Dexmedetomidine-ketamine sedation during bone marrow aspirate and biopsy in a patient with Duchenne muscular dystrophy

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ABSTRACT

Sedation during invasive procedures not only provides appropriate humanitarian care for patients, but also facilitates the completion of invasive procedures. Although generally safe and effective, adverse effects may occur especially in patients with co-morbid diseases. We present the successful use of a combination of dexmedetomidine and ketamine to provide sedation and analgesia in a 21-year-old patient with Duchenne muscular dystrophy (DMD) undergoing bone marrow aspiration and biopsy. Co-morbidities included both depressed myocardial function and impaired respiratory function. Dexmedetomidine was administered as a loading dose of 1 μg/kg over 5 min followed by an infusion of 1 μg/kg/h. Ketamine (20 mg) was administered along with the dexmedetomidine loading dose. An additional 10 mg of ketamine was administered to treat the pain experienced during the placement of the local anesthetic agent prior to the procedure. No clinically significant hemodynamic or respiratory changes were noted. The patient tolerated the procedure well and was discharged home. A review of previously published reports of dexmedetomidine and ketamine for procedural sedation are reviewed.

Key words: *Dexmedetomidine, Duchenne muscular dystrophy, ketamine, procedural sedation*

INTRODUCTION

Duchenne muscular dystrophy (DMD) is an X-linked disorder which occurs with an incidence of 1 in 3,300 male births. It generally presents as weakness during the first decade of life usually between four and eight years of age. The genetic defect results in a deficiency of the protein dystrophin in skeletal, cardiac, and smooth muscle. Although skeletal muscle involvement with weakness predominates as the major clinical feature of this disorder, as these patients enter the second and the third decade of life, progressive myocardial involvement leads to impaired myocardial contractility, conduction disturbances, and arrhythmias. The potential impact of this disorder on perioperative morbidity and even mortality cannot be ignored as the literature has demonstrated a significantly increased risk during anesthetic care in these patients.[1]

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Although general anesthesia may be required for specific procedures, moderately painful procedures such as bone marrow aspiration and biopsy can be performed with procedural sedation and the maintenance of spontaneous ventilation. In cases like these, there are many options for the provision of such care although frequently used agents such as propofol may result in respiratory depression.[2] Given these issues, there remains a need for a better agent or agents for procedural sedation. We report our experience with a combination of ketamine and dexmedetomidine for sedation during bone aspirate and biopsy in an adolescent with DMD and co-morbid respiratory and cardiac involvement. The potential applications of this combination in procedural sedation are discussed and previous reports from the literature reviewed.

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 the Nationwide

Children's Hospital (Columbus, Ohio). The patient was a 21-year-old, 43-kg man with DMD, who presented for sedation during bone marrow aspiration and biopsy. There were no cognitive effects of the DMD and the patient was cognizant of the procedure and the plan for anesthetic care. He, his parents, and his pediatric pulmonologist specifically requested avoidance of endotracheal intubation and general anesthesia. Pulmonary function testing performed two days prior to the procedure revealed a forced vital capacity (FVC) that was 16% of that predicted for his age and weight and a forced expiratory volume in one second (FEV_1) that was 18% of the predicted value. The forced expiratory flow rate (FEF) 25–75 was 30% of the predicted normal value. Administration of an aerosolized bronchodilator resulted in a decrease of these values to 14, 16 and 16% of predicted normal values, respectively. Transesophageal echocardiography conducted three months before the procedure showed moderately depressed left ventricular systolic function with a left ventricle ejection fraction of 34%.

The patient was kept *nil per os* for 6 h. A 24-gauge peripheral intravenous cannula was started in the preoperative area. Initial vital signs in the preoperative holding area included an heart rate (HR) of 80 beats/min, a respiratory rate of 20 breaths/minute, a blood pressure (BP) of 76/48 mmHg and an oxygen saturation of 100%. On arrival to the operating room, standard American Society of Anesthesiologists' monitors were placed. Supplemental oxygen (3 liters/min) was administered and end-tidal carbon dioxide ($EtCO_2$) measured via a nasal cannula. Baseline vital signs in the operating room revealed an HR of 77 beats/min, respiratory rate of 18-20 breaths/min, BP of 73/34 mmHg, an oxygen saturation of 97-98%, and an $EtCO_2$ of 42-44 mmHg. Dexmedetomidine was administered as a loading dose of 1 μg/kg over 5 min followed by an infusion of 1 μg/kg/h. Ketamine (20 mg) was administered along with the loading dose of dexmedetomidine. An additional 10 mg of ketamine was administered during the procedure. There was no clinically significant change in the oxygen saturation, $EtCO_2$ or respiratory rate. The HR varied from 77 to 93 beats/min and the BP from 52-78/29-49 mmHg. The lowest recorded BP reading was 52/29 mmHg. As the parents reported preoperatively that there were periodic episodes of low BP during previous overnight admissions while the patient was asleep, no therapy was initiated. The BP reverted back to baseline without intervention. The procedure was completed without difficulty and the patient was taken to the post-anesthesia care unit. He required no additional analgesic medications or sedation. He denied any memory of the procedure or pain during it. He was discharged home in his usual state of health.

DISCUSSION

Dexmedetomidine is an α_2-adrenergic agonist which initially received 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. While FDA-approved only for use in adults, dexmedetomidine has been used safely and 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.[3] Although generally effective for sedation during non-invasive procedures, dexmedetomidine as the sole agent has not been uniformly successful for invasive procedures.[4] Given these issues, the combination of ketamine and dexmedetomidine may be preferred for invasive procedures.

Although limited when compared to reports using only dexmedetomidine, there have been previous reports in the literature regarding the use of a dexmedetomidine-ketamine combination for procedural sedation in the pediatric population. Koruk *et al.*, prospectively compared sedation using dexmedetomidine and ketamine to a regimen using midazolam with ketamine during