doi: 10.1111/j.1368-5031.2005.00476.x

Cophenylcaine spray vs. placebo in flexible nasendoscopy: a prospective double-blind randomised controlled trial

C. GEORGALAS,[1] G. SANDHU,[2] A. FROSH,[3] J. XENELLIS[4]

Department of Otolaryngology/Head and Neck Surgery,[1] Whipps Cross Hospital, Department of Otolaryngology/Head and Neck Surgery,[2] Charing Cross Hospital, London, Department of Otolaryngology/Head and Neck Surgery,[3] Lister Hospital, Stevenage, Hertfordshire, UK, Academic Department of Otolaryngology,[4] Ippokration University Hospital, Athens, Greece

SUMMARY

Practices vary across the UK on the use of topical preparation prior to flexible fibreoptic nasendoscopy. In this double-blind study, we randomised 98 patients to receive cophenylcaine or placebo nasal spray before flexible nasendoscopy. A visual analogue scale (1–100) was used to record pain, unpleasantness of taste and overall discomfort experienced. Overall, the procedure was associated with minimal pain and discomfort in both groups. There was no significant difference in pain or overall discomfort experienced between the two groups; however, the sensation of bad taste was significantly worse in the cophenylcaine group. In linear regression, factors that predicted the overall unpleasantness of the experience were primarily pain experienced and secondarily unpleasantness of taste. We conclude that the routine use of cophenylcaine for nasal preparation is not justified before flexible nasendoscopy.

Keywords: Anaesthesia; topical; endoscopy; nasal cavity; lignocaine (lidocaine); phenylcaine

INTRODUCTION

Traditionally, cocaine has been the drug of choice for the preparation of the nasal mucosa prior to instrumentation in the nasal cavity. Its excellent vasoconstrictive and anaesthetic properties have facilitated for many years the examination as well as surgery in the nose, providing improved quality of view for the surgeon as well as minimising patient discomfort. However, the use of cocaine in the UK has progressively decreased, as a result of concerns about its toxicity and narrow therapeutic margins, its side effects including euphoria and excitatory effects even at sub-toxic levels and the logistic problems created by the storage of a controlled drug. A combination of a local anaesthetic (lidocaine) and adrenergic vasoconstrictive (phenylephrine) in a ratio of 5 : 0.5 (cophenylcaine forte) has been introduced as an alternative. It is being increasingly used in the outpatient clinic as preparation for fibreoptic flexible endoscopy, although there are concerns in many departments about its efficacy and effectiveness, concerns that are even more pronounced in view of its costs. We undertook this study to examine in an unbiased, systematic way its effects compared to placebo (normal saline) on the overall discomfort experienced by fibreoptic nasendoscopy.

Correspondence to:
Christos Georgalas, MRCS DLO, Department of Otolaryngology, Southend Hospital, Westcliff-On-Sea SSO 0RY, UK
Email: cgeorgalas1@yahoo.co.uk

MATERIALS AND METHODS

After obtaining ethics committee approval for the protocol, we recruited a total of 100 volunteers about to undergo diagnostic nasendoscopy in the otolaryngology outpatients department. Two had to be excluded from the study because of poor English resulting in communication problems; informed consent was obtained from the remaining 98 patients who were included in the study. Forty-two were males and 56 were females, with ages ranging from 22 to 91 years. Patients were excluded if they had undergone the procedure before (so that their previous experience would not introduce bias to their responses), were pregnant or had known allergy to either phenylephrine or lidocaine.

Once recruited for this trial, the patients were randomly allocated, through the use of envelopes containing computer-generated random numbers, into one of the two study groups. Two identical vials labelled simply 'A' and 'B' were used for the administration of the cophenylcaine spray and placebo. A total of 51 patients were thus allocated to the first group and received cophenylcaine (lidocaine 5% with phenylephrine 0.5%) spray and 47 patients were allocated to the second group and received normal saline spray. Each patient received two puffs of the relevant spray to each nostril (a total of 260 μl per nostril) by a nurse 10 min prior to their endoscopy. The nurse administering the nasal spray, the patient and the doctor performing nasendoscopy were unaware of the type of spray used. In all cases, the tip of the instrument was de-misted with a sterile alcohol wipe and the 3.7 mm tip of the Olympus ENF P3 nasendoscope was passed through

the anatomically most-accommodating nostril. At the end of the consultation, the patient filled out a Visual Analogue Score Scale (VAS) from 0 to 100, commenting on taste unpleasantness, the pain experienced and the overall discomfort caused by the procedure. At the end of the study, the randomisation code was broken and the data on the spray administered became available.

The data were statistically analysed using SPSS 10.0 software. Success of randomisation regarding age and sex was assessed, and all variables were tested for normality, with normality plots and Kolmogorov–Smirnov testing. Normally distributed data were described with the use of means and standard deviations, while medians and range were used to describe nonparametric variables. Comparisons between nonparametric outcome variables were done after logarithmic transformation. Subsequently, multivariate linear regression was performed to assess for the presence of confounding factors and interactions.

