Topical anaesthesia and decongestion in rhinology*

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Abstract

Topical anaesthesia and decongestion of the sinonasal mucosa are used commonly in rhinology practice to facilitate nasal endoscopy, as well as debridement and biopsies. Topical agents used for sinonasal anaesthesia include lignocaine, tetracaine and cocaine. Unlike lignocaine and tetracaine, cocaine also has a decongestant effect. Phenylephrine, oxymetazoline, xylometazoline or adrenaline are usually added to lignocaine and tetracaine to provide decongestion. Several studies have been performed seeking to identify the optimal nasal preparation for nasal endoscopy in the clinic setting. However, there remains no clear consensus in the literature resulting in ongoing wide variation between anaesthetic-decongestant preparations used in clinical practice. Indeed, some authors have argued that no anaesthetic is required at all for flexible nasendoscopy despite the apparent consensus that nasal instrumentation is generally uncomfortable, inferred by the persistence of ongoing research in this area. This review provides a practical summary of local anaesthetic and decongestant pharmacology as it relates to rhinologic practice and summarises the literature to date, with the goal of identifying current gaps in the literature and guiding future research efforts.

Key words: anaesthetics, topical, vasoconstrictors, nasal, vocaine, phenylephrine, lidocaine drug combination

Introduction

The use of topical mucosal anaesthesia is a daily feature of modern rhinologic practice. Most commonly, local anaesthetics are applied with decongestants to the nasal cavity prior to in-office nasal endoscopy and instrumentation, or as a preoperative preparation. The agents used, either alone or in various combinations, include cocaine, lignocaine and tetracaine for anaesthesia (cocaine also providing a vasoconstrictive effect), and phenylephrine, adrenaline, oxymetazoline and xylometazoline for decongestion [1,2].

Cocaine was the first local anaesthetic discovered and subsequently incorporated into clinical practice. It retains an important place in modern rhinologic practice as the only local anaesthetic to also provide vasoconstriction. However, it is highly restricted as a drug of abuse with significant potential for toxicity and addiction [3]. Other local anaesthetics are at least as effective, and modern vasoconstrictors applied topically provide equivalent decongestion. Combination anaesthetic-decongestant products such as *Co-Phenylcaine* (5% lignocaine and 0.5% phenylephrine; ENT Technologies Pty Ltd., Melbourne, VIC, Australia) have been developed which provide anaesthesia and decongestion without the use of cocaine.

Several studies have been published which examine the efficacy of topical anaesthetic-decongestant preparations by measuring changes in sensory thresholds of the nasal mucosa, as well as by recording patient-reported comfort during flexible and rigid nasal endoscopy. The results of these studies vary, with some even suggesting that for flexible nasendoscopy, withholding anaesthetic spray provides equivalent overall patient comfort as its use does.

As many patients continue to receive topical nasal anaesthetic and decongestant agents, it is important to ensure that the optimal agents and dosages are used. This review provides a short summary of local anaesthetic and decongestant pharmacology and reviews the published studies of the clinical efficacy of these agents for endoscopy in the clinic setting. The efficacy of these agents in the operative setting, both for preoperative sinonasal preparation and for haemostasis, are outside the scope of this review. Topics requiring further research are suggested.

Table 1. Chemical parameters of common local anaesthetics used topically on the sinonasal mucosa.

Anaesthetic	Structure	pKa	Proportion of non-ionised drug at pH 7.4	logP [53]
cocaine	ester	8.6 [8]	6%	2.30
lignocaine	amide	7.95 [53]	22%	2.44
tetracaine	ester	8.49 [53]	8%	3.51

Local anaesthetics are categorised according to whether their aromatic and amine groups are linked by an amide or an ester group. pKa is the pH at which ionised and non-ionised forms are present in solution in equal concentrations. As pKa increases further above physiological pH, the proportion of non-ionised drug available to diffuse into neuronal axons decreases. logP is a log transformation of the octanol-water partition coefficient, a measure of hydrophobicity or hydrophilicity of a molecule. A higher positive value indicates greater hydrophobicity and predicts greater potency.

