The feasibility of topical cocaine use in fiberoptic bronchoscopy

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Objective. To test the hypothesis that the application of 4% cocaine-soaked cotton pledgets to each piriform sinus for one minute represents a safe and efficacious method of providing additional topical anesthesia for fiberoptic bronchoscopy. **Materials and Methods**. We retrospectively reviewed all FBs performed at Mayo Clinic Jacksonville from January 1999 to April 2004. Data abstracted included periprocedural complications and doses of midazolam and fentanyl used in the FBs with or without topical cocaine application in addition to the usual anesthesia with topical xylocaine. The Wilcoxon rank sum test was used for statistical analysis. **Results**. We identified 92 FBs where topical 4% cocaine was used. A sample of 80 FBs without cocaine use served as the control group. There were no periprocedural complications in either group. There was significantly less fentanyl use in the cocaine versus the control group (P<0.0001, the median dose 75 vs. 100 mcg, respectively). There was no significance in midazolam use in the cocaine versus the control group (p = 0.16). **Conclusions**. Topical application of 4% cocaine to each piriform sinus in addition to standard xylocaine is safe. Its use is associated with significantly less use of fentanyl. **Clinical implications**. The use of topical cocaine may allow FB to be performed with less systemic narcotic use.

Introduction

Fiberoptic bronchoscopy (FB) is a common and useful procedure in a variety of clinical settings. There is consensus that FB should be performed in the safest and most comfortable manner possible. Interventions to maximize safety and comfort include appropriate monitoring, topical airway anesthesia and sedative medication use. However, the ideal anesthetic for diagnostic FFB remains undefined (1-4).

Cocaine is an extremely useful drug for various endoscopic procedures, with unrivaled vasoconstrictive and decongestant properties (5, 6). Cocaine has been successfully used topically as an anesthetic in FB (7-9). It was first introduced as a surface an-

esthetic in 1884 in Vienna, by Koler in ophthalmology and by Jelinek in laryngology (10). The "merits" of cocaine made the back cover of the first issue of the Laryngoscope in 1896. In the early 1900's, it was prescribed for colds and hay fever in addition to being sold directly to the public. However, the subsequent development of cocaine abuse resulted in regulation of its use in 1914 with the passage of the Harrison Anti-Narcotic Act (11). Continued medical use of cocaine was limited to topical anesthesia. However, because of concerns with toxicity, abuse potential, and extensive record keeping, even the use of topical cocaine began to decrease in the late 1980s (12).

Intratracheal instillation of cocaine, which results in rapid systemic absorption, has led to cardiovascular toxicity (13, 14). However, different methods of anesthetic application have different absorption profiles (5, 15). We hypothesized that the application of cotton pledgets soaked in topical 4% cocaine to the piriform sinuses may result in potentially less systemic absorption and side effects. The rationale for piriform sinus application is that the superior laryngeal nerve conveys impulses for the laryngeal cough reflex (16, 17) and the laryngeal sensory fibers innervate the caudal end of the piriform sinus (18). Previous reports have confirmed that laryngeal anesthesia with topical cocaine application resulted in a substantial decrease or a complete disappearance of afferent superior laryngeal nerve (SLN) activity (19). Similarly, complete anesthesia of the SLN abolished the cough reflex after inhalation of a nebulized chemoirritant solution of tartaric acid (16).

Although others and we utilize this technique successfully, no study has previously examined its safety or efficacy. In order to study the feasibility of topical cocaine application to the bilateral piriform sinuses as a supplemental anesthesia for FB, we performed a review of all FBs performed at Mayo Clinic Jacksonville from January 1999 to April 2004.

Materials and methods

The study was approved by Mayo Clinic's Institutional Review Board as a minimal risk study. From the medical record data, we identified 1615 bronchoscopies performed at our institution over a period of 5 years. This database included patients undergoing bronchoscopy in the outpatient, inpatient, and intensive care unit settings as well as following lung transplant.

We aimed to identify 100 outpatient FBs performed with the use of topical cocaine in addition to routine anesthesia with xylocaine. The control group was formed by selecting every 16th FB from the medical record list to match the proposed number of one hundred FBs with cocaine use. These two groups, cocaine and control, were compared by required doses of sedation with midazolam and fentanyl. Statistical analysis was performed using the Wilcoxon rank sum test.

