A comparison of cocaine, oxymetazoline, and saline for nasotracheal intubation

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Topical vasoconstrictive agents were compared to assess their effectiveness in decreasing the epistaxis associated with nasotracheal intubation. Cocaine, oxymetazoline, and a saline control were randomly administered by nasal spray in a double-blind study to 36 outpatients presenting for extraction of impacted molars. Twelve intubations were performed in each group. The incidence of epistaxis was recorded following each intubation before the start of the surgical procedure. The data were analyzed by Fisher's exact test for the presence or absence of epistaxis in each group. In each case there was no significant difference between the groups studied ($p > 0.05$).

Resulting data suggest that if vasoconstrictors are used, the selection of cocaine over the safer alternative oxymetazoline offers no significant advantage in decreasing epistaxis. These data also support previous findings which suggest that the addition of any vasoconstrictor does not significantly alter the incidence of epistaxis.

Cocaine is unique among local anesthetics in that it has additional property as a vasoconstrictor. This dual action has made it the most frequently recommended adjunct to nasotracheal intubation. The local anesthesia that it provides in an awake patient allows the intubation to be comfortable and tolerable. Cocaine also has been proposed to be beneficial during nasal intubation after the induction of general anesthesia, because it decreases the circulatory response to the passage of the tube. Vasoconstriction has been considered important to facilitate the insertion of the tube in both awake and asleep patients, and to decrease the incidence of trauma to tissues of the nasal passages. This effect was thought to occur due to the decongestive effect that vasoconstriction has on the nasal tissues, shrinking the mucosal tissues and increasing the internal diameter of the nasal passage.

Recently, however, the use of cocaine for nasotracheal intubation has been questioned due to several problems associated with its use. Among these problems are cocaine's potential for unpredictable toxic reactions, its many potential adverse drug interactions and its regulation as a narcotic due to its potential for diversion and illicit use. Additionally, the sympathomimetic properties of cocaine may predispose the patient to develop significant arrhythmias and may increase anesthetic requirements during general anesthesia, although research examining the former problem has yielded conflicting results. Patients with known succinylcholine sensitivities due to either genetic predisposition or the use of anticholinesterase medications...
have been shown to maintain significantly higher levels of cocaine in their plasma and thus are more likely to develop toxic reactions. This may explain why toxic reactions have been reported in patients with doses as low as 10 mg, while others have tolerated doses of more than 1000 mg.1

What has resulted is a search by many investigators for a safer alternative to cocaine for nasotracheal intubation. Recent studies have provided some surprising results, however, that not only question the continued use of cocaine for such purposes but also question the underlying benefit of including a local anesthetic and/or a vasoconstrictor in the preparation for an asleep nasotracheal intubation.5,10

This study was undertaken to compare the ability of cocaine, the alternative vasoconstrictor oxymetazoline, and saline in decreasing the incidence of epistaxis seen during nasotracheal intubation after the induction of general anesthesia.

Methods

A complete research proposal was submitted and approved by the New Britain General Hospital Human Experimentation and Research Committee prior to beginning this investigation.

The dose of cocaine employed was 100 mg in a 10% solution with sterile water. This represented a total volume of 1 ml, half of which (50 mg) was sprayed into each nostril of selected patients. A 0.5% solution of oxymetazoline (Afrin®) was used as a starting concentration. The recommended dosage for nasal decongestion is approximately 3 drops per nostril. A 0.2 ml measure of the solution, corresponding to approximately 7 drops or 0.01 mg, was diluted with 0.8 ml of sterile water. The result was a recommended dosage of oxymetazoline in a concentration which allowed for the same 1 ml volume as in the cocaine samples.

A double-blind study was constructed in which numbered vials contained the same volumes of unknown solutions. The pharmacy randomly numbered 36 vials which contained the unknown solutions: 12 of the vials contained the cocaine solution, 12 contained oxymetazoline, and 12 contained saline. Only the pharmacy knew the coded contents of each numbered vial. The code was not revealed until the completion of the study, but the agents used in the first 20 intubations were revealed early for preliminary data analysis to be presented at a seminar. For each selected patient, 0.5 ml of the assigned unknown solution was removed from the vial and sprayed into each nostril.