Pharmacology

Local anaesthetics

The advent of local anaesthesia came with the discovery in 1884 by an ophthalmologist that cocaine, when applied topically, abolished corneal sensation [4]. Modern local anaesthetics are derivatives of cocaine and share its basic structure of an aromatic ring and an amine, connected either by an ester or an amide functional group [5]. This forms the basis of the classification of local anaesthetic drugs into "esters" and "amides," which is highly relevant to drug metabolism as amides undergo hepatic metabolism and excretion, whereas esters undergo enzymatic digestion in the plasma and tissues [6]. The amides are therefore metabolised more slowly, particularly at the extremes of age or in those with hepatic disease, leading to a risk of accumulation with multiple dosing [7]. The esters are metabolised much more rapidly. However, their primary metabolite, para-aminobenzoic acid, is allergenic, and adverse reactions are reported more commonly for esters than for amides for this reason [8,9]. Overall, allergy to local anaesthetics is rare [9].

Local anaesthetics are weak bases and exist in chemical equilibrium between their ionised and non-ionised forms. With few exceptions, they act intracellularly and must diffuse into the axon in their non-ionised form before re-equilibrating in the cytoplasm. The ionised drug then binds to voltage-gated sodium channels, blocking the passage of sodium ions and preventing the generation of action potentials [6,8,10].

The ratio between ionised and non-ionised molecules is determined by the pKa (Table 1). At physiological pH, a drug with a higher pKa will exist in its ionised form in greater proportion. With a higher pKa and consequently lower concentration of non-ionised drug, the concentration gradient down which the anaesthetic diffuses into the axon is weaker [8,10]. The pKa of a local anaesthetic therefore influences its rate of onset. This may be mitigated by increasing the pH of the local anaesthetic solution, for example by the addition of sodium bicarbonate, or by increasing the local anaesthetic concentration [8]. The difference between pKa and tissue pH is one of the reasons why local anaesthetics are less effective in inflamed tissue. With tissue inflammation, pH decreases, widening the gap between pH and pKa and swinging the equilibrium towards the ionised form of the drug, subsequently reducing intracellular diffusion [6,8].

Anaesthetic potency is strongly influenced by the hydrophobicity of the molecule (Table 1) [7,8]. This may be due to the partial hydrophobicity of the subunit of the voltage gated sodium channel to which local anaesthetics bind: a more hydrophobic anaesthetic molecule with greater affinity for this binding site will be more potent [7]. More hydrophobic molecules also diffuse more easily through the axonal membrane, leading to a faster onset of anaesthesia [8].

Decongestants

Topical decongestants are primarily α-adrenergic agonists. Phenylephrine and adrenaline are sympathomimetic amines, and oxymetazoline and xylometazoline are imidazoline derivatives. All act by direct α-adrenergic receptor activation in vascular smooth muscle, causing vasoconstriction with consequent reduction in mucosal blood flow and engorgement [2,11]. The exception is cocaine, which acts by catecholamine reuptake inhibition to achieve the same effect (Figure 1). This also gives cocaine its euphoric effects and its systemic toxicity profile in overdose [3,12].

Toxicity

Local anaesthetics are generally safe, but systemic toxicity may arise when recommended dosage ranges are exceeded [6]. Local anaesthetic systemic toxicity (LAST) has a well-described constellation of symptoms, including perioral paraesthesia, seizures, generalised CNS depression and cardiovascular collapse [7,10]. However, the doses typically used in topical sinonasal anaesthesia are well within safe limits. Lignocaine with vasoconstrictor may be administered up to 7 mg per kilogram body weight (490mg in a 70 kg patient compared to only ~5 mg lignocaine per spray of *Co-Phenylcaine*) [8]. The dosage range of tetracaine is less clear. A report from 1956 on fatalities following topical anaesthesia identified several instances of LAST where unknown or excessive doses (greater than 160 mg) of topical tetracaine were administered. This toxicity was thought to be due in part to the rapid absorption of tetracaine from mucous membranes, and maximum

