A randomised controlled trial assessing the efficacy of co-phenylcaine nasal spray in flexible transnasal pharyngolaryngoscopy

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ABSTRACT

INTRODUCTION The aim of this study was to assess whether using co-phenylcaine nasal spray before flexible transnasal pharyngolaryngoscopy results in reduced pain and discomfort during the procedure.

METHODS This was a randomised controlled trial. Eighty-four patients were randomised to receive either co-phenylcaine nasal spray or placebo nasal spray before performing transnasal flexible pharyngolaryngoscopy. Patient reported outcome measures included pain, discomfort, unpleasantness and willingness to repeat the procedure while clinician reported outcome measures comprised ease of examination and quality of view obtained during the procedure.

RESULTS There was no statistically significant difference in scores for pain, discomfort, unpleasantness and willingness to repeat the procedure between the co-phenylcaine and placebo groups. On the other hand, ease of examination scores were significantly better for the co-phenylcaine group than for the placebo group.

CONCLUSIONS The majority of patients do not find flexible pharyngolaryngoscopy unpleasant or painful with or without topical nasal anaesthesia. However, the spray does appear to help the examiner in completing a satisfactory assessment.

KEYWORDS

Endoscopy – Topical anaesthesia – Nasal cavity – Randomised controlled trial

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Flexible transnasal pharyngolaryngoscopy (NPL) is one of the most common procedures in otolaryngology performed in both outpatient and ward settings. Although NPL is safe and straightforward, it is often uncomfortable and sometimes intolerable. A small proportion of patients may also refuse to allow the procedure to be repeated.

The efficacy of topical anaesthesia before NPL remains controversial. Two studies published in 2008 (a meta-analysis)¹ and 2011 (a Cochrane review)² did not find any evidence to support the use of topical treatment before flexible nasal endoscopy. However, the majority of the studies included in the Cochrane review were impaired by small sample sizes and poor data reporting, and failed to address significant confounding variables. The authors concluded that further randomised controlled trials should be performed and that the trials should follow the recommendations of the CONSORT (Consolidated Standards of Reporting Trials) statement³ in order to ensure that reporting is clear, that the methods can be properly assessed and that the data are in a form that can be used in meta-analysis.

There have also been two recently published randomised controlled trials, which have shown a significant reduction

in the discomfort associated with flexible nasal endoscopic examination after using topical lidocaine spray with Listerine[®] mouthwash (Johnson & Johnson, New Brunswick, NJ, US).^{4,5} Furthermore, our personal experiences indicate that there are still variations in practice within and between ear, nose and throat (ENT) departments across the UK. We therefore conducted a double blind randomised controlled trial to assess whether preparation of the nose prior to NPL is effective.

Methods

A parallel randomised controlled trial was conducted at a district general hospital in August 2014. Allocation of the participants was carried out using a computer generated list of random numbers (<http://www.sealedenvelope.com/>). Participants were stratified with 1:1 allocation using block sizes of 4, 6 and 8. For this trial, co-phenylcaine (5% lidocaine and 0.5% phenylephrine) topical nasal spray (Aurum Pharmaceuticals, Brentwood, UK) was chosen as the investigative medicine as it is one of the most commonly used and readily available nasal sprays in ENT departments in the UK. The

co-phenylcaine spray and placebo spray were prepared in identical bottles, numbered consecutively for each patient according to the randomisation schedule. One of the research coordinators who was not involved in the enrolment, randomisation, intervention administration or examination undertook the preparation of the sprays.

Blinding

This was a double blind study. The allocation sequence was concealed from the rest of the research team in sequentially numbered, opaque and sealed envelopes. All the NPLs were performed by a single clinician who was not involved in the randomisation process.

Participants

Patients over the age of 16 years undergoing NPL as part of their routine clinical assessment in an ENT outpatient clinic were invited to participate in the study. By definition, NPL included assessment of the postnasal space, base of tongue, vallecula, pyriform fossae and larynx. Exclusion criteria comprised pregnancy, allergy or sensitivity to co-phenylcaine and patients who had undergone NPL previously as their earlier experiences could have biased their assessment.

Interventions

Patients were assigned randomly to receive two puffs of co-phenylcaine topical nasal spray or placebo nasal spray (normal saline) into each nostril ten minutes before the examination. The drugs were delivered using a pump dispenser, with a dose volume of 150µl in each spray. In the co-phenylcaine group, each spray was equivalent to 6.5mg of lidocaine hydrochloride and 0.65mg of phenylephrine hydrochloride.

An ENT trainee not involved in the NPL examinations carried out administration of the nasal sprays. Two sprays were directed posteriorly along the floor of the nasal cavity towards the inferior turbinate and nasopharynx. If the spray malfunctioned and no solution was administered, the area was sprayed a second time. All examinations were performed within 15 minutes of spray application. In all cases, the tip of the endoscope was demisted with a sterile alcohol wipe before inserting it into the most accommodating nostril. All endoscopic examinations were conducted using a 3.5mm flexible rhinolaryngoscope (Karl Storz, Tuttlingen, Germany).