Data abstracted included patient characteristics (age, gender, indication for FB), periprocedural complications (arrhythmias, desaturations and intractable cough), and doses of midazolam and fentanyl used in the FBs with or without topical cocaine application. All patients were routinely monitored according to the institutional protocol. Pulse oximetry and a single lead EKG were continuously recorded during the procedure, and automated non-invasive blood pressure was monitored every 5 minutes. All patients received supplemental oxygen at 2 to 5 l/minute via nasal cannula to maintain oxygen saturation above 90%. Conscious sedation was achieved with midazolam and fentanyl in almost all patients, with doses administered initially and during the procedure at the bronchoscopist's discretion.

Anesthesia was achieved with a 2% viscous xylocaine gargle and 4% nebulized xylocaine prior to procedure and aliquots of 2% xylocaine instilled during the procedure. In the cases where cocaine was used, cotton pledgets soaked in 4 ml of 4% cocaine were applied via Jackson laryngeal forceps to the bilateral piriform sinuses for the duration of one minute, in addition to routine anesthesia with xylocaine.

Results

We identified 92 FBs where topical 4% cocaine was applied to the bilateral piriform sinuses for the duration of one minute prior to the procedure. A sample of 80 FBs without cocaine use served as the control group. Twenty cases out of the original 100 cases in the control group were excluded because either they were performed on intubated or post-transplant patients or cocaine use was subsequently documented. No further control cases were included to match the 92 cases with cocaine use due to adherence to the pre-study protocol.

Indications and patient data

The median age of all 172 patients was 69 years. There were 88 males and 84 females. The most common indications for the bronchoscopy were: known or suspected cancer, pulmonary infiltrate and pulmonary nodule. The remainder of bronchoscopies were performed for: hemoptysis, cough or other miscellaneous reasons. The baseline characteristics of patients in both groups are shown in Table 1. There were no significant differences between the cocaine and the control groups in regards to age, gender or indication for FB, except for patients with infiltrates.

Table 1 General characteristics

Characteristics	Cocaine (n = 92)	Control (n = 80)	p
Age, median (1st and 3rd quartile)	70 (64, 75)	67 (59, 75)	NS
Male/Female	51/41	37/43	NS
Indication (n; %)			
Infiltrate	12 (13)	24 (30)	< 0.044
Cancer	44 (48)	31 (39)	NS
Nodule	13 (14)	9 (11)	NS
Hemoptysis	11 (12)	6 (7.5)	NS
Cough	5 (5.5)	6 (7.5)	NS
Other	7 (7.5)	4 (5)	NS

Safety

The application of topical anesthesia with 4% cocaine by the technique previously described did not result in adverse effects. There were no episodes of arrhythmias and no procedure had to be prematurely terminated because of desaturations in either group. There was no intractable cough periprocedurally in either group.

Efficacy

The topical application of cocaine resulted in the use of less conscious sedation. Fentanyl use in the cocaine group was significantly lower than the control group ($P<0.0001$, the median dose 75 vs. 100 mcg, respectively). There was no significant difference of midazolam use in the cocaine compared to the control group ($p = 0.16$) (Table 2).

Table 2 Doses of fentanyl and midazolam used in the cocaine and the control group

Median dose (1st, 3rd quartile)	Cocaine	Control	P-value
Fentanyl (mcg)	75 (50, 75)	100 (50, 125)	<0.0001
Midazolam (mg)	2 (2, 3)	2 (2, 3.5)	0.16

Discussion

Bronchoscopic technique is not standardized. Controversies exist with regard to premedication before FB and this depends on the personal experience of individual operators (1, 3, 15). For local anesthesia, a variety of agents have been used (7-9). The preferred sedative medications are opiates and benzodiazepines, alone or in combination (15, 20-21). Combined sedation with a benzodiazepine and an opiate allows a reduction in the dose of supplemental local anesthesia (22). However, the routine use of sedative medications may potentially have untoward side effects (15, 21). Since there are reports of routine diagnostic FB being performed adequately with little or without any sedation (23-25), the risk-benefit considerations become more important.

In order to evaluate the safety and efficacy of topical cocaine, we analyzed the group of patients that received topical anesthesia with 4% cocaine applied to the bilateral piriform sinuses in addition to routine anesthesia with xylocaine. When applied topically with the technique described, cocaine use did not result in any known adverse effects among 92 patients in our cohort.

