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Kinetics of olfactory function following endonasal sinus surgery for nasal polyposis*

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SUMMARY

Introduction: *Sinus surgery is known to improve olfactory function in patients with nasal polyposis. However, little is known about the kinetics of this process.*

Material and Methods: *Fifty-two adult patients with nasal polyposis underwent endonasal sinus surgery. Olfactory testing was performed with the Sniffin' Sticks assessing threshold (T), discrimination (D) and identification (I) giving the TDI score. Testing was performed 2 days prior to surgery (T1), as well as 1 week (T2), 1 month (T3), 3 months (T4), and 6 months (T5) following surgery.*

Results: *The median TDI score was 15.4 (range 8.0 - 35.5) at T1, indicating that half the patients were anosmic before surgery, while 13.5% were normosmic. At T2, the median TDI score dropped to 8.0 (range 8.0 – 32.1). Thereafter, it improved to 21.7 (range 8.0 – 36.9) at T3 ($p = 0.04$), 22.8 (range 8.0 – 38.0) at T4 ($p < 0.0005$), and 27.0 (range 8.0 – 37.9) at T5 ($p < 0.0005$), respectively. 43.1% of patients were normosmic at T5, however, 21.6% remained anosmic. Each subtest followed the same pattern. No significant effect on the kinetics of olfactory function could be found for variables such as systemic steroids, partial resection of the middle turbinate, inferior turbinotomy, and allergic rhinitis.*

Conclusion: *Endonasal sinus surgery significantly improved the severely impaired olfactory function in patients with nasal polyposis. Olfactory function dropped shortly after surgery, and subsequently increased steadily up to the endpoint of the study 6 months postoperatively.*

Key words: olfaction, sinus surgery, nasal polyposis, steroid treatment, middle turbinate resection

INTRODUCTION

Besides nasal blockage, many patients with nasal polyposis complain about impaired sense of smell [(1)]. In terms of pathophysiology, it may not only be the blocked airway to the olfactory region, which compromises the patients' sensory abilities, but additionally there may be disease specific factors involved such as thickening of the olfactory mucosa, or dyscrasia of olfactory mucus. Still, ventilation of the olfactory region is a prerequisite in the olfactory process [(2)]. Consequently, sinus surgery improves olfactory function [(3,4)]. However, little is known about the kinetics of this process and whether patients with improved olfaction actually reach normal levels of olfactory function. Therefore, we prospectively evaluated the patients' olfactory performance with regards to threshold, discrimination and identification on 4 points in time within 6 months following surgery according to the physiological stages of paranasal sinus wound healing [(5)]. While there are numerous olfactory test available [(6)], we preferred to use the Sniffin' Sticks Test introduced by Kobal and co-workers [(7-9)].

MATERIALS AND METHODS

Initially, 63 adult patients with nasal polyposis scheduled for primary endonasal sinus surgery were prospectively included in the study after giving informed consent. We did not include patients with a history of previous sinus surgery, traumatic anosmia, malignant disease, or any neurological disorder known to influence the olfactory function, e.g. Alzheimer's dementia. Eleven patients were excluded due to no show at follow-up visits, resulting in 52 patients eligible for statistical evaluation. There were 19 female and 33 male patients ranging from 26 to 83 years of age with an average age of 47 years. Twenty-two out of 52 patients (43%) had allergic rhinitis diagnosed by allergen testing. Four patients (8%) suffered from intolerance to acetylsalicylic acid.

Treatment

Sinus surgery was performed exclusively by the endonasal route with the aid of rigid endoscopes according to the technique described by Wigand [(10)]. All patients had complete ethmoidectomy with antrostomy, sphenoidotomy and opening of

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the frontal recess. The middle turbinates of 20 patients (38%) were partially resected. Septoplasty was performed in combination with sinus surgery in 25 out of 52 patients (48%). Partial resection of the lower turbinates was performed in 29 cases (54%). Twenty-eight patients (54%) received topic (budesonide) and systemic corticosteroids (prednisolone) postoperatively at a starting dose of 1 mg / kg body weight tapered over 4 weeks. The indication for systemic steroid treatment at the time of the study was a history of asthma, acetylsalicylic acid sensitivity, allergic rhinitis, massive polyposis ("white out" in CT scan) and revision surgery of any extent (the latter was excluded in the present study). As the study was not randomized, steroid allocation reflects severity of disease and / or risk factors. There was no randomization of surgical and / or medical treatment.

