the middle turbinate, needle aimed at the level of the superior two-thirds of the middle turbinate, repeated contralaterally using 30 degree rigid endoscope. 2. Patients observed for 15 min after procedure for potential adverse events Single injection. All injections done by same practitioner, an assistant was used to aspirate and deliver 0.9ml PRP.	1. Age more than or equal to 18 years. 2. Abrupt onset of COVID-19 OD. 3. OD subjective duration equal than or greater than 12 months. 4. Sniffin' Sticks score less than or equal to 7 at point of PRP injection. 5. No response to previous olfactory training and adjuvant therapy measured by minimum two consecutive Sniffin' Sticks threshold evaluations 3 months apart. 6. Able to give informed consent.	1. Chronic rhinosinusitis 2. History of head trauma with loss of consciousness 3. Pre-existing OD prior to COVID-19 infection. 4. Pregnancy. 5. Previous neurosurgery or endoscopic nasal surgery. 6. Known olfactory bulb lesions on imaging. 7. Known neurologic disease (e.g. Parkinson's, dementia or epilepsy). 8. Major psychiatric disease. 9. Inability to tolerate nasal endoscopy. 10. Known platelet or coagulation disorders. 11. Undergoing anti-inflammatory or anticoagulant therapy, or concurrent pathology presumably requiring anti-inflammatory treatment 30 days following injection

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Reference	PRP protocol				Inclusion criteria	Exclusion criteria
	Blood draw	PRP preparation	Local anaesthesia	PRP administration		
ELNaeem et al. 2025	8ml venous blood collected in glass tubes containing ACD.	1. Soft spin for 10 minutes, 2000 rpm using Hettchi bench top centrifuge, Rotoix 32 A, Tokyo, Japan. 2. Platelet-containing supernatant plasma transferred to another sterile tube without anticoagulant (Kemico Z serum plain tube). 3. Second tube centrifuged at 3000 rpm for 10 minutes using Hettchi bench top centrifuge, Rotoix 32 A, Germany, to obtain a platelet concentrate. The lower 1/3 contains PRP (platelet pellets), whereas the top 2/3 contains platelet-poor plasma. 4. Platelet-poor plasma removed and PRP was suspended in 1 ml by heavy mixing.	Xylometazoline chlorhydrate 0.1% and 10% Xylocaine soaked in nasal pack, placed both in spheno-ethmoidal recess and the area between nasal septum and inferior turbinate for 10 minutes using 0 degree/ 4mm rigid endoscope (Storz, Germany)	1. Patients were placed in semi-recumbent position, head end of bed elevated 20 degrees. 2. PRP mixed with 0.1ml of calcium gluconate to activate secretion growth factors. 3. PRP injected submucosally using a syringe and 22-G needle into the olfactory area, particularly in the posterior part of the middle turbinate and adjacent part of nasal septum. 4. Patients observed for 15 minutes for adverse effects. Three injections given, one month interval.	1. Persistent post-COVID-19 OD for more than 6 months All patients had medical history and clinical examination (general, neurological and nasopharyngeal examination using rigid endoscopy - 0 degree/4mm, Storz endoscope, Germany). All patients had laboratory and radiological investigations and baseline TDI Sniffin' Sticks.	1. Lesions obstructing nasal airway (nasal polyps, tumors, chronic sinusitis, and structural abnormalities) 2. Previous sinonasal surgery. 3. Atrophic rhinitis. 4. Nasal granulomas. 5. History of bleeding disorders or receiving any medication affecting platelets or bone marrow function.

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Reference	PRP protocol				Inclusion criteria	Exclusion criteria
	Blood draw	PRP preparation	Local anaesthesia	PRP administration		
El Naga et al. 2022	8.5 ml of venous blood taken, mixed with 1.5 ml of acid citrate dextrose (ACD). No blood cooling before or during platelet separation.	1. Soft spin at 800 rpm for 10 min. 2. Sterile syringes used to transfer platelet-containing supernatant plasma into another sterile tube without anticoagulant. 3. Hard spin of separated plasma at 2000 rpm. The lower 1/3 contains PRP (platelet pellets), whereas the top 2/3 contains platelet-poor plasma. 4. Platelet-poor supernatant extracted using sterile syringes. 5. Platelet pellets suspended in a minimum amount of plasma (1–2 ml) by gently shaking the tube. 6. Platelet count assessed following PRP preparation to ensure adequate platelet yielding.	Emla 5% and 10% Xylocaine spray, soaked on cotton wool and inserted into nose for 30 min	PRP injection into the olfactory region at 1cm2 intervals using a 1-ml syringe, 30-G needle and nasal endoscope. Three injections given, three week interval.	1. Age over 18 years. 2. Positive PCR test more than 3 months prior. 3. Parosmia without response to 3 months of olfactory training, topical corticosteroids, omega-three, vitamin B12, and zinc supplementation.	1. Active COVID-19 infection. 2. Previous nasal surgery. 3. Bleeding tendency.
Elsheikh et al. 2024	8.5 ml of venous blood taken using a wide bore canula into a vacutainer containing ACD. No blood cooling before or during platelet separation.	1. Soft spin at 1000rpm for 15 minutes by Hitachi himac CT6E, Taiwan. 2. Sterile syringes used to transfer Platelet-containing supernatant plasma to another sterile tube without anticoagulant. 3. Platelet count evaluated to guarantee sufficient platelet yield using XN-330 Sysmex CBC analyser, USA.	Not stated	Not stated Three injections, interval unspecified.	1. Age over 18 years old. 2. Anosmia lasting 3 months or greater with a history of COVID-19 infection. 3. No other reasons for anosmia. 4. Previous medical treatment for anosmia without response.	1. Age less than 18 years 2. Infection, e.g. influenza, atrophic rhinitis, sinusitis, etc. 3. Previous nasal trauma. 4. Previous nasal surgery. 5. Benign or malignant nasal tumors 6. Nasal polyps.

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Reference	PRP protocol				Inclusion criteria	Exclusion criteria
	Blood draw	PRP preparation	Local anaesthesia	PRP administration		
Evman et al. 2023	Not stated	Not stated	Not stated	1ml PRP injected into olfactory cleft region. Single injection.	1. Age over 18 years 2. OD for 1 year or more after COVID-19 infection. 3. No response to nasal steroids, nasal D-panthenol/ vitamin A combination sprays and olfactory rehabilitation training for 1 month after initial presentation to clinic.	1. Severe nasal septal deviation 2. Allergic rhinitis. 3. Nasal polyps 4. Previous sinonasal surgery 5. Previous neurological pathology
Fieux et al. 2025	30cm3 blood taken from patient.	PRP isolated following manufacturer instructions from the PurePRP preparation kit (Emcyte Corporation) involving a two-step centrifugation process.	Not stated	1. 1 ml autologous PRP injected into each side of the superior septum mucosa within the olfactory cleft (2ml total). Three injections given, two weeks interval.	1. Age over 18 years 2. OD following COVID-19 lasting for more than 6 months and less than 12 months. 3. UPSIT greater than or equal to 30/40. All patients underwent nasal endoscopy.	1. Sinonasal mass or tumor. 2. Ongoing sinonasal inflammation or infection. 3. Structural obstruction to the olfactory cleft such as severe septal deviation.
Lechien et al. 2023	20 mL blood taken into tube with sodium citrate anticoagulant.	1. Centrifugation at 4200 rpm for 10 minutes. 2. Supernatant drawn up into a 10 mL syringe. 3. PRP transferred into a 1 mL syringe.	Xylocaine 10% spray, and xylometazoline chlorhydrate drops.	1. Several points of 0.2-0.5ml injections into middle turbinate and nasal septum opposing head of middle turbinate using 27-G needle and 0 degree rigid scope, repeated contralaterally. In some cases of septal deviation, the needle was bent to have better access to the olfactory cleft. 2. All PRP injections performed by the same otolaryngologist. 3. Patients observed for 15 min after procedure for potential adverse events. Single injection.	Not stated All patients had normal tomodensitometry or magnetic resonance imaging.	1. OD prior to COVID-19 pandemic. 2. Alternative causes of anosmia including post-viral, post-traumatic, neurological, and idiopathic. 3. Chronic rhinosinusitis with or without nasal polyposis. 4. Nasal obstruction related to rhinitis. 5. Previous nasal radiation. 6. Previous functional endoscopic sinus surgery.

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Reference	PRP protocol				Inclusion criteria	Exclusion criteria
	Blood draw	PRP preparation	Local anaesthesia	PRP administration		
Lechien et al. 2024 (note: not included in data analysis)	20ml blood taken into tube with sodium citrate anticoagulant.	1. Centrifugation at 4200 rpm for 10 minutes. 2. Supernatant drawn up into 10 ml syringes, PRP transferred into 1ml syringe.	Xylometazoline chlorhydrate drops into the nasal fossae, then Xylocaine 10% spray 2 minutes after.	1. Several points of 0.2-0.5ml injections into middle turbinate, nasal septum opposing head of middle turbinate and anteriorly in the same region using 27-G needle and 0 degree rigid scope, repeated contralaterally (total 2.2ml). In cases of anatomical deviation, closest possible injection to olfactory cleft is achieved. The needle is occasionally bent 30 degrees for improved access. 2. Patient observed for 15 min after procedure for potential adverse events. Single injection.	Proposed inclusion criteria: 1. Post-viral anosmia or hyposmia lasting over 6 months. 2. Severe parosmia. 3. recent (<2 years) post-traumatic or idiopathic hyposmia or anosmia or neurological disease related anosmia or hyposmia.	Proposed exclusion criteria: 1. Acute or chronic sinonasal infection. 2. Anosmia or hyposmia lasting over 2 years. 3. History of nasal cancer or aggressive tumour such as inverted papilloma. 4. OD related to nasal polyposis. Pre-injection nasoendoscopy is important to exclude above conditions and explore olfactory cleft anatomy.
Lechien et al. 2025	20ml blood taken into tube with sodium citrate anticoagulant.	1. Centrifugation at 4200 rpm for 10 minutes. 2. Supernatant drawn up into 10 ml syringes, PRP transferred into 1ml syringe.	Xylometazoline chlorhydrate drops followed by Xylocaine 10% spray.	1. 4-6 0.2ml injections performed in the nasal septum of the olfactory cleft bilaterally, depending on access and length of olfactory cleft. A 27-G needle, occasionally bent for better access in case of septal deviation, alongside a 30 degree rigid endoscope was used. 2. Patients observed for 15 min after procedure for potential adverse events. Single injection. In case of septal deviation limiting injection to only one side, over 1ml of PRP injected contralaterally. Both cohort and control underwent 3 month olfactory training protocol.	1. Self-reporting COVID-19-related OD for more than 6 months. 2. TDI score below 30.75 3. Parosmia present on a validated structured parosmia questionnaire, >8/12 parosmia score in Fr-ODQ, and reporting parosmia symptoms were more severe than anosmia/hyposmia complaints.	1. Sinus or olfactory region abnormalities on nasoendoscopy or imaging. 2. Chronic rhinosinusitis with or without nasal polyps. 3. Olfactory or nasal tumor. 4. Post-traumatic, neurological, idiopathic OD before COVID-19 pandemic. 5. Nasal obstruction related to rhinitis. 6. History of nasal chemotherapy or radiation. 7. History of functional endoscopic sinus surgery. 8. Severe neurological or psychiatric comorbidities.

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Reference	PRP protocol				Inclusion criteria	Exclusion criteria
	Blood draw	PRP preparation	Local anaesthesia	PRP administration		
Sadek et al. 2023	20ml blood taken from patient, mixed with sodium citrate.	1. Centrifugation at 4200 rpm for 10 minutes. 2. The supernatant containing 2ml of PRP was transferred to two distinct syringes of 1ml each.	10% xylocaine spray, then, two minutes afterwards, xylometazoline chlorhydrate drops placed in the nasal fossae.	1. Injection in the middle turbinate and nasal septum related to the head of the middle turbinate using a 27-G needle using a 0 degree rigid endoscope, repeated contralaterally. 2. Patients observed for 15 min after procedure for potential adverse events. Single injection.	1. Age 18 years or older	1. Less than 18 years old. 2. Previous nasal surgery. 3. Nasal diseases e.g. allergy or sinonasal polyposis. 4. Immuno-compromised patients. 5. General co-morbidity/ debilitating disease.
Steffens et al. 2022	Followed Yan et al. protocol	Followed Yan et al. protocol	Followed Yan et al. protocol States local anaesthesia was given, no further details.	Followed Yan et al. protocol 1ml PRP injected into each olfactory cleft Single injection.	1. Age over 18 years with COVID-19 OD	1. Abnormal findings on nasal endoscopy (e.g., polyposis, rhinosinusitis). 2. Blood disorders, or blood thinner use.
Yan et al. 2023	25 mL of venous blood obtained via peripheral blood draw and added to a prefilled syringe with 5 mL of sodium citrate.	1. Centrifugation at 4200rpm for 1 min. 2. Platelet plasma suspension aspirated and recentrifuged at 4200 rpm for 5 min. 3. Subsequent supernatant containing platelet-poor plasma discarded, 4. Remaining 2.5 mL of PRP resuspended and drawn up into two separate 1- mL sterile syringes. Emcyte GS30-PURE II PRP kits (EmCyte Corporation) were utilised and PRP isolation was performed per GS30- PURE II Protocol A.	Not stated	Submucosal injection at two sites within the olfactory cleft along the superior septum, posterior to the head of the middle turbinate. Three injections, two week interval.	1. Objective OD duration of over 6 months but less than 12 months. 2. Age over 18 years 3. Confirmed OD scoring more than or equal to 33 points on UPSIT. 4. Previously trialled olfactory training and topical budesonide nasal irrigations for at least 3 months. 5. Normal endoscopic examination of the nasal cavity and olfactory cleft.	1. History of inflammatory sinonasal disease. 2. Evidence of rhinitis or sinusitis on endoscopy. 3. Prior sinonasal or anterior skull base surgery. 4. Self-reported OD prior to COVID-19 infection. 5. Neuro-degenerative disease. 6. History of bleeding disorders, or use of blood thinner medications.

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Systematic search: Platelet rich plasma for COVID anosmia

Date: 02 July 2025

Disclaimer: We have taken care in the preparation of this literature search, but we make no warranty as to its accuracy and we will not be liable to any person relying on or using it for any purpose. We would also like to advise our requesters to use caution in interpreting or generalising findings as inherent publication bias towards predominantly white, northern hemisphere countries may limit the applicability of some research to certain patient populations (*Library and Archives, RCS England, 2024)*

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PICOS and search notes

Search title	Platelet rich plasma for COVID anosmia
Research question	Platelet rich plasma is a novel treatment for smell dysfunction related to COVID-19. This involves a special preparation of plasma, donated by the patient themselves, which is then injected into the olfactory mucosa in the nose and potentially can reduce inflammation as well as promoting growth of new smell nerves, therefore leading to smell regeneration. We are aiming to investigate the efficacy of PRP for COVID-19 related OD.
Population(s)	Clinical study conducted on human populations with olfactory dysfunction related to COVID-19 regardless of age, gender, or ethnicity
Intervention(s)	Patients treated with Platelet-Rich Plasma (PRP) for COVID-19
Comparators	A non-exposed control group including alternative treatment or placebo
Outcomes	1. Validated psychophysical Olfaction scoring systems including but not limited to “Sniffin’ Sticks” (TDI), UPSIT, or CCCRC. 2. Health-related QoL measured by validated disease-specific scoring systems such as ODQ. 3. Disease severity and extent through validated objective and subjective symptom scores such as VAS. 4. Short-term, medium-term and long-term reported adverse events and length of follow-up. 5. Epidemiological data surrounding populations in which PRP was administered including but not limited to demographics, previous treatment and length of olfactory dysfunction. 6. Description of PRP administration protocols including but not limited to preparation, amount, timing and duration.
Exclusion criteria	Populations with COVID-19 without relation to olfactory dysfunction Populations treated with PRP for indications outside of COVID-19 Control groups which included administration of PRP Studies where no outcome measures are directly related to efficacy of PRP on olfactory or clinical outcomes in patients with COVID-19

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	Case reports, abstracts, reviews. Studies without full-text English translation Animal studies
Search period	Since inception
Types of studies included	Full-text primary studies written in English or with full-text English translation available. Exclude case reports, abstracts, reviews, studies without full-text English translation or animal studies.
Comments	MEDLINE, EMBASE, Web of Science, Google Scholar and Cochrane

Search notes:

- Broader subject headings were searched for. Only respiratory tract infections was an option, but see below - it proved possible to dispense with this concept altogether.
- The Ovid and Cochrane database searches were rerun without date limits and using fewer search concepts: olfaction disorders + PRP. This is a more sensitive way to do the search as it does not rely at all on respiratory infection terms.
  A key systematic review was found in Embase that did not use any respiratory infection terms, but it had already been included from another source.
  This approach does capture non-relevant studies on traumatic anosmia.
  Overall effect: unique search output increased to 145 references.
- A missing synonym line in the Cochrane search has now been added. However, adding this line made no change in output.
- This seems a topic with relatively little research, however you search for it. There is a high proportion of duplicates, which backs up this impression. You could try citation tracking of your included references. This is a labour-intensive technique but can be semi-automated if you use a tool such as CitationChaser or Web of Science. It provides extra methodological assurance.

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Database Results

The searches were conducted on 02 July (Ovid Medline, Ovid Embase, Cochrane Library, Google Scholar).