RESULTS

Of the 98 patients included in the study, 42 were males and 56 were females, with a mean age of 50.7 (SD 16.2). Nineteen were males and 32 were females in the cophenylcaine group, while 23 were males and 24 were females in the placebo group ($p = 0.24$, Pearson Chi-square) (Table 1). The mean age in the placebo group was 55.2 (SD 15.8) vs. 46.5 (SD 15.5) in the cophenylcaine group, the difference being statistically significant ($t = -2.7$, $p = 0.007$) (Table 2). Although this did not invalidate our randomisation, it meant that we had to adjust our comparisons for age. The three main outcome variables were negatively skewed (i.e. the vast majority of patients recorded low levels of discomfort) and were logarithmically transformed. After this transformation, Kolmogorov–Smirnov testing and normality plots confirmed the normal distribution of the three newly generated variables (natural logarithms of taste, pain and overall discomfort score).

Univariate parametric analysis (*t*-test assuming equal variances for pain and overall discomfort and *t*-test with unequal variances for taste) showed no significant difference between the two groups in the overall unpleasantness of the procedure and pain, while it showed significantly increased discomfort related to taste unpleasantness in the cophenylcaine group ($t = 3.9$, $p < 0.001$) (Table 3). To better understand the comparisons, we include a table of median values of the main outcome variables for the two groups. (Figure 1).

Table 1 Demographic characteristics of study sample – gender

		Spray used		
		Cophenylcaine	*Saline*	*Total*
Sex	Male	19	23	42
	Female	32	24	56
Total		51	47	98

$p = 0.24$.

Table 2 Demographic characteristics of study sample – age

	Spray used	*n*	*Mean*	*Standard deviation*
Age	Saline	47	55.2	15.5
	Cophenylcaine	51	46.5	15.8

$p = 0.007$.

As mentioned earlier, although randomisation has been performed, the difference in age between the two groups was significant. This does not invalidate the randomisation; however, it makes it important that we adjust for age by performing linear regression.

We used age, sex and type of nasal preparation as predictors for the (logarithmic transformed) scores. It was shown that age or patient gender was not correlated with any of the three outcome variables, while the increased discomfort related to taste in the cophenylcaine group remained unchanged.

Finally, to explore patients' overall discomfort with procedure, we performed linear regression of the overall discomfort of the procedure and its possible predictor variables (age, sex, spray used, taste unpleasantness and pain). The final model showed a good fit ($R^2 = 0.57$, $p < 0.001$) and showed that 58% of the total variability in the overall discomfort experienced could be explained by two variables: Pain incurred during the procedure ($t = 7.6$, $p < 0.001$) and secondarily taste unpleasantness ($t = 6.1$, $p < 0.001$). Interestingly, the type of spray used ($p = 0.24$) as well as the patient age ($p = 0.16$) or gender ($p = 0.55$) were not correlated with the overall discomfort and were excluded from the final model.

DISCUSSION

One of the commonest minor invasive procedures performed in the otolaryngology outpatient clinic is nasendoscopy, having almost completely replaced the traditional laryngeal mirror. Many otolaryngologists, however, are concerned that it can be a significant source of discomfort for the patient and try to reduce this discomfort by the application of local anaesthetics: In the past, cocaine was the main local anaesthetic and vasoconstrictor agent used, but over the last years its use in the outpatient clinic has all but ceased. However, there are significant variations between the practices of different otolaryngology departments across the UK, with some consultants advocating the use of lidocaine or cophenylcaine or even otrivine prior to nasendoscopy and others maintaining that there is no need for any local agent. This difference in practice is hard to justify, more so in our present era of

Table 3 Independent samples test

				95% CI of the difference	
	df	*Significance (two-tailed)*	*Mean difference*	*Lower*	*Upper*
LN overall discomfort	93	0.290	–0.1980	–0.5710	0.1720
LN pain	93	0.812	–5.10E–02	–0.4990	0.3920
LN unpleasant taste	92	0.000	–0.7910	–1.1960	–0.3870

LN, natural logarithms.

limited resources and cost-effectiveness, where a clear evidence base is required to underlie our practice. The use of a local agent prior to nasendoscopy is not only associated with increased costs and clinic time but could have potential local or systemic side effects. In a study of 108,000 cases of cocaine use for submucous resection and rhinoplasty procedures, 291 mild side effects, 34 severe side effects and five deaths were reported (1). Cophenylcaine nasal spray appears to be a safer alternative (2); however, the possibility of systemic effects cannot be completely excluded.