Outcome measures

The patient-reported outcome measures were pain, discomfort, unpleasantness, and willingness to repeat the procedure. For pain, patients were instructed report on the actual pain they experienced during the procedure. In contrast to this, for discomfort patients were instructed to rate their discomfort based on all negative sensations they experienced during the examination. For unpleasantness, patients were asked to also report on their experience with the nasal spray. The clinician performing the NPL was asked to record the ease of examination and quality of view obtained during the procedure.

Patients and clinicians reported each outcome on 100mm Visual Analogue Scales (VAS).

Sample size

Based on previously published trials,^{1,4,6} a sample size calculation was performed to determine the minimum sample required to detect differences in patient reported pain and discomfort. Based on this data, this study required a minimum of 42 patients in each group to achieve the desired power of 90% at an alpha of 0.05.

Statistical analysis

All outcome measures were tested for normal distribution with normality plots and the Kolmogorov-Smirnov test. As all the data obtained were skewed and not normally distributed, the non-parametric Mann-Whitney U test was used to compare treatment and control groups for all outcome measures. Analysis was performed on an intention-to-treat basis. After applying the Bonferroni correction for the four patient reported outcome measures, statistical significance was defined as $p < 0.0125$.

Ethical considerations

All patients recruited in this trial were informed that the use of a topical local anaesthetic spray for flexible NPL was controversial but that there have been some published trial results indicating that it may reduce discomfort. Only patients who gave informed consent and required a NPL examination based on standard clinical indications were eligible to participate in the study. The study was approved by the local research ethics committee and conducted in accordance with the Declaration of Helsinki.

Results

A total of 93 patients were invited for inclusion in the study. Nine patients refused to participate: six preferred to have the local anaesthetic spray and three did not want to take part in the study at all (Fig 1). As a result, 84 patients (31 men, 53 women) were included in the analysis. Of the 42 patients in the co-phenylcaine group, 16 were men and 26 were women while the 42 patients in the placebo group comprised 15 men and 27 women. There was no significant difference in the sex ratio between the groups ($p=1.00$, chi-squared test). The overall age range was 20–86 years (mean: 56.6 years). The mean age in the co-phenylcaine group was 58.1 years compared with 55.1 years for the placebo group ($p=0.38$).

All randomised patients completed the study protocol and there were no missing data. No adverse events occurred during the trial.

Patient reported outcome measures

Patients completed the VAS for pain, discomfort, unpleasantness and willingness to repeat the procedure (Fig 2). There was no statistically significant difference in median pain scores between the co-phenylcaine group (2.0mm, 95% confidence interval CI: 0.0–5.0) and the placebo group (7.0mm, 95% CI: 2.0–14.0) ($p=0.048$). There was also no significant reduction in discomfort in the co-phenylcaine group

(median: 6.5mm, 95% CI: 4.0–10.0) compared with the placebo group (median: 10.0mm, 95% CI: 5.0–16.0) ($p=0.19$).

Furthermore, there was no difference in unpleasantness associated with the whole procedure, including the experience of the nasal spray itself, between the co-phenylcaine group (median: 8.5mm, 95% CI: 3.0–15.0) and the placebo group (median: 12.0mm, 95% CI: 5.0–15.0) ($p=0.62$). In terms of the patients' willingness to repeat the procedure, there was also no significant difference between the co-phenylcaine group (median: 98.0mm, 95% CI: 92.0–100.0) and the placebo group (median: 97.5mm, 95% CI: 93.0–100.0) ($p=0.80$).

Clinician reported outcome measures

The clinician performing the NPL completed the VAS for ease of examination and quality of view obtained during the

procedure (Fig 3). The median score for ease of examination was significantly better for the co-phenylcaine group (median: 100.0mm, 95% CI: 98.0–100.0) than for the placebo group (median: 84.5mm, 95% CI: 75.0–96.0) ($p<0.0001$). Scores for quality of view obtained during examination were also better for the co-phenylcaine group (median: 100.0mm, 95% CI: 99.0–100.0) than for the placebo group (median: 98.0mm, 95% CI: 91.0–99.0). Despite not being clinically significant, this difference was nevertheless statistically significant ($p=0.0016$).

Discussion

The use of topical anaesthesia before NPL continues to be a frequently discussed topic in many ENT clinics, and there still appears to be variation in practice in the use of topical

Figure 2 Median visual analogue scale (VAS) scores for patient reported outcome measures with 95% confidence intervals

local anaesthetic and vasoconstrictor sprays before performing flexible NPL. Many patients find NPL uncomfortable and this occasionally results in refusal to repeat the procedure. On the other hand, the use of a local anaesthetic spray prior to NPL is associated with increased costs, time, possible local or systemic side effects and unpleasant experiences from the use of the spray itself.⁷

Our study has shown that using a local anaesthetic/vasoconstrictor nasal spray before performing NPL does not confer any significant benefit in reducing patient pain, discomfort or unpleasantness during the procedure. Similar results have been obtained in other trials comparing local anaesthetic sprays with a placebo spray and/or no nasal preparations^{6,8,9} but in most of these studies, other confounding variables were also present, such as the use of lubricant gel and multiple examiners involved in performing the NPL.

