Intranasal Topical Local Anesthetic and Decongestant for Flexible Nasendoscopy in Children
A Randomized, Double-blind, Placebo-Controlled Trial

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IMPORTANCE To our knowledge, the present study is the first double-blind, randomized, placebo-controlled trial in children to compare nasal preparation sprays administered before flexible nasendoscopy with placebo.

OBJECTIVE To compare the degree of pain experienced by children undergoing flexible nasendoscopy after 1 of 3 intranasal sprays: placebo, decongestant with topical local anesthetic (TLA), or decongestant without TLA.

DESIGN, SETTING, AND PARTICIPANTS A randomized placebo-controlled trial with blinding of participants, caregivers, observers, and otolaryngologists was conducted in a tertiary pediatric otolaryngology ambulatory clinic. Participants included a consecutive sample of children aged 3 to 12 years requiring flexible nasendoscopy. Exclusion criteria included concomitant respiratory tract infection, known allergy to a trial agent, or previous flexible nasendoscopy. One hundred fifty-one children were assessed for eligibility; 24 eligible children refused participation and 69 were included and block-randomized. All completed the study, and there were no adverse events.

INTERVENTIONS Nasal spray administration of placebo (normal saline); xylometazoline hydrochloride, 0.05% (decongestant); or lidocaine hydrochloride, 1%, with xylometazoline hydrochloride, 0.05% (TLA with decongestant) was performed 10 minutes before flexible nasendoscopy.

MAIN OUTCOMES AND MEASURES Primary outcome measure was the child-reported Wong-Baker Faces Pain (WBFP) scale. Secondary outcomes included the caregiver-proxy WBFP scale; the Face, Legs, Activity, Cry, and Consolability (FLACC) scale; and the physician-reported Difficulty of Procedure Visual Analog Scale (DPVAS).

RESULTS Twenty-three children were recruited in each of the intervention arms. Baseline characteristics were comparable between groups. The mean child-rated WBFP scale scores were 2.4, 1.8, and 2.2 for the placebo, decongestant, and TLA with decongestant groups, respectively (P = .45). Although the finding was statistically nonsignificant, decongestant had the lowest mean caregiver-proxy WBFP scale score, lowest observer-rated FLACC scale score, and highest physician-rated DPVAS score. Subgroup analysis did not demonstrate any correlation between the outcomes and age or sex.

CONCLUSIONS AND RELEVANCE This study revealed no statistically significant difference in the discomfort experienced by children undergoing flexible nasendoscopy after placebo, decongestant, or TLA with decongestant. Decongestant was associated with the least discomfort (on child, caregiver, and observer-rated pain scale scores) and the lowest rating for difficulty of procedure. With these findings, the study suggests that there is no significant benefit of topical decongestant with or without TLA compared with placebo in reducing pain associated with pediatric flexible nasendoscopy.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01351298

Published online October 24, 2013.

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Flexible nasendoscopy is a minimally invasive diagnostic procedure that involves passing a thin fiberoptic endoscope through the nasal cavity. Otolaryngologists frequently require this procedure in the complete assessment of pediatric outpatients. Children who have nasal or breathing symptoms (eg, sleep-disordered breathing and nasal discharge) may have an abnormality anywhere from the anterior nasal cavity (eg, allergy and nasal polyps) to the posterior nasal cavity or nasopharynx (eg, adenoid hypertrophy and nasopharyngeal tumor). For more than 2 decades, flexible nasendoscopy has been considered to be the criterion standard method for assessment of the posterior nasal cavity and nasopharynx in children.1

To attempt to minimize discomfort, many otolaryngologists administer an intranasal spray before the procedure, usually consisting of either a decongestant or a decongestant combined with topical local anesthetic (TLA). There is currently clinical equipoise as to whether these sprays are warranted in children. The theoretical benefits of decongestant and TLA are a reduction of resistance to flexible nasendoscopy passage and reduced sensation, respectively. However, the actual benefit to the child is unclear. In an uncontrolled study2 of pain perception after decongestant and TLA, children reported moderate pain during the nasendoscopy. The only randomized clinical study3 to compare nasal sprays before nasendoscopy in children determined no significant difference in discomfort between children who received decongestant and those who received decongestant combined with TLA. However, a placebo group was not included, and only proxy measures of discomfort were used.

In adults, there have been inconsistent results from studies of nasal sprays before flexible nasendoscopy. One adult randomized clinical trial4 showed that using TLA made the nasendoscopy experience worse than using a placebo normal saline spray.

To our knowledge, the present study was the first randomized placebo-controlled trial to systematically investigate the potential benefit of using topical decongestant alone or topical decongestant with TLA before pediatric flexible nasendoscopy.