Databases searched	Number of results
Ovid MEDLINE(R) ALL <1946 to 01 July 2025	[33]
Embase <1974 to 2025 Week 26>	[61]
Cochrane Central Register of Controlled Trials (CENTRAL)	[16]
Cochrane Database of Systematic Reviews (CDSR)	[0]
Google Scholar search	[76]
Google Scholar related articles to Platelet-rich plasma for the treatment of COVID-19 related olfactory dysfunction: a systematic review. B. AlRajhi, et al. Rhinology 2023 Vol. 61 Issue 6 Pages 498-507	[26]
Total results retrieved	**[212]**
Total results after deduplication	**[145]** NB: Some duplicates may remain as EndNote does not capture all duplicates
Search designer	**Janet Clapton, BSc (Hons), MSc**
Suggested acknowledgement	With thanks to Janet Clapton, Information Specialist, Royal College of Surgeons of England Library and Archives Team, for conducting the literature searches
If you require updated results beyond the date this search was completed, or advice on how to represent the full search strategies in any publications, please contact us at evidencesupport@rcseng.ac.uk **Please see our guide on Reporting surgical search results at: https://www.rcseng.ac.uk/-/media/Files/RCS/Library-and-publications/Library/Literature-search-service/Reporting-search-results.pdf**	

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Search Strategies

Database:	Ovid MEDLINE(R) ALL <1946 to Jul 1, 2025>	Results per line:
Date:	02/07/2025	
1	olfaction disorders/ or anosmia/	6710
2	((olfactory or olfaction or smelling) adj3 (dysfunction* or disorder*)).ti,ab,kw,kf.	4505
3	(anosmia or cacosmia or dysosmia or hyperosmia or hyposmia or parosmia or phantosmia).ti,ab,kw,kf.	6860
4	or/1-3	12334
5	platelet-rich plasma/ or platelet-rich fibrin/	8118
6	(platelet rich plasma or platelet-rich plasma or PRP).ti,ab,kw,kf.	27293
7	(platelet-rich fibrin or platelet rich fibrin).ti,ab,kw,kf.	2968
8	(thrombocyte rich plasma or thrombocyte-rich plasma).ti,ab,kw,kf.	10
9	or/5-8	30370
10	4 and 9	33

Database:	Embase <1974 to 2025 Week 26>	Results per line:
Date:	02/07/2025	
1	smelling disorder/ or exp anosmia/ or cacosmia/ or dysosmia/ or hyperosmia/ or hyposmia/ or olfactory hallucination/ or parosmia/	24324
2	((olfactory or olfaction or smelling) adj3 (dysfunction* or disorder*)).ti,ab,kw,kf.	5861
3	(anosmia or cacosmia or dysosmia or hyperosmia or hyposmia or parosmia or phantosmia).ti,ab,kw,kf.	10050
4	or/1-3	27273
5	thrombocyte rich plasma/ or platelet-rich fibrin/	24864
6	(platelet rich plasma or platelet-rich plasma or PRP or platelet rich fibrin or platelet-rich fibrin).ti,ab,kw,kf.	41803
7	(thrombocyte rich plasma or thrombocyte-rich plasma).ti,ab,kw,kf.	22
8	or/5-7	47077
9	4 and 8	61

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Database:	Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Database of Systematic Reviews (CDSR)	Results per line:
Date:	02/07/2025	
#1	MeSH descriptor: [Olfaction Disorders] explode all trees	282
#2	((olfactory or olfaction or smelling) NEAR/3 (dysfunction* or disorder*)):ti,ab,kw	574
#3	(anosmia or cacosmia or dysosmia or hyperosmia or hyposmia or parosmia or phantosmia):ti,ab,kw	690
#4	#1 or #2 or #3	1059
#5	MeSH descriptor: [Platelet-Rich Plasma] explode all trees	1280
#6	(platelet rich plasma or (platelet NEXT rich plasma) or PRP):ti,ab,kw	5340
#7	(platelet rich fibrin or platelet NEXT rich fibrin):ti,ab,kw	5405
#8	(thrombocyte rich plasma or (thrombocyte NEXT rich plasma)):ti,ab,kw	1473
#9	{OR #5-#8}	6869
#10	#4 and #9	16
#11	#10 in Trials	16

Database:	Sources	Results per line:	Number of results:
Date:	02/07/2025		
	Google Scholar related search		
	Platelet-rich plasma for the treatment of COVID-19 related olfactory dysfunction: a systematic review B. AlRajhi, O. A. Alrodiman, A. F. Alhuzali, H. Alrashed, Y. A. Alrodiman and B. Alim Rhinology 2023 Vol. 61 Issue 6 Pages 498-507 DOI: https://dx.doi.org/10.4193/Rhin23.168	about 100' - scanned top 60 by relevance	26 articles
	Google Scholar search		
	platelet rich plasma anosmia	about 2570' - scanned top 120 by relevance	76 articles

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Search results

Links will take you to full text where RCS England holds a subscription. For ease of access, we strongly recommend that you log in to the RCS website before viewing any articles or journal issues. If you require assistance with your login or with full text access, please email us: evidencesupport@rcseng.ac.uk

1. Wang, E. and Z. M. Patel (2025).
"Smell Recovery After Platelet-Rich Plasma After Trauma-Induced Anosmia "
JAMA Otolaryngology-- Head & Neck Surgery 151(4): 412-413.

https://dx.doi.org/10.1001/jamaoto.2024.4992
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=prem&NEWS=N&AN=39913151
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:39913151&id=doi:10.1001%2Fjamaoto.2024.4992

2. Lechien, J. R., et al. (2025).
"Recovery of misattributed congenital anosmia after platelet-rich plasma injections: Report of two cases."
Brazilian Journal of Otorhinolaryngology 91(2): 101538.

https://dx.doi.org/10.1016/j.bjorl.2024.101538
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=prem&NEWS=N&AN=39608252
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:39608252&id=doi:10.1016%2Fj.bjorl.2024.101538

3. Lechien, J. R. and S. Saussez (2025).
" Platelet-Rich Plasma for Treating COVID-19-Related Anosmia , Hyposmia , and Parosmia : A Controlled Longitudinal Study."
Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 172(4): 1450-1458.

https://dx.doi.org/10.1002/ohn.1149
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=39888025
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:39888025&id=doi:10.1002%2Fohn.1149

OBJECTIVE: To investigate the effectiveness of platelet-rich plasma (PRP) injection into the olfactory clefts of coronavirus disease 2019 (COVID-19) patients with persistent anosmia , hyposmia , and parosmia ., STUDY DESIGN: Controlled study., SETTING: Multicenter study., METHODS: From March 2022 to July 2024, 514 COVID-19 patients undergoing PRP injection and olfactory training versus olfactory training (controls) for a persistent olfactory dysfunction (OD) were consecutively recruited from two medical centers. Subjects were evaluated from pre- to 3 months post-injection with the olfactory disorder questionnaire (ODQ) and the threshold, discrimination, and identification (TDI) test. Olfactory outcomes were compared between controls and patients considering the type of OD (anosmia , hyposmia , and parosmia)., RESULTS: The PRP group was composed of 416 patients with anosmia (N = 111; 26.7%), hyposmia (N = 160; 38.5%), and parosmia (N = 145; 34.9%). The baseline ODQ of patients with parosmia was significantly higher than those of

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the other groups (P = .001). The increase in TDI subscores and total score was significantly higher in all PRP subgroups compared to controls (P = 0.001). The ODQ significantly reduced from pre- to post-PRP injection in hyposmia and parosmia groups (P = 0.001). Patients with parosmia showed a significantly greater reduction in ODQ scores compared to the control group. The 3-month TDI score was negatively influenced by the age of patients (rs = -0.263; P = 0.001) and the duration of OD (rs = -0.213; P = .001)., CONCLUSION: Patients with parosmia experienced a stronger impact of OD on quality of life (QoL), and showed greater QoL improvement following PRP injections compared to other groups. Copyright © 2025 American Academy of Otolaryngology-Head and Neck Surgery Foundation.

4. Kim, D. H., et al. (2025).
"Short-term efficacy of platelet-rich plasma in the treatment of persistent olfactory dysfunction : systematic review and meta-analysis."
European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery 282(1): 37-46.

https://dx.doi.org/10.1007/s00405-024-08885-6
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=39098960
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:39098960&id=doi:10.1007%2Fs00405-024-08885-6

PURPOSE: To assess the short-term effects of topical platelet-rich plasma (PRP) injection on persistent refractory olfactory dysfunction ., METHODS: A comprehensive literature search of the PubMed, SCOPUS, EMBASE, Web of Science, Google Scholar, and Cochrane databases was conducted for articles up to November 2023. The search focused on studies that compared the amelioration of olfactory dysfunction between a topical PRP treatment cohort and a control group (receiving either placebo or no treatment), along with pre- and post-treatment comparisons. Subgroup analysis of the evaluation of olfactory function was also performed., RESULTS: The improvement in olfactory scores 1-3 months post-treatment (standardized mean difference = 1.5354 [95% confidence interval: 0.7992; 2.2716], I2 = 83.8%) was greater in the treatment group than in the control group. In the treatment group, PRP increased the threshold, discrimination, and identification (TDI) score for Sniffin' Sticks by > 5.5 (minimum clinically significant difference; mean difference = 6.1789 [3.9788; 8.3789], I2 = 0.0%), indicating clinically significant improvement based on verified examinations. The rate of significant improvement among patients was 0.6683 [0.5833; 0.7436] after treatment. All TDI subdomains were significantly and similarly improved after treatment., CONCLUSION: This meta-analysis suggests that injection of PRP into the olfactory fissure or surrounding mucosal areas is an effective treatment for persistent refractory olfactory dysfunction in the short term. Copyright © 2024. The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature.

5. Fieux, M., et al. (2025).
"Long-term Outcomes of PRP Injections for Post-viral Olfactory Loss: A Prospective Cohort Study."
International Forum of Allergy & Rhinology 15(4): 420-427.

https://dx.doi.org/10.1002/alr.23505
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=39740091
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:39740091&id=doi:10.1002%2Falr.23505

BACKGROUND: Platelet-rich plasma (PRP) injections have previously been shown to benefit coronavirus disease 2019 (COVID-19)-induced smell loss. It is unknown if that benefit is stable over

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time. The aim of this study was to assess outcomes at 1-year post-intervention., METHODS: Prospective cohort study. Sixteen patients (10 PRP and six placebo) from the original PRP randomized placebo-controlled clinical trial, and a further 16 patients from smell clinic who were a year out from initial treatment (six PRP patients and 10 non-PRP) were enrolled. University of Pennsylvania Smell Identification Tests (UPSITs) and visual analog scale (VAS) subjective scores were compared to initial scores., RESULTS: There was no difference between groups with respect to age, gender, race, duration of smell loss prior to intervention, smoking or diabetes status, Charlson comorbidity index, presence of phantosmia or parosmia , or baseline UPSIT score. The PRP group had a significantly higher change in UPSIT score at 1 year (p = 0.001), a higher number of patients who met the minimal clinically important difference for the UPSIT (87.5% vs. 31.2%, p = 0.004), and a significantly greater change in VAS at 1 year (p = 0.001), compared to those who did not receive injections. On multivariate logistic regression analysis, no factors appeared to have a significant effect on these findings., CONCLUSION: PRP injections into the olfactory cleft now have long-term data suggesting benefit in both subjective and psychophysical measures of smell, and improvements in both realms at 1 year are significantly higher than in those who do not receive the injections. Copyright © 2024 ARS-AAOA, LLC.

6. Sharifi, A., et al. (2024).
"Utilization and efficacy of platelet-rich plasma and platelet-rich fibrin in otolaryngology: a systematic evidence-based review."
European Archives of Oto-Rhino-Laryngology 281(10): 5091-5110.

7. Satyarini, N. C. and S. Rasyidah (2024).
"The Systematic Review of Platelet Rich Plasma Induced Olfactory In Patients With Covid 19."
Al Makki Health Informatics Journal 2(1): 153-161.

8. Png, L. H., et al. (2024).
"Infectious disease for the rhinologist."
Current opinion in otolaryngology & head and neck surgery 32(1): 28-34.

https://dx.doi.org/10.1097/MOO.0000000000000947
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med25&NEWS=N&AN=37997887
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:37997887&id=doi:10.1097%2FMOO.0000000000000947

PURPOSE OF REVIEW: The purpose of this review is to summarize the recent literature relating to viral, fungal and bacterial infections and their interactions within the sinonasal tract in the past 18 months., RECENT FINDINGS: Coronavirus disease 2019 (COVID-19)-associated olfactory dysfunction (OD) is variant dependent. Magnetic resonance imaging studies have found greater olfactory cleft opacification and higher olfactory bulb volume in post-COVID-19 OD. Olfactory training remains the mainstay of treatment, while platelet-rich plasma injections and ultramicronized palmitoylethanolamide and luteolin combination oral supplementation have shown early promise.Consensus statements on paranasal sinus fungal balls and acute invasive fungal sinusitis have

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been released.Studies on the nasal microbiome have reported Staphylococcus and Corynebacterium as the most abundant genera, with higher levels of Staphylococcus and Corynebacterium being found in patients with chronic rhinosinusitis (CRS) and healthy individuals respectively. However, there is conflicting evidence on the significance of biodiversity of the nasal microbiome found in CRS versus healthy patients., SUMMARY: While the peak of the COVID-19 pandemic is behind us, its sequelae continue to pose treatment challenges. Further studies in OD have implications in managing the condition, beyond those afflicted post-COVID-19 infection. Similarly, more research is needed in studying the nasal microbiome and its implications in the development and treatment of CRS.
Copyright © 2023 Wolters Kluwer Health, Inc. All rights reserved.

9. Nct (2024).
"The Effect of Platelet-rich Plasma Nasal Injection in the Treatment of Traumatic Olfactory Dysfunction."
https://clinicaltrials.gov/ct2/show/NCT06290219.

https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02681054/full

Causes of olfactory impairment include sinus diseases, post-viral olfactory dysfunction, neurological diseases, and post-traumatic lesions of the olfactory nerve. Since the outbreak of the COVID-19 in 2019, there has been a significant increase in the number of patients suffering from olfactory disorders, and the duration of loss of smell and taste varies. According to follow-up studies, nearly 46% of those patients still have symptoms of olfactory impairment one year after diagnosis, and nearly 7% have even completely lost their ability to smell. In recent years, injecting platelet-rich plasma into the nasal cavity has been a new method to improve the sense of smell. The effects of platelet-rich plasma can reduce chronic inflammation and cell-related damage and promote regeneration of olfactory tissue, while hyaluronic acid can promote the release of growth factors from platelets. The purpose of this study is to explore the efficacy of injecting high-concentration platelet plasma combined with hyaluronic acid into the nasal olfactory mucosa in the treatment of traumatic anosmia. A total of 80 patients with olfactory dysfunction were collected from otolaryngology, head and neck outpatient clinics. Selection criteria are 18 years of age or older, and loss of olfactory function for more than 6 months after head trauma. Exclusion criteria are pregnant or lactating women, patients with compromised immune function, patients with acute or chronic sinus infection, patients with nasal polyps, patients with a history of sinonasal cancer, and patients with low platelets or hemophilia and other blood and blood cell-related diseases. This study will establish experimental groups and control groups according to random distribution. Subjects in both groups received zinc tablets and olfactory training for 12 weeks. The experimental group additionally received an injection of platelet-rich plasma combined with hyaluronic acid. After treatment, patients return to the clinic to track the olfactory condition. Before treatment, the subjects evaluated their olfactory function using a Visual Analogue Scale (VAS) and performed the phenyl ethyl alcohol odor detection threshold test and the traditional Chinese version of the University of Pennsylvania Olfactory Identification Test. In the experimental group, 10cc of blood will be drawn from the subjects in the experimental group, the drawn blood will be centrifuged, the centrifuge tube will be inverted 20 times to mix the plasma and hyaluronic acid, and finally 5cc of the plasma mixed with hyaluronic acid will be drawn out using an empty syringe. The project investigator injects plasma mixed with hyaluronic acid into the nasal septum and the medial side of the middle turbinate of the patient's nasal cavity under a nasal endoscope. The two groups will undergo the same olfactory tests three months later to compare the changes in olfactory function of the two groups of patients before and after treatment to explore the efficacy of injecting high-concentration platelet plasma combined with hyaluronic acid into the nasal olfactory mucosa to treat traumatic anosmia.

Corrected Proof

10. Nct (2024).
"Randomized Clinical Trial of Intranasal Injection of Platelet-Rich Plasma for Treatment of Parosmia."
https://clinicaltrials.gov/ct2/show/NCT06283745.

https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02672657/full

This randomized clinical trial will evaluate the benefit of platelet-rich plasma (PRP) inthe treatment of qualitative olfactory dysfunction (parosmia). PRP can be isolated from apatient's own blood and has been found in previous studies to have anti-inflammatory andpro-regenerative properties. It has been used across multiple specialties, such asOrthopedics, Facial Plastics, Dermatology, Neurology in injected form to treat a widevariety of tissues to encourage the body's inherent regenerative capacity. Theinvestigators have completed a randomized controlled trial here, ending in 2022,evaluating it's use in post-SARS-CoV-2 olfactory loss which demonstrated safety andefficacy. Therefore, the investigators aim to assess the ability of PRP to improveolfactory function in patients with parosmia.