A trial by Frosh *et al* found that the pain of nasoendoscopy was worsened by using a local anaesthetic spray.¹⁰ Their study, however, used Xylocaine spray (lidocaine), which is commonly observed to cause nasal discomfort.⁹ In another trial by Bonaparte *et al*, pain scores were significantly reduced with local anaesthetic spray in patients with an inflammatory disorder of the nasal cavity compared to those without an inflammatory condition. However, in this trial all patients underwent extended or full bilateral nasal examination, which differs from the pharyngo-laryngeal examination in our study. The patients in the study by Bonaparte *et al* also performed an oral rinse with Listerine® to mask the negative flavour of the nasal spray. One can argue that although Listerine® mouthwash can help offset the adverse effects of the nasal spray, it is unlikely to play a role in reducing pain during the NPL itself.

Discomfort differs from pain in that it quantifies any other negative sensations associated with the procedure. Similar to our findings, other trials have shown that using a topical nasal spray does not reduce the severity of discomfort during NPL.^{6,9,11} One of these studies, however, used sheaths, which increase the diameter of the endoscope, and also a one-minute interval between the spray and examination, which is insufficient for topical local anaesthesia to reach maximum effect.¹¹ The only trials that have shown significant reduction in discomfort were the two studies performed by Bonaparte *et al*.^{4,5} As both of these also included use of a Listerine® oral rinse before performing NPL, the improved scores for discomfort could be attributed to the effect of the mouthwash rinse offsetting the overall bad taste of the nasal spray.

Local anaesthesia can produce unwanted side effects. These include reduced sensitivity of the oropharynx and pharynx (which can affect the safety of swallowing, choking and gagging sensations) along with the remote possibility of hypersensitivity reactions.^{8,11} Another common side effect is the unpleasant taste. This sensation can be very bothersome for the patient and may on its own result in refusal of anaesthetic spray before the examination. In a study by Sadek *et al*, local anaesthetic spray was associated with an increased perception of unpleasant taste, with patients in the co-phenylcaine group having the highest scores.⁸ In another study by Georgalas *et al*, unpleasantness of taste was also significantly increased for the co-phenylcaine group.⁶

In our study when patients were asked to report on their unpleasantness feeling with the procedure including their experience with the spray itself, there was no significant difference seen between both groups. No patients had any choking or gagging sensations and there were no allergic reactions to the nasal spray. This suggests that most of the

patients in our trial did not feel that the local anaesthetic spray had an adverse effect on them. Furthermore, when patients in each group were asked whether they were willing to repeat the procedure, there was again no significant difference between the groups.

Some other studies have also reported on the effect of local anaesthetic nasal spray on ease of examination.^{9,12} In our study, a significant difference was seen with the clinician finding the examination easier in patients who received the co-phenylcaine spray. This is at odds with the results of Cain *et al*, where there was no significant difference in this outcome measures.⁹ Singh *et al* also reported comparable scores in terms of ease of procedure for both the local anaesthetic and the placebo groups.¹² The high scores in our study for ease of examination and quality of view could be due to a combination of a single experienced clinician performing all the examinations and the passage of the scope through the most accommodating nostril. They may also be a consequence of the vasoconstrictor decongestant component of the spray rather than the local anaesthetic.

Study limitations

This study assessed the potential benefits of topical medication in flexible endoscopy of the pharynx and larynx rather than detailed nasal examination. Patients with inflammatory disorders of the nasal cavity may derive more benefit from the use of a local anaesthetic spray before NPL than has been demonstrated here.

In order to conduct a double blind study, a placebo nasal spray was used for the control group. Other adjuncts such as lubrication with gel or water were not compared.

Comparison of co-phenylcaine with no medication at all might have produced more obvious differences in outcome measures. In addition, some of the differences that were observed might have resulted from the phenylephrine rather than from the lidocaine in the co-phenylcaine spray.

Only one experienced clinician performed all the NPLs in this study. It is possible that less experienced clinicians might benefit more from the effects of local anaesthesia and the results of this study are not necessarily generalisable to all endoscopists.

Conclusions

Despite the concerns many clinicians have about subjecting patients to uncomfortable procedures, it appears that the majority of patients do not find flexible pharyngolaryngoscopy unpleasant or painful regardless of whether any topical nasal anaesthesia is used. However, the spray has been shown to help the examiner in completing a satisfactory assessment. We would recommend that junior doctors with less experience of flexible endoscopy consider the use of local anaesthetic decongestant spray. Future studies could address the question of whether a decongestant spray used alone improves ease of examination for the clinician without the unpleasant side effects of local anaesthesia for the patient.

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