**Methods**

A parallel, randomized, 3-arm, double-blind, placebo-controlled superiority trial was conducted at the pediatric otolaryngology ambulatory clinic at the British Columbia Children’s Hospital after research and ethics board approval. Children aged 3 to 12 years who were determined by the treating pediatric otolaryngologist to require a flexible nasendoscopy during their clinical assessment were offered participation in the study. Exclusion criteria included concomitant respiratory tract infection, known allergy to a trial agent, and previous flexible nasendoscopy. Potential participants and their caregivers received a detailed explanation of the study from a research assistant, and fully informed consent and assent (where applicable) were obtained before participation. Participants were randomized in blocks of 3 to one of the 3 intranasal spray solutions using a pregenerated random number table. The 3 preparations were: (1) sodium chloride, 0.9% (normal saline), solution (placebo, group A); (2) xylometazoline hydrochloride, 0.05% (equal volumes of xylometazoline hydrochloride, 0.1%, and normal saline solution) (decongestant, group B); and (3) xylometazoline hydrochloride, 0.05%, with lidocaine hydrochloride, 1% (equal volumes of xylometazoline hydrochloride, 0.1%, and lidocaine hydrochloride, 2%, solution) (decongestant with TLA, group C). Administration of the test solution was performed by a nurse practitioner behind closed doors using a pharmacy-coded labeled bottle. The otolaryngologist, independent observer, caregiver, and child were blinded to the intervention group. The nurse practitioner was aware of the code of the spray used for the participants (A, B, or C) but not of the identity of the spray. Only the hospital pharmacy was aware of the spray identity.

Each patient received 0.5 mL of the solution in each nostril 10 minutes before nasendoscopy. The child was asked not to comment on the taste of the agent, both during the explanation of the study and again during administration of the spray. The nasal preparation was administered using a mucosal administration device, which has the advantage of administering a consistent dosage and volume in the form of a fine mistlike spray, thereby targeting the desired mucosal region of the nasal cavity.

After administration of the solution, the child and caregiver were transferred to the endoscopy clinic room, and the otolaryngologist explained the procedure to them. All endoscopies were performed by an experienced fellowship-trained attending pediatric otolaryngologist. The equipment was shown to the child, who was subsequently encouraged to touch the tip of the endoscope to become familiar with it. The image of the child’s finger and face were then displayed on the endoscopy video monitor for the child to see. The child was then given a choice to sit on his or her own or on the caregiver’s lap. To ensure that the child could not move during the procedure, an assistant or the caregiver was asked to help support the child’s head on either side. A 2.4-mm flexible fiberoptic nasendoscope (ENT-4500; Vision-Sciences Inc) was slowly introduced into one of the nostrils and carefully advanced to the nasopharynx. The image was projected onto a video monitor and could be followed by the child, caregiver, and otolaryngologist.

**Outcome Measures**

The primary outcome measure was the self-reported Wong-Baker Faces Pain (WBFP) scale,5 a validated, long-established, non–procedure-specific scoring system for pain in children using cartoon faces in a Likert scale ranging from 0 (no hurt) to 5 (hurts worst).6 The secondary outcome measures were the caregiver-proxy WBFP scale; the Face, Legs, Activity, Cry, and Consolability (FLACC) scale,7 and the Difficulty of Procedure Visual Analog Scale (DPVAS).3 The FLACC scale requires an observer to assign a rating from 0 to 2, based on predetermined descriptors of behavior, for each of 5 domains (face, legs, activity, cry, and consolability) to determine a total pain score from 0 to 10.7 The DPVAS consisted of a visual analog scale based on a 100-mm line ranging from easiest to most difficult.
At the end of the procedure, the children rated the level of their discomfort using the WBFP scale. The caregiver rated the level of the child’s discomfort using the caregiver-proxy WBFP scale. The observer rated the level of discomfort using the FLACC scale. The pediatric otolaryngologist subjectively rated the difficulty of performing the flexible nasendoscopy with the DPVAS. Any adverse events were documented.

Sample Size Calculation
A sample size calculation was performed a priori to determine the required number of participants. The previously reported mean (SD) child-rated WBFP scale score or a comparable population was 2.74 (1.8).² We aimed to detect a reduction in this interval measure of 2. This was based on expert opinion consensus among the authors of an anticipated average improvement that would favor routine use of intranasal preparation over placebo, ie, a clinically relevant difference. We therefore calculated that we needed at least 22 children in each group to reject the null hypothesis that the population means of the experimental and control groups were equal with probability (power) of 0.90. The α value associated with this test of the null hypothesis was .017, giving an effective type I error probability across the three 2-sided comparisons of \( P = 0.05\). 