11. Murphy, C., et al. (2024).
"Integrating the patient's voice into the research agenda for treatment of chemosensory disorders "
Chemical senses 49.

https://dx.doi.org/10.1093/chemse/bjae020
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med26&NEWS=N&AN=38761171
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:38761171&id=doi:10.1093%2Fchemse%2Fbjae020

World-wide some 658 million people were infected with coronavirus disease 2019 (COVID-19) and millions suffer from chemosensory impairment associated with long COVID. Current treatments for taste and smell disorders are limited. Involving patients has the potential to catalyze the dynamic exchange and development of new ideas and approaches to facilitate biomedical research and therapeutics. We assessed patients' perceptions of the efficacy of treatments for chemosensory impairment using an online questionnaire completed by 5,815 people in the US Logistic regression determined variables predictive of reported treatment efficacy for patients aged 18 to 24, 25 to 39, 40 to 60, and 60+ yrs. who were treated with nasal steroids, oral steroids, zinc, nasal rinse, smell training, theophylline, platelet-rich plasma , and Omega 3. The most consistent predictor was age, with the majority of those 40 to 60 and 60+ reporting that nasal steroids, oral steroids, zinc, nasal rinse, and smell training were only slightly effective or not effective at all. Many of these treatment strategies target regeneration and immune response, processes compromised by age. Only those under 40 reported more than slight efficacy of steroids or smell training. Findings emphasize the need to include patients of all ages in clinical trials. Older adults with olfactory impairment are at increased risk for Alzheimer's disease (AD). We speculate that olfactory impairment associated with long COVID introduces the potential for a significant rise in AD. Long COVID-associated chemosensory impairment increases the urgency for translational and clinical research on novel treatment strategies. Suggestions for high-priority areas for epidemiological, basic, and clinical research on chemosensory impairment follow. Copyright © The Author(s) 2024. Published by Oxford University Press.

12. Moffa, A., et al. (2024).
" Platelet-Rich Plasma for Patients with Olfactory Dysfunction : Myth or Reality? A Systematic Review."
Journal of Clinical Medicine 13(3).

Corrected Proof

https://dx.doi.org/10.3390/jcm13030782
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=pmnm9&NEWS=N&AN=38337476
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:38337476&id=doi:10.3390%2Fjcm13030782

BACKGROUND: With promising outcomes, platelet-rich plasma (PRP) has recently been suggested as a treatment for olfactory dysfunction (OD)., METHODS: Clinical studies utilizing PRP in OD caused by COVID-19, trauma, anesthetic exposure, viral infection, and chronic rhinosinusitis were included in a systematic review., RESULTS: Ten clinical studies were qualitatively analyzed. Six of these studies used the PRP for OD caused by COVID-19, one on OD after functional endoscopic sinus surgery, and three on post-infectious or post-trauma OD. The population included 531 patients, ranging in age from 15 to 63., CONCLUSION: The use of PRP may be a risk-free and efficient therapeutic option with very encouraging outcomes. Indeed, it enhances olfactory perception in patients who not only exhibit COVID-19 infection aftereffects, but also in those who have lost their sense of smell due to trauma, rhinosinusitis, rhinitis, or even surgery. To evaluate the PRP's therapeutic benefits in OD patients and to compare the efficacy of different therapeutic protocols with regard to treatment schedules, there is an urgent need for focused controlled trials.

13. Mehraeen, E., et al. (2024).
"Treatments for Olfactory Dysfunction in COVID-19: A Systematic Review."
International Archives of Otorhinolaryngology 28(04): e728-e743.

14. Maniaci, A., et al. (2024).
" Platelet-Rich Plasma (PRP) in the Treatment of Long COVID Olfactory Disorders : A Comprehensive Review."
Biomedicines 12(4).

https://dx.doi.org/10.3390/biomedicines12040808
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=pmnm9&NEWS=N&AN=38672163
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:38672163&id=doi:10.3390%2Fbiomedicines12040808

Background: Long COVID has brought numerous challenges to healthcare, with olfactory dysfunction (OD) being a particularly distressing outcome for many patients. The persistent loss of smell significantly diminishes the affected individual's quality of life. Recent attention has been drawn to the potential of platelet-rich plasma (PRP) therapy as a treatment for OD. This comprehensive review aims to evaluate the effectiveness of PRP therapy in ameliorating OD, especially when associated with long-term COVID-19. Methods: We executed a comprehensive search of the literature, encompassing clinical trials and observational studies that utilized PRP in treating OD limited to COVID-19. We retrieved and comprehensively discussed data such as design, participant demographics, and reported outcomes, focusing on the efficacy and safety of PRP therapy for OD in COVID-19 patients. Results: Our comprehensive analysis interestingly found promising perspectives for PRP in OD following COVID-19 infection. The collective data indicate that PRP therapy contributed to a significant improvement in olfactory function after COVID-19 infection. Conclusions: The evidence amassed suggests that PRP is a promising and safe therapeutic option for OD, including cases attributable to Long COVID-19. The observed uniform enhancement of olfactory function in patients receiving PRP highlights the necessity for well-designed, controlled trials. Such studies would help to

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refine treatment protocols and more definitively ascertain the efficacy of PRP in a broader, more varied patient cohort.

15. Lechien, J. R., et al. (2024).
"Effectiveness of Platelet-Rich Plasma for COVID-19-Related Olfactory Dysfunction : A Controlled Study."
Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 170(1): 84-91.

https://dx.doi.org/10.1002/ohn.460
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med25&NEWS=N&AN=37522295
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:37522295&id=doi:10.1002%2Fohn.460

OBJECTIVE: To investigate the effectiveness of platelet-rich plasma (PRP) injection into the olfactory clefts of coronavirus disease 2019 (COVID-19) patients with persistent olfactory dysfunction (OD)., STUDY DESIGN: Controlled study., SETTING: Multicenter study., METHODS: From March 2022 to November 2022, COVID-19 patients with persistent OD were recruited from three European hospitals to undergo PRP injections into the olfactory clefts. Olfactory function was evaluated at baseline and 10 weeks postinjection with the Olfactory Disorder Questionnaire (ODQ) and threshold, discrimination, and identification (TDI) test. Data were compared with a control group of untreated patients., RESULTS: Eighty-one patients who underwent PRP injection and 78 controls were included. Sixty-five PRP patients (80.3%) experienced subjective smell improvement after a mean duration of 3.4 +/- 1.9 weeks. The parosmia , life quality statement, and ODQ sub- and total scores significantly decreased from pre- to 10-week postinjection in the PRP group. The TDI sub- and total scores significantly increased 10 weeks postinjection. In controls, the ODQ score did not change over time, while the discrimination, identification, and total TDI scores significantly increase after 10 weeks of follow-up. The 10-week TDI and ODQ scores were significantly better in the PRP group compared with the controls., CONCLUSION: Patients who underwent PRP injection reported better 10-week subjective and objective smell outcomes than controls. Future randomized-controlled studies using saline injection into the olfactory cleft of controls are needed to determine the superiority of PRP over placebo. Copyright © 2023 American Academy of Otolaryngology-Head and Neck Surgery Foundation.

16. Lechien, J. R. and S. Saussez (2024).
"Injection of Platelet Rich Plasma in the Olfactory Cleft for COVID-19 Patients With Persistent Olfactory Dysfunction : Description of the Technique."
Ear, Nose, & Throat Journal 103(1_suppl): 115S-119S.

https://dx.doi.org/10.1177/01455613221124773
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med25&NEWS=N&AN=36219733
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:36219733&id=doi:10.1177%2F01455613221124773

In this paper, we described technique of platelet rich plasma injection into the olfactory cleft in a 22-year-old female with 24-month post-COVID-19 anosmia . The technique starts with the blood extraction and the isolation of PRP through a 10-min centrifugation. The supernatant was injected in nasal regions after a local anesthesia through a 0degree rigid optic. Several points of .2-.5 mL were performed in the nasal septum in regard of the head of the middle turbine and in the head of the middle turbine in both sides. The baseline threshold, discrimination, and identification scores were 1, 8, and 0, and the Olfactory Disorder Questionnaire score was 51, respectively. The injection of PRP

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in olfactory cleft was done without complication and mild pain. The patient perception of recovery of smell sense occurred at 3-week post-injection. From this time, the smell sense progressively improved to the 2-month consultation. At 2-month post-injection, the TDI scores reached 16, 16, and 16 (48), while the Olfactory Disorder Questionnaire was 73. The injection of PRP into the olfactory cleft appears to be a safe and easiness new approach that may improve the recovery of smell sense. Future controlled studies are needed.

17. Lechien, J. R. and S. Saussez (2024).
"Effectiveness of platelet-rich plasma in long-lasting post-viral olfactory dysfunction : a case-series."
European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery 281(11): 5841-5846.

https://dx.doi.org/10.1007/s00405-024-08816-5
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med26&NEWS=N&AN=38992193
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:38992193&id=doi:10.1007%2Fs00405-024-08816-5

OBJECTIVE: To investigate the platelet-rich plasma (PRP) effectiveness in patients with a long-lasting postviral olfactory dysfunction (LPOD)., METHODS: Forty-three consecutive patients with a long-lasting postviral OD were prospectively recruited. The injection of 1 mL of PRP was carried out in both olfactory clefts. The pre- to 6-month post-PRP injection change in olfaction was assessed with the olfactory disorder questionnaire (ODQ) and the threshold, discrimination, and identification (TDI) tests., RESULTS: Forty-three patients received bilateral PRP injections (24 females). The mean age of patients was 58.9 +/- 16.8 years. The mean duration of LPOD was 8.7 years. The pre to 6-month post-injection mean TDI significantly improved from 10.3 +/- 10.2 to 20.12 +/- 12.07 (p = 0.001). The mean ODQ significantly decreased from 29.8 +/- 13.0 to 23.4 +/- 11.3 (p = 0.013). The average change of the TDI and the ODQ were 9.8 and 6.4, respectively. Age was inversely associated with the 6-month threshold score., CONCLUSION: PRP appears to be a promising therapeutic strategy for long-lasting postviral OD. Our findings support the conduction of controlled randomized trial in this population of patients. Copyright © 2024. The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature.

18. Lechien, J. R. (2024).
"Determinants of long-lasting postviral COVID-19 and non-COVID-19 olfactory Dysfunction: The sanctuary theory."
Medical Hypotheses 187: 111357.

https://dx.doi.org/10.1016/j.mehy.2024.111357
https://www.sciencedirect.com/science/journal/03069877
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed27&NEWS=N&AN=2032008448
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:10.1016%2Fj.mehy.2024.111357

Since the onset of the Coronavirus disease 2019 (COVID-19) pandemic, the long-lasting postviral olfactory dysfunction (POD) became a prevalent symptom in Western country populations. However, the pathophysiology of long-lasting POD remains poorly understood. The effectiveness of platelet-rich plasma (PRP) injections into the olfactory clefts and recent findings from COVID-19 studies brought new elements in the understanding of the pathophysiology of COVID-19 and non-COVID-19 long-lasting POD. The present hypothesis suggests that the long-lasting POD could be related to a long-

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lasting silent chronic inflammation in the neuroepithelium due to the persistence of virus antigen into stem cells. The immune response could limit the regenerative and recovery processes, making the olfactory region an incomplete immune sanctuary for some viruses according to some specific pathophysiological phenomena (syncytia formation).Copyright © 2024 Elsevier Ltd

19. Krygier, J., et al. (2024).
"A case of airborne allergic contact dermatitis to essential oils used for olfactory training in post-COVID-19 anosmia."
Otolaryngology Case Reports 30: 100584.

https://dx.doi.org/10.1016/j.xocr.2024.100584
https://www.sciencedirect.com/science/journal/24685488
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed27&NEWS=N&AN=2030437110
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:10.1016%2Fj.xocr.2024.100584

Allergic contact dermatitis (ACD) is a delayed hypersensitivity reaction occurring on the skin site of contact after direct exposure to an allergen. Airborne ACD can also exist and is caused by allergens released into the air and settled later on the exposed skin. Essential oils that are highly concentrated plant extracts have been widely described as possible contact allergens for susceptible individuals. Since the beginning of the 2020 COVID-19 pandemic, anosmia has revealed to be one of the earliest and most specific symptoms of this infection. This is generally contemporaneous with the infection and with self-limiting action, but cases of long-lasting or even permanent anosmia have been reported. Anosmia therapy with the greatest degree of supporting evidence is olfactory training. We report a case of airborne ACD in relation with essential oils use during olfactory training for anosmia associated with COVID-19 infection.Copyright © 2024 The Authors

20. Jiang, R.-S. and Y.-F. Chiang (2024).
"The Effect of Platelet-Rich Plasma and Hyaluronic Acid Nasal Injections in the Treatment of Traumatic Olfactory Dysfunction "
Ear, Nose, & Throat Journal: 1455613241291710.

https://dx.doi.org/10.1177/01455613241291710
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medp&NEWS=N&AN=39404838
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:39404838&id=doi:10.1177%2F01455613241291710

Objective: Platelet-rich plasma (PRP) has been injected into the olfactory cleft to treat olfactory dysfunction related to coronavirus disease 2019. In this study, we aimed to evaluate the effect of PRP combined with hyaluronic acid (HA) nasal injection in the treatment of traumatic olfactory dysfunction . Methods: Patients who had lost olfactory function after experiencing head trauma and were willing to receive PRP and HA nasal injections for treatment were enrolled. Before nasal injection, 10 cc of blood was drawn from the patients. The drawn blood was injected into a centrifuge tube for processing, and finally, 5 cc of the PRP mixed with HA was drawn out using an empty syringe. The PRP mixed with HA was injected into the upper part of the middle nasal septum and the medial side of the middle turbinate of the patient's nasal cavity under a nasal endoscope. The olfactory function of each patient was evaluated by the phenyl ethyl alcohol (PEA) odor detection threshold test before and at both 1 and 3 months after nasal injection and the traditional Chinese version of the University of Pennsylvania Smell Identification Test at 3 months after nasal injection. Results: A total of 28 patients received PRP and HA nasal injections between August and December of 2023 and came back for evaluation of the effect. In all, 20 (71.4%) patients felt their olfactory function improved 1

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month after injection, and 24 of 28 (85.7%) patients reported their olfactory function improved at 3 months after injection. The bilateral or unilateral PEA threshold decreased in 22 (78.6%) patients 1 month after injection, and decreased in 15 (53.6%) patients 3 months after injection. Conclusions: Our results show that PRP and HA nasal injections were associated with favored patient-reported outcomes and improved the olfactory threshold in the treatment of traumatic olfactory dysfunction .

21. Irct20230127057244N (2024).
"comparing the Effect of corticosteroids and PRP on anosemia with placebo."
https://trialsearch.who.int/Trial2.aspx?TrialID=IRCT20230127057244N2.

https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02797782/full

INTERVENTION: Intervention 1: Intervention group:Injection of a mixture of one cc platelet-rich plasma solution obtained from centrifugation of patients' blood samples and in one cc triamcinolone from Iran Hormon Pharmaceutical Company in the olfactory cleft area of ??the patients in a space of one centimeter in patients with chronic sinusitis with polyps who have undergone endoscopic sinus surgery. This procedure will be performed at the end of the surgery and will not be repeated. Intervention 2: Control group: Injecting one cc of normal saline from Iran Injectable and Pharmaceutical Products Company following endoscopic sinus surgery in the olfactory cleft area of ??patients in a space of one centimeter in patients with chronic sinusitis with polyps who have undergone endoscopic sinus surgery. This procedure will be performed at the end of the surgery and will not be repeated. CONDITION: Chronic Sinusitis. ; Chronic pansinusitis J32.4 PRIMARY OUTCOME: Olfactory Outcomes. Timepoint: before intervention and 6 month after. Method of measurement: I_SIT Score. INCLUSION CRITERIA: Nasal polyposis , Having different severities of olfactory disorder based on the olfactory recognition test score and duration of anosmia less than 2 years.

22. Irct20230127057244N (2024).
"A comparative study of injecting platelet-rich plasma solution versus normal saline injection on olfactory outcomes following endoscopic sinus surgery in patients with chronic sinusitis accompanied by nasal polyps."
https://trialsearch.who.int/Trial2.aspx?TrialID=IRCT20230127057244N3.

https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02797783/full

INTERVENTION: Intervention 1: Intervention group: Injection of platelet-rich plasma solution on olfactory outcome after endoscopic sinus surgery in sick patients to chronic sinusitis with polyps. Intervention 2: Control group: Normal saline injection on olfactory outcome following endoscopic sinus surgery in patients with chronic sinusitis with polyps. CONDITION: Chronic Sinusitis. ; Chronic pansinusitis J32.4 PRIMARY OUTCOME: Olfactory Outcomes. Timepoint: At entrance time to trial and 6 months later. Method of measurement: Sino-nasal Outcome Test. INCLUSION CRITERIA: Patients aged 15 to 50 years with nasal polyps. Having different severities of olfactory disorder based on the olfactory recognition test score and duration of anosmia less than 2 years.

23. Elsheikh, E. M., et al. (2024).
"Effect of Plasma Rich Protein Use in Post (COVID 19) Anosmic Patients."
Zagazig University Medical Journal 30(1.6): 2910-2920.

