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Dexmedetomidine-ketamine sedation during upper gastrointestinal endoscopy and biopsy in a patient with Duchenne muscular dystrophy and egg allergy

Vidya Raman,¹ Desale Yacob,² and Joseph D Tobias^{1,2}¹Department of Anesthesiology, Nationwide Children's Hospital and the Ohio State University, Columbus, Ohio, United States²Department of Pediatrics, Nationwide Children's Hospital and the Ohio State University, Columbus, Ohio, United States**Address for correspondence:** Dr. Vidya Raman, Department of Anesthesiology and Pain Medicine, Nationwide Children's Hospital, 700 Children's Drive, Columbus, Ohio 43205, United States E-mail: vidya.raman@nationwidechildrens.org**Copyright :** © International Journal of Critical Illness and Injury Science

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Abstract

Sedation during invasive procedures provides appropriate humanitarian care as well as facilitating the completion of procedure. Although generally safe and effective, adverse effects may occur especially in patients with co-morbid diseases. In many cases, given its rapid onset and offset, propofol is chosen to provide sedation during various invasive procedures. We present a nine-year-old, 45 kg child with Duchenne muscular dystrophy (DMD) who presented for esophagogastroduodenoscopy (EGD). Given the egg allergy, which was a relative contraindication to the use of propofol, and the potential risk of malignant hyperthermia due to DMD, a combination of dexmedetomidine and ketamine was used for procedural sedation. Dexmedetomidine was administered as a loading dose of 1 µg/kg along with a single bolus dose of ketamine (1 mg/kg). This was followed by a dexmedetomidine infusion at 0.5 µg/kg/hour. The patient tolerated the procedure well and was discharged to home. Previous reports regarding the use of dexmedetomidine and ketamine for procedural sedation are reviewed and the potential efficacy of this combination is discussed.

Keywords: Dexmedetomidine, gastrointestinal endoscopy, ketamine, procedural sedation

INTRODUCTION

Invasive and/or non-invasive procedures remain both a common component in the management of children with acute and chronic diseases. In recent years, there has been a shift in the philosophy regarding procedural sedation given the increasing recognition of the negative aspects of inadequate sedation. Although procedural sedation is generally safe and effective, patients with underlying co-morbid conditions are at increased risk for complications during and after the procedure.[1]

Duchenne muscular dystrophy (DMD) is an X-linked disorder that occurs in males with an incidence of 1 in 3,300 births. A deficiency of the protein, dystrophin, in skeletal, cardiac, and smooth muscle results in progressive muscle weakness with eventual respiratory and cardiac compromise during the second and third decades of life. Previous reports have demonstrated the impact of this disorder on perioperative morbidity and mortality.[2] Additionally, postoperative mechanical ventilation may be required when general anesthesia, endotracheal intubation, and mechanical ventilation are needed.[3,4] Given the potential for adverse effects including MH (malignant hyperthermia), rhabdomyolysis, and hyperkalemia in patients with DMD, avoidance of inhalational anesthetic agents is generally recommended.[5,6]

The intravenous anesthetic agent, propofol, is a commonly chosen alternative to inhalational anesthetic agents in patients with MH susceptibility and in those with DMD.[7] The only

contraindication to propofol listed by its manufacturer is hypersensitivity to the product or its components, which include egg lecithin and soybean oil. Although there is limited evidence-based medicine to support the potential for allergic reactions following propofol use in patients with egg allergies,[8] many healthcare providers consider such allergies a contraindication to its use. Given these issues, there remains a need for alternative agents for procedural sedation in this population. We report our experience with a combination of ketamine and dexmedetomidine for sedation during esophagogastroduodenoscopy (EGD) in a 9-year-old pediatric patient with DMD. The potential applications of this combination in procedural sedation are discussed with particular emphasis on their use in the patient with potential MH susceptibility.