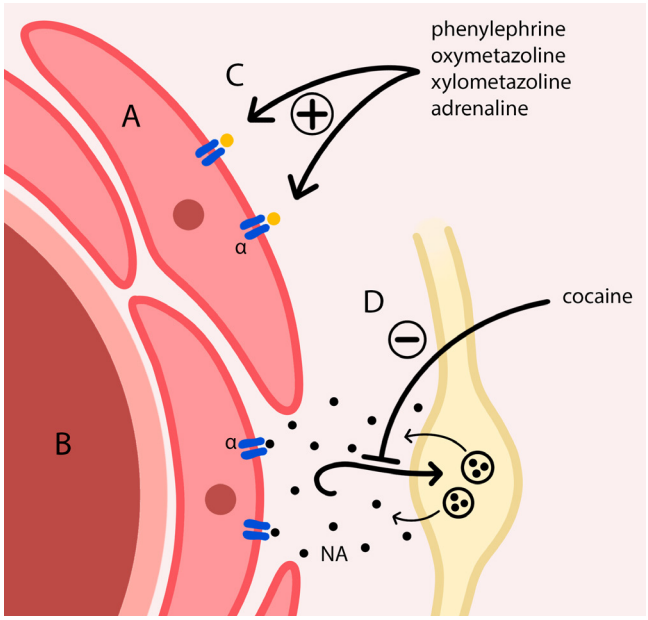

Figure 1. Sites of action of topical decongestants used in nasal preparation. Smooth muscle (A) in the wall of an arteriole (B) contracts in response to α-adrenergic receptor activation. Phenylephrine (the vasoconstrictor in *Co-phenylcaine*), oxymetazoline, xylometazoline and adrenaline act by direct agonism of α-adrenergic receptors on vascular smooth muscle (C). Cocaine acts by inhibition of catecholamine reuptake in sympathetic neuronal varicosities. When noradrenaline is released from vesicles in the neuron, inactivation by reuptake is blocked, leading to a buildup of endogenous vasoconstrictor (D). α: alpha-adrenergic receptor. NA: noradrenaline.

total doses of between 20 mg and 50 mg were suggested [13]. However, a more recent study in which a mean dose of 120mg topical tetracaine was given before 537 flexible bronchoscopies demonstrated no instances of LAST, and no adverse events were identified in any studies investigating tetracaine reviewed below [14]. A newer consensus is that a topical dose of 100 mg should not be exceeded [15,16]. Cocaine has a different toxicity profile, which results primarily from catecholamine excess rather than cardiac and central nervous system (CNS) depression [12]. A maximum safe dose of 1.5 mg/kg has been suggested [8]. When appropriate doses are given, major toxicity is rare. Although vasoconstriction leading to cardiac and cerebral ischaemia is observed when cocaine is abused, clinical and population-based studies have not identified an increased risk of such events following nasal preparation [17–19]. The results of these studies do not prove safety, however: dose-independent coronary vasospasm has been described, and in one survey of 4017 American otolaryngologists, a quarter of respondents reported adverse events related to cocaine in their practice [15,20]. Of 1180 adverse events reported, tachycardia, hypertension, hyperactivity, and dysphoria accounted for 1006, with the remaining 174 comprised of stroke, seizure, syncope, chest pain, myocardial infarction, cardiac arrhythmia, cardiac arrest, and death [20].

Local adverse effects of topical anaesthesia are relatively common and include overflow pharyngeal anaesthesia, a transient reduction in sensation of nasal airflow and subjective hyposmia. This hyposmia does not consistently correlate with reduction in olfactory thresholds or discrimination using Sniffin' Sticks or olfactory event-related potentials [21,22]. However, aggressively anaesthetising the olfactory cleft may result in temporary anosmia and headache [21].

