COCaine TOXICity AFTER LARYNGOSCOpy IN AN INFANT

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ABSTRACT

Iatrogenic cocaine toxicity was observed in a 5.5-month-old male who received intranasal cocaine as a topical anesthetic for laryngoscopy. He became agitated, diaphoretic, tachycardic, and hypertensive shortly following the procedure. To control his signs and symptoms, he required 3 doses of IV lorazepam. Systemic absorption and toxicity can vary amongst individuals, making it difficult to determine appropriate dosing. The maximum dose of 1 mg/kg in children has not been validated and toxicity may appear at a much lower dose in certain individuals. Pediatric patients receiving topical cocaine as an anesthetic must be given the lowest possible dose, and then carefully monitored for signs of systemic absorption.

Key Words: Cocaine toxicity, pediatric patients, topical cocaine

Cocaine is the oldest local anesthetic drug. It is derived from the leaves of Erythroxylon coca.¹ Its first use was as a local anesthetic in 1884 by the Austrian ophthalmologist Karl Koller, who instilled cocaine into the conjunctival sac.¹ To this day, cocaine is still used as a topical anesthetic for ophthalmologic procedures.

Among local anesthetics, cocaine still remains a popular topical anesthetic for procedures in the nose, throat, and oral cavity.²,³ It is excellent for this purpose, having a rapid onset of action and a prolonged duration of activity up to one hour or more.⁴ In addition, its strong vasoconstricting effect provides mucosal decongestion and decreased risk of hemorrhage, obviating the need for epinephrine.⁴

The mechanism of action of cocaine involves inhibition of conduction in nerve fibers by blockade of sodium channels.⁵ In turn, this results in the prevention of an action potential from being generated and can produce prolongation of the QRS and the QTc similar to type 1A and 1C antiarrhythmic agents because of its sodium channel blockade properties.⁶ Cocaine is the only local anesthetic that is a potent sympathomimetic agent. It blocks reuptake of norepinephrine and epinephrine both in the central nervous system and systemically.⁶ If absorbed systemically, cocaine has multiple effects on the central nervous system, resulting in intense behavioral stimulation, euphoria, and arousal.⁴ The seizure threshold is initially raised but with increasing doses of cocaine, it is lowered, and seizures may result. The adrenergic effects of cocaine are responsible for the tachycardia, hypertension, mydriasis, tremor, and perspiration seen with cocaine toxicity.⁴

In spite of the use of topical cocaine in pediatric patients, limited data are available for appropriate use, dosing, and monitoring guidelines in these patients. We present a 5.5-month-old male with iatrogenic cocaine toxicity following flexible direct nasopharyngoscopy. As well, literature involving other cases of iatrogenic cocaine toxicity will be reviewed and discussed.

Case report

A 5.5 month-old boy was electively admitted for the investigation of cough since one month of age and increasing hoarseness. He was a healthy term infant. His postnatal period was unremarkable other than moderately severe eczema for which he was being treated with 1% hydrocortisone ointment. He was developmentally appropriate for age. On admission, he was alert with normal vital signs. His growth was symmetrical with his...
weight 9.7 kg, his height 71 cm, and his head circumference 44.75 cm. The physical examination was within normal limits, except for eczematous lesions of the face and torso.

While in the hospital, investigations identified a number of congenital abnormalities. He had vertebral anomalies with fusion of the right side of vertebral bodies T2 to T5, duodenal malrotation, congenital left kidney agenesis, and left-sided aortic arch with anomalous right subclavian artery. A modified barium swallow determined the presence of direct aspiration. An esophagogram revealed a persistent smooth impression on the posterior aspect of the esophagus at the expected level of the aortic arch, consistent with an anomalous right subclavian artery. Cytogenetic analysis of cultured peripheral lymphocytes revealed no numerical or structural abnormalities. Magnetic resonance imaging of his brain was normal.

As part of his investigation for chronic hoarseness, he underwent direct flexible nasopharyngoscopy through the left nasal cavity to visualize the vocal cords. 0.1 cc of 4% of topical cocaine was instilled by dropper in the left nasal cavity prior to procedure. The procedure was carried out uneventfully. The vocal cord mobility was normal. There was mild edema of the vocal cords and evidence of visual aspiration of saliva at the time of the examination.

Upon return to the Pediatric ward 90 minutes following the procedure, he was noted to be very agitated, diaphoretic, with dilated pupils. He was constantly moving his limbs and picking at his clothes. He was tachycardic with a heart rate of 190 and hypertensive with a blood pressure of 135/115. ECG was not performed. He was diagnosed with cocaine toxicity and was treated with Lorazepam 0.5 mg IV (0.05mg/kg) over 3 minutes. In order to control recurrent cardiovascular excitability and neurological irritation, he was given two further doses of lorazepam within one hour apart. He had complete resolution of his symptoms within 4 hours of the procedure without any sequelae with heart rate of 110 and blood pressure of 95/70.