The subjects selected were all young, healthy, ASA class I adult patients presenting for extraction of impacted molars under general nasotracheal anesthesia. Each subject was screened preoperatively to rule out the presence of preexisting factors which might predispose to epistaxis, toxic reactions, or interactions with the agents used. The screening included both a predetermined set of questions and a brief nasal examination. Any patient who had one or more predisposing factors to epistaxis was not accepted for the study. For example, any patient who had taken aspirin within one week prior to the study was not included due to the possibility of aspirin-induced platelet dysfunction. Several patients with obviously deviated septa and others with nasal polyps were not included. Any patient with a systemic disease or who was taking medication which might interfere with the study or potentially result in adverse interactions was also not included.

Spraying was chosen as the method of administering the agents used in the study. After a review of the methods commonly used, it was determined to be the only method which would allow precise quantification of the delivered dose while at the same time ensuring consistently uniform dispersal. The spray device used was a modification of the Devilbiss® model 15 atomizer specifically designed for this study.11

Administration of the agents was performed by an individual other than the intubator. The intubator was not present in order to prevent inadvertent identification of the unknown agent by subjective patient reports. For example, it was felt that those patients administered the cocaine might report, unsolicited, a numbness in their upper airway due to the unique anesthetic effects of the agent.

All the subjects were ambulatory or day care patients and did not receive any preoperative medication prior to arriving in the operating room. A standard induction sequence which emphasized typical pharmacologic preparation was selected. Each patient received 0.2 mg of glycopyrrolate to control the incidence of bradycardia during the induction. Following this, 50 to 100 µg of fentanyl were administered intravenously to decrease the circulatory response to the intubation.

A 3 mg defasciculating dose of d-Tubocurarine was given 3 minutes prior to induction to prevent muscle fasciculations and postoperative muscle soreness following the administration of succinylcholine. Anesthesia was induced with a 3 to 5 mg/kg dose of thiopental followed by 1.5 mg/kg dose of succinylcholine to facilitate laryngoscopy and
intubation. After a waiting period of about 1.5 minutes, the selected nasotracheal tube was then inserted into the selected nostril as described below.

The tube selected for this study was the Rusch® red rubber cuffed nasotracheal tube. Three different tubes are used currently in the authors' clinical setting, each with some slight differences in characteristics such as external versus internal diameters, shape, pliability, and softness of the construction material. There are a few other tube types which can be used either nasally or orally that are also clinically available. It was determined, following a preliminary examination of the characteristics of available tubes for nasal intubation, that the Rusch® tube selected offered several advantages.

One of the most difficult factors to control in a study involving the trauma of nasotracheal intubation is the appropriateness of tube size selection. Individual variations in anatomy do occur and the sex, size, and external nasal characteristics of the patient are frequently taken into account when selecting a particular size nasotracheal tube. For this study, a size 6.0 or 6.5 mm internal diameter tube could be selected for females and a 6.5 or 7.0 mm internal diameter tube could be selected for males. By allowing this range of tube sizes it was hoped that the tube size could be more appropriately matched to the patient and that the selection of an inappropriately sized tube for any given patient would be minimized. Tube size represents the least controllable factor of any study in this area and is one of the most important limitations to the results obtained. It was felt that allowing such a range of tube sizes offered the best control over this factor.