Statistical Analysis
Analysis of the primary outcome measure was performed using the analysis of variance test if the scores were normally distributed or the Kruskal-Wallis test if not normally distributed. Analyses of the secondary outcome measures were also performed using one of these tests depending on the data being parametric or nonparametric. Subgroup analysis involved a comparison of the treatment effect in boys vs girls using a test of statistical interaction between treatment and sex. Comparison of pain scores vs age of the participant was performed using the Pearson product moment correlation coefficient for normally distributed data or Spearman \( \rho \) correlation coefficient for nonnormally distributed data. All statistical analyses were performed using commercial software (STATA, version 10; StataCorp LP).

Results
Sixty-nine patients were successfully recruited between June 1, 2011, and April 30, 2012. Of 151 children undergoing flexible nasendoscopy who were initially considered, 58 individuals (38%) did not meet the inclusion criteria and 24 children (16%) declined to participate (Figure 1). The recruited children comprised 49 boys (71%) and 20 girls (29%), with a median age of 6 years (range, 3-12 years). All recruited children completed the study. Through block randomization, the number of children in each intervention group was equal (n = 23). There were no significant differences between baseline characteristics of the 3 groups (Table).

Mean child-rated WBFP scale scores, the primary outcome, were 2.4, 2.2, and 1.8 for the placebo, decongestant with TLA, and decongestant alone groups, respectively, with no statistically significant differences (\( P = .45\)). The decongestant group also had the lowest pain score on the mean caregiver-proxy WBFP scale score and the mean observer-rated FLACC scale score, although differences again were not statistically significant (\( P = .52 \) and \( P = .63 \) respectively). The mean physician-rated DPVAS rated the least difficult procedure as the decongestant group but again without statistical significance (\( P = .51\)). Subgroup analysis did not demonstrate any statistically significant interaction between the primary outcome or secondary outcome measures and participant age or sex. All correlations between the different outcome measures were significant (Figure 2). For example, a scatterplot demonstrates the statistically significant correlation between the child-rated and...
caregiver-rated WBFP scale scores (Figure 3), with a Pearson correlation coefficient of 0.68 (P < .001).

Discussion

The diagnostic procedure of flexible fiberoptic nasendoscopy often forms an essential component of the otolaryngologic assessment of a child.1 The theoretical benefit of preparing the nose with a decongestant is a reduction of resistance to flexible nasendoscope passage, making the procedure more comfortable; the theoretical benefit of TLA is reduced contact sensitivity and therefore reduced pain. However, the actual benefit to the child of either product has been unclear. The results of our study suggest that there is no clinically significant benefit to administering either a combination of these agents or decongestant alone in comparison with a normal saline spray. This correlation matrix demonstrates Pearson correlation coefficients for each cross-correlation between the study outcome measures. Significance of all correlations was P < .001. DPVAS indicates Difficulty of Procedure Visual Analog Scale; FLACC, Face, Legs, Activity, Cry, and Consolability; and WBFP, Wong-Baker Faces Pain.

One previous uncontrolled study2 of 23 children aged 4 to 18 years found that after spraying with decongestant (phenylephrine hydrochloride, 0.5%) combined with local anesthetic (lidocaine hydrochloride, 5%), children perceived moderate pain during flexible nasendoscopy. In that study, the mean child-rated WBFP scale score was 2.7, which is consistent with the scores in our study.

The only previous randomized clinical study3 attempting to test efficacy of nasal sprays preceding pediatric flexible nasendoscopy compared only decongestant alone (oxymetazoline hydrochloride, 0.05%) directly against decongestant with TLA (oxymetazoline, 0.05%, and lidocaine hydrochloride, 4%). That study included 53 children aged 5 to 10 years and used an observer-rated visual analog scale from 0 to 10 as the primary pain outcome measure. The observers reported scores of 4 for decongestant alone vs 4.3 for the decongestant and TLA combined, which were not statistically significantly different. Again, those scores are consistent with the scores in our

Table. Group Demographics and Mean Outcome Scores

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placeboa (n = 23)</th>
<th>Decongestantb (n = 23)</th>
<th>Decongestant With TLAc (n = 23)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, No. (%)</td>
<td>17 (74)</td>
<td>15 (65)</td>
<td>17 (74)</td>
<td>.56</td>
</tr>
<tr>
<td>Median age at study (range) [SD], y</td>
<td>6 (3-12) [2.8]</td>
<td>7 (4-12) [2.5]</td>
<td>6 (3-12) [2.2]</td>
<td>.56</td>
</tr>
<tr>
<td>Wong-Baker Faces Pain scale[1]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child-rated</td>
<td>2.4</td>
<td>1.8</td>
<td>2.2</td>
<td>.45</td>
</tr>
<tr>
<td>Parent/caregiver-rated</td>
<td>2.0</td>
<td>1.6</td>
<td>1.8</td>
<td>.52</td>
</tr>
<tr>
<td>Face, Legs, Activity, Cry, and Consolability scale[4]</td>
<td>4.2</td>
<td>3.3</td>
<td>3.6</td>
<td>.63</td>
</tr>
</tbody>
</table>

Abbreviation: TLA, topical local anesthetic.