**DISCUSSION**

The safe dose level for topically applied cocaine is thought to be 200 to 300 mg (3 mg/kg) in an adult. This is not based on studies, but rather on early clinical experience during tonsillectomy.\(^7\) Determination of a safe dose of cocaine is complicated by multiple factors including route of administration, site and method of application, and rate of metabolism, which can influence toxicity.\(^8,9\) Patients who exhibit intrinsically low cholinesterase activity or those who are being treated with cholinesterase inhibitors are thought to have impaired ability to metabolize cocaine.\(^4\) This may account for the rare events of toxicity found in patients receiving doses of cocaine as low as 10 mg.\(^7\)

Systemic absorption does occur when cocaine is applied to mucosal surfaces, and there is some evidence that suggests that absorption occurs more readily from some sites than from others.\(^9,10\) Cocaine spray applied to the larynx as a glossopharyngeal and superior laryngeal nerve block permits good visualization by direct laryngoscopy.\(^4\) Greinwald and Holtel studied nasally applied cocaine by absorption of cocaine from cottonoid pledgets.\(^11\) Their study demonstrated that approximately one third of a 160-mg cocaine solution placed on cotton pledgets was absorbed via the nasal mucosa. They did not find any correlation between age, sex, plasma levels, and nasal absorption of cocaine.

They concluded that significant amounts of cocaine to induce toxic manifestations would rarely be absorbed by the nasal mucosa using the 160-mg dose on cotton pledgets. Johnson surveyed a group of otolaryngologists and plastic surgeons on their use of cocaine as a local anesthetic.\(^12\) He found that a majority of physicians continue to use cocaine as a topical anesthetic. As well, physicians reported that adverse reactions to cocaine, although uncommon, were potentially severe and occurred even with appropriate dosing.

There are few specific pediatric studies examining the use of topical cocaine. Bonadio evaluated the safety and efficacy of cocaine in combination with tetracaine and adrenaline (TAC) for minor oral lacerations in a small group of children older than 5 years of age.\(^13\) Bonadio did not see any adverse reaction related to TAC in his small study group. Case reports of iatrogenic cocaine toxicity in children include an 11-week old female infant.\(^14\) She developed irritability, arched back, jittery movements of her arms and
legs, and crossed eyes for 30 minutes following intranasal instillation of two drops of 4% cocaine solution equal to the total of 4 mg (0.6 mg/kg). Her symptoms were resolved promptly with intravenous lorazepam. Finally, cocaine toxicity was reported in a 14-month old boy when 30 mg (2.3 mg/kg) of topical cocaine was administered through a bronchoscope. The infant presented with dilated pupils, hyperventilation, and continuous movements of the extremities. He continued having symptoms for eight to ten hours despite the administration of Apoozem, meperidine, and metohexitone.

Our patient received 0.1 cc of 4% topical cocaine instilled intranasally, or a total dose of 4 mg (0.4 mg/kg). This is less than the recommended maximum dose of 1 mg/kg that originally initiated from adult dose. Reasons for his toxicity may include that he aspirated some of the cocaine into the trachea where it is known to absorb more readily. Aspiration was visualized during the procedure itself, and previously noted on a modified barium swallow. Perhaps injury to the airway induced by chronic aspiration resulted in increased permeability of the mucosal lining of the airway. This is further supported by the presence of edema of the vocal cords, suggesting abnormalities of the mucosa. As well, perhaps individual variation in cocaine metabolism such as low cholinesterase activity was present in this patient, as implicated in previous studies. This, however, is less likely. From an anatomical point of view, nasal drops are an ideal mode of drug delivery for infants, since their nasal cavity is so small that one or two drops can cover the whole mucosa. However, because of poor accuracy in dosing as compared with syringes, nasal drops may not be a reliable method for administering highly potent drugs. Although there may be the possibility of a dosing error, it would appear to be slim in this case. The patient’s chart was reviewed extensively and the responsible ENT surgeon was interviewed, with no evidence of an apparent error.

Given current information available, we recommend that dosing guidelines for topical cocaine use in infants and children be more clearly established. Cocaine as a topical anesthetic should be used with extreme caution in children with risk factors for underlying abnormalities of the mucosal lining of the aero digestive tract such as gastroesophageal reflux disease, direct and/or indirect aspiration. These underlying risk factors can result in increased absorption and iatrogenic toxicity. However, there is a great body of evidence that suggests that the use of cocaine, even in experienced hands, can cause rapid, unexpected and severe toxic reactions. Since better-tolerated alternatives are available, cocaine use in endonasal procedures should be cautiously considered. These alternatives include lidocaine and tetracaine in combination with ephinephrine, naphazoline, or oxymetazoline.

Further, if one is in favor of cocaine use as local anesthetic, we advocate monitoring children for systemic effects for 4 to 8 hours (cocaine approximate half life of 1 hour) following such administration. With the development of cocaine toxicity, patients may need to be monitored by EKG.

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