

Combination of oral ketamine and midazolam as a premedication for a severely autistic and combative patient

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Abstract

Patients with impaired ability to understand and communicate can be difficult to manage perioperatively. They frequently require lateral thinking on the part of the anesthesiologists to make the induction process as smooth as possible. We present a case of a severely autistic and violent patient scheduled for dental rehabilitation under general anesthesia. A combination of oral ketamine and midazolam was mixed in the beverage Dr Pepper to mask the taste and the appearance of the drugs. The unique flavor of Dr Pepper is well suited to increase the palatability and the acceptability of medications in children and patients with developmental delay.

Key words Premedication · Oral ketamine · Oral midazolam · Autistic patient

Introduction

Autism is a very common syndrome characterized by a qualitative impairment in both verbal and nonverbal communications and social interaction. Patients may display maladaptive features such as self-injurious behavior, aggression, and tantrums, which are common and frequently severe enough to limit educational and developmental progress. The patients are frequently withdrawn and often maintain a ritualistic behavior reflecting the need to be kept in a consistent, predictable environment [1,2]. Placing such patients in a new environment with strangers can therefore be stressful and problematic for both the patient and the caregivers. When such patients are encountered, it may require ingenuity and adaptability on the part of the anesthesiologists to make the process of anesthetic induction and emergence as smooth as possible. We report the anesthetic management of one such patient.

Case report

A 16-year-old, 80-kg, 190-cm-tall male with severe autism was scheduled for dental rehabilitation under general anesthesia. During a dental rehabilitation procedure under general anesthesia 1 year previously, the patient had refused to cooperate and drink his premedication and had become very agitated in the preoperative holding area. This necessitated physical restraint and forcible intramuscular injection with ketamine to sedate him. The anesthesia was otherwise uneventful, but it was an emotionally distressing experience for the parents for them to see their child being physically wrestled with and subdued. They were extremely reluctant to go through the same ordeal again.

The history obtained the day prior to the procedure revealed that this patient usually behaved in a violent and unpredictable manner in unfamiliar surroundings and with strangers. He did not have any other medical problem and was not on any medications. On the day of the dental procedure, the patient was pacing back and forth in his pre-operative room and appeared anxious. He was clearly agitated and withdrew to a corner when the anesthesiologist entered his room. He even punched one of the nurses when she tried to talk to him. He would not allow his parents to go near him until the anesthesiologist and the nurse left the room.

Given this scenario, we decided to use a combination of ketamine 240 mg ($3 \text{ mg}\cdot\text{kg}^{-1}$) and midazolam 20 mg ($0.25 \text{ mg}\cdot\text{kg}^{-1}$) as an oral premedication to sedate the patient. However, he refused to take the oral premedication mixed in sweet syrup. Learning that Dr Pepper (Dr Pepper Snapple Group, Plano, TX, USA) was one of his favored beverages, we mixed the oral medications with 15 ml of Dr Pepper to mask the appearance and change the flavor of the drug. In this disguised form, the patient took the drug readily from his parents. He was then left undisturbed in his bed, and he fell asleep in 20 min. He was quietly taken to the operating room. A

“steal” inhalational induction was done with oxygen, nitrous oxide, and sevoflurane and minimal disturbance, using only the pulse oximeter for monitoring. Once anesthesia was induced, he was transferred to the operating table. All the other American Society of Anesthesiologists (ASA) standard monitors were attached and intravenous access was easily obtained. He was given 100 µg of fentanyl and 50 mg of rocuronium to facilitate endotracheal intubation. The patient’s airway was secured with a well-lubricated 6.0-mm cuffed nasal RAE ETT (Mallinckrodt, Tyco Healthcare, St Louis, MO, USA) endotracheal tube via the right nostril. The dental procedure lasting 90 min was uneventful and the patient was extubated in a deep plane of anesthesia at the completion of the procedure. He was recovered in a quiet secluded environment with his mother at his bedside. The patient woke up 30 min later and was calm and mildly detached to the surroundings. He was observed for an additional 4 h to assure he did not have any residual effects from the sedatives and the anesthetics used. Subsequently the patient was discharged in a calm and stable condition.