Topical decongestants other than cocaine are well tolerated at doses used for endoscopy in the clinic setting. Most data come from studies in the operative setting, where minor changes in heart rate and blood pressure are variably reported and are rarely of clinical importance [23,24]. Topical adrenaline 1:1000 has been used in several studies without event although in one study on participants undergoing transsphenoidal pituitary surgery, hypertension without change in heart rate was observed in around a quarter of their patient cohort after six adrenaline-soaked pledgets were placed [19,25–27]. The significance of this finding for the use of adrenaline in the clinic setting, where less adrenaline is typically used, is unclear. Note is made that injected adrenaline 1:100,000 has a greater haemodynamic effect than concentrated topical adrenaline, with the difference likely due to the slowing of absorption in topical application caused by local vasoconstriction (26). Phenylephrine, oxymetazoline and xylometazoline are used safely in the operative setting in children without clinically significant haemodynamic effects [23,24,28].

Previous literature

A literature search was performed in the MEDLINE database using the following MeSH terms: Administration, Topical; Anesthetics, Local; Nasal Cavity; Nasal Decongestants; Paranasal Sinuses. Additional studies were identified from the reference lists of original articles and reviews. Agents investigated in the included studies are summarised in Table 2. The methodologies and main outcomes of the included papers are summarised in Table 3.

Nasal mucosal anaesthesia

Several studies have examined the efficacy of topical anaesthesia for the sinonasal mucosa, primarily focussing on lignocaine (alone or combined with decongestants), cocaine and tetracaine.

Studies testing mucosal sensory thresholds and pain perception in healthy volunteers have used various methodologies. One study used pin-prick testing 15 minutes following application of cocaine 6% or lignocaine 4% and xylometazoline 0.1%, with no significant difference in pain scores observed between these

Table 2. Local anaesthetics and decongestants investigated in the clinical studies reviewed.

Class	Agent
Local anaesthetics	Cocaine [3,32–34,42] Lignocaine [1,3,32–41,44,46,48] Tetracaine [35,36,43]
Decongestants	Cocaine [3,32–34,42] Phenylephrine [1,3,32,33,37–41,46,48] Xylometazoline [1,40] Oxymetazoline [35,36] Adrenaline [34] Ephedrine [43]

The most frequently investigated agents are lignocaine and phenylephrine followed by cocaine.

agents [29]. Others have used Semmes-Weinstein monofilaments, which are standardised nylon filaments that flex when pushed with a specified force onto skin or mucosa. Anaesthetic/decongestant solutions were applied to the nasal cavity on pledgets for 10 min, then sensory thresholds measured, and a painful stimulus exerted by the filament pressure exceeding the sensory threshold. Lignocaine 2% with oxymetazoline 0.025% provided equivalent or superior anaesthesia compared to cocaine 4% in terms of sensory thresholds and pain perception, both in the period after removal of the pledgets and following a delay of approximately one hour [16,30]. Tetracaine 1% with oxymetazoline 0.05% gave superior reductions in nasal mucosal sensation and pain perception compared with both preparations at the same time points [16,31].

These studies in healthy participants were largely corroborated by the findings from studies comparing topical anaesthesia in clinic patients undergoing nasal endoscopy. Cocaine 10% and lignocaine-based sprays including *Co-Phenylcaine* or lignocaine 4% with adrenaline 1:1000 offered equivalent patient comfort and ease of endoscopy when applied 10 to 15 min prior to rigid or flexible nasendoscopy [3,32–34]. When comparing lignocaine and tetracaine, the results are mixed: one study demonstrated the superiority of tetracaine over lignocaine in terms of patient comfort, whereas another found equivalent efficacy between preparations [35,36]. In the former study, anaesthetics were applied on neurosurgical sponges for 10 min prior to endoscopy; in the latter, anaesthetics were given as sprays with a wait time of 3 min. Patients were given oxymetazoline separately for decongestion in both studies.