The main reasons why cocaine use decreased over the years were its toxicity due to systemic absorption, the potential for transfer of infectious agents and extensive record keeping (12-13, 27-28). In our cohort, the dose used for anesthesia was relatively small and with topical administration as described, systemic absorption was likely insignificant. This is supported by the lack of untoward side effects. In the past, a cocaine topical solution had to be prepared by pharmacy personnel, but currently a commercial, 4 ml-vial of 4% cocaine is available. This eliminates the risk of contamination with various microorganisms that was reported in the past (27-28). In contrast to the colorless cocaine solution, which was used in the past and could not be distinguished by the naked eye from other anesthetic solutions, the commercially available solution is dark green in color and no dye needs to be added. Following these improvements in manufacturing and packaging, the requirements for record keeping for medical usage of cocaine are similar to those indicated for any other controlled substance. The results of the study also showed that patients who had additional anesthesia with 4% cocaine required less opiate medication. The proposed mechanism is that the cough reflex is abolished or significantly decreased after anesthesia of the piriform sinuses, thus allowing bronchoscopy to be performed with less systemic sedation, especially with less narcotic medication use. A study on both human and animal subjects demonstrated abolishment of the cough reflex after laryngeal anesthesia with topical cocaine application (19). The nerve responsible for afferent impulses for the cough reflex is the superior laryngeal nerve (16-17), which also innervates piriform sinus (18).

The control of coughing was shown to be of paramount importance for the quality of a bronchoscopy, as this facilitates ease of viewing the bronchial tree and obtaining good biopsy samples (29). Moreover, an excessive cough can increase the risk of complications or prevent the performance of invasive procedures during bronchoscopy. Coughing raises intrathoracic pressure leading to an increased risk of pneumothorax during transbronchial biopsies (30). In a Swiss study, a significant number of patients considered a cough to be the worst side effect of bronchoscopy (31). For all these reasons and to have better control of coughing, bronchoscopists tend to use opiate medications. The primary action of the currently available opiates is on the central cough pathway. The antitussive effect is mediated predominantly by μ receptors with a possible role for κ receptors (32).

Although efficient in controlling the cough, opiate medications were shown to result in more hypoxic complications (29), more unwanted dysphoria (24) and their use prolongs recovery time (33). The results of our study and these observations call for a proper balance between sedation and anesthesia with the goals of increased comfort, safety, and efficacy as well as reduced cost in bronchoscopic procedures.

Potential shortcomings of this study are inherent in its retrospective design, patient sampling, and lack of standardized approach to sedative dosing. However, potential uncontrolled variables were unlikely to affect the major statistical significance that was observed in fentanyl use. Based on our results that suggest improvements in safety and efficacy of cocaine, its use has recently increased at our institution.

Conclusion

In conclusion, our data suggest that topical application of 4% cocaine to each piriform sinus, in addition to standard xylocaine, is safe and feasible. Its use is associated with the use of significantly lower doses of fentanyl. This may allow FB to be performed with less systemic narcotic use. Future prospective studies systematically addressing the impact of reduced narcotic use in the setting of topical cocaine use would be instructive.

Conflict of interest: The authors declare that they have no conflict of interest. This study was not sponsored by any external organization.

References

1. Ernst A, Silvestri G, Johnstone D. Interventional Pulmonary Procedures; Guidelines from the American College of Chest Physicians. Chest. 2003;123:1693-717.
2. Lenox RJ. A proper balance. Chest. 2004;125(1):13-4.
3. Pickles J, Jeffrey M, Datta A, Jeffrey AA. Is preparation for bronchoscopy optimal? Eur Respir J. 2003;22(2):203-6.
4. British Thoracic Society guidelines on diagnostic flexible bronchoscopy. Thorax. 2001;56(Suppl I):i1-21.
5. Verlender JM Jr, Johns ME. The clinical use of cocaine. Otolaryngol Clin N Am. 1981;14(3):521-31.
6. Johnson PE, Belafsky PC, Postma GN. Topical nasal anesthesia for transnasal fiberoptic laryngoscopy: a prospective, double-blind, cross-over study. Otolaryngology-Head & Neck Surgery. 2003;128(4):452-4.
7. Graham DR, Hay JG, Clague J, Nisar M, Earis JE. Comparison of three different methods used to achieve local anesthesia for fiberoptic bronchoscopy. Chest. 1992;102(3):704-7.
8. Middleton RM, Shah A, Kirkpatrick MB. Topical nasal anesthesia for flexible bronchoscopy. A comparison of four methods in normal subjects and in patients undergoing transnasal bronchoscopy. Chest. 1991;99(5):1093-6.
9. Teale C, Gomes PJ, Muers MF, Pearson SB. Local anaesthesia for fibreoptic bronchoscopy: comparison between intratracheal cocaine and lignocaine. Respir Med. 1990;84(5):407-8.
10. Feldmann H. Diagnosis and therapy of diseases of the larynx in the history of medicine. Part III. After the invention of laryngoscopy. Laryngo-Rhino-Otologie. 2002;81(8)596-604.
11. The merits of cocaine. Laryngoscope. 1996;106(6):680.
12. Goodell JA, Gilroy G, Huntress JD. Reducing cocaine solution use by promoting the use of a lidocaine-phenylephrine solution. Am J Hosp Pharm. 1988;45(12):2510-3.
13. Osula S, Stockton P, Abdelaziz MM, Walshaw MJ. Intratracheal cocaine induced myocardial infarction: an unusual complication of fibreoptic bronchoscopy. Thorax. 2003;58(8):733-4.
14. Davies L, Mister R, Spence DP, Calverley PM, Earis JE, Pearson MG. Cardiovascular consequences of fibreoptic bronchoscopy. Eur Respir J. 1997;10(3):695-8.
15. Putinati S, Ballerin L, Corbetta L, Trevisani L, Potena A. Patient satisfaction with conscious sedation for bronchoscopy. Chest. 1999;115(5):1437-40.
16. Addington WR, Stephens RE, Goulding RE. Anesthesia for the superior laryngeal nerves and tartaric acid-induced cough. Arch Phys Med Rehab. 1999;80(12):1584-6.