CASE REPORT

Approval for the retrospective review of this case and presentation of the material in this format was approved by the Institutional Review Board at Nationwide Children's Hospital (Columbus, Ohio). A nine-year-old, 45 kg child with DMD and positive celiac serology presented for an EGD with biopsies to complete his workup of celiac disease. His only past anesthetic was at the age of three years in his home country of Jordan prior to the diagnosis of DMD. Currently, the patient was non-ambulatory and wheelchair bound. His last echocardiogram preformed the week prior to this anesthetic as part of the preoperative work-up revealed a shortening fraction of 30% and an ejection fraction of 63%. Current medications included lisinopril 5 mg once a day and metoprolol 12.5 mg twice a day. Other pertinent history was that the child had not eaten eggs or egg products for several years after developing a rash. Premedication with oral midazolam (15 mg) was followed by transportation to the operating room and the placement of routine American Society of Anesthesiologists' monitors including continuous pulse oximetry, continuous electrocardiography, intermittent non-invasive blood pressure, and end-tidal carbon dioxide monitoring. Following the administration of 70% nitrous oxide and 30% oxygen for three minutes, a peripheral intravenous cannula was placed without movement or response. Supplemental oxygen was delivered at two liters per minute and end-tidal carbon dioxide (ETCO₂) measured via a nasal cannula. Dexmedetomidine (1 µg/kg) and ketamine (1 mg/kg) were administered as a bolus dose over 10 minutes. Following these medications, the heart rate decreased from 80-90 to 60-64 beats/minute without a change in the blood pressure which remained at 110-120/60-70 mmHg. Oxygen saturation, respiratory rate (RR), and ETCO₂ remained unchanged. The oxygen saturation measured by pulse oximetry remained at 98-100%, the ETCO₂ was 35-40 mmHg, and the respiratory rate was 14-20 breaths/minute. Following the bolus dose, a continuous dexmedetomidine infusion was started at 0.5 µg/kg/hour. At this point, the EGD scope was introduced into the patient's mouth without response. The EGD with biopsies from the small bowel, stomach, and esophagus were completed without incident during the 15 minute procedure. During the procedure, the heart rate (HR) remained at 60-70 beats and the blood pressure (BP) varied from 88-104/50-68 mmHg. Pulse oximetry remained at 97-100%, ETCO₂ at 35-40 mmHg, and the respiratory rate at 14-20 breaths/minute. The patient was transported to the post-anesthesia care unit. He was awake and alert, answering questions within 20 minutes. His postoperative course was uneventful and he was discharged home after two hours to ensure temperature, respiratory, and cardiovascular stability.

DISCUSSION

Our patient was somewhat unique in that his co-morbid disease process (DMD) was a relative contraindication to the use of the inhalational anesthetic agents while his egg allergy was a relative contraindication to the use of propofol. Given his underlying disease process, we also felt that performance of procedural sedation while maintaining spontaneous ventilation and avoiding general anesthesia and endotracheal intubation was the optimal choice. Although general anesthesia may be required for specific procedures, many procedures can be performed with procedural sedation and the maintenance of spontaneous ventilation. In addition to the associated egg allergy which may preclude its use, propofol may also result in respiratory depression and apnea.[9–11]

Dexmedetomidine is an α_2 -adrenergic agonist which initially received Food and Drug Administration (FDA) approval in the United States in 1999 for the sedation of adults during mechanical ventilation

and subsequently in 2009 for monitored anesthesia care (MAC) of adults. Although FDA-approved only for use in adults, it has been used successfully in several different clinical scenarios in infants and children including sedation during mechanical ventilation, procedural sedation, supplementation of postoperative analgesia, prevention of emergence delirium, control of post-anesthesia shivering, and the treatment of withdrawal.[12]

Although effective for non-invasive procedures, dexmedetomidine has not been universally effective when used as the sole agent for invasive procedures including gastrointestinal (GI) endoscopy. In fact, early experience with this agent demonstrated it to be ineffective during upper endoscopy in a pediatric patient.[13] In a prospective, randomized trial in adults comparing dexmedetomidine with fentanyl or meperidine-midazolam for sedation during colonoscopy, dexmedetomidine resulted in less effective sedation, a higher incidence of adverse effects, and a delay in the time to discharge readiness.[14] There was clinically significant bradycardia with a heart rate of 40 beats/min in 2 of 19 patients and a decrease in the blood pressure to less than 50% of the initial value in 4 of 19 patients. Time to home readiness was 85 ± 74 minutes with dexmedetomidine, 39 ± 21 minutes with meperidine-midazolam and 32 ± 13 minutes with fentanyl ($P = 0.007$). The study, which had planned to enroll 90 patients, was terminated early after 64 patients due to the adverse effects noted with dexmedetomidine.