Discussion

Perioperative management of autistic patients can be difficult. Some of the methods described include the use of physical restraints, forcible intramuscular injections, and oral medications using sedatives and anxiolytics [3].

The use of physical restraints and forcible intramuscular injections in patients who have limited ability to communicate can be traumatic for the patient and the family. The use of oral benzodiazepines, barbiturates, and butyrophenones alone is not always successful in achieving sedation and the cooperation of patients with severe behavioral problems [3]. In contrast, oral ketamine has been safely and effectively used as a premedication for operative procedures both in children and adults [3–7]. Another advantage is that ketamine can be administered by multiple routes.

There is very little published literature dealing with premedication in combative autistic patients. One case report, by Christiansen and Chambers [8], described an autistic 13-year-old boy who had several anesthetics, all requiring restraints and forcible premedication, in order to have a successful induction of anesthesia. The patient in this case report refused or spat out the oral premedication drugs, possibly because the beverage used did not successfully hide the taste of the premedicant drugs. A correspondence (letter to the editor) piece by Bachenberg [3] mentioned use of oral ketamine as premedication in an autistic combative patient.

In the present patient, we used ketamine mixed with midazolam, based on the study by Darlong et al. [9]. In this prospective, randomized, double-blind study, the combination of oral ketamine (3 mg·kg⁻¹) and midazolam (0.25 mg·kg⁻¹) had minimal side effects and provided a faster onset and more rapid recovery than ketamine 6 mg·kg⁻¹ or midazolam 0.5 mg·kg⁻¹ for premedication in children. Funk et al. [10] also investigated whether the addition of a low dose of oral ketamine (3 mg·kg⁻¹) to oral midazolam (0.5 mg·kg⁻¹) resulted in better premedication compared with oral midazolam 0.5 mg·kg⁻¹ or ketamine 6 mg·kg⁻¹ alone. There was improved anxiolysis and separation in the combined ketamine-and-midazolam group. Vertigo and emesis before induction were found to be significantly more frequent after ketamine alone compared to a mixture of ketamine and midazolam; during recovery, there were no differences between the groups in sedation or time to discharge. In a study by Trabold et al. [11], the combination of midazolam and ketamine as oral preanaesthetic medication did not significantly affect the recovery time of children after sevoflurane anesthesia.

Palatability is a crucial factor in children and developmentally delayed patients in whom the acceptability of a medication and, hence, its ease of administration may be greatly affected by the taste and appearance of the drug [3,12]. We want to emphasize in this case report the unique taste of Dr Pepper, which is well suited to mask the bitter taste of midazolam and ketamine. Dr Pepper is a carbonated soft drink with a very distinct flavor, and is marketed in North America and South America by the Dr Pepper Snapple Group. In addition, the pH of Dr Pepper (pH 2.5) is close to those of both midazolam (pH 3.3) and ketamine (pH 3.5–4.1), providing stability to the drug mixture [13,14].

We preferred not to risk awakening the patient by trying to obtain an intravenous access prior to induction of anesthesia. Instead, we opted for a “steal induction” technique with inhalational anesthetic agents to achieve a smooth induction. In 1977, Meyers and Muravchick [15] compared postoperative behavioral responses in a group of children who underwent a “steal induction” (asleep induction technique) versus a group of children who underwent an “awake” induction. They showed that the asleep induction technique was associated with far fewer behavioral upsets postoperatively than awake induction techniques. The steal induction technique was particularly useful in our patient.

In summary, lateral thinking is frequently the key while dealing with violent autistic patients. Disguising the premedication drugs in a compatible and palatable beverage greatly increases the ease of administration of these drugs in uncooperative patients.

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