Corrected Proof

24. Duffy, A., et al. (2024).
"Topical platelet-rich plasma as a possible treatment for olfactory dysfunction-A randomized controlled trial."
International Forum of Allergy & Rhinology 14(9): 1455-1464.

https://dx.doi.org/10.1002/alr.23363
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med25&NEWS=N&AN=38722276
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:38722276&id=doi:10.1002%2Falr.23363

BACKGROUND: Olfactory dysfunction (OD) affects many survivors of COVID-19. Prior studies have investigated the use of platelet-rich plasma (PRP) injections for OD. We describe the first randomized controlled trial investigating topical PRP for OD treatment and contribute to existing literature illustrating PRP as an emerging therapeutic., METHODS: This is a single-blinded, randomized controlled trial conducted from July 2022 to December 2023. Adult patients with OD >=6 months secondary to COVID-19 with Brief Smell Identification Test (BSIT) scores of <=8/12 or SCENTinel odor intensity of <=40/100 were included. Patients were randomized to three, monthly PRP or placebo-impregnated Surgifoam treatments into bilateral olfactory clefts. The BSIT, SCENTinel, and Questionnaire of Olfactory Disorders-Negative Statements (QOD-NS) were completed monthly through month 12., RESULTS: Of 104 patients screened, 83 participated. No significant differences in age, OD duration, BSIT, SCENTinel, or QOD-NS scores were found between PRP (n = 42) and placebo (n = 41) patients at baseline. PRP patients experienced a statistically significant increase in BSIT scores from baseline at months 5-9, 11, and 12, while placebo patients did not ($p < 0.05$). However, total BSIT scores were similar between the two groups throughout the study. Neither the SCENTinel odor intensity scores nor the change from baseline were significantly different between the treatment groups. At month 12, PRP patients experienced minor improvement in OD-related quality-of-life compared with placebo., CONCLUSIONS: This study is the first to describe topical PRP as a safe, experimental treatment for OD in humans. PRP may impact odor identification in post-COVID-19 OD patients, although the lack of difference in total BSIT scores highlights the need for further study.
Copyright © 2024 The Authors. International Forum of Allergy & Rhinology published by Wiley Periodicals LLC on behalf of American Academy of Otolaryngic Allergy and American Rhinologic Society.

25. Cantone, E., et al. (2024).
"Persistent COVID-19 parosmia and olfactory loss post olfactory training: randomized clinical trial comparing central and peripheral-acting therapeutics."
European Archives of Oto-Rhino-Laryngology 281(7): 3671-3678.

26. Bischoff, S., et al. (2024).
"Treatment of COVID-19 Associated Olfactory Dysfunction : A Systematic Review."
Current Allergy and Asthma Reports 25(1): 2.

https://dx.doi.org/10.1007/s11882-024-01182-6
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med26&NEWS=N&AN=39477832

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https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:39477832&id=doi:10.1007%2Fs11882-024-01182-6

PURPOSE OF REVIEW: COVID -19 associated olfactory dysfunction is widespread, yet effective treatment strategies remain unclear. This article aims to provide a comprehensive systematic review of therapeutic approaches and offers evidence-based recommendations for their clinical application., RECENT FINDINGS: A living Cochrane review, with rigorous inclusion criteria, has so far included 2 studies with a low certainty of evidence. In this systematic review we list clinical data of 36 randomised controlled trials (RCTs) and non-randomised studies published between Jan 1, 2020 and Nov 19, 2023 regarding treatment options for COVID-19 associated olfactory dysfunction . Nine treatment groups were analysed, including olfactory training, local and systemic corticosteroids, platelet-rich plasma (PRP), calcium chelators, vitamin supplements including palmitoylethanolamide with luteolin, insulin, gabapentin and cerebrolysin. Primary objective was the effect of the studied treatments on the delta olfactory function score (OFS) for objective/psychophysical testing. Treatments such as PRP and calcium chelators demonstrated significant improvements on OFS, whereas olfactory training and corticosteroids did not show notable efficacy for COVID-19 associated olfactory dysfunction . Copyright © 2024. The Author(s).

27. Bae, A. Y., et al. (2024).
"Efficacy of Platelet-Rich Plasma in the Treatment of Persistent Olfactory Impairment After COVID-19: A Systematic Review and Meta-Analysis."
Journal of rhinology : official journal of the Korean Rhinologic Society 31(1): 1-7.

https://dx.doi.org/10.18787/jr.2024.00006
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=pmnm9&NEWS=N&AN=39664044
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:39664044&id=doi:10.18787%2Fjr.2024.00006

Background and Objectives: This study aimed to evaluate the impact of topical platelet-rich plasma (PRP) injection on persistent refractory olfactory dysfunction after COVID-19 infection., Methods: A systematic review was conducted, focusing on studies that compared the efficacy of topical PRP treatment with a control group (receiving either placebo or no treatment) in ameliorating olfactory dysfunction . Pre- and post-treatment comparisons were evaluated, along with a subgroup analysis of olfactory function evaluation., Results: The analysis revealed a significant improvement in olfactory scores between 1 to 3 months post-treatment (standardized mean difference=1.4376; 95% confidence interval [CI]=0.5934-2.2818; I2=84.1%) in the treatment group compared to the control group. Moreover, a notable disparity was observed between the two groups in the incidence of substantial recovery from anosmia or hyposmia (odds ratio=8.6639; 95% CI=2.9752-25.2292; I2=0.0%). PRP treatment led to a clinically significant increase in the threshold, discrimination, and identification (TDI) score for the Sniffin' Sticks test by >5.5 (minimum clinically significant difference; mean difference, 6.3494; 95% CI=4.0605-8.6384; I2=0.0%), as confirmed by verified examinations. The odds ratio for significant improvement among patients after treatment was determined to be 0.7654 (95% CI=0.6612-0.8451). Furthermore, all TDI subdomains exhibited significant and comparable improvements post-treatment., Conclusion: This meta-analysis indicates that the injection of PRP into the olfactory fissure or surrounding mucosal areas is an effective treatment for persistent refractory olfactory dysfunction . Copyright © 2024 by The Korean Rhinologic Society.

28. Albazee, E., et al. (2024).
" Platelet-rich plasma following endoscopic sinus surgery in patients with chronic sinusitis: A systematic review and meta-analysis of randomised controlled trials."

Corrected Proof

Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery 49(5): 567-577.

https://dx.doi.org/10.1111/coa.14186
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med26&NEWS=N&AN=38816910
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:38816910&id=doi:10.1111%2Fcoa.14186

INTRODUCTION: To comprehensively evaluate the reported clinical effectiveness of platelet-rich plasma (PRP) in patients with chronic sinusitis undergoing endoscopic sinus surgery (ESS)., METHODS: We performed a systematic review and meta-analysis of randomised controlled trials (RCTs). Five digital online databases (PubMed, Scopus, Web of Science, Google Scholar and Cochrane CENTRAL) were searched from inception up to 1st May 2023. Our specific outcomes involved postoperative nasal endoscopy scores measured via Lund-Kennedy score or Meltzer score, olfactory sensation scores and pre-operative anosmia duration. All data were pooled as standardised mean difference (SMD) with a 95% confidence interval (CI), using the RevMan software., RESULTS: Six RCTs were included in this systematic review and meta-analysis, with a total of 169 patients. The risk of bias in the included RCTs was low in three RCTs, some concerns in one RCT and high risk in two RCTs. The overall analysis of the postoperative nasal endoscopy scores showed that the PRP group had lower scores compared to the control group (n = 3 RCTs, SMD = -1.19; 95% CI [-1.94, -0.44], p = .002). There was no significant difference between the PRP and control groups regarding anosmia duration (n = 2 RCTs, SMD = 0.21; 95% CI [-0.17, 0.59], p = 0.28) or olfactory sensation scores, despite the PRP group having higher scores (n = 2 RCTs, SMD = 0.53; 95% CI [-0.32, 1.39], p = 0.22)., CONCLUSION: This study highlights the potential advantages of using PRP as an additional treatment for individuals with chronic sinusitis undergoing ESS. The improvements associated with PRP include facilitating wound healing, reducing inflammation and enhancing surgical outcomes. To optimise the use of PRP in clinical settings, future research should focus on conducting larger trials with standardised protocols.
Copyright © 2024 John Wiley & Sons Ltd.

29. (2024).
"The Effect of Platelet-rich Plasma and Hyaluronic Acid Nasal Injection in the Treatment of Traumatic Olfactory Dysfunction A1 - Anonymous."
clinicaltrials.gov.

https://clinicaltrials.gov/study/NCT06290219
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emctr&NEWS=N&AN=NCT06290219
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:&issn=&isbn=&volume=&issue=&spage=&pages=&date=2024&title=clinicaltrials.gov&atitle=The+Effect+of+Platelet-rich+Plasma+and+Hyaluronic+Acid+Nasal+Injection+in+the+Treatment+of+Traumatic+Olfactory+Dysfunction&aulast=

Brief Summary, The purpose of this study is to explore the efficacy of injecting high-concentration platelet plasma combined with hyaluronic acid into the nasal olfactory mucosa in the treatment of traumatic anosmia., Detailed Description, Causes of olfactory impairment include sinus diseases, post-viral olfactory dysfunction, neurological diseases, and post-traumatic lesions of the olfactory nerve. Since the outbreak of the COVID-19 in 2019, there has been a significant increase in the number of patients suffering from olfactory disorders, and the duration of loss of smell and taste varies. According to follow-up studies, nearly 46% of those patients still have symptoms of olfactory impairment one year after diagnosis, and nearly 7% have even completely lost their ability to smell. In recent years, injecting platelet-rich plasma into the nasal cavity has been a new method to improve

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the sense of smell. The effects of platelet-rich plasma can reduce chronic inflammation and cell-related damage and promote regeneration of olfactory tissue, while hyaluronic acid can promote the release of growth factors from platelets. The purpose of this study is to explore the efficacy of injecting high-concentration platelet plasma combined with hyaluronic acid into the nasal olfactory mucosa in the treatment of traumatic anosmia. A total of 80 patients with olfactory dysfunction were collected from otolaryngology, head and neck outpatient clinics. Selection criteria are 18 years of age or older, and loss of olfactory function for more than 6 months after head trauma. Exclusion criteria are pregnant or lactating women, patients with compromised immune function, patients with acute or chronic sinus infection, patients with nasal polyps, patients with a history of sinonasal cancer, and patients with low platelets or hemophilia and other blood and blood cell-related diseases. This study will establish experimental groups and control groups according to random distribution. Subjects in both groups received zinc tablets and olfactory training for 12 weeks. The experimental group additionally received an injection of platelet-rich plasma combined with hyaluronic acid. After treatment, patients return to the clinic to track the olfactory condition. Before treatment, the subjects evaluated their olfactory function using a Visual Analogue Scale (VAS) and performed the phenyl ethyl alcohol odor detection threshold test and the traditional Chinese version of the University of Pennsylvania Olfactory Identification Test. In the experimental group, 10cc of blood will be drawn from the subjects in the experimental group, the drawn blood will be centrifuged, the centrifuge tube will be inverted 20 times to mix the plasma and hyaluronic acid, and finally 5cc of the plasma mixed with hyaluronic acid will be drawn out using an empty syringe. The project investigator injects plasma mixed with hyaluronic acid into the nasal septum and the medial side of the middle turbinate of the patient's nasal cavity under a nasal endoscope. The two groups will undergo the same olfactory tests three months later to compare the changes in olfactory function of the two groups of patients before and after treatment to explore the efficacy of injecting high-concentration platelet plasma combined with hyaluronic acid into the nasal olfactory mucosa to treat traumatic anosmia.Copyright © 2025 clinicaltrials.gov

30. (2024).
"Randomized Clinical Trial of Intranasal Injection of Platelet-Rich Plasma for Treatment of Parosmia A1 - Anonymous."
clinicaltrials.gov.

https://clinicaltrials.gov/study/NCT06283745
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emctr&NEWS=N&AN=NCT06283745
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:&issn=&isbn=&volume=&issue=&spage=&pages=&date=2024&title=clinicaltrials.gov&atitle=Randomized+Clinical+Trial+of+Intranasal+Injection+of+Platelet-Rich+Plasma+for+Treatment+of+Parosmia&aulast=

Brief Summary, This randomized clinical trial will evaluate the benefit of platelet-rich plasma (PRP) in the treatment of qualitative olfactory dysfunction (parosmia). PRP can be isolated from a patient's own blood and has been found in previous studies to have anti-inflammatory and pro-regenerative properties. It has been used across multiple specialties, such as Orthopedics, Facial Plastics, Dermatology, Neurology in injected form to treat a wide variety of tissues to encourage the body's inherent regenerative capacity. The investigators have completed a randomized controlled trial here, ending in 2022, evaluating it's use in post-SARS-CoV-2 olfactory loss which demonstrated safety and efficacy. Therefore, the investigators aim to assess the ability of PRP to improve olfactory function in patients with parosmia.Copyright © 2025 clinicaltrials.gov

31. Yan CH, J. S., Lin H-FC, et al. (2023).
"Use of platelet-rich plasma for COVID-19–related olfactory loss: a randomized controlled trial."

Corrected Proof

International Forum of Allergy & Rhinology 13: 989–997.

https://doi.org/10.1002/alr.23116

32. Yan, C. H., et al. (2023).
"Use of platelet-rich plasma for COVID-19-related olfactory loss: a randomized controlled trial."
International Forum of Allergy & Rhinology 13(6): 989-997.

https://dx.doi.org/10.1002/alr.23116
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med23&NEWS=N&AN=36507615
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:36507615&id=doi:10.1002%2Falr.23116

INTRODUCTION: The current study evaluated the use of platelet-rich plasma (PRP), an autologous blood product with supraphysiologic concentrations of growth factors, in the treatment of prolonged coronavirus disease 2019 (COVID-19)-related smell loss., METHODS: This multi-institutional, randomized controlled trial recruited patients with COVID-19 who had objectively measured smell loss (University of Pennsylvania Smell Identification Test [UPSIT] <= 33) between 6 and 12 months. Patients were randomized to three intranasal injections of either PRP or sterile saline into their olfactory clefts. The primary outcome measure was change in Sniffin' Sticks score (threshold, discrimination, and identification [TDI]) from baseline. The secondary end point measures included responder rate (achievement of a clinically significant improvement, >=5.5 points TDI), change in individual TDI olfaction scores, and change in subjective olfaction via a visual analog scale., RESULTS: A total of 35 patients were recruited and 26 completed the study. PRP treatment resulted in a 3.67-point (95% CI: 0.05-7.29, p = 0.047) greater improvement in olfaction compared with the placebo group at 3 months and a higher response rate (57.1% vs 8.3%, odds ratio 12.5 [95% exact bootstrap confidence interval, 2.2-116.7]). There was a greater improvement in smell discrimination following PRP treatment compared with placebo but no difference in smell identification or threshold. There was no difference in subjective scores between PRP and placebo. No adverse effects were reported., CONCLUSION: Olfactory function following COVID-19 can improve spontaneously after 6 months and can improve to a greater extent with PRP injection. These data build on the promise of PRP to be a safe potential treatment option for patients with COVID-19-related smell loss, and larger-powered studies will help further assess its efficacy. Copyright © 2022 ARS-AAOA, LLC.

33. Vaira, L. A., et al. (2023).
"COVID-19 related persistent olfactory disorders represent an unprecedented challenge."
American Journal of Otolaryngology - Head and Neck Medicine and Surgery 44(1): 103667.

https://dx.doi.org/10.1016/j.amjoto.2022.103667
http://www.elsevier.com/inca/publications/store/6/2/3/1/1/9/index.htt
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed25&NEWS=N&AN=2020753811
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:36270236&id=doi:10.1016%2Fj.amjoto.2022.103667

34. Sorour, S. S., et al. (2023).
"Assessment of olfactory dysfunction after treatment with platelet-rich plasma."
The Egyptian Journal of Hospital Medicine 91(1): 5094-5099.

Corrected Proof

35. Shawky, M. A. and A. M. Hadeya (2023).
" Platelet-rich Plasma in Management of Anosmia (Single Versus Double Injections)."
Indian journal of otolaryngology and head and neck surgery : official publication of the Association of Otolaryngologists of India 75(Suppl 1): 1004-1008.

https://dx.doi.org/10.1007/s12070-023-03553-3
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=pmnm8&NEWS=N&AN=37206725
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:37206725&id=doi:10.1007%2Fs12070-023-03553-3

Background: Anosmia is a common problem with a significant impact on quality of life and increased mortality. People with anosmia may not be able to fully taste foods and may lose interest in eating. This can lead to weight loss or malnutrition. Anosmia can also lead to depression because it may impair one's ability to smell or taste pleasurable foods. Platelet-rich plasma (PRP) is an autologous biologic product with anti-inflammatory and neuroprotective effects. This prospective study evaluated the role of PRP on olfactory neuroregeneration in patients with anosmia and compare the results of single and double injections., Methods: 54 patients were included in the study who had olfactory loss greater than 6 months in duration, no evidence of sinonasal inflammatory disease, and no improvement with olfactory training and topical steroids. 27 patients received a single intranasal injection of PRP into the mucosa of the olfactory cleft and 27 patients received a double injections with 3 weeks interval between them. The Q-Sticks Test was administered at the beginning of the study and at 1 and 3 months., Results: All patients reported a subjective improvement of their smell shortly after injection but then stabilized. At 3-month post-treatment, 16 patients improved significantly after single injection and 19 patients improved significantly after double injections. There were no adverse outcomes from intranasal PRP injections., Conclusion: PRP appears safe for use in the treatment of olfactory loss, and preliminary data suggest possible efficacy, especially for those with persistent loss. Further studies will help determine optimal frequency and duration of use. Copyright © Association of Otolaryngologists of India 2023, Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.