However, conflicting results demonstrating the efficacy of dexmedetomidine have been reported by other investigators. Dere *et al.* reported that dexmedetomidine (loading dose of $1 \mu\text{g/kg}$ followed by an infusion of $0.5 \mu\text{g/kg/hr}$) was superior to midazolam (0.05 mg/kg) and fentanyl ($1 \mu\text{g/kg}$) during colonoscopy in 60 adult patients.[15] Demiraran *et al.* demonstrated that dexmedetomidine (loading dose of $1 \mu\text{g/kg}$ followed by an infusion of $0.2 \mu\text{g/kg/hr}$) was more effective than midazolam (0.07 mg to a maximum of 5 mg) during upper endoscopy in adults.[16]

Part of the variability in the efficacy of dexmedetomidine may be explained by the doses used and the patient populations studied. Mason *et al.* demonstrated improved efficacy (increased percentage of patients successfully completing the exam) with dexmedetomidine as the sole agent for sedation during radiologic imaging with the use of higher doses of dexmedetomidine.[17] The dosing regimen included a 10-minute loading dose of $3 \mu\text{g/kg}$ followed by an infusion of $2 \mu\text{g/kg/hr}$. The success rate increased from 91.8% to 97.6% with a reduction of both the need for supplemental pentobarbital as well as the recovery time when compared to their previous regimen (loading dose of $2 \mu\text{g/kg}$ followed by an infusion of $1.5 \mu\text{g/kg/hr}$). However, although no intervention was required, many of the patients developed significant decreases in their heart rate. Despite the success reported by Mason *et al.* others have reported failures with dexmedetomidine when used alone as the sole agent for invasive or painful procedures.

Given our concerns with escalating the dexmedetomidine dose due to its potential effects on chronotropy and cardiac function especially in a patient population like DMD in which myocardial involvement may be present, we decided that the combination of dexmedetomidine with a second agent may be preferable. In such scenarios, we have found that the combination of dexmedetomidine with ketamine may be used to provide the optimal level of sedation and analgesia with limited effects on respiratory and cardiovascular function. The use of ketamine provides several benefits including the provision of analgesia which is not present with dexmedetomidine, an increase in HR and BP to offset the bradycardia of dexmedetomidine, and a more rapid onset when compared to dexmedetomidine alone. Dexmedetomidine prevents several of the potential deleterious effects of ketamine including emergence agitation, excessive salivation, and stimulation of the cardiovascular system (increased HR and BP).[18] Although our patient also received midazolam in an effort to limit such problems, limited data in the adult population demonstrate that dexmedetomidine alone may be sufficient.[18] Additionally, given the limited adverse effects on respiratory function of dexmedetomidine, we were able to maintain spontaneous ventilation in our patient.[11,19]

To date, clinical experience with the combination of dexmedetomidine and ketamine are limited compared with the wide range of clinical reports using dexmedetomidine alone. Two previous reports have demonstrated the efficacy of a bolus dose of ketamine and dexmedetomidine followed by a

dexmedetomidine infusion for sedation.[20,21] Mester *et al.* retrospectively evaluated the combination of dexmedetomidine and ketamine for sedation during cardiac catheterization in the pediatric population.[20] The dosing regimen included a bolus dose of ketamine (2 mg/kg) and dexmedetomidine (1 µg/kg) administered over three minutes followed by a continuous infusion of dexmedetomidine. The regimen provided effective sedation with only 3 of the 16 patients requiring supplementation with an additional bolus dose of ketamine. Two patients developed upper airway obstruction which responded to repositioning of the airway. No central apnea was noted. The PaCO₂ was ≥ 45 mmHg in seven patients.

In another case series, McVey *et al.* described the successful use of dexmedetomidine and ketamine for procedural sedation during lumbar puncture for spinal anesthesia in 12 pediatric patients.[21] The dosing regimen for the ketamine and dexmedetomidine was similar to that reported by Mester *et al.* Additional anecdotal experience in small case series or individual case reports have outlined the use of a dexmedetomidine-ketamine regimen for procedural sedation in an additional 11 patients.[22–26] These reports provide further evidence for the efficacy of this combination for procedures in which a deep level of sedation is required, while maintaining spontaneous respiration.

CONCLUSION

Our patient's clinical scenario was somewhat unique given the association of an egg allergy and his underlying co-morbid disease process, DMD, which placed him at high risk for respiratory compromise during procedural sedation. We found that a bolus dose of ketamine and dexmedetomidine followed by a dexmedetomidine infusion provided effective sedation for EGD with limited effects on respiratory function. Regardless of the agent or agents used for procedural sedation, there is a potential for not only hemodynamic, but also respiratory depression. Given these concerns, appropriate monitoring and access to resuscitation medications and airway equipment is mandatory during procedural sedation. Given our concerns regarding the patient's associated co-morbid conditions and his MH risk, we monitored his status for two hours following the procedure. Although some of the previous studies have shown a prolonged recovery time of dexmedetomidine compared with propofol,[11,19] we noted no such issues in our patient. With these caveats in mind, we believe that in this and other clinical scenarios, the combination of dexmedetomidine and ketamine should be considered when choosing agents for procedural sedation.

Footnotes

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Conflict of Interest: None declared.

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