Olfactory testing

Olfactory function was measured in a well-aerated and quiet room by the Sniffin' Sticks introduced by Kobal and co-workers [7-9]. The test is evaluating the threshold (T) for n-butanol presented at 16 concentrations, odour discrimination (D) based on 16 odour triplets and identification (I) of 16 odours while using a forced choice testing paradigm. The TDI score is calculated as the sum of the 3 subtests, thus ranging from 0 to 48. The median of normal for patients aged 36 to 55 years is 35.5 with the 10^{th} percentile of normal being at 28.8 and the 90th percentile at 41.5 [9]. A TDI score of less than 15 is indicating anosmia. During the testing, the patient was blinded with a mask. Each side was tested separately. Food intake was restricted to drinking water within 3 hours before the test. Alike, smoking was not allowed within the same time period.

Timing of testing

The base line olfactory testing was performed 2 days prior to surgery (T1). Postoperative testing was scheduled at 1 week (T2), 1 month (T3), 3 months (T4) and 6 months (T5) following surgery. T2 corresponds to the first stage of paranasal wound (bloody crusting) according to Hosemann and co-workers [5]. T3 is timed at the end of the second stage (obstructive lymphedema). T4 is within the third stage (mesenchymal restructuring) and T5 is after completion of the fourth stage (scar formation).

Statistics

A one-way repeated measures analysis of covariance (RM-ANCOVA) controlling for systemic steroid treatment, partial resection of the middle turbinate, inferior turbinotomy, and allergic rhinitis was used for significance testing. A saturated model was fitted including the fixed effects of treatment (between-group factor), the follow-up points (within-group factor) and the treatment by time interaction. The sphericity assumption was tested by the Mauchly test. If the sphericity assumption was violated ($p < 0.05$) the Huynh-Feldt epsilon correction was applied.

The results were graphically displayed in box plots. The boxes range from the first to the third quartile (interquartile range IQR). The median is represented by a horizontal line within the box. The whiskers range from the minimum to the maximum. Outliers are values between 1.5 IQR's and 3 IQR's from the end of a box. Values more than 3 IQR's from the end of a box are defined as extreme. Statistical analysis was performed by using SPSS™ 13.0 (SPSS Inc., Chicago, USA) running on a Microsoft Windows™ personal computer.

RESULTS

Forty-eight out of 52 patients (92%) complained about nasal blocking. On the right hand side, nasal flow at 150 Pa was 150.12 $cm^3/s \pm 23.23$ cm^3/s before surgery and 243.53 $cm^3/s \pm 22.21$ cm^3/s at the endpoint of our investigation 6 months postoperatively. On the left hand side, nasal flow at 150 Pa was 182.94 $cm^3/s \pm 25.57$ cm^3/s before surgery and 212.70 $cm^3/s \pm 26.23$ cm^3/s at 6 months postoperatively. The change was significant on the right side ($p = 0.006$), but not on the left side ($p = 0.311$).

Forty-one out of 52 patients (79%) subjectively judged their olfactory performance as impaired prior to surgery. Indeed, the median TDI score was 15.4 (range 8.0 - 35.5) at T1. 26 patients (50%) were anosmic with a TDI score below 15. 13.5% of patients were normosmic (above the 10^{th} percentile of normal). At T2, 1 week after surgery, the median olfactory performance dropped to 8.0 (range 8.0 – 32.1). Thereafter, the TDI score improved to 21.7 (range 8.0 – 36.9) at T3, 22.8 (range 8.0 – 38.0) at T4, and 27.0 (range 8.0 – 37.9) at T5, respectively. Statistically, the improvement was highly significant at all times when compared to the base line level at T1 as indicated in Figure 1. The rise of the TDI score between T3 and T4 was also significant ($p = 0.04$), whereas the change from T4 to T5

