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Case report

Intranasal flumazenil and naloxone to reverse over-sedation in a child undergoing dental restorations

CHRISTOPHER HEARD MD*, PAUL CREIGHTON DDS† AND JERROLD LERMAN MD FRCPC FANZCA‡

**Department of Pediatric Anesthesiology and Division of Pediatric Critical Care, †Department of Pediatric Dentistry and ‡Department of Pediatric Anesthesiology, Women & Children's Hospital of Buffalo, Buffalo, NY, USA*

Summary

We describe a 3-year-old child who became over-sedated after receiving intranasal (IN) midazolam (0.53 $mg \cdot kg^{-1}$) and IN sufentanil (1 $mcg \cdot kg^{-1}$) for dental restorations in the dental office. Desaturation was attributed to laryngospasm, which was managed with positive pressure ventilation and oxygen. The sedation was reversed with a combination of IN flumazenil and naloxone.

Keywords: sedation; intranasal; reversal

Introduction

Moderate sedation is a frequent technique to facilitate dental treatment to a child in the dental office setting. Although moderate sedation is considered to be safe, complications do occur. These complications are usually respiratory in origin and may result in a hypoxic cardio-respiratory arrest if they are not recognized and treated in a timely and an appropriate manner. We report a child whose level of sedation became excessive, resulting in airway obstruction, which was managed successfully with a favorable outcome.

Case report

A 3-year-old, 14-kg female, ASA 1, was scheduled for elective dental restoration with moderate sedation in the dental chair. The child was fasted after midnight and was not premedicated. She had no anesthesia or sedation experience. Her physical examination was unremarkable; her airway was normal, and her tonsils were not enlarged.

Sedation that included 15 mcg of sufentanil (1 $mcg \cdot kg^{-1}$) and 5 mg midazolam (0.3 $mg \cdot kg^{-1}$) was administered intranasally [IN; using a mucosal atomization device (MAD®; Wolfe Tory Medical, UT, USA)] by a pediatric anesthesiologist. During the sedation, she was monitored continuously in the preprocedure waiting area. Fifteen minutes after the administration of sedation, she was seated in the dental chair and lightly restrained in a papoose. Monitors included pulse oximetry and noninvasive blood pressure. Five minutes after being seated in the dental chair, she continued to struggle, remaining agitated, and uncooperative. Her sedation level at that time was scored as 1 on the Ramsay Score (RS; Table 1). In order to facilitate her dental care, a second dose of 2.5 mg midazolam IN was administered. Five minutes later, her sedation level was scored 2–3 on the RS. At that time, the sedation was supplemented with

Correspondence to: Paul Creighton, Department of Pediatric Dentistry, Women & Children's Hospital of Buffalo, 219 Bryant Street, Buffalo, NY 14222, USA (email: creighto@buffalo.edu).

Table 1
Ramsay Score

1	Anxious and agitated or restless or both
2	Cooperative, orientated, and tranquil
3	Responding to commands only
4	Brisk response to light glabellar tap
5	Sluggish response to light glabellar tap
6	No response to light glabellar tap

50% N_2O by nasal mask and the dental surgery commenced. Twenty minutes after receiving the second dose of midazolam, her level of sedation had deepened (no response to painful stimulus) to a RS of 6, and her airway became obstructed. Her oxygen saturation decreased to the 80–85% range. Surgery was interrupted, 100% O_2 was given by nasal mask, chin lift and jaw thrust were applied, and a 70-mm oral airway was inserted into her mouth. Her oxygen saturation, breathing rate, and pattern returned to normal. Her heart rate remained unchanged between 140 and 150.

When the oral airway was removed, however, her oxygen saturation decreased to the 90–95% range. At that time, the decision was made to terminate the dental treatment and allow her to recover with an oral airway *in situ*. A jaw thrust maneuver was applied to support her airway. Despite this and other maneuvers, her oxygen saturation continued to decrease. Chest movement suggestive of respiratory efforts was observed, although the reservoir bag did not move. A presumptive diagnosis of laryngospasm was made, and a treatment plan consisting of positive pressure ventilation through a full facemask and 100% O_2 was instituted. The laryngospasm resolved in response to these measures, without further decreases in either the oxygen saturation or the heart rate. Spontaneous respirations resumed at 20–30 breaths·min^{-1}, although she remained unarousable (RS = 6). At that time, the decision was made to awaken her to prevent a recurrence of the laryngospasm. The opioid effects were antagonized with an IN dose of naloxone 0.4 mg using the MAD. This resulted in an increase in the respiratory rate, but no change in the depth of sedation. To antagonize the sedation, two 100 mcg doses of IN flumazenil (one dose in each opening of the nares) were administered using a MAD. Three minutes later, she opened her eyes and was fully awake (RS = 1). She was taken to the recovery area and monitored for 2 h without sequelae. During this recovery period, the child's RS was 2 for the first 30 min, and after that she remained fully awake, with no evidence of resedation. She was discharged and rescheduled to complete her dental work under general anesthesia on another day.