36. Saraswathula, A., et al. (2023).
"Reimbursement for Olfactory Testing: A Growing Need at a Unique Time in History."
JAMA Otolaryngology - Head and Neck Surgery 149(7): 567
EP - 568.

https://dx.doi.org/10.1001/jamaoto.2023.0837
http://archotol.jamanetwork.com/issues.aspx
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed25&NEWS=N&AN=2025858953
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:37166819&id=doi:10.1001%2Fjamaoto.2023.0837

37. Sadek, A. A., et al. (2023).
"Role Of platelet-Rich Plasma in Treatment of Post COVID-19 Olfactory Dysfunction."
Minia Journal of Medical Research 34(4): 123-132.

Corrected Proof

38. Murphy, C., et al. (2023).
"Patient Centered Olfactory Research in the COVID era: Age-related Differences and Implications for Neurodegenerative Disease."
Chemical senses 48: 96.

http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed24&NEWS=N&AN=643299454
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:&issn=0379-864X&isbn=&volume=48&issue=&spage=96&pages=96&date=2023&title=Chemical+Senses&atitle=Patient+Centered+Olfactory+Research+in+the+COVID+era%3A+Age-related+Differences+and+Implications+for+Neurodegenerative+Disease&aulast=Murphy

World-wide some 15 million people may suffer from olfactory impairment associated with long COVID. Current treatments and research on new treatments for taste and smell disorders are limited. Actively involving patients in research has the potential to catalyze the dynamic exchange and development of new ideas and approaches to facilitate biomedical research, discovery, and therapeutics. We assessed patients' perceptions of the efficacy of treatments for olfactory impairment with a focus on age using an online questionnaire completed by 5,352 people in the United States. Logistic regression was used to determine predictive variables of reported treatment efficacy for patients 18-24, 25-39, 40-60 and 60+ years old who were treated with nasal steroids, oral steroids, zinc, nasal rinse, smell training, theophylline, PRP, and Omega 3. The most consistent predictor was age, with the majority of those 40-60 and 60+ reporting that nasal steroids, oral steroids, zinc, nasal rinse and smell training were only slightly effective or not effective at all. There were no differences between those who found theophylline or PRP effective, though numbers treated were small. Many of these treatment strategies target regeneration and immune response, processes compromised by age. Findings suggest that older patients may have a more limited regeneration potential in the setting of olfactory impairment and emphasize the need to include patients of all ages in clinical trials. Older adults with olfactory impairment are at increased risk for Alzheimer's disease (AD). We speculate that olfactory impairment associated with long COVID introduces the potential for a significant rise in AD. Long COVID-associated olfactory impairment increases the urgency for translational and clinical research on novel treatment strategies.

39. Lewthwaite, H., et al. (2023).
"Treatable traits for long COVID."
Respirology 28(11): 1005
EP - 1022.

https://dx.doi.org/10.1111/resp.14596
http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1440-1843
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed25&NEWS=N&AN=2025449984
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:37715729&id=doi:10.1111%2Fresp.14596

Long COVID, or post-acute COVID-19 sequelae, is experienced by an estimated one in eight adults following acute COVID-19. Long COVID is a new and complex chronic health condition that typically includes multiple symptoms that cross organ systems and fluctuate over time; a one-size-fits-all

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approach is, therefore, not likely to be appropriate nor relevant for long COVID treatment. 'Treatable Traits' is a personalized medicine approach, purpose-built to address the complexity and heterogeneity of complex chronic conditions. This comprehensive review aimed to understand how a treatable traits approach could be applied to long COVID, by first identifying the most prevalent long COVID treatable traits and then the available evidence for strategies to target these traits. An umbrella review of 22 systematic reviews identified 34 symptoms and complications common with long COVID, grouped into eight long COVID treatable trait clusters: neurological, chest, psychological, pain, fatigue, sleep impairment, functional impairment and other. A systematic review of randomized control trials identified 18 studies that explored different intervention approaches for long COVID prevention (k = 4) or management (k = 14). While a single study reported metformin as effective for long COVID prevention, the findings need to be replicated and consensus is required around how to define long COVID as a clinical trial endpoint. For long COVID management, current evidence supports exercise training or respiratory muscle training for long COVID treatable traits in the chest and functional limitation clusters. While there are studies exploring interventions targeting other long COVID treatable traits, further high-quality RCTs are needed, particularly targeting treatable traits in the clusters of fatigue, psychological, pain and sleep impairment.Copyright © 2023 The Authors. Respirology published by John Wiley & Sons Australia, Ltd on behalf of Asian Pacific Society of Respirology.

40. Lechien, J. R., et al. (2023).
" Platelet-rich plasma injection in the olfactory clefts of COVID-19 patients with long-term olfactory dysfunction "
European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery 280(5): 2351-2358.

https://dx.doi.org/10.1007/s00405-022-07788-8
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med23&NEWS=N&AN=36520209
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:36520209&id=doi:10.1007%2Fs00405-022-07788-8

OBJECTIVE: To investigate safety, feasibility, and effectiveness of platelet-rich plasma (PRP) injection into the olfactory clefts of COVID-19 patients with persistent olfactory dysfunction (OD)., METHODS: From March 2022 to July 2022, COVID-19 patients with persistent OD were consecutively recruited to benefit from PRP injection into the olfactory clefts. Patient pain, annoyance, time of procedure, and adverse events were evaluated. Olfactory function was evaluated at baseline and 2-month post-injection with the olfactory disorder questionnaire (ODQ) and threshold, discrimination, and identification (TDI) test., RESULTS: Eighty-seven patients with anosmia (N = 30), hyposmia (N = 40), or parosmia (N = 17) with a mean OD duration of 15.7 months completed the evaluations. The PRP injection was successfully performed in all patients with a mean procedure time of 18.4 +/- 3.4 min. The adverse events included transient epistaxis (N = 31), parosmia related to xylocaine spray (N = 10), and vasovagal episode (N = 2). The injection procedure was evaluated as somewhat or moderately painful by 41 (47%) and 22 (25%) patients, respectively. Thirty-seven patients were assessed after 2 months post-injection. The mean ODQ and TDI scores significantly improved from baseline to 2-month post-injection ($p < 0.01$). The olfactory improvement occurred after a mean of 3.6 +/- 1.9 weeks., CONCLUSION: The injection of PRP into the olfactory clefts is safe and associated with adequate patient-reported outcomes. The findings of this preliminary study suggest possible efficacy on subjective and psychophysical evaluations, but future randomized controlled studies are needed to determine the superiority of PRP injection over placebo. Copyright © 2022. The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature.

Corrected Proof

41. Jegatheeswaran, L., et al. (2023).
"Assessment of COVID-19-related olfactory dysfunction and its association with psychological, neuropsychiatric, and cognitive symptoms."
Frontiers in Neuroscience 17: 1165329.

https://dx.doi.org/10.3389/fnins.2023.1165329
https://www.frontiersin.org/journals/neuroscience#
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed25&NEWS=N&AN=2024929361
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:10.3389%2Ffnins.2023.1165329

Purpose of review: To provide a detailed overview of the assessment of COVID-19-related olfactory dysfunction and its association with psychological, neuropsychiatric, and cognitive symptoms. Recent findings: COVID-19-related olfactory dysfunction can have a detrimental impact to the quality of life of patients. Prior to the COVID-19 pandemic, olfactory and taste disorders were a common but under-rated, under-researched and under-treated sensory loss. The pandemic has exacerbated the current unmet need for accessing good healthcare for patients living with olfactory disorders and other symptoms secondary to COVID-19. This review thus explores the associations that COVID-19 has with psychological, neuropsychiatric, and cognitive symptoms, and provide a framework and rationale for the assessment of patients presenting with COVID-19 olfactory dysfunction. Summary: Acute COVID-19 infection and long COVID is not solely a disease of the respiratory and vascular systems. These two conditions have strong associations with psychological, neuropsychiatric, and cognitive symptoms. A systematic approach with history taking and examination particularly with nasal endoscopy can determine the impact that this has on the patient. Specific olfactory disorder questionnaires can demonstrate the impact on quality of life, while psychophysical testing can objectively assess and monitor olfaction over time. The role of cross-sectional imaging is not yet described for COVID-19-related olfactory dysfunction. Management options are limited to conservative adjunctive measures, with some medical therapies described.Copyright © 2023 Jegatheeswaran, Gokani, Luke, Klyvyte, Espehana, Garden, Tarantino, Al Omari and Philpott.

42. Hummel, T., et al. (2023).
"Olfactory Dysfunction: Etiology, Diagnosis, and Treatment."
Deutsches Arzteblatt International 120(9): 146
EP - 154.

https://dx.doi.org/10.3238/arztebl.m2022.0411
https://www.aerzteblatt.de/int/archive/article/230045
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed25&NEWS=N&AN=2027597027
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:36647581&id=doi:10.3238%2Farztebl.m2022.0411

Background: Disorders of the sense of smell have received greater attention because of the frequency with which they occur as a symptom of SARS-CoV-2 infection. Olfactory dysfunction can lead to profound reduction in quality of life and may arise from many different causes. Method(s): A selective literature review was conducted with consideration of the current version of the guideline issued by the Association of the Scientific Medical Societies in Germany. Result(s): The cornerstones of diagnosis are the relevant medical history and psychophysical testing of olfactory function using standardized validated tests. Modern treatment strategies are oriented on the cause of the dysfunction. While treatment of the underlying inflammation takes precedence in patients with sinunasal dysosmia, olfactory training is the primary treatment option for other forms of the disorder. The prognosis is determined not only by the cause of the olfactory dysfunction and the patient's age, but also by the

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olfactory performance as measured at the time of diagnosis. Conclusion(s): Options for the treatment of olfactory dysfunction are available but limited, depending on the cause. It is therefore important to carry out a detailed diagnostic work-up and keep the patient informed of the expected course and prognosis.Copyright © 2023 Deutscher Arzte-Verlag GmbH. All rights reserved.

43. Gary, J. B., et al. (2023).
"Qualitative olfactory dysfunction and COVID-19: an evidence-based review with recommendations for the clinician."
American journal of rhinology & allergy 37(1): 95-101.

44. Evman, M. D. and Z. E. Cetin (2023).
"Effectiveness of platelet-rich plasma on post-COVID chronic olfactory dysfunction "
Revista da Associacao Medica Brasileira (1992) 69(11): e20230666.

https://dx.doi.org/10.1590/1806-9282.20230666
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med24&NEWS=N&AN=37909619
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:37909619&id=doi:10.1590%2F1806-9282.20230666

OBJECTIVE: The aim of this study was to investigate the efficacy of platelet-rich plasma injection on the olfactory cleft of patients with post-COVID olfactory dysfunction lasting over 1 year, who were unresponsive to common treatments., METHODS: Patients over 18 years of age with post-COVID olfactory dysfunction over 1 year whose complaints did not improve with intranasal steroids and D-panthenol/vitamin A combination nasal sprays with olfactory rehabilitation training for 1 month were prospectively collected and randomized into two groups: intranasal platelet-rich plasma group and control group. At the end of 1 month, Connecticut Chemosensory Clinical Research Center olfaction test scores of smell detection threshold and smell identification test were compared accordingly., RESULTS: A total of 25 patients were randomized into platelet-rich plasma (n=12) and control (n=13) groups. In the platelet-rich plasma group, the mean smell detection threshold score increased from 5.63 (SD 0.68) to 6.46 (SD 0.45), and the mean smell identification test score increased from 11.42 (SD 1.17) to 15.17 (SD 0.39). In the control group, the mean smell detection threshold score changed from 5.69 (SD 0.66) to 5.77 (SD 0.70), and the mean smell identification test score changed from 11.20 (SD 1.12) to 11.85 (SD 1.57). Post-hoc analysis revealed that similar mean smell detection threshold (mean difference 0.07; p=0.994) and smell identification test (mean difference -0.50; p=0.703) scores were transformed into a significant difference between groups (smell detection threshold mean difference 0.69; p=0.037; smell identification test mean difference 3.32; p<0.001)., CONCLUSION: At the end of the first month, there was a significant improvement in olfactory threshold values in the platelet-rich plasma group compared to the control group. No side effect or adverse event related to platelet-rich plasma injection was observed.

45. de Sousa, F. A., et al. (2023).
"Use of platelet rich plasma in persistent olfactory dysfunction after COVID-19: a prospective study."
Revista Portuguesa de Otorrinolaringologia-Cirurgia de Cabeça e Pescoço 61(4): 345-354.

Corrected Proof

46. Asvapoositkul, V., et al. (2023).
"Therapeutic options of post-COVID-19 related olfactory dysfunction: a systematic review and meta-analysis."
Rhinology 61(1): 2-11.

47. AlRajhi, B., et al. (2023).
" Platelet-rich plasma for the treatment of COVID-19 related olfactory dysfunction : a systematic review."
Rhinology 61(6): 498-507.

https://dx.doi.org/10.4193/Rhin23.168
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med24&NEWS=N&AN=37772881
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:37772881&id=doi:10.4193%2FRhin23.168

INTRODUCTION: Olfactory Dysfunction (OD) is a prevalent issue with a significant number of cases attributed to COVID-19. This systematic review aimed to evaluate the effectiveness of platelet-rich plasma (PRP) in the treatment of COVID-19 related OD, including anosmia , hyposmia , and parosmia ., METHODS: A comprehensive literature search was conducted using Medline, Scopus, Directory of Open Access Journals (DOAJ), and Google Scholar from inception until December 22, 2022. The eligibility criteria were confirmed COVID-19 patients with OD, whether it was measured objectively and/or subjectively, who received PRP treatment. The study followed a pre-specified protocol registered in PROSPERO (ID: CRD42023386803) and adhered to PRISMA guidelines., RESULTS: Four studies that enrolled 233 patients were included. The degree of improvement was assessed using threshold-discrimination-identification (TDI) scores at baseline and 1 and 2 months after PRP injection. Parosmia was assessed using the Visual Analog Scale (VAS) scores. Treatment of OD with PRP injections resulted in variable degrees of improvement. However, PRP injections can be considered safe, effective, and promising therapeutic options, as revealed by pooled studies., CONCLUSIONS: This systematic review indicated that PRP may be an effective treatment for COVID-19 related OD. However, additional large-scale studies are required to further investigate PRP efficacy in the treatment of OD following COVID-19.

48. Aaraj, M. A., et al. (2023).
"The use of Platelet rich Plasma in COVID-19 Induced Olfactory Dysfunction : Systematic Review."
Indian journal of otolaryngology and head and neck surgery : official publication of the Association of Otolaryngologists of India: 1-5.

https://dx.doi.org/10.1007/s12070-023-03938-4
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medp&NEWS=N&AN=37362129
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:37362129&id=doi:10.1007%2Fs12070-023-03938-4

PURPOSE: Different modalities of treatment have been suggested in the treatment for post COVID-19 olfactory dysfunction (OD). Starting with lifestyle modification, smoking cessation, for example, was shown to improve the symptoms for patients with OD. Intranasal and oral corticosteroids have been

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described in the literature for the treatment of OD. In this review, we are looking at a novel intervention using platelet-rich plasma injection into the nasal cleft for treatment of post COVID-19 infection olfactory dysfunction ., METHODS: A literature search was done using the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) 2020 Guidelines, the databases of PMC, Medline, CINAHL, Wiley online library were searched from their year of inception until February 2023. Search terms were used and included a combination of the following keywords; " platelet-rich plasma ", " platelet rich plasma ", " PRP ", " Anosmia ", " olfactory dysfunction " and "COVID"., RESULTS: The four studies in this review included a total of 238 adult patients who presented with olfactory dysfunction . The studies were heterogenic in terms of follow up period which was not long enough through all the included studies. Additionally, different protocol of injecting was seen in different studies., CONCLUSION: Injecting PRP for treatment of COVID-19 induced olfactory dysfunction is a safe technique with what seems like promising initial results with low complication rate. However, there are not enough studies assessing its effectiveness compared to other treatment modalities. Further randomized controlled trials with shared protocol are needed to establish further understanding of its role in treatment of COVID-19 induced OD. Copyright © Association of Otolaryngologists of India 2023. Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.

49. Aaraj, M. A., et al. (2023).
"The use of platelet rich plasma in covid-19 induced olfactory dysfunction: Systematic review."
Indian Journal of Otolaryngology and Head & Neck Surgery 75(4): 3093-3097.

50. Wu, T. J., et al. (2022).
"Management of post-COVID-19 olfactory dysfunction."
Current Treatment Options in Allergy: 1-18.