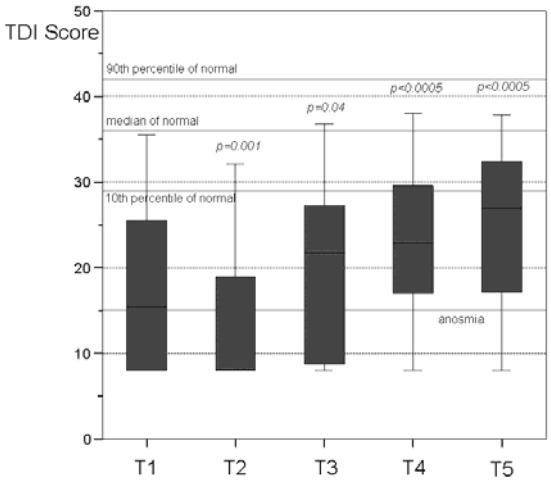

Figure 1. Box plot showing the kinetic of olfactory function as measured by the Sniffin' Sticks TDI score over time. The median of normal as well as the range from the 10th to the 90^{th} percentile for the age group 36 to 55 years (9) as well as the limit of anosmia (TDI below 15) are displayed. T1-5 are the points of testing as explained in the Material and Methods section. The p values give the significance level of a one-way repeated measures analysis of covariance (RM-ANCOVA) comparing to the score at T1 (see Material and Methods).

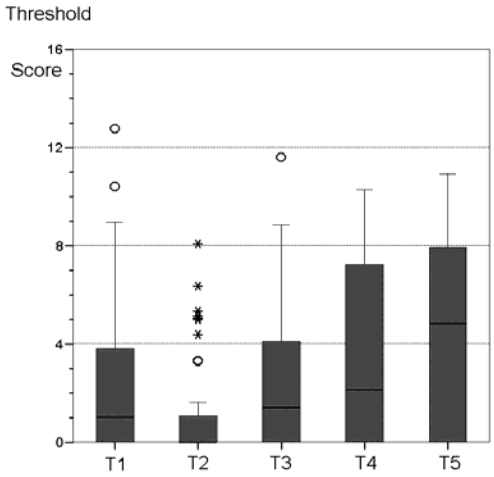

Figure 2. Box plot showing the kinetic of Sniffin' Sticks threshold scores over time. Outliers are represented by a circle; extremes by an asterisk (see Material and Methods).

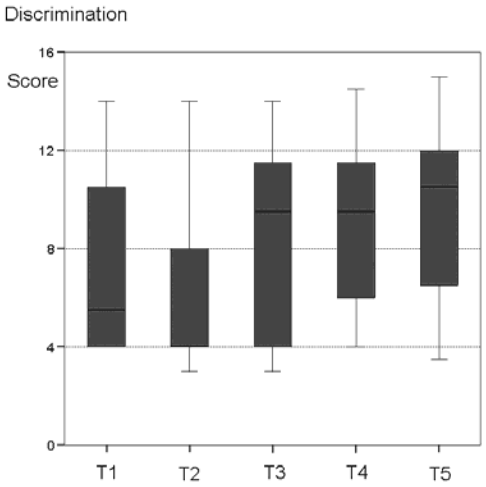

Figure 3. Box plot showing the kinetic of Sniffin' Sticks discrimination scores over time.

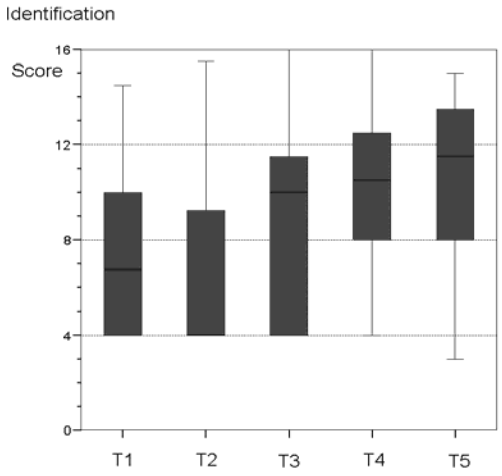

Figure 4. Box plot showing the kinetic of Sniffin' Sticks identification scores over time.

was not. About 43% of patients became normosmic at T5, with a maximum TDI score of 37.9. While 50% of the patients were anosmic before surgery, 6 months after surgery 21.6% (11 patients) remained anosmic. There were 7 patients who deteriorated in olfactory function below their preoperative value, however all changes were within 1 score point, and statistically not significant.

Each subtest followed the same pattern (Figures 2-4) over time. We could not find any significant differences between the two sides.