Discussion

This case report demonstrates two interesting and important principles regarding sedation in children. First, that laryngospasm and airway obstruction are potential complications regardless of the intended level of sedation. In particular, moderate sedation can be difficult to achieve in younger children, and the risks of deep sedation and anaesthesia must be anticipated. Also, all the complications that may be associated with general anesthesia, including laryngospasm, can occur. Managing this complication in the dental office may be a challenge, even for the pediatric anesthesiologist. A review of a 30 000 pediatric sedation database by the Pediatric Sedation Research Consortium (1) suggested that potentially serious adverse events were not as rare as generally perceived. In dental clinics in which sedation is administered, succinylcholine is often not available, and IV access is rarely established. Hence, the management of laryngospasm is limited to continuous positive airway pressure (CPAP), jaw thrust, and oxygen. In this report, laryngospasm was successfully using these maneuvers. Had the laryngospasm not abated, atropine and succinylcholine would have been administered immediately followed by tracheal intubation. The third treatment option that we followed was to discontinue the procedure and awaken the child.

The second important issue from this case report is that the nose is a readily accessible to administer medications in emergency situations. Flumazenil a competitive benzodiazepine receptor antagonist, antagonizes benzodiazepine overdose/complications. In children, 40 mcg·kg^{-1} IN flumazenil (2) provides therapeutic plasma levels (10–30 ng·ml^{-1}), with a peak concentration of 68 ng·ml^{-1}. The time to maximum blood concentration is 2 min, and its elimination half-life is 2 h. The use of the MAD® optimizes mucosal absorption and speeds the onset of the drug effect. We chose a dosing regimen of 1 ml (100 mcg·ml^{-1}) flumazenil per opening of the

nares (a simple, easy to remember, and effective dose for most children). The absorption of intranasal administrated medications is better with a smaller drug volume. Excess volume is wasted in the posterior pharynx. This dose may be repeated as required (3).

Naloxone has also been administered via the nasal route (4). Plasma levels in rats (5) showed peak naloxone concentrations and bioavailability similar via both IV and IN routes. Naloxone (2 mg, divided dose) given IN in a prospective study yielded a clinical response in 83% of opioid overdoses with an average response time of 3 min. We administered naloxone, 0.2 mg per opening of the nares, and repeated it as clinically required.

Unplanned over-sedation can occur after any sedation technique, irrespective of the drug used or the route of administration. In this case, the sedation technique used included three sedatives: midazolam, sufentanil, and nitrous oxide. A previous study reported more complications after moderate sedation when three or more sedatives were used (1).

The intranasal administration of potent medications such as sufentanil may be associated with an increased risk of respiratory compromise. Although our study was negative in this respect, other studies (6) have reported such complications.

Furthermore, the addition of nitrous oxide to other sedatives in children increases the risk of over-sedation occurring (7). Intranasal administration of reversal agents offers a quick and an effective route to treat over-sedation from opioids and benzodiazepines. However, this route of drug administration does not supplant the need to have those qualified and skilled in airway management present. Parenthetically, one should exercise caution when administering intranasal drugs that may be neurotoxic as the cribriform plate is only a theoretical barrier between the nasal passages and the brain.

Although laryngospasm is a well-recognized complication of general anesthesia, it is less commonly considered a substantive risk during and after sedation. Because hypoxic brain damage and/or a death may occur if laryngospasm is not immediately and effectively treated, a strategy to prevent and treat laryngospasm, especially when IV access is not immediately available, is urgently needed. If succinylcholine is immediately available, then 4 $mg \cdot kg^{-1}$, given through the intramuscular route, is an effective treatment. Theoretically, it is safer to use sedatives that can be reversed and have those reversal agents immediately available because the immediate reversal of the sedation may be needed to attenuate the side effects from laryngospasm. The IN approach allows delivery of such agents in an easy, reliable and rapid manner that should facilitate a successful outcome.

If reversal agents have been used, then the patient should not be discharged immediately, but rather observed to ensure whether no re-sedation occurs. We felt that at least 2 h postreversal event was an appropriate period.

We believe this to be the first case report to describe the treatment and prevention of laryngospasm and airway obstruction during moderate sedation, using intranasally administered reversal agents.

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