51. Uzun, G., et al. (2022).
"Platelets and Sera from Donors of Convalescent Plasma after Mild COVID-19 Show No Procoagulant Phenotype."
Hamostaseologie 42(7): S14
EP - S23.

https://dx.doi.org/10.1055/a-1797-0564
https://www.thieme-connect.com/products/ejournals/journal/10.1055/s-00034925
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed23&NEWS=N&AN=2020942360
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:36288732&id=doi:10.1055%2Fa-1797-0564

Coronavirus disease-2019 (COVID-19) is associated with increased thromboembolic complications. Long-term alteration in the coagulation system after acute COVID-19 infection is still a subject of research. Furthermore, the effect of sera from convalescent subjects on platelets is not known. In this

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study, we investigated platelet phenotype, coagulation, and fibrinolysis in COVID-19 convalescent plasma (CCP) donors and analyzed convalescent sera-induced effects on platelets. We investigated CCP donors who had a history of mild COVID-19 infection and donors who did not have COVID-19 were used as controls. We analyzed phosphatidylserine (PS) externalization, CD62p expression, and glycoprotein VI (GPVI) shedding both in platelet-rich plasma (PRP) and after incubation of washed healthy platelets with donors' sera using flow cytometry. Coagulation and fibrinolysis systems were assessed with thromboelastometry. Forty-seven CCP donors (22 males, 25 females; mean age (+/-SD): 41.4 +/- 13.7 years) with a history of mild COVID-19 infection were included. Median duration after acute COVID-19 infection was 97 days (range, 34-401). We did not find an increased PS externalization, CD62p expression, or GPVI shedding in platelets from CCP donors. Sera from CCP donors did not induce PS externalization or GPVI shedding in healthy platelets. Sera-induced CD62p expression was slightly, albeit statistically significantly, lower in CCP donors than in plasma donors without a history of COVID-19. One patient showed increased maximum clot firmness and prolonged lysis time in thromboelastometry. Our findings suggest that procoagulant platelet phenotype is not present after mild COVID-19. Furthermore, CCP sera do not affect the activation status of platelets.Copyright © 2022. Thieme. All rights reserved.

52. Steffens, Y., et al. (2022).
"Effectiveness and safety of PRP on persistent olfactory dysfunction related to COVID-19."
European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery 279(12): 5951-5953.

https://dx.doi.org/10.1007/s00405-022-07560-y
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med22&NEWS=N&AN=35904632
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:35904632&id=doi:10.1007%2Fs00405-022-07560-y

INTRODUCTION: Olfactory dysfunction (OD) is a well know symptom of coronavirus disease 2019 (COVID-19), accounting for 48 to 85% of patients. In 1 to 10% of cases, patients develop a chronic olfactory dysfunction (COD), lasting more than 6 months. Recently, platelet-rich plasma (PRP) was used in patients with non-COVID-19 COD and authors reported encouraging results., METHODS: In the present study, we investigated the usefulness and safety of PRP injection in 56 patients with COVID-19 COD by the Sniffing Stick test (TDI score) and a linker-scale from 0 (none) to 3 (strong) and we compare the result to a control group., RESULTS: At 1 month post-PRP injection, the mean TDI scores significantly improved by 6.7 points in the PRP group ($p < 0,001$), the mean self-assessment of improvement in smell function was 1.8 (mild-to-moderate) in the PRP group, which was significantly higher than the score (0.3) in the control group ($p < 0,001$)., CONCLUSION: Our results showed that PRP in the olfactory cleft can increase the olfactory threshold 1 month after the injection. Moreover, our results suggest that timing of treatment may be an important factor and that PRP is a safe treatment, because no adverse effects were reported throughout the study., TRIAL REGISTRATION NUMBER: NCT05226546. Copyright © 2022. The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature.

53. Steffens, Y., et al. (2022).
"Effectiveness and safety of PRP on persistent olfactory dysfunction related to COVID-19: Towards a new therapeutic hope."
medRxiv.

https://dx.doi.org/10.1101/2022.02.14.22270109
https://www.medrxiv.org/

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http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=empp&NEWS=N&AN=2017166069
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:10.1101%2F2022.02.14.22270109

Olfactory dysfunction (OD) is a well know symptom of coronavirus disease 2019 (COVID-19), accounting for 48 to 85% of patients. In 1 to 10% of cases, patients develop a chronic olfactory dysfunction (COD,) lasting more than 6 months. Recently, platelet-rich plasma (PRP) was used in patients with non-COVID-19 COD and authors reported encouraging results. In the present study, we investigated the usefulness and safety of PRP injection in 56 patients with COVID-19 COD. Our results showed that PRP in the olfactory cleft can increase the olfactory threshold one month after the injection. Moreover, our results suggest that timing of treatment may be an important factor and that PRP is a safe treatment because no adverse effects were reported throughout the study.Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC-ND 4.0 International license.

54. Nct (2022).
""Platelet Rich Plasma for the Management of Post-Viral Olfactory Dysfunction."
https://clinicaltrials.gov/show/NCT05666492.

https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02508754/full

The investigators hypothesize that the use of topical PRP will improve smell identification, threshold, and smell-related quality of life in comparison to a placebo. This study will provide critical information for a promising new treatment of olfactory dysfunction with the highest level of evidence, in a randomized, placebo-controlled trial. Preliminary results from an ongoing pilot study investigating topical PRP is the basis for the hypothesis. By investigating the efficacy of topical PRP in smell restoration, the investigators will provide a less-invasive way to deliver this autologous product. A randomized trial will set a precedent for the use of this treatment to serve a growing population of patients affected with post-COVID olfactory dysfunction. Over a period of one year, participants with post-viral olfactory dysfunction will be randomly assigned to a test or control group and will visit the clinic monthly for three months to receive PRP or saline based on their randomized group. This will be followed by 9 months of at-home electronic visits. At each visit both the test and control groups will undergo smell testing and will fill quality of life questionnaire.

55. Lupia, E., et al. (2022).
"Thrombopoietin participates in platelet activation in COVID-19 patients."
EBioMedicine 85: 104305.

https://dx.doi.org/10.1016/j.ebiom.2022.104305
http://www.journals.elsevier.com/ebiomedicine/
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed23&NEWS=N&AN=2020654878
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:36242922&id=doi:10.1016%2Fj.ebiom.2022.104305

Background: The pathogenesis of coronavirus disease 2019 (COVID-19) is characterized by enhanced platelet activation and diffuse hemostatic alterations, which may contribute to immunothrombosis/thromboinflammation and subsequent development of target-organ damage. Thrombopoietin (THPO), a growth factor essential to megakariocyte proliferation, is known to prime platelet activation and leukocyte-platelet interaction. In addition, THPO concentrations increase in several critical diseases, such as acute cardiac ischemia and sepsis, thus representing a potential

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diagnostic and prognostic biomarker. Furthermore, several data suggest that interleukin (IL)-6 is one of the most important inflammatory mediators involved in these phenomena, which led to explore the potential therapeutic role of IL-6 inhibitors. In this prospective cohort study, we aimed to study THPO and IL-6 concentrations in COVID-19 patients at the time of first clinical evaluation in the Emergency Department (ED), and to investigate their potential use as diagnostic and prognostic biomarkers. In addition, we sought to explore the role of THPO contained in plasma samples obtained from COVID-19 patients in priming in vitro platelet activation and leukocyte-platelet interaction. Method(s): We enrolled 66 patients presenting to the ED with symptoms suggestive of COVID-19, including 47 with confirmed COVID-19 and 19 in whom COVID-19 was excluded (Non-COVID-19 patients). As controls, we also recruited 18 healthy subjects. In vitro, we reproduced the effects of increased circulating THPO on platelet function by adding plasma from COVID-19 patients or controls to platelet-rich plasma or whole blood obtained by healthy donors, and we indirectly studied the effect of THPO on platelet activation by blocking its biological activity. Finding(s): THPO levels were higher in COVID-19 patients than in both Non-COVID-19 patients and healthy subjects. Studying THPO as diagnostic marker for the diagnosis of COVID-19 by receiver-operating-characteristic (ROC) statistics, we found an area under the curve (AUC) of 0.73, with an optimal cut-off value of 42.60 pg/mL. IL-6 was higher in COVID-19 patients than in healthy subjects, but did not differ between COVID-19 and Non-COVID-19 patients. THPO concentrations measured at the time of diagnosis in the ED were also higher in COVID-19 patients subsequently developing a severe disease than in those with mild disease. Evaluating THPO as biomarker for severe COVID-19 using ROC analysis, we found an AUC of 0.71, with an optimal cut-off value of 57.11 pg/mL. IL-6 was also higher in severe than in mild COVID-19 patients, with an AUC for severe COVID-19 of 0.83 and an optimal cut-off value of 23 pg/ml. THPO concentrations correlated with those of IL-6 (r=0.2963; p=0.043), and decreased 24 h after the administration of tocilizumab, an IL-6 receptor blocking antibody, showing that the increase of THPO levels depends on IL-6-stimulated hepatic synthesis. In vitro, plasma obtained from COVID-19 patients, but not from healthy subjects, primed platelet aggregation and leukocyte-platelet binding, and these effects were reduced by inhibiting THPO activity. Interpretation(s): Increased THPO may be proposed as an early biomarker for the diagnosis of COVID-19 and for the identification of patients at risk of developing critical illness. Elevated THPO may contribute to enhance platelet activation and leukocyte-platelet interaction in COVID-19 patients, thus potentially participating in immunothrombosis/thromboinflammation. Funding(s): This work was supported by Ministero dell'Universita e della Ricerca Scientifica e Tecnologica (MURST) ex 60% to GM and EL.Copyright © 2022 The Authors

56. Kutuk, S. G., et al. (2022).
"The effectiveness of platelet rich plasma therapy in chronic sinusitis patients with odor disorder undergoing endoscopic sinus surgery."
European Research Journal 8(6): 869
EP - 881.

https://dx.doi.org/10.18621/eurj.910253
https://dergipark.org.tr/en/pub/eurj/issue/73067/910253
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed23&NEWS=N&AN=2021624016
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:10.18621%2Feurj.910253

Objectives: Objectives: In this study, the objective was to compare the effectiveness of fluticasone dipropionate and platelet-rich plasma treatments added to the treatment in patients undergoing functional endoscopic sinus surgery in patients with chronic sinusitis involving odor dysfunction, different stages and types of sinusitis. Method(s): The study included a total of 60 patients between 18 and 60 years who underwent endoscopic sinus surgery due to chronic paranasal sinus infection

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followed by olfactory dysfunction. Group 1: paranasal sinus surgery + steroid therapy (first 30 patients) and Group 2: paranasal sinus surgery + steroid therapy + PRP therapy (second 30 patients) were grouped together without the patients' knowledge of the operating physician and of the treatment protocol. For the paranasal sinus CT evaluation, Lund-Mackey staging was used and the degree of the disease was determined using the Kennedy staging system. Modified Sniffin Stick test was applied to all patients in the preoperative 1st week and in the 3rd month postoperatively. The Modified Sniffin Stick test was conducted on all patients during the preoperative 1st week and the postoperative 3rd month. The modified Sniffin Stick test and endoscopic evaluation score were evaluated and whether or not the patients benefited from PRP treatment were compared. Result(s): According to the postoperative endoscopy score, there was a difference between the experimental group and the control group in terms of postoperative endoscopy score, and it was found to be statistically significant. Besides, the postoperative endoscopy score of the experimental group was found to be lower than the control group. The average of Modified Sniffin' Stick Test scores in the postoperative period of the patients in the study was 28.27 +/- 7.88 for the experimental group, while it was determined as 20.08 +/- 5.75 for the control group, and this difference was statistically significant. The average anosmia times of the experimental and control group patients in the study were compared, and the mean duration of anosmia was 48.53 +/- 20.40 (6-96) for the experimental group and 44.27 +/- 19.45 (6.96) for the control group. The difference in the mean duration of anosmia between the experimental and control groups was not found statistically significant. Conclusion(s): In this research, PRP, which is applied to functional endoscopic sinus surgery and fluticasone dipropionate treatment, has been shown to be a readily applicable, safe and highly efficient method of treatment in patients with chronic sinusitis accompanied by smell dysfunction.Copyright 2021 by The Association of Health Research & Strategy.

57. Duffy, A., et al. (2022).
"Topical Platelet-Rich Plasma: A Novel Delivery Method for an Emerging Treatment of Olfactory Dysfunction."
Otolaryngology - Head and Neck Surgery 167(1 Supplement): P151.

https://dx.doi.org/10.1177/01945998221107672
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed23&NEWS=N&AN=639220472
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:10.1177%2F01945998221107672

Introduction: Olfactory dysfunction (OD) affects more than 3 million US adults. The number of patients with post viral olfactory dysfunction (PVOD) is expected to increase secondary to the worldwide COVID-19 pandemic. Preliminary studies have demonstrated the efficacy of platelet-rich plasma (PRP) in restoration of smell in both animals and humans. To date, human studies have utilized injectable PRP only. We describe our pilot study investigating the use of topical PRP as a novel delivery method for smell restoration and contribute to existing literature demonstrating the promise of PRP as a therapeutic. Method(s): Pilot study from September 2020 to January 2022. Patients >18 years with hyposmia diagnosed via Brief Smell Identification Test (B-SIT) score <8 were included. PRPimpregnated Surgifoam was placed into bilateral olfactory clefts monthly for at least 3 months. Patients completed the B-SIT at baseline and 1 month after each treatment. Result(s): Eight patients underwent at least 3 treatments and completed the B-SIT at month 4. Average age was 56.3 years; mean smell loss duration was 19.3 months. Etiologies included PVOD, post-COVID (5), and idiopathic. Mean change in B-SIT after 3 treatments was +1.06. Of patients, 62.5% had achieved the minimal clinically significant difference of >1 on B-SIT after treatments 2 and 3. Patients with smell loss <12 months demonstrated greater B-SIT scores at 4 months (+1.6 vs +0.2). Two patients achieved B-SIT >8 after 3 treatments. Of patients who have returned thus far for a fourth treatment, 1 additional patient scored >8. Conclusion(s): We present the largest pilot study to date for the use of PRP in treatment of OD and the

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first study to develop methods for topical delivery in human subjects. Topical PRP may serve as a less invasive, efficacious therapy for patients. Further, randomized control trials are warranted to investigate the required number of topical PRP treatments for smell restoration.

58. Chang, M. T. and Z. M. Patel (2022).
"Novel Therapies in Olfactory Disorders "
Current otorhinolaryngology reports 10(4): 427-432.

https://dx.doi.org/10.1007/s40136-022-00436-z
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=pmnm7&NEWS=N&AN=36312744
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:36312744&id=doi:10.1007%2Fs40136-022-00436-z

Purpose of Review: To summarize and critically review the recent literature on novel treatments for olfactory disorders (OD)., Recent Findings: Emerging therapies in the management of OD include multiple vitamins and supplements, biologics, neuromodulators, and intranasal agents. There is also an active investigation into treatments that harness the neuroregenerative properties of the olfactory epithelium, such as platelet-rich plasma and stem cell transplantation., Summary: Successful management of OD is multimodal and tailored to the underlying etiology. As the findings of further investigations accrue, the management of OD will undoubtedly continue to be advanced and refined, and likely harness the intrinsic neuroregenerative properties of the olfactory system. Copyright © The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022, Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.

59. Abo El Naga, H. A., et al. (2022).
"The potential therapeutic effect of platelet-rich plasma in the treatment of post-COVID-19 parosmia."
Egyptian Journal of Otolaryngology 38(1).

10.1186/s43163-022-00320-z
https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02558766/full

Background: COVID-19-related olfactory dysfunction is an emerging problem with a significant impact on the quality of life of affected individuals. Different lines of treatment have been used with varying results. This study aimed to assess the potential therapeutic effect of PRP in the treatment of post-COVID olfactory dysfunction. This work aimed to assess the potential therapeutic effect of platelet-rich plasma (PRP) in treating post-COVID-19 parosmia. A pilot study was conducted on 60 patients with post-COVID parosmia without responding to a 3-month course of olfactory training, topical corticosteroids, omega-three, vitamin B12, and zinc supplementation. The patients were distributed randomly and equally among 2 groups. The case group was subjected to three PRP injections in the olfactory cleft at 3 weeks intervals. The control group continued the pre-study treatment protocol for 6 weeks. The degree of parosmia was assessed before and after treatment subjectively using a visual analog scale (VAS) from 0 to 10. Reaching 0–1 on the visual analog scale was a complete improvement. The primary outcome was assessing the post-treatment score for parosmia 1 month after the third injection in the case group. The second outcome was the comparison between both groups regarding the degree of improvement 1 month after cessation of treatment. Results: There was a highly significant improvement in VAS for parosmia ($p < 0.00001$) in the case group and a significant improvement in VAS for parosmia in the control group ($p = P = 0.00148$). There was a significant

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difference between both groups regarding the degree of improvement favoring the case group (p = 0.002). Conclusion: Platelet-rich plasma injection in the olfactory cleft offers a therapeutic option for treating patients with post-COVID-19 olfactory parosmia who failed to respond to traditional conservative treatment.