RM-ANCOVA did not reveal any significant effect on the kinetics of olfactory function of variables such as systemic steroids, partial resection of the middle turbinate, inferior turbinotomy and allergic rhinitis.

DISCUSSION

The kinetics of olfactory function are clearly dependant on the stages of paranasal wound healing as described by Hosemann and co-workers [5]. While the drop at T1 is explained by airway blockage due to bloody crusts in stage 1, there is a constant improvement over time thereafter. At the end of stage 2 with obstructive lymphedema, olfactory function has already improved, but not yet to the possible maximum. In this study, the maximum of the TDI score was reached at the endpoint of the study 6 months after surgery when healing is complete with scar formation. The further course of olfactory function remains unknown.

Olfactory performance was very low in this patient population with nasal polyposis, highlighted by a rate of 50% anosmic patients. However, statistically speaking the improvement in olfactory function was highly significant. 43.1% of patients reached normal levels of olfactory function (i.e. the 10th percentile of normal controls being at 30.3 for the age group 16-35 years, 28.8 for the age group 36 to 55 years, or 27.5 for the age group above 55 years [9]. However, 21% of patients remained anosmic at T5. All subtests exhibited the same pattern over time. The difference in the absolute value of the identification and discrimination score compared to the threshold score is due to the test design.

The effect of sinus surgery on olfaction has been evaluated in several studies. Delank and Stoll [3] examined olfactory function in 78 patients undergoing endonasal surgery for chronic rhinosinusitis by the squeeze bottle method before and an average of 46 days following surgery. While in 9% of patients olfactory function deteriorated, 71% of hyposmic and anosmic patients improved after surgery. Judging from our study results, these authors might have found an even greater percentage of improvement when testing at a later stage after surgery. Klimek and co-workers [11] studied the olfactory threshold of 31 patients following microscopic sinus surgery for patients with nasal polyps by the CCCRC test up to 6 months. Before surgery, the patients were on average classified as moderately hyposmic. They also noticed a significant improvement at 2 and 3 months after surgery, however, there was a (not significant) drop after 6 months. On the other hand, Jankowski and Bodino [4] proved stable results in subjective rating of olfactory function by the

patients via a visual analogue scale at 3, 6, 9, and 12 months following radical ethmoidectomy with the nasalisation principle combined with one depot injection of 80 mg triamcinolone and a low dose of nasal steroids [4]. Middle turbinate resection did not alter the possibility to improve olfaction, as it could be supported by our study, keeping in mind that the amount of resection has differed. Neither could Friedman and co-workers [12] find any significant effects of partial middle turbinate resection on olfaction with the UPSIT in 64 patients undergoing endoscopic sinus surgery. However, even though there are no proven negative effects of partial or subtotal middle turbinate resection on olfactory function, we are not advocating its deliberate sacrifice.

Corticosteroids have long been shown to improve olfactory function in patients with nasal polyposis [13]. Nasal corticosteroids have demonstrated an improvement of olfactory function in patients with hyposmia due to perennial rhinitis [14]. Nasal corticosteroids are also effective in patients with nasal polyposis by reducing symptoms of nasal blockage [15]. However, while the effect of nasal corticosteroids on olfactory function may be small, systemic corticosteroids do improve olfaction in patients with nasal polyposis [16]. We were unable to reveal any significant effect of systemic steroids on the kinetics of olfactory function. However, as this medical treatment was not randomly assigned, the steroid subgroup had a worse TDI score prior to surgery. Whether steroids would have displayed a positive effect if given to all patients cannot be concluded from this study. However, perioperative steroids are probably beneficial in terms of improving olfactory function. The data of Jankowski and Bodino [4] indicate that those patients with hyposmia responsive to steroids are those who will recover olfactory function after surgery.

CONCLUSION

Patients with nasal polyposis can be severely handicapped with regards to olfactory function. Endonasal sinus surgery significantly improved olfactory function with a continuous increase up to the endpoint of the study at 6 months, equally for all 3 subtests. Around 43% of patients were normosmic at T5, however, 21.6% remained anosmic. No significant effect on the kinetics of olfactory function could be found for variables such as systemic steroids, partial resection of the middle turbinate, inferior turbinotomy, and allergic rhinitis.

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