* Normal saline.

** Xylometazoline hydrochloride, 0.05%.

† Lidocaine hydrochloride, 1%, with xylometazoline hydrochloride, 0.05%.

[1] Range, 0 to 5.
[3] Range, 0 to 10 (easiest, 0; most difficult, 10).

Figure 2. Correlation Matrix

This correlation matrix demonstrates Pearson correlation coefficients for each cross-correlation between the study outcome measures. Significance of all correlations was P < .001. DPVAS indicates Difficulty of Procedure Visual Analog Scale; FLACC, Face, Legs, Activity, Cry, and Consolability; and WBFP, Wong-Baker Faces Pain.

Figure 3. Scatterplot of Child vs Parent/Caregiver Wong-Baker Faces Pain (WBFP) Scale Score

This scatterplot includes the best-fit regression line of WBFP scale score as rated by the child vs parent/caregiver. Size of scatter points denotes frequency of duplicate data points.
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tive option to reduce self-reported discomfort; however, other reported the use of decongestant alone as being the most effective effect, the delay of 10 minutes between spray administering and reducing reporting bias. Although we cannot therefore support the use of decongestant alone as being the most effective option to reduce self-reported discomfort; however, other studies were unable to demonstrate a difference in discomfort or ease of examination from the operator’s perspective. An additional study suggested that the use of TLA spray alone compared with placebo made things worse through the unpleasant sensation it caused, which may have outlasted the procedure.

One potential limitation of the present study is that the active sprays were tested against normal saline as placebo as opposed to nothing. This was of course essential to facilitate blinding and reduce reporting bias. Although we cannot therefore rule out the possibility that the placebo spray had some beneficial effect, the delay of 10 minutes between spray administration and the nasendoscopy would be expected to make any nasal cavity lubrication or moisturizing effect of the normal saline spray very minimal. Another limitation of this study is the lack of testing for different flexible endoscope sizes. There are flexible nasendoscopes in use at other centers that are smaller or larger than the 2.4-mm diameter used in our study. With other nasendoscope diameters, different responses may have been seen to the nasal sprays investigated in the present study.

The placebo effect is an example of the powerful influence that psychological factors can have on pain perception, and recent studies have shown that placebo analgesia can have measurable effects on nociceptive processing, for example, in the spinal cord. The use of nonpharmacologic interventions, such as distraction techniques, has been shown to have the potential to reduce pain in children undergoing medical procedures, such as venipuncture. Although our study did not show any statistically significant or clinically significant benefit in using a nasal spray with decongestant or TLA with decongestant over placebo, we recognize that if offered a choice, some children or caregivers would still elect to have a nasal spray before nasendoscopy in the hope that this might reduce the associated discomfort. Based on the results of this study, in this circumstance, we suggest the use of a decongestant because this resulted in the most comfortable procedure independent of the rater.

In conclusion, this study revealed no statistically significant difference in the discomfort experienced by children undergoing flexible nasendoscopy after intranasal spray of placebo, decongestant, or TLA with decongestant. Decongestant spray was associated with the least discomfort (on child-rated, caregiver-rated, and observer-rated pain scores) and the lowest rating for difficulty of procedure by the nasendoscopist.

ARTICLE INFORMATION

Submitted for Publication: April 3, 2013; final revision received July 23, 2013; accepted August 19, 2013.


Author Contributions: Dr Chadha had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: All authors.

Acquisition of data: Chadha. Lam, Ludemann, Lam, Patsy Regan, RN

Analysis and interpretation of data: Chadha, Ludemann, Ziegler, Lam, Ludemann, Kozak.

Drafting of the manuscript: Chadha. Lam.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Chadha.

Obtained funding: Chadha, Kozak.

Administrative, technical, and material support: All authors.

Study supervision: Chadha.

Conflict of Interest Disclosures: None reported.

Previous Presentation: This study was presented at the American Society of Pediatric Otolaryngology Spring Meeting, April 27, 2013; Arlington, Virginia.

Additional Contributions: Patsy Regan, RN (pediatric otolaryngology nurse), and J. Paul Moxham, MD, FRCSC (pediatric otolaryngologist), contributed to data acquisition, and Rachelle (Dar Santos) Moslehgh, BSc, CCRP (clinical research coordinator), provided administrative, technical, and material support. There was no financial compensation for these contributions.

REFERENCES