60. (2022).
"Value of Platelet-Rich Plasma in Post Severe Acute Respiratory Syndrome Coronavirus 2 Smell Disorders A1 - Anonymous."
clinicaltrials.gov.

https://clinicaltrials.gov/study/NCT05395845
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emctr&NEWS=N&AN=NCT05395845
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:&issn=&isbn=&volume=&issue=&spage=&pages=&date=2022&title=clinicaltrials.gov&atitle=Value+of+Platelet-Rich+Plasma+in+Post+Severe+Acute+Respiratory+Syndrome+Coronavirus+2+Smell+Disorders&aulast=

Brief Summary, The study will be conducted to evaluate : The efficacy of Platelet Rich plasma in treatment of smell disorders post severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) via the growth factors involved in accelerating and enhancing healing., Detailed Description, Smell is essential sensory function for good quality of life as its preservation helps in identifying several harmful odors . Viral URTIs can lead to olfactory disorders of varying degree and duration 70% of URTI caused by rhinovirus, adenovirus ,influenza and parainfluanza virus Smell disorders are divided into two types Quantitative (anosmia and hyposmia) Qualitative (parosmia and phantosmia) Anosmia is a total loss of smell . hyposmia is a decrease in the sense of smell. parosmia is a distortion of the smell in presence of an existing stimulus . Phantosmia (Cacosmia) is distortion of the smell in absence of an existing stimulus severe acute respiratory syndrome coronavirus2 (SARS-coV-2)which is a global pandemic started in china 2019 one of respiratory tract infection that affect olfaction and cause varying types of smell impairment. Smell disorders seem to be more common in SARS-coV2 than other respiratory infections as in some patient persist for long time after resolution of respiratory symptoms Current evidence suggest that olfactory impairment results from propensity of SARS-coV2 for neuroinvasion and neurotrophic activities . Majority of patients experience some level of smell impairment most often temporary as olfactory neuroepithelium has regenerative power . European study published on 16 July 2020 reported that some patient affected by SARS -coV2 come solely with olfactory symptoms and most of patient recovered within 2 weeks ,smell not recovered in one quarter of patient 15 Once olfactory dysfunction persists more than 2 weeks a therapy should be considered to avoid persistent impairment of smell One of therapies can be used in ttt of smell disorders (Platelet _rich plasma) PRP is a process in which a small amount of blood from test subject is separated by special centrifugation process. PRP contains many growth factor which have a neuroregenerative feature as well as therapeutic effectCopyright © 2025 clinicaltrials.gov

61. (2022).
"Effectiveness and Safety of Platelet Rich Plasma (PRP) on Persistent Olfactory Dysfunction Related to COVID-19: Towards a New Therapeutic Hope A1 - Anonymous."
clinicaltrials.gov.

https://clinicaltrials.gov/study/NCT05226546
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emctr&NEWS=N&AN=NCT05226546
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:&issn=&isbn=&volume=&issue=&spage=&pages=&date=2022&title=clinicaltrials.gov&atitle=Effectiveness+and+Safety+of+Plat

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elet+Rich+Plasma+%28PRP%29+on+Persistent+Olfactory+Dysfunction+Related+to+COVID-19%3A+Towards+a+New+Therapeutic+Hope&aulast=

Brief Summary, Olfactory dysfunction (OD) is a well know symptom of coronavirus disease 2019 (COVID-19), accounting for 48 to 85% of patients. In 1 to 10% of cases, patients develop a chronic olfactory dysfunction (COD,) lasting more than 6 months. Recently, platelet-rich plasma (PRP) was used in patients with non-COVID-19 COD and authors reported encouraging results. In the present study, the investigators investigated the usefulness and safety of PRP injection in 56 patients with COVID-19 COD. Our results showed that PRP in the olfactory cleft can increase the olfactory threshold one month after the injection. Moreover, our results suggest that timing of treatment may be an important factor and that PRP is a safe treatment because no adverse effects were reported throughout the studyCopyright © 2025 clinicaltrials.gov

62. (2022).
""Platelet Rich Plasma for the Management of Post-Viral Olfactory Dysfunction A1 - Anonymous."
clinicaltrials.gov.

https://clinicaltrials.gov/study/NCT05666492
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emctr&NEWS=N&AN=NCT05666492
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:&issn=&isbn=&volume=&issue=&spage=&pages=&date=2022&title=clinicaltrials.gov&atitle=%22Platelet+Rich+Plasma+for+the+Management+of+Post-Viral+Olfactory+Dysfunction&aulast=

Brief Summary, SARS COV-19 has resulted in prolonged olfactory dysfunction in many patients. The investigators aim to compare the effect of topical platelet-rich plasma (test) vs saline (placebo) in patients with covid-related post-viral olfactory dysfunction., Detailed Description, The investigators hypothesize that the use of topical PRP will improve smell identification, threshold, and smell-related quality of life in comparison to a placebo. This study will provide critical information for a promising new treatment of olfactory dysfunction with the highest level of evidence, in a randomized, placebo-controlled trial. Preliminary results from an ongoing pilot study investigating topical PRP is the basis for the hypothesis. By investigating the efficacy of topical PRP in smell restoration, the investigators will provide a less-invasive way to deliver this autologous product. A randomized trial will set a precedent for the use of this treatment to serve a growing population of patients affected with post-COVID olfactory dysfunction. Over a period of one year, participants with post-viral olfactory dysfunction will be randomly assigned to a test or control group and will visit the clinic monthly for three months to receive PRP or saline based on their randomized group. This will be followed by 9 months of at-home electronic visits. At each visit both the test and control groups will undergo smell testing and will fill quality of life questionnaire.Copyright © 2025 clinicaltrials.gov

63. Klug, T., et al. (2021).
"Treatment of refractory anosmia with topical platelet rich plasma."
Otolaryngology - Head and Neck Surgery 165(1 SUPPL): P344
EP - P345.

https://dx.doi.org/10.1177/01945998211030910i
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed22&NEWS=N&AN=636201142
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:10.1177%2F01945998211030910i

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Introduction: We assess the role of topical platelet-rich plasma (PRP) in the management of anosmic patients; aim to understand the mechanism of action of topical PRP in the olfactory groove; and differentiate and analyze objective vs subjective improvement in patients receiving topical PRP for anosmia. Anosmia affects up to 20% of the general population, has significant negative impact on quality of life, and has been associated with increased mortality. Further, an estimated 30% to 75% of patients who contract COVID-19 develop anosmia or hyposmia. Despite the commonality and adverse impact of this disorder, there are very few effective treatment options. This abstract/ manuscript presents encouraging, late-breaking data showing that topical PRP placed in the olfactory groove may show some efficacy in managing persistent, long-standing anosmia. Method(s): Ten patients with persistent anosmia for at least 6 months were included in this pilot study. All 10 patients had failed previous medical management and olfactory training. An absorbable sponge was soaked in PRP and placed in the patient's olfactory groove on one side in a single-blinded and randomized fashion. The other side received an absorbable sponge soaked in saline. The patient was subsequently seen at 4-week intervals for an additional 2 months, with this procedure repeated at each interval. The same side of the nose was treated with PRP at each encounter and was randomized only at the beginning of the trial. At each interval, a Brief Smell Identification Test (B-SIT) was performed on each nostril independently. Result(s): Nine patients completed 3 treatment sessions, and 1 patient was lost to follow-up after two treatments. The average overall presenting B-SIT score was 3.5 +/- 1.76 (scores <4 are considered anosmic); 3.9 +/- 2.02 in the treatment nostril and 3.1 +/- 1.37 in the control nostril. B-SIT scores improved after each subsequent visit, regardless of the nostril side treated. After completion of the 3 treatments, or at the time of exiting the study, the average overall B-SIT score improved to 4.5 +/- 1.92; 4.6 +/- 1.81 in the treatment nostril and 4.4 +/- 2.12 in the control nostril. All patients reported subjective improvement in their sense of smell. Conclusion(s): Topical PRP placed in the olfactory groove appears to show some efficacy in managing persistent, longstanding anosmia.

64. Kapoor, D., et al. (2021).
"Post viral olfactory dysfunction after SARS-CoV-2 infection: anticipated post-pandemic clinical challenge."
Indian Journal of Otolaryngology and Head & Neck Surgery: 1-8.

65. Goljanian Tabrizi, A., et al. (2021).
"Efficacy of Platelet-Rich Plasma as an Adjuvant Therapy to Endoscopic Sinus Surgery in Anosmia Patients with Sinonasal Polyposis: A Randomized Controlled Clinical Trial."
Medical journal of the Islamic Republic of Iran 35: 156.

https://dx.doi.org/10.47176/mjiri.35.156
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=pmnm6&NEWS=N&AN=35341080
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:35341080&id=doi:10.47176%2Fmjiri.35.156

Background: Treatment of patients with anosmia is a major therapeutic challenge. The present study evaluated the efficacy of platelet-rich plasma (PRP) in the treatment of anosmia in patients with sinonasal polyposis. Methods: In the present clinical trial, atotal of 48 patients with sinonasal polyposis with theIran Smell Identification Test (I-SIT) score of <6 who completed the medical treatment and were observed 3 months after the sinus surgery were included and randomly divided in to 2groups. After endoscopic sinus surgery, the intranasal injection of 1 mL PRP and normal saline was performed in the olfactory region in the intervention and control groups, respectively. Odor function was

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assessed using the I-SIT at the baseline and at the end of the studyby an independent samples ttest. Results: Based on the findings of the present study, the I-SIT improved in both groups during the follow-up, as it reached from 2.63 +/- 2.63 to 5.85 +/- 2.46 after oral steroid administration and 18.93 +/- 1.14 after surgery in the intervention group and from the baseline of 2.10 +/- 2.83 to 5.62 +/- 2.99 after receiving standard medical treatment and 18.43 +/- 1.36in the control groupafter surgery. Although this improvement was significant in both groups in either time interval (all with p<0.001), there was no significant difference between the 2groups in terms of changes in the I-SIT score (p=0.802). Conclusion: According to the current study, PRP injection showed no short-term effect on the recovery of olfactory function in patients with sinonasal polyposis. Copyright © 2021 Iran University of Medical Sciences.

66. Addison, A. B., et al. (2021).
"Clinical Olfactory Working Group consensus statement on the treatment of postinfectious olfactory dysfunction."
Journal of allergy and clinical immunology 147(5): 1704-1719.

67. Aboelmagd, E. A., et al. (2021).
"Platelet-rich plasma in the management of anosmia."
Egyptian Journal of Neck Surgery and Otorhinolaryngology 7(1): 10-19.

68. Yan, C. H., et al. (2020).
"The use of platelet-rich plasma in treatment of olfactory dysfunction : A pilot study."
Laryngoscope Investigative Otolaryngology 5(2): 187-193.

https://dx.doi.org/10.1002/lio2.357
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=pmnm5&NEWS=N&AN=32337347
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:32337347&id=doi:10.1002%2Flio2.357

BACKGROUND: Olfactory dysfunction is a prevalent problem with a significant impact on quality of life and increased mortality. Limited effective therapies exist. Platelet-rich plasma (PRP) is an autologous biologic product with anti-inflammatory and neuroprotective effects. This novel pilot study evaluated the role of PRP on olfactory neuroregeneration in patients with hyposmia ., METHODS: Seven patients who had olfactory loss greater than 6 months in duration, no evidence of sinonasal inflammatory disease, and no improvement with olfactory training and budesonide topical rinses were enrolled in this preliminary study. Patients received a single intranasal injection of PRP into the mucosa of the olfactory cleft. The Sniffin' Sticks olfactory test consisting of threshold, discrimination, and identification measurements (TDI) was administered at the beginning of the study and at 1 and 3 months., RESULTS: All patients reported a subjective improvement of their smell shortly after injection but then stabilized. At 3-month post-treatment, two patients with functional anosmia (TDI < 16) did not improve significantly. Five patients with hyposmia (TDI > 16 but <30) showed an improvement with 60% achieving normosmia (TDI > 30) at 3-month follow-up. On average, patients with baseline TDI > 16 improved by 5.85 points with the most significant improvement in the threshold

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subcomponent. There were no adverse outcomes from intranasal PRP injections., CONCLUSION: PRP appears safe for use in the treatment of olfactory loss, and preliminary data suggest possible efficacy, especially for those with moderate yet persistent loss. Further studies will help determine optimal frequency and duration of use., LEVEL OF EVIDENCE 2B: Copyright © 2020 The Authors. Laryngoscope Investigative Otolaryngology published by Wiley Periodicals, Inc. on behalf of The Triological Society.

69. Tutar, B., et al. (2020).
"The impact of platelet-rich fibrin (PRF) on olfactory function and pain after septoplasty operations."
European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery 277(4): 1115-1120.

https://dx.doi.org/10.1007/s00405-020-05839-6
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med18&NEWS=N&AN=32048028
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:32048028&id=doi:10.1007%2Fs00405-020-05839-6

BACKGROUND: We aimed to investigate the effect of platelet-rich fibrin (PRF) on olfactory function and pain score in patients who underwent septoplasty., METHODS: This prospective randomized observational study was performed between 2018 January and 2019 April with 148 patients who had septoplasty operation. Patients were divided two groups and 74 patients were placed in group 1 to which PRF was applied after the completion of septoplasty whereas 67 patients were put in group 2 which did not undergo PRF. Sniffin' Sticks test was applied to all patients at pre-op, post-op 1-week, 6-week, and 6-month. Pain scores of patients were measured with visual analogue scale at 1 and 3 week., RESULTS: The distribution of patients according to pre-op olfactory function (normo-hypo-anosmia), there was no significant differences statistically ($p > 0.05$). When we compared the 1-week post-op results of Sniffin' Sticks test of patients, we found differences between the groups ($p < 0.05$). It was observed in the early postoperative period that according to the Sniffin' Sticks test scores, the results of the PRF group were better than those of the non-PRF group. At 6-week and 6-month, between the groups; there was no differences in terms of olfactory function. When we looked at the pain score of patients at 1 and 3 week after septoplasty; significant differences were obtained between groups., CONCLUSION: The application of PRF to the mucosal surface after the completion of septoplasty, has positive effect on olfactory function and pain especially in the early postoperative period. During the healing process, it was observed that prf maintained better odor functions. It is a minimally invasive technique with low risks and satisfactory clinical results.

70. Nct (2020).
"Intranasal Injection of PRP Versus Saline for Treatment of Olfactory Dysfunction."
https://clinicaltrials.gov/show/NCT04406584.

https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02124993/full

Olfactory dysfunction constitutes a common impairment in the general population, affecting nearly 20 million in the USA and severely impairing quality of life. Unfortunately, this problem is often permanent, and no effective treatment is available at this time. Although many etiologies exist for olfactory loss, the underlying pathology is thought to be permanent damage to the olfactory bulb, nerves or basal cells of the olfactory system. Platelet-rich plasma (PRP) is an autologous treatment derived from a patient's own blood and has been found to have pro-nerve regenerative properties in animal and human studies. A small pilot study at the principal investigator's institution demonstrated

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improved olfactory thresholds in patients with partial olfactory loss who received PrP injections. In this randomized clinical trial, the investigators aim to further evaluate the ability of PRP injections to restore olfactory function in human subjects. Given the lack of effective current treatments, a therapeutic benefit of PrP would represent a crucial advancement in research and treatment of olfactory loss, which affects a large swath of the population. Patients will be seen at the Stanford Sinus center, or at the newly added collaborating institution UCSD, and those with smell loss will be identified by the clinically validated patient directed survey: The UPSIT (University of Pennsylvania Smell Identification Test). They will undergo nasal endoscopy to exclude structural causes of smell loss including mass or tumor. Nasal endoscopy will be performed to exclude structural causes of olfactory, using topical anesthesia (1% phenylephrine & 4% lidocaine topical spray). THESE ABOVE STEPS CONSTITUTE STANDARD OF CARE FOR EVALUATION OF OLFACTORY LOSS. The timing of the initial research visit will depend on the evolution of the current covid-19 pandemic and adhere to Stanford guidelines regarding research visits. At the initial research visit, patients meeting inclusion criteria will be evaluated in a procedure room at the Stanford Sinus center. A baseline Sniffin' sticks smell test will be performed (see below). A small vial of blood will be drawn from the patient at the Blake Wilbur first floor laboratory. The research coordinator will walk the patient back to clinic along with the patient's blood smple. PRP will be isolated from the blood by the study investigator, following manufacturer instructions from the PurePRP preparation kit (Emcyte corporation), which will involve use of a centrifuge located in the clinic for this purpose. 0.5 mL of the PRP solution will be set aside for platelet quantification. From the remaining PRP solution, patients will then receive 1ml of autologous PrP or sterile saline (0.9% Sodium Chloride), which will be injected into the superior septum mucosa near the olfactory groove bilaterally. Patients will be blindfolded during injection to prevent identification of the injected specimen, and will previously be randomized in a 1:1 ratio via a random number generator. Patients will be monitored for side effects for 15 minutes. (We routinely perform nasal endoscopy with injection and associated procedures in our clinic, which patients tolerate very well.) Injections will then be performed twice more at 2-weeks and 4-weeks after the initial injection, for a total of 3 biweekly injections. ALL OF THE ABOVE STEPS ARE FOR RESEARCH PURPOSES. The Sniffin' Sticks test is a validated, non-invasive assessment of olfactory function via presentation of scented felt pens to blindfolded patients. The output is the TDI score (threshold, discrimination, identification). The TDI score will be recorded at baseline (initial research visit), and then at 1-month and 3-months after the initial test, for a total of 3 tests. The first test will occur before the first injection, and the second test will be performed before the third injection. There will be no injection at the last (third) test. THE ABOVE VISITS ARE FOR RESEARCH PURPOSES. The study time-line is summarized as follows Visit 1: 1st Sniffin' Sticks t st, 1st injection Visit 2: 2 weeks after Visit 1, second injection Visit 3: 4 weeks after Visit 1, second test, third injection Visit 4: 3 months after Visit 1, third test

71. Irct20200211046464N (2020).
"Effect of PRP in treatment of anosmia."
https://trialsearch.who.int/Trial2.aspx?TrialID=IRCT20200211046464N1.

https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02171443/full

INTERVENTION: Intervention 1: Intervention group: Patients in both groups underwent sinus endoscopic surgery by only one specific ENT specialist. At this stage, in the intervention group, a platelet-rich plasma was injected into the patient's nose inside the operating room and during general anesthesia. To do this, platelet-rich plasma was injected with a 1 cc syringe in the olfactory area within 1 cm2 with the help of a nasal endoscope and by the same surgeon from specific ENT specialists. The whole process of preparing platelet-rich plasma was performed in the sports medicine group under the supervision of the sports medicine professor and using Arjangian platelet-rich plasma kits. The temperature during these steps to prevent plaque clots was 21-24. C. Intervention 2: Control