When topical anaesthetics have been compared to decongestant alone or placebo prior to endoscopy, the results are surprising. When *Co-Phenylcaine* was compared with xylometazoline 0.1% for rigid nasal endoscopy, or placebo for flexible nasendoscopy, a non-significant trend towards greater comfort was observed at best in the *Co-Phenylcaine* groups [1,37–39]. Another study found that the only factor associated with reduced discomfort for flexible nasendoscopy among topical nasal preparations was the administration of a vasoconstrictor [40]. A further study compared pain scores in patients who received *Co-Phenylcaine* 5 min prior to endoscopy and/or simple distraction by watching their examination on a screen and found that patients reported greater comfort with distraction regardless of whether or not *Co-Phenylcaine* had been given [41]. However, participants assigned themselves to each intervention, giving a high likelihood of bias: patient anxiety is associated with greater discomfort, and it is conceivable that more highly anxious patients would opt for *Co-Phenylcaine* and choose not to watch their examination [39]. Taken together, however, these studies overall demonstrate the value of decongestion for patient comfort prior to endoscopy along with the relative inefficacy of lignocaine in this setting. Further, randomised trials investigating cocaine 5% and tetracaine 2% failed to demonstrate superiority of either over placebo [42,43].

The unpleasant taste of anaesthetic-decongestant preparations may form a partial explanation for the overall failure to improve patient comfort. Unpleasant taste was a confirmed or potential contributor to overall discomfort in several studies, and a separate study in which *Vanilla Mint Listerine* mouthwash (Johnson & Johnson Inc., New Brunswick, NJ, USA) was used as a flavour mask prior to applying lignocaine spray demonstrated significant reductions in overall discomfort with lignocaine compared with placebo [38,40,44]. Masking the taste of anaesthetic-decongestant nasal preparations or choosing less offensive-tasting preparations may therefore be a simple way to improve patient comfort [44,45].

Few studies have measured the time to achieve peak anaesthesia of different topical anaesthetics. Most have begun testing 10 minutes after application of the anaesthetic, which is an unrealistically long waiting period in the setting of a busy clinic. However, one study assessed pain perception by palpation of the inferior turbinate with a Jobson-Horne probe, before and every three minutes after application of three sprays of *Co-Phenylcaine*. Pain scores were lowest at 9 minutes post-spray [3]. In another study, participants undergoing rigid nasal endoscopy using a 4 mm endoscope were randomised to either a 1 min or 10 min waiting period between receiving *Co-Phenylcaine* and beginning endoscopy. Discomfort was rated significantly lower after a 10 min waiting period on visual analogue scales completed by the patient, and ease of passage of the endoscope and clarity of view was significantly better on visual analogue scales completed by the clinician [46].

Table 3. Summary of the studies reviewed.