17. Sant'Ambrogio G, Sant'Ambrogio FB. Role of laryngeal afferents in cough. Pulm Pharm. 1996;9(5-6):309-14.

18. Yoshida Y, Tanaka Y, Hirano M, et al. Sensory innervation of the pharynx and larynx. Am J Med. 2000;108(Suppl4)a51S-61S.

19. Kuna ST, Woodson GE, Sant'Ambrogio G. Effect of laryngeal anesthesia on pulmonary function testing in normal subjects. Am Rev Respir Dis. 1988;137(3):656-61.

20. Prakash UB, Offord KP, Stubbs SE. Bronchoscopy in North America: the ACCP survey. Chest. 1991;100:1668-75.

21. Shelley MP, Wilson P, Norman J. Sedation for fibreoptic bronchoscopy. Thorax. 1989;44:769-75.

22. Tsunezuka Y, Sato H, Tsukioka T, Nakamura Y, Watanabe Y. The role of codeine phosphate premedication in fibre-optic bronchoscopy under insufficient local anaesthesia and midazolam sedation. Respir Med. 1999;93(6):413-5.

23. Colt HG, Morris JF, Fiberoptic bronchoscopy without premedication: a retrospective study. Chest. 1990;98:1327-30.

24. Hatton MQ, Allen MB, Vathenen AS, Mellor E, Cooke NJ. Does sedation help in fibreoptic bronchoscopy? BMJ. 1994;309(6963):1206-7.

25. Pearce SJ. Fiberoptic bronchoscopy: is sedation necessary? BMJ. 1980;281:779-80.

26. Stolz D, Chhajed PN, Leuppi JD, Brutsche M, Pflimlin E, Tamm M. Cough suppression during flexible bronchoscopy using combined sedation with midazolam and hydrocodone: a randomised, double blind, placebo controlled trial. Thorax. 2004;59(9):773-6.

27. Schleupner CJ, Hamilton JR. A pseudoepidemic of pulmonary fungal infections related to fiberoptic bronchoscopy. Infection Control. 1980;1(1):38-42.

28. Steere AC, Corrales J, von Graevenitz A. A cluster of Mycobacterium gordonae isolates from bronchoscopy specimens. Am Rev Respir Dis. 1979;120(1):214-6.

29. Greig JH, Cooper SM, Kasimbazi HJ, Monie RD, Fennerty AG, Watson B. Sedation for fibre optic bronchoscopy. Respir Med. 1995;89(1):53-6.

30. Hattotuwa K, Gamble EA, O'Shaughnessy T, Jeffery PK, Barnes NC. Safety of bronchoscopy, biopsy and BAL in research patients with COPD. Chest. 2002;122:1909-12.

31. Mendes de Leon C, Bezel R, Karrer W, Brändli O. [Premedication in fiber optic bronchoscopy from the patient's and the physician's viewpoint--a randomized study for the comparison of midazolam and hydrocodone]. Schweiz Med Wochenschr. 1986;116(37):1267-72.

32. Homsi J, Walsh D, Nelson KA. Important drugs for cough in advanced cancer. Support Care Cancer. 2001;9:565-74.

33. Hug CC Jr. Opioids: Clinical use as anesthetic agents. J Pain Symptom Manag. 1992;7(6):350-5.