

Is Cocaine a Safe Topical Agent for Use During Endoscopic Sinus Surgery?

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BACKGROUND

Adequate surgical visualization is paramount to safe and successful endoscopic sinus surgery (ESS). Minimizing bleeding facilitates identification of anatomical landmarks, ensuring a safer surgery. Topical vasoconstriction is a fundamental method for controlling intraoperative hemorrhage, and there are several different agents available for this purpose. Topical cocaine has traditionally been used by otolaryngologists and is particularly attractive given its unique dual local anesthetic and vasoconstrictive properties.¹ A maximal safe dose of 200 mg, or 1.5 mg/kg to 3 mg/kg, of intranasal cocaine is widely published; however, this value is largely based on historical anecdote and untested clinical practice rather than rigorous scientific evidence.¹ In recent years, the safety and role of cocaine in endoscopic sinus surgery has been questioned largely due to occasional case reports of adverse events (predominantly cardiac) and administrative control measures surrounding access and storages. Yet, other topical medication options lack the aforementioned dual properties of cocaine that made it ideal for sinus surgery in the first place. The question thus arises as to whether topical cocaine is still an appropriate and safe topical vasoconstrictor for continued routine use in modern ESS practice.

LITERATURE REVIEW

A large survey of active members of the American Academy of Otolaryngology–Head and Neck Surgery was published in 2004 by Long et al.¹ The survey aimed to reassess the current trend in the medicinal use of cocaine and its apparent toxicity in comparison to an earlier survey by Johns and Henderson in 1977. The survey returned

4,717 responses (54% response rate). Fifty percent of respondents reported using cocaine as a topical agent during ESS over the preceding calendar year. Of note, the overwhelming majority reported applying cocaine using a 4% liquid solution on nasal pledgets for topical application, reflecting more modern concentration dosing of cocaine during sinus surgery rather than the more historic doses of 10% cocaine, or even 25%. Twenty-six percent of the total respondents reported adverse events that were either directly or indirectly attributed to cocaine application; a total of 14 mortalities and 1,166 cases of morbidity were reported. It was unclear how the adverse events were actually attributed to the cocaine use (beyond simple respondent opinion). Many of these morbidities were mild in nature, with tachycardia and hypertension being the most commonly reported nonfatal adverse effects (84.1%). In comparison, the 1977 survey by Johns and Henderson revealed that 92% of respondents used cocaine routinely in their practice. Furthermore, of otolaryngologists who used cocaine for nasal anesthesia, 47% routinely used dosing greater than 200 mg. Overall, based on these surveys it seems that cocaine administration by U.S. otolaryngologists has decreased significantly over the past 25 years, likely due to a combined result of potential toxicities, nuances associated with safe storing and dispensing of the controlled agent, and increased availability of other vasoconstrictive agents.

In comparison, in 2003 De et al. published a review of cocaine use by otolaryngologists in the United Kingdom, as well as the incidences and types of adverse reactions to cocaine administration.² A survey of members of the British Association of Otolaryngology–Head and Neck Surgery returned a total of 378 responses (65% response rate). Sixty-seven percent of all surgeons used cocaine regularly, and only 11% reported that they had experienced complications potentially related to cocaine administration. One mortality and 39 cases of morbidity were reported, although yet again it was unclear how, or even if, causation was established. The report concluded that, although cocaine has possible adverse drug interactions and side effects, the risks from toxicity are nonetheless quite low, and cocaine remains a common topical agent used by British Association of Otolaryngology–Head and Neck Surgery during ESS.

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A small prospective study published by Liao et al. evaluated the absorption of topical cocaine from the nasal mucosa in rhinologic procedures.³ Twelve recruited patients were divided into three groups. Group I received pledgets soaked with 4 mL of a 4% cocaine solution (160 mg) for 10 minutes, group II received 4 mL of a 4% cocaine solution (160 mg) for 20 minutes, and group III received 4 mL of a 10% cocaine solution (400 mg) for 20 minutes. Absorption rate was determined by measuring serum cocaine concentration at 5-, 10-, 15-, and 20-minute intervals following topical application of the cocaine-soaked pledgets. The study found that only one-third of cocaine from the cotton pledgets is absorbed via nasal mucosa when applied topically. Although the 4% cocaine solutions did not result in any adverse hemodynamic events, 50% of group III patients (10% cocaine) experienced intraoperative hypertension and transient ventricular tachycardia. It was therefore concluded that 10% cocaine solutions should be avoided given undesirable complications. Finally, although absorption rates were largely linear, idiosyncratic absorption was observed in one group II patient, and the report concluded that caution should be exercised with any concentration dosing of cocaine due to the unpredictable nature of systemic effects.