Study	Drugs tested	Study design	Method of application	Method of anaesthetic assessment	Method of decongestant assessment	Summary of findings
Biggs et al. 2018[41]	*Co-Phenylcaine* distraction	Observational study	Sprays (if used) then 5 min wait time	FNE then VAS for discomfort	-	Lower discomfort scores with distraction regardless of whether anaesthetic was applied
Javed et al. 2017[37]	*Co-Phenylcaine* saline	RCT	Sprays then 10 min wait time	FNE then VAS for patient experiences	VAS for ease of endoscopy and quality of view	No significant difference in overall discomfort between sprays. Easier endoscopy with better views when *Co-phenylcaine* was used.
Gaviola et al. 2013[35]	lignocaine 4% with oxymetazoline tetracaine 2% with oxymetazoline	RCT	Sprays then 3 min wait time	FNE then 10-point scales for patient experiences	-	No significant difference in overall discomfort between sprays
Bonaparte et al. 2011[44]	lignocaine 10% saline	Split-body randomised trial	Sprays then 5–15 min wait time	FNE then VAS for pain/discomfort	-	Reduced discomfort with lignocaine 10% compared with saline control (median VAS 18.6 mm for lignocaine, 44.6 mm for saline, $p = 0.01$)
Bourolias et al. 2010[36]	lignocaine 10% with oxymetazoline 0.1% tetracaine 2% with oxymetazoline 0.1%	RCT	Oxymetazoline given as a spray; anaesthetics given on pledgets for 10 min	FNE then VAS for pain/discomfort	-	Reduced discomfort with tetracaine 2% compared with lignocaine 10% (mean VAS 2.29 for tetracaine, 3.04 for lignocaine, $p < 0.001$)
McCluney et al. 2009[1]	*Co-Phenylcaine* xylometazoline 0.1%	RCT	Sprays then 10 min wait time	Rigid endoscopy then questionnaires completed by patients	Questionnaire for quality of view	No significant difference in comfort or quality of view between sprays
Pothier et al. 2007[46]	*Co-Phenylcaine*	RCT	Sprays then 1 or 10 min wait time	Rigid endoscopy then VAS for pain/discomfort	VAS for ease of endoscopy and quality of view	Significantly lower discomfort after 10 min wait time (median VAS score 39 mm at 1 min compared with 8 mm at 10 min, $p = 0.02$); easier endoscopy with better views after 10 min
Douglas et al. 2006[48]	*Co-Phenylcaine* lignocaine 5%	Randomised crossover trial	Spray then 10 min wait time	Rigid endoscopy then VAS for pain/discomfort	VAS for ease of endoscopy and quality of view	No significant difference in overall discomfort between sprays. Greater technical ease with *Co-phenylcaine*.
Georgalas et al. 2005[38]	*Co-Phenylcaine* saline	RCT	Sprays then 10 min wait time	FNE then VAS for patient experiences	-	No significant difference in overall discomfort between sprays
Cain et al. 2002[39]	*Co-Phenylcaine* saline no spray	RCT	Sprays (if used) then 10 min wait time	FNE then VAS for patient experiences	VAS for ease of endoscopy and quality of view	No significant difference in overall discomfort between sprays
Smith et al. 2002[3]	cocaine 10% *Co-Phenylcaine*	Semi-objective sensory testing in healthy volunteers, then RCT	Sprays then 5 min wait time	Healthy volunteers: VAS of perception of standardised painful stimulus RCT: FNE then VAS for pain	PNIF, acoustic rhinometry	Lowest pain scores at 9 min after receiving *Co-phenylcaine* spray in healthy volunteers. No significant difference in PNIF or overall discomfort between sprays in RCT.
Walshe et al. 2002[32]	cocaine 10% *Co-Phenylcaine*	Split-body randomised trial	Sprays (*Co-Phenylcaine*), pledgets (cocaine), 10 min wait time	Rigid endoscopy then 10-point scale for pain	Questionnaire for quality of view	No significant difference in overall discomfort or quality of view between preparations

RCT: randomised controlled trial. PNIF: peak nasal inspiratory flow. VAS: visual analogue scale. FNE: flexible nasendoscopy. *Co-Phenylcaine* contains 5% lignocaine and 0.5% phenylephrine.