A scale was used to record the incidence of epistaxis. If no blood was noted, the words "Epistaxis: None" were recorded. If there was visible blood which was only enough to coat the inside of the 14 french suction catheter prior to the trap, the

<table>
<thead>
<tr>
<th>Table I</th>
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<td>Summary of double-blind comparison of the effects of intranasally applied cocaine, oxymetazoline, and saline on the incidence of epistaxis during asleep nasotracheal intubations.</td>
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<table>
<thead>
<tr>
<th>Agent</th>
<th>n-total</th>
<th>No blood</th>
<th>Epistaxis</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Trace</td>
<td></td>
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<tr>
<td>Trace</td>
<td>Measurable/amount</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>12</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>O</td>
<td>12</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>S</td>
<td>12</td>
<td>6</td>
<td>3</td>
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C = Cocaine, O = Oxymetazoline, S = Saline

Both trace and measurable occurrences of epistaxis were combined for statistical analysis of data. The incidence of epistaxis versus no blood was then compared for each group using Fisher's Exact Test.
words “Epistaxis: Trace” were recorded. If enough blood was present to be suctioned into the trap, the words “Epistaxis: Measurable” were recorded and the amount in milliliters was measured on the calibrated side of the clear suction trap and noted. In only five cases was there enough blood to measure, averaging about 2 ml for these particular patients. For this reason the “Trace” and “Measurable” occurrences were grouped together and compared to those intubations in which there was no occurrence of epistaxis.

Once the result was recorded, the study was completed for that patient and anesthetic management and surgery progressed according to the dictates of the nurse anesthetist, anesthesiologist, and surgeon.

Results

Table I illustrates the grouping of the data prior to statistical analysis. Both “Trace” and “Measurable” occurrences of epistaxis were grouped together and compared to the occurrences of no epistaxis for each agent. Fisher’s Exact Test was utilized to test for significant differences between the three groups.

Table II illustrates the results of statistical analysis of the data. A p value of less than 0.05 was considered significant. Comparison of the three groups indicated no significant differences in the incidence of epistaxis during asleep nasotracheal intubations when either cocaine, oxymetazoline, or saline was used.

Discussion

The results of this investigation were not foreseen when the study was first conceived and undertaken. At that time there were no reports of previous studies specifically involving the use of vasoconstrictors during nasotracheal intubation, and the related research tended to suggest that vasoconstrictors were beneficial. Computed tomograms of the upper airway before and after application of vasoactive substances had vividly and graphically demonstrated the effects on the nasal mucosa.

Application of a vasodilator closed off the nasal passages completely, primarily by forward and medial expansion of the turbinates and surrounding tissues. Application of a vasoconstrictor caused just the reverse to occur, with significant increases in intranasal diameters as the tissues became decongested.

This information, as well as results disclosed in other related studies, contributed to the belief held by many clinicians that vasoconstrictive agents decrease the incidence of epistaxis and related complications during nasotracheal intubation. For the reasons just described, cocaine had enjoyed relative popularity for such purposes.

<table>
<thead>
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<th>Table II</th>
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<tr>
<td>Analysis of data from double-blind comparison of the effects of intranasally applied cocaine, oxymetazoline, and saline on the incidence of epistaxis during asleep nasotracheal intubations.</td>
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<table>
<thead>
<tr>
<th>Group I</th>
<th>No blood</th>
<th>Epistaxis</th>
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<tbody>
<tr>
<td>Agent</td>
<td>C</td>
<td>9</td>
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<tr>
<td>S</td>
<td>6</td>
<td>6</td>
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<table>
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<tr>
<th>Group II</th>
<th>No blood</th>
<th>Epistaxis</th>
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<tbody>
<tr>
<td>Agent</td>
<td>O</td>
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<td>S</td>
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<th>Group III</th>
<th>No blood</th>
<th>Epistaxis</th>
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<tbody>
<tr>
<td>Agent</td>
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<td>9</td>
</tr>
<tr>
<td>O</td>
<td>9</td>
<td>3</td>
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C = Cocaine, O = Oxymetazoline, S = Saline

Levels of significance were determined between each group after application of Fisher’s Exact Test in which p < 0.05 was considered significant.
However, cocaine has more recently been associated with several problems\(^8,9\) which have caused alternatives for vasoconstriction, such as oxymetazoline, to appear to be more attractive and safer. This study was initially conceived to evaluate this alternative in the hope that it could be successfully used in place of cocaine for topical vasoconstriction during asleep nasal intubations.