Singh et al. (3) in a double-blind randomised trial compared the proportion of patients having significant pain or gagging reflex following preparation of the nose with cocaine vs. placebo. He showed that there was no indication for the routine use of cocaine prior to nasendoscopy and also demonstrated that the presence of a deviated nasal septum did not dictate its use. A study by Frosh et al. in 1998 compared the discomfort incurred by the use of local lidocaine with the use of placebo or no spray prior to nasendoscopy and concluded that lidocaine was associated with significantly more pain and overall discomfort than placebo or no spray (4). The effects of cophenylcaine and cocaine on nasal patency (measured through nasal inspiratory peak flow) and pain were compared in another study (5). This showed increased vasoconstrictive effect of cophenylcaine as compared with cocaine but equal local anaesthetic potency.

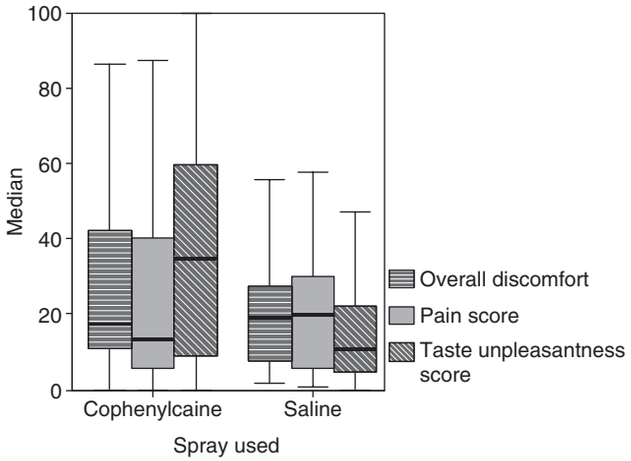

Figure 1 Overall discomfort, pain and taste unpleasantness score in cophenylcaine and normal saline groups

Finally, two studies have compared the use of cophenylcaine with placebo. A recent study (6) examined the overall ease of examination as well as the pain and overall discomfort in 90 patients and concluded (although the use of mean values for the description of nonparametric data makes the interpretation problematic) that there is no difference in pain or overall discomfort between cophenylcaine and placebo. An earlier trial by Sadek et al. (7) compared four groups (local anaesthetic ± vasoconstrictive agent) in a balanced, two-way factorial design. In that study, it was concluded that only vasoconstriction had a limited effect (0.8 in a 10-point scale) in reducing overall discomfort. What is striking in all these studies, including our own, are the quite low levels of discomfort associated with flexible nasendoscopy that ranged from 0.3 (7) to 1.2–2.2 (5,6) in a 10-point scale, explaining thus the very limited efficacy and the need for topical anaesthetic.

Our study confirms that the use of the anaesthetic/vasoconstrictive agent such as cophenylcaine prior to nasendoscopy is not superior to placebo in terms of decreased pain, and, in the contrary, by producing an unpleasant taste sensation, it may actually add to the overall discomfort of the procedure. However, it must be kept in mind that the normal saline spray used as a placebo could have had a limited effect on the overall unpleasantness of the procedure, by acting as a lubricant and facilitating the introduction of the nasendoscope. However, its use was unavoidable if we wanted to perform a really blinded trial. Overall, we feel the lack of efficacy, and the cost and potential side effects of cophenylcaine suggest that, in the majority of cases, the routine use of cophenylcaine prior to fibreoptic nasendoscopy is not justified.

REFERENCES

1 Feehan HF, Mancusi-Ungaro A. The use of cocaine as a topical anesthetic in nasal surgery. A survey report. *Plast Reconstr Surg* 1976; **57**: 62–5.
2 Myers MG, Iazzetta JJ. Intranasally administered phenylephrine and blood pressure. *Can Med Assoc J* 1982; **127**: 365–8.
3 Singh V, Brockbank MJ, Todd GB. Flexible transnasal endoscopy: Is local anesthetic necessary? *J Laryngol Otol* 1997; **111**: 616–8.

4 Frosh AC, Jayaraj S, Porter G, Almeyda J. Is local anaesthesia beneficial in flexible fibreoptic nasendoscopy? *Clin Otolaryngol* 1998; **23**: 259–62.
5 Lennox P, Hern J, Birchall M, Lund V. Local anaesthesia in flexible nasendoscopy. A comparison between cocaine and co-phenylcaine. *J Laryngol Otol* 1996; **110**: 540–2.
6 Cain AJ, Murray DP, Mcclymont LG. The use of topical nasal anaesthesia before flexible nasendoscopy: a double blind, randomized controlled trial comparing cophenylcaine with placebo. *Clin Otolaryngol* 2002; **27**: 485–8.
7 Sadek SAA, De R, Scott A, White AP, Wilson PS, Carlin WV. The efficacy of topical anesthesia in flexible nasendoscopy: a double blind randomized controlled trial. *Clin Otolaryngol* 2001; **26**: 25–8.

Paper received September 2004, accepted November 2004