Table continues on the next page

Study	Drugs tested	Study design	Method of application	Method of anaesthetic assessment	Method of decongestant assessment	Summary of findings
Sadek et al. 2001[40]	*Co-Phenylcaine* lignocaine 10% xylometazoline 0.1% no spray	RCT	Sprays then 10 min wait time	FNE then VAS for patient experiences	-	Overall discomfort was reduced only by the presence of a vasoconstrictor (mean VAS 21.54 without vasoconstrictor, 12.30 with vasoconstrictor, p = 0.02)
Leder et al. 1997[43]	tetracaine 2% ephedrine 3% saline with flavouring	RCT	Sprays then 1 min wait time	FNE then 5-point scale for discomfort	-	No significant difference in overall discomfort between sprays
Singh et al. 1997[42]	cocaine 5% saline	Split-body randomised trial	Sprays then 10 min wait time	FNE then 5-point scales for pain and gag	5-point scales for ease of endoscopy	No significant difference in overall discomfort between sprays. Ease of endoscopy comparable between cocaine and saline control.
Kasemsuwan et al. 1996[34]	cocaine 10% lignocaine 4% with adrenaline 1:1000	Split-body non-randomised trial	Sprays then 10 min wait time	FNE then discomfort rated mild/moderate/severe	Rhinomanometry	Equivalent comfort during nasendoscopy and reduction in nasal resistance with both sprays
Lennox et al. 1996[33]	cocaine 10% *Co-Phenylcaine*	RCT	Sprays then 15 min wait time	FNE then VAS for pain	PNIF	No significant difference in overall discomfort; equivalent increases in PNIF observed with each spray
Noorily et al. 1995[31]	lignocaine 2% with oxymetazoline 0.025% tetracaine 1% with oxymetazoline 0.05%	Semi-objective sensory testing in healthy volunteers	On pledgets for 10 min	Semmes-Weinstein monofilaments, VAS of perception of standardised painful stimulus	-	Significantly higher sensory thresholds and greater reduction in pain perception with tetracaine compared to lignocaine, at both 10 and 70 min following application.
Noorily et al. 1995[16]	cocaine 4% lignocaine 2% with oxymetazoline 0.025% tetracaine 1% with oxymetazoline 0.05%	Semi-objective sensory testing in healthy volunteers	On pledgets for 10 min	Semmes-Weinstein monofilaments, VAS of perception of standardised painful stimulus	-	Significantly higher sensory thresholds and greater reduction in pain perception with tetracaine compared to lignocaine and cocaine, at both 10 and 70 min following application.
Tarver et al. 1993[30]	cocaine 4% lignocaine 2% with oxymetazoline 0.025%	Semi-objective sensory testing in healthy volunteers	On pledgets for 10 min	Semmes-Weinstein monofilaments	Laser doppler	Greater reduction in pain perception at 50 min after application of lignocaine compared to cocaine; no significant difference at 10 min. No difference in sensory thresholds between preparations. Blood flow was reduced by around 40% with lignocaine-oxymetazoline, and around 20% with cocaine.
Campbell et al. 1992[29]	cocaine 6% lignocaine 4% with xylometazoline 0.1% saline	Semi-objective sensory testing in healthy volunteers	Sprays then 15 min wait time	10-point scale of perception of standardised painful stimulus	Rhinomanometry	Significant reductions in pinprick sensation and cross-sectional area compared to saline control but no significant difference between cocaine and lignocaine-xylometazoline
Wight et al. 1990[47]	cocaine 10% xylometazoline 0.1%	Randomised crossover trial	Solution applied to head of inferior turbinate	-	Rhinomanometry, laser doppler	Decrease in nasal resistance of 49% with xylometazoline compared to 14.5% with cocaine ($p < 0.005$). Reduction in blood flow by approximately 50% with xylometazoline and approximately 10% with cocaine at 15 minutes after application ($p < 0.001$)

Decongestants

Several studies have used objective techniques to compare decongestants. In those using laser doppler, xylometazoline 0.1% and oxymetazoline 0.025% gave greater reductions in nasal mucosal blood flow compared with up to 10% cocaine, with the difference reaching significance after 8 minutes and 3 minutes, respectively [30,47]. Using rhinomanometry, xylometazoline 0.1% is variably found to give equivalent or superior decongestion compared with up to 10% cocaine in terms of reductions in transnasal resistance and effective cross-sectional area [29,47]. Adrenaline 1:1000 and cocaine 10% were found to be equivalent [34]. When peak nasal inspiratory flows were measured, cocaine 10% and *Co-Phenylcaine* give equivalent decongestion at 5 min, but *Co-Phenylcaine* is superior at 15 min [3,33].

In the clinic setting, nasal preparation with cocaine 10%, *Co-Phenylcaine* and xylometazoline 0.1% were associated with equivalent ease of endoscopy and quality of endoscopic views when rated subjectively by clinicians [1,32]. When compared to nasal preparations without decongestant, *Co-Phenylcaine* is variably reported to provide equivalent or superior endoscopic views and ease of endoscopy [37,39,48].

Discussion

Previously published systematic reviews have concluded that there is insufficient evidence to justify the routine use of anaesthetic-decongestant nasal preparations prior to flexible nasendoscopy, acknowledging study heterogeneity and the consequent difficulty in undertaking meaningful meta-analysis [49–51]. That such research continues to be undertaken despite the literature generally indicating inefficacy of local anaesthetics would suggest a general agreement that nasal endoscopy may often be unpleasant for patients, as well as a collective desire to improve tolerability of this procedure.