Essentially, the initial objective was accomplished. Based on the results, oxymetazoline appears to be no less and no more effective than cocaine for such purposes and, as such, represents a safer, more practical alternative. However, a saline control was employed also, due to the general lack of concrete data involving the efficacy of vasoconstrictors in decreasing the incidence of epistaxis. It was demonstrated that neither vasoconstrictor was significantly better than saline in this regard.

Two other studies to examine the effect of vasoconstrictors on the incidence of epistaxis compared the combination of lidocaine and phenylephrine to cocaine.\(^8,9\) Both studies primarily examined the effects of these agents on the circulatory response to the intubation and secondarily on the incidence of epistaxis. In the study by Mitchell and associates,\(^9\) a saline control was added also. In neither case was the lidocaine/phenylephrine combination found to be significantly different from cocaine in decreasing the circulatory response to nasal intubation or the incidence of epistaxis. Also, in the Mitchell study, neither cocaine nor the lidocaine/phenylephrine mixture proved to be significantly different from saline in decreasing either of these occurrences.

Despite some similarities, there were differences in the experimental designs of these three studies relative to the effect of vasoconstrictors on the incidence of epistaxis. Although most are probably of little consequence, one major difference should be considered. Gross and his associates\(^8\) measured the incidence of epistaxis upon extubation following the surgical procedure, while this study and that by Mitchell measured epistaxis following each intubation before the surgery began. The limitation to measuring epistaxis immediately following intubation is that the tube itself may tamponade some of the bleeding from traumatized tissue. The authors believed that the chances of this occurring were unlikely given the small sizes of the tubes selected, as well as the fact that there should still be some evidence of blood on the visible distal end of the tube during the measurement if trauma did occur.

The limitation to the method employed by Gross, however, may be more important. When the epistaxis is measured upon extubation, it becomes very difficult to ascertain whether the blood noted is the result of the intubation or of the oral surgical procedure which followed. Despite posterior pharyngeal packs and meticulous suturing, irrigation, and suctioning at completion of the surgery, there is invariably blood on some portion of the distal tube as a result of the surgery. The "blood on the tube" or "blood in the nose" noted by Gross following extubation could easily have been picked up by the tube in its course through the operative site. Even blood noted on the proximal portions of the tube could have resulted from extraction of a deeply seated molar, for example, which required surgical entry into one of the sinuses. These limitations were unfortunate, because the study by Gross utilized a sample size nearly three times larger than that of this study or the Mitchell study.

Although different agents were evaluated in the three studies cited here, and there were critical differences in experimental design, essentially the same conclusions were drawn regarding the role of vasoconstrictors in nasotracheal intubation. What this means for those who employ the use of the safer alternatives for topical vasoconstriction is unclear. The alternative agents appear to be relatively benign, and more research on their use is necessary before it can be recommended that they be abandoned. At the most they would only represent a waste of time in preparing the patient for nasal intubation.

This is not necessarily the case for cocaine, however. It is far from a benign agent and its continued use for asleep nasotracheal intubations is highly questionable; particularly in light of both the recent evidence regarding its effects on the circulatory responses to nasal intubation as well as on the incidence of epistaxis.\(^9,10\) It will probably continue to be the drug of choice for many procedures in the awake patient including nasotracheal intubation. However, it must be used with great care for the reasons described in this text, and the search for suitable alternatives should continue. A more predictable agent with less tendency for abuse would present multiple benefits for the patient as well as the clinician. Clearly, before cocaine is abandoned for procedures in the awake patient, other alternatives must be shown to be at least as effective in producing local anesthesia and patient comfort.

REFERENCES


Vitaliti JC, Sessler CN, Cooper KR, et al. 1984. Vasosstiction of nasal mucosa by 5% cocaine compared to 4% lidocaine/0.5% phenylephrine. Anesthesiology. (3A): A216.

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