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group:After Functional endoscopic sinus surgery, in the control group, instead of platelet-rich plasma, normal saline serum was injected into the patient's olfactory area with the same amount and under the same conditions. The injector was also unaware of the group of patients and the injected substance. CONDITION: Condition 1: Nasal Polyp. Condition 2: Anosmia. ; Nasal polyp ; Anosmia R43.0 PRIMARY OUTCOME: Olfactory score less than 6 in the Iranian Smell Identification Test. Timepoint: Measurement of olfactory score at the beginning of the study (before the intervention), After receiving oral treatment and 3 months after surgery and injection of platelet-rich plasma. Method of measurement: Iranian Smell Identification Test. INCLUSION CRITERIA: Age between 15 and 50 years Having chronic sinusitis with polyps Anosmia lasts less than 2 years Existence of anosmia confirmed by olfactory diagnosis test

72. (2020).
"Intranasal Injection of Platelet-rich Plasma Versus Saline for Treatment of Olfactory Dysfunction A1 - Anonymous."
clinicaltrials.gov.

https://clinicaltrials.gov/study/NCT04406584
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emctr&NEWS=N&AN=NCT04406584
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:&id=doi:&issn=&isbn=&volume=&issue=&spage=&pages=&date=2020&title=clinicaltrials.gov&atitle=Intranasal+Injection+of+Platelet-rich+Plasma+Versus+Saline+for+Treatment+of+Olfactory+Dysfunction&aulast=

Brief Summary, This randomized clinical trial will evaluate the benefit of platelet-rich plasma (PrP) in the treatment of olfactory dysfunction. PrP can be isolated from a patient's own blood and has been found in previous studies to have anti-inflammatory and pro-regenerative properties. It has been used across multiple specialties, such as Orthopedics, Facial Plastics, Dermatology, Neurology in injected form to treat a wide variety of tissues to encourage the body's inherent regenerative capacity. The investigators have completed a pilot study here evaluating it's use in olfactory loss which demonstrated safety and also suggested efficacy. Therefore, the investigators aim to assess the ability of PrP to improve olfactory function in patients with decreased sense of smell., Detailed Description, Olfactory dysfunction constitutes a common impairment in the general population, affecting nearly 20 million in the USA and severely impairing quality of life. Unfortunately, this problem is often permanent, and no effective treatment is available at this time. Although many etiologies exist for olfactory loss, the underlying pathology is thought to be permanent damage to the olfactory bulb, nerves or basal cells of the olfactory system. Platelet-rich plasma (PRP) is an autologous treatment derived from a patient's own blood and has been found to have pro-nerve regenerative properties in animal and human studies. A small pilot study at the principal investigator's institution demonstrated improved olfactory thresholds in patients with partial olfactory loss who received PrP injections. In this randomized clinical trial, the investigators aim to further evaluate the ability of PRP injections to restore olfactory function in human subjects. Given the lack of effective current treatments, a therapeutic benefit of PrP would represent a crucial advancement in research and treatment of olfactory loss, which affects a large swath of the population. Patients will be seen at the Stanford Sinus center, or at the newly added collaborating institution UCSD, and those with smell loss will be identified by the clinically validated patient directed survey: The UPSIT (University of Pennsylvania Smell Identification Test). They will undergo nasal endoscopy to exclude structural causes of smell loss including mass or tumor. Nasal endoscopy will be performed to exclude structural causes of olfactory, using topical anesthesia (1% phenylephrine \& 4% lidocaine topical spray). THESE ABOVE STEPS CONSTITUTE STANDARD OF CARE FOR EVALUATION OF OLFACTORY LOSS. The timing of the initial research visit will depend on the evolution of the current covid-19 pandemic and adhere to Stanford guidelines regarding research visits. At the initial research visit, patients meeting inclusion criteria will

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be evaluated in a procedure room at the Stanford Sinus center. A baseline Sniffin' sticks smell test will be performed (see below). A small vial of blood will be drawn from the patient at the Blake Wilbur first floor laboratory. The research coordinator will walk the patient back to clinic along with the patient's blood smple. PRP will be isolated from the blood by the study investigator, following manufacturer instructions from the PurePRP preparation kit (Emcyte corporation), which will involve use of a centrifuge located in the clinic for this purpose. 0.5 mL of the PRP solution will be set aside for platelet quantification. From the remaining PRP solution, patients will then receive 1ml of autologous PrP or sterile saline (0.9% Sodium Chloride), which will be injected into the superior septum mucosa near the olfactory groove bilaterally. Patients will be blindfolded during injection to prevent identification of the injected specimen, and will previously be randomized in a 1:1 ratio via a random number generator. Patients will be monitored for side effects for 15 minutes. (We routinely perform nasal endoscopy with injection and associated procedures in our clinic, which patients tolerate very well.) Injections will then be performed twice more at 2-weeks and -weeks after the initial injection, for a total of 3 biweekly injections. ALL OF THE ABOVE STEPS ARE FOR RESEARCH PURPOSES. The Sniffin' Sticks test is a validated, non-invasive assessment of olfactory function via presentation of scented felt pens to blindfolded patients. The output is the TDI score (threshold, discrimination, identification). The TDI score will be recorded at baseline (initial research visit), and then at 1-month and 3-months after the initial test, for a total of 3 tests. The first test will occur before the first injection, and the second test will be performed before the third injection. There will be no injection at the last (third) test. THE ABOVE VISITS ARE FOR RESEARCH PURPOSES. The study time-line is summarized as follows Visit 1: 1st Sniffin' Sticks test, 1st injection Visit 2: 2 weeks after Visit 1, second injection Visit 3: 4 weeks after Visit 1, second test, third injection Visit 4: 3 months after Visit 1, third testCopyright © 2025 clinicaltrials.gov

73. Yasak, A. G., et al. (2018).
"The effectiveness of platelet-rich plasma in an anosmia-induced mice model."
The Laryngoscope 128(5): E157-E162.

https://dx.doi.org/10.1002/lary.27029
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med15&NEWS=N&AN=29243256
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:29243256&id=doi:10.1002%2Flary.27029

OBJECTIVE: In this study, we aimed to functionally and morphologically demonstrate the effectiveness of platelet-rich plasma (PRP) on anosmia in a mouse model of anosmia ., STUDY DESIGN: Animal study., METHODS: A total of 16 male mice were included. When selecting the mice, the food-finding test (FFT) was used to make sure that the animals could smell, and anosmia was induced by administration of intraperitoneal 3-methylindole. The mice were randomly divided into two groups of eight (groups A and B). After 1 week, topical PRP was administered to the mice in group A and topical saline was administered to the mice in group B. The FFT was again administered at 7, 14, and 21 days. The mice were sacrificed on day 21, the olfactory neuroepithelium was histopathologically examined, and the epithelial damage scores and epithelial thickness were measured., RESULTS: After topical administration of PRP and saline, the difference in the average FFT values of the groups was statistically significant at 7, 14, and 21 days (P < 0,005). During the histopathological examination, the epithelial damage score was statistically significantly lower in the PRP group (P = 0.001) than in the saline group, and epithelial thickness was statistically significantly greater in the PRP group compared to the saline group (P = 0.003)., CONCLUSION: We showed that PRP administration has a curative effect on olfactory functions in an anosmia-induced mice model. However, there is a need for further research before PRP can be considered for use in patients with anosmia in clinical practice., LEVEL OF EVIDENCE: NA. Laryngoscope, 128:E157-E162, 2018. Copyright © 2017 The American Laryngological, Rhinological and Otological Society, Inc.

Corrected Proof

74. Khafagy, Y. W., et al. (2018).
"Leukocyte- and platelet-rich fibrin: a new graft material in endoscopic repair of spontaneous CSF leaks."
European Archives of Oto-Rhino-Laryngology 275(9): 2245
EP - 2252.

https://dx.doi.org/10.1007/s00405-018-5048-7
https://link.springer.de/link/service/journals/00405/index.htm
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed19&NEWS=N&AN=622952340
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:29982939&id=doi:10.1007%2Fs00405-018-5048-7

Background: Spontaneous CSF leak is a challenging condition, with frequent recurrences following attempted surgical closure. The selection of graft materials depends on the experience of the operating surgeon. Leukocyte- and platelet-rich fibrin (L-PRF) is a second-generation platelet concentrate that has currently invaded every surgical specialty. To our knowledge, no previous reports about the use of L-PRF in repair of CSF leak were published. The study was conducted to assess the potential role of L-PRF in spontaneous CSF leaks repair. Method(s): This prospective controlled study was conducted on 40 patients who were randomly divided into 2 groups: In group A, L-PRF was used in addition to another layer, while patients in group B underwent multilayer repair using traditional graft materials. Result(s): Preoperative HRCT scan showed bony dehiscence (n = 30) and opacity in a nearby sinus (n = 9). MRI findings varied between empty sella in 28 patients, and meningocele in 19 patients. Mean preoperatively measured CSF pressure was 26.6 cm H2O. Cribriform plate was identified as the commonest site of leaks. Multiple skull defects were detected in 2 cases. Failure of repair was found in 3 patients (15%) of group B and 1 patient (5%) of group A, this difference was statistically insignificant (P value = 0.28). Significance correlation between recurrence of CSF leak and elevated intracranial pressure was observed (P value; 0.04). Conclusion(s): L-PRF was found to be a good adjunct material in endoscopic spontaneous CSF leaks repair. It helps in decreasing the number of layers needed for defect closure.Copyright © 2018, Springer-Verlag GmbH Germany, part of Springer Nature.

75. Mavrogeni, P., et al. (2017).
" Anosmia treatment by platelet rich plasma injection."
The international tinnitus journal 20(2): 102-105.

https://dx.doi.org/10.5935/0946-5448.20160019
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med14&NEWS=N&AN=28452719
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:28452719&id=doi:10.5935%2F0946-5448.20160019

INTRODUCTION: Platelets are known for their key role in hemostasis and controlling the bleeding after injury. The fact that platelets secrete growth factors and active metabolites means that their applied use can have a positive influence in clinical situations requiring rapid healing and tissue regeneration., OBJECTIVES: Platelet Rich Plasma has been described as a promising but unproven therapy., MATERIALS AND METHODS: Whole blood was undergoing one stage of centrifugation. The whole blood was then separated into three layers. One ml of the lowest layer of plasma was administered to the patient's nose., RESULTS: After the third and finally the fourth therapy, 4 of 5 patients said that "their smell came back", while the remaining one patient said that he could smell a lot but not everything., CONCLUSION: Based on our results, platelet rich plasma administration to the olfactory region could be a promising, last chance therapy for complete anosmia .

Corrected Proof

76. Zhang, S., et al. (2015).
" Olfactory dysfunction and neurotransmitter disturbance in olfactory bulb of transgenic mice expressing human A53T mutant alpha-synuclein."
PloS one 10(3): e0119928.

https://dx.doi.org/10.1371/journal.pone.0119928
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med12&NEWS=N&AN=25799501
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:25799501&id=doi:10.1371%2Fjournal.pone.0119928

Parkinson disease is a multi-system neurodegenerative disease characterized by both motor and non-motor symptoms. Hyposmia is one of the early non-motor symptoms occurring in more than 90% of Parkinson disease cases, which can precede motor symptoms even several years. Up to now, the relationship between hyposmia and Parkinson disease remains elusive. Lack of proper animal models of hyposmia restricts the investigation. In this study we assessed olfactory function in Prp-A53T-alpha-synuclein transgenic (alphaSynA53T) mice which had been reported to show age-dependent motor impairments and intracytoplasmic inclusions. We also examined cholinergic and dopaminergic systems in olfactory bulb of alphaSynA53T mice by immunofluorescent staining, enzyme linked immunosorbent assay and western blot. We found that compared to wild type littermates, alphaSynA53T mice at 6 months or older displayed a deficit of odor discrimination and odor detection. No significant changes were found in olfactory memory and odor habituation. Furthermore compared to wildtype littermates, in olfactory bulb of alphaSynA53T mice at 10 months old we detected a marked decrease of cholinergic neurons in mitral cell layer and a decrease of acetylcholinesterase activity, while dopaminergic neurons were found increased in glomerular layer, accompanied with an increase of tyrosine hydroxylase protein. Our studies indicate that alphaSynA53T mice have olfactory dysfunction before motor deficits occur, and the cholinergic and dopaminergic disturbance might be responsible for the Parkinson disease-related olfactory dysfunction .

77. Onodera, T., et al. (2014).
"Review of studies that have used knockout mice to assess normal function of prion protein under immunological or pathophysiological stress."
Microbiology and Immunology 58(7): 361
EP - 374.

https://dx.doi.org/10.1111/1348-0421.12162
http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1348-0421
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed15&NEWS=N&AN=373475090
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:24866463&id=doi:10.1111%2F1348-0421.12162

Deletion of cellular isoform of prion protein (PrPC) increases neuronal predisposition to damage by modulating apoptosis and the negative consequences of oxidative stress. In vivo studies have demonstrated that PrPC-deficient mice are more prone to seizure, depression, and induction of epilepsy and experience extensive cerebral damage following ischemic challenge or viral infection. In addition, adenovirus-mediated overexpression of PrPC reduces brain damage in rat models of cerebral ischemia. In experimental autoimmune encephalomyelitis, PrPC-deficient mice reportedly have a more aggressive disease onset and less clinical improvement during the chronic phase than wild-type mice mice. In mice given oral dextran sulfate, PrPC has a potential protective role against inflammatory bowel disease. PrPC-deficient mice demonstrate significantly greater increases in blood glucose concentrations after intraperitoneal injection of glucose than wild-type mice. Further in vivo challenges to PrP gene-deficient models and conditional knockout models with siRNA and in vivo

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administration of PrP-ligating agents may assist in refining knowledge of the lymphoid function of PrPC and predicting the effects of anti-PrP treatment on the immune system. Together, these findings indicate that PrPC may have multiple neuroprotective and anti-inflammatory roles, which explains why this protein is so widely expressed. © 2014 The Societies and Wiley Publishing Asia Pty Ltd.

78. Zanusso, G., et al. (2009).
"Different prion conformers target the olfactory pathway in sporadic creutzfeldt-jakob disease."
International Symposium on Olfaction and Taste 1170: 637
EP - 643.

https://dx.doi.org/10.1111/j.1749-6632.2009.03905.x
http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1749-6632
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emexb&NEWS=N&AN=355092767
https://rcseng.ovidds.com/resolver/full?sid=OVID:embase&id=pmid:19686205&id=doi:10.1111%2Fj.1749-6632.2009.03905.x

Prion diseases, or transmissible spongiform encephalopathies (TSEs), are mammalian neurodegenerative diseases that occur as sporadic, inherited, or iatrogenic forms. Human TSEs exhibit a wide spectrum of phenotypic variability, which is influenced by (1) the conformation of the pathologic prion protein, or PrPSc; (2) the polymorphic codon 129 of the prion protein gene (PRNP), involving synonymous or nonsynonymous expression of Met or Val; and (3) the site of formation or entry of the self-replicating PrPSc. Brain deposition of PrPSc occurs in a phenotype-specific regional pattern, either as extracellular amyloid plaques and plaque-like aggregates, or as fine granular immunoreactivity at intracellular sites and presynaptic and postsynaptic locations, including dendrites. We previously demonstrated PrP Sc deposition in ciliated dendrites of olfactory sensory neurons in sporadic Creutzfeldt-Jakob disease (sCJD), the most common human prion disease. PrPSc immunoreactivity was not limited to the olfactory neuroepithelium. But additionally involved the central olfactory pathway. More recently, we have found that the pathology of the olfactory pathway occurs early in the disease course, either in the myoclonic or classic sCJD or in the ataxic variant. Intriguingly, in the ataxic or cerebellar variant, mainly observed in patients with the MetVal polymorphism (2) carrying PrPSc type 2, olfactory involvement is accompanied by pathologic changes in the dorsal motor nucleus of the vagus and other brainstem nuclei. These findings suggest that different molecular events and distinct routes of PrPSc spread contribute to the prominent heterogeneity of sCJD, conceivably providing support to the olfactory pathogenesis theory of neurodegenerative diseases. © 2009 New York Academy of Sciences.

79. Le Pichon, C. E., et al. (2009).
" Olfactory behavior and physiology are disrupted in prion protein knockout mice."
Nature Neuroscience 12(1): 60-69.

https://dx.doi.org/10.1038/nn.2238
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med7&NEWS=N&AN=19098904
https://rcseng.ovidds.com/resolver/full?sid=OVID:medline&id=pmid:19098904&id=doi:10.1038%2Fnn.2238

The prion protein PrP (C) is infamous for its role in disease, but its normal physiological function remains unknown. Here we found a previously unknown behavioral phenotype of Prnp(-/-) mice in an odor-guided task. This phenotype was manifest in three Prnp knockout lines on different genetic backgrounds, which provides strong evidence that the phenotype is caused by a lack of PrP (C) rather than by other genetic factors. Prnp(-/-) mice also showed altered behavior in a second olfactory task, suggesting that the phenotype is olfactory specific. Furthermore, PrP (C) deficiency affected

Corrected Proof

oscillatory activity in the deep layers of the main olfactory bulb, as well as dendrodendritic synaptic transmission between olfactory bulb granule and mitral cells. Notably, both the behavioral and electrophysiological alterations found in Prnp(-/-) mice were rescued by transgenic neuronal-specific expression of PrP (C). These data suggest that PrP (C) is important in the normal processing of sensory information by the olfactory system.