There are multiple sources of heterogeneity between studies, including the specific preparations used and their concentrations, the mode of application (typically either sprayed or on pledgets), and the endoscopic stimulus. Rigid endoscopy may be more stimulating than flexible nasendoscopy, and there is wide variation within both rigid and flexible endoscopic examinations. For example, there is a marked difference in stimulus between flexible endoscopy with examination of multiple areas within the sinonasal cavity, and flexible endoscopic examination of the larynx in which the endoscope passes straight through the nasal passage [44]. It is difficult to draw meaningful conclusions from the published studies about anaesthetic efficacy as the type and strength of stimulus for which patients were rating their discomfort was not always described in detail.

From this review, it would appear that when the efficacy of topical anaesthetics using semi-objective measurements of mucosal sensation is tested, tetracaine is a more potent anaesthetic than lignocaine and cocaine. These results are consistent with the greater relative hydrophobicity and therefore potency of tetracaine over other local anaesthetics (Table 1). The non-superiority of cocaine as both an anaesthetic and a decongestant is borne out in studies with patients undergoing nasal endoscopy in the clinic. When assessed using objective measures of nasal mucosal vasoconstriction, cocaine appeared inferior to other decongestants, but all decongestants reviewed appear equivalent on subjective assessments of ease of endoscopy and quality of views obtained. Based on these results, cocaine should not have a role in the setting of office-based nasal endoscopy when safer preparations are more easily available. However, any recommendations about the use of cocaine and other anaesthetic-decongestant combinations for pre-operative nasal preparation are beyond the scope of this review.

In these studies, local anaesthetics generally improved patient comfort during endoscopy less than may be expected given their efficacy at causing mucosal anaesthesia. This may be because sensory testing isolates only one facet of the patient experience, but in most trials patients were asked to rate their overall comfort. Any unpleasant features of these nasal preparations, such as an unpleasant taste or pharyngeal numbness, may therefore negate any benefits [44].

Few studies have investigated the time to peak anaesthetic and decongestive effect for these preparations. As a result, clarity around how long we should wait after application of local anaesthetic prior to beginning endoscopy is limited. It is important in the setting of a busy otolaryngology clinic to ensure that enough time is allowed for topical anaesthetics to work.

Future research directions

The adoption of standardised methods of anaesthetic application, patterns of endoscopy, and careful patient selection would help improve future study designs. For example, testing sprays of anaesthetic-decongestant preparations in patients undergoing routine post-operative debridement following bilateral comprehensive functional endoscopic sinus surgery, with a standardised pattern of nasal instrumentation, may be more discriminatory as the sensory stimulus would be greater. Results may be more consistent due to the relatively standardised post-operative anatomy, and patients with inflamed mucosa are likely to show greater reductions in discomfort than those with normal tissue undergoing endoscopy [44].

Reducing the unpleasant tastes of many of these preparations, either by masking bad tastes or choosing inoffensive-tasting drugs, may improve the patient experience [44]. This may mean

choosing sprays with constituents like tetracaine and imidazoline derivatives rather than lignocaine, cocaine, or phenylephrine, all of which are bitter tasting [3,45,52]. Tetracaine-based topical anaesthesia is a rational choice based on its pharmacodynamics, and imidazoline-derived decongestants do not taste strongly and are generally well tolerated.

Finally, greater clarity is needed regarding time to peak anaesthetic and decongestant effect to determine the optimum time between applying sprays and beginning endoscopy.

Conclusion

There is currently no clear consensus regarding optimal sinonasal preparation prior to endoscopy in the clinic setting. This may be due to the wide heterogeneity in published studies with respect to methods by which topical preparations are applied and by which outcomes are measured, and importantly due to the lack of clarity around the extent of endoscopy and other instrumentation and therefore the sensory stimulus being rated by patients in clinical trials. The taste of anaesthetic-decongestant preparations has been identified as a significant contributor to overall unpleasantness of nasal endoscopy, and studies in which unpleasant tastes are masked or less offensive-tasting preparations are tested are likely to be of value. Future studies should focus on development of a local anaesthetic and decongestant preparation with minimal taste, maximal efficacy and minimal risk of adverse effects.

Authorship contribution

SH reviewed literature and drafted the manuscript. RK and RGD undertook manuscript revision.

Conflict of interest

None to disclose.

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