In 2011, a systematic review was published by Higgins et al. that examined the safety of several topical vasoconstrictors in ESS, including cocaine.⁴ A total of 42 articles of various types and levels of evidence were included. Reported adverse cardiovascular reactions associated with intraoperative cocaine use included hypertension, tachyarrhythmias, myocardial infarction, cardiogenic shock, cardiovascular arrest, and death. Other sympathomimetic effects included mydriasis and glaucoma. The rate of these documented events was extremely low, and the majority occurred with concentrations of cocaine much higher than those used today. The authors recognized that the many confounding factors and literature heterogeneity made it difficult to accurately assess morbidity given the effects of systemic anesthetic agents, amount of drug used and absorbed, and concomitant local injections. Of the nine identified randomized controlled trials, three examined use of a cocaine and epinephrine mixture (Moffett's solution). Two of the three studies found an improved surgical field with the addition of epinephrine, but the scoring system was not validated. Conflicting results were found regarding the effect on systemic absorption of cocaine with the addition of epinephrine. The authors' final recommendations were to use topical cocaine judiciously and to avoid using concentrated topical cocaine in patients with a history of cardiovascular disease.

The systematic review by Higgins et al. also evaluated other topical vasoconstrictors in ESS, such as adrenaline, phenylephrine, and oxymetazoline. Of all topical vasoconstrictors evaluated, oxymetazoline appears to have the greatest safety profile, with no studies or cases reporting adverse events. However, many feel that performing safe ESS at times requires better hemostasis than that provided by oxymetazoline. Other vasoconstrictors such as phenylephrine and epinephrine were not without risk. Adverse reactions of hypertensive crisis, postoperative myocardial

infarction, and cardiogenic shock are reported with the use of 1:1,000 epinephrine packing. In regards to phenylephrine, the authors go so far as to conclude avoiding its use, if possible, due to reports of adverse cardiac events and deaths. A clinical review conducted in New York evaluating the morbidity with intranasal phenylephrine identified four pediatric and five adult patients who suffered hypertensive crisis or pulmonary edema, three who subsequently died after going into cardiac arrest. Unfortunately, there are few high-powered, higher level comparison studies to accurately and confidently compare one agent to another. The literature is heterogenous in the concentrations of vasoconstrictor used, method of application, and concurrent use of multiple vasoconstrictors during a single procedure.

Most recently, Valdes et al. in 2014 performed a blinded randomized, controlled trial assessing the effect of 4% cocaine in comparison to 1:1,000 epinephrine on surgical field visualization and intraoperative bleeding during functional endoscopic sinus surgery (FESS).⁵ Their small study enrolled a total of 37 patients and randomized each side of the nose to either epinephrine or cocaine-soaked patties. Their study concluded that there was no mean difference in surgical site visualization or blood loss between the two. Both agents were noninferior for topical decongestion, and additionally, no adverse intraoperative or postoperative events were experienced with either drug. They concluded that a 4% cocaine mixture was safe and effective for topical decongestion during FESS, with the same safety profile of epinephrine, so long as patients were free of cardiac risk factors.

BEST PRACTICE

Although the potential toxicities and adverse reactions associated with cocaine topical application are well recognized, their incidences are extremely infrequent and apparently idiosyncratic in nature, whereas the benefits of cocaine are unique in terms of its singular ability to both vasoconstrict and anesthetize the nasal mucosa. Further higher level studies investigating the systemic absorption of topical cocaine, the actual incidence of directly attributable adverse effects, and its safety and utility in comparison to other topical vasoconstrictor agents should be conducted. Based on the available evidence, no specific recommendation for or against the use of cocaine during ESS can be made at this time, and surgeons can use their own judgment when weighing benefits versus risks of topical cocaine while also recognizing that there is no direct replacement for its useful unique characteristics. Consideration should be given to use of alternative topical vasoconstrictive agents such as oxymetazoline in patients with a strong history of comorbid cardiovascular risk factors.

LEVEL OF EVIDENCE

In this review the evidence levels included in the analysis were: one level 1b study (blinded randomized-control trial); one level 2a study (heterogenous systematic review), one level 2c study (experimental outcomes study) and two level 3b studies (retrospective cross-sectional surveys).

BIBLIOGRAPHY

1. Long H, Greller H, Mercurio-Zappala M, Nelson L, Hoffman R. Medicinal use of cocaine: a shifting paradigm over 25 years. *Laryngoscope* 2004; 114;1625–1629.
2. De R, Uppal HS, Shehab ZP, Hilger AW, Wilson PS, Courteney-Harris R. Current practices of cocaine administration by UK ororhinolaryngologists. *J Laryngol Otol* 2003;117:109–112.
3. Liao BS, Hilsinger RL Jr, Rasgon BM, Matsuoka K, Adour KK. A preliminary study of cocaine absorption from the nasal mucosa. *Laryngoscope* 1999;109: 98–102.
4. Higgins TS, Hwang PH, Kingdom TT, Orlandi RR, Stammberger H, Han JK. Systematic review of topical vasoconstrictors in endoscopic sinus surgery. *Laryngoscope* 2011;121:422–432.
5. Valdes C, Bogado M, Rammal A, Samaha M, Tewfik M. Topical cocaine vs adrenaline in endoscopic sinus surgery: a blinded randomized controlled study. *Int Forum Allergy Rhinol* 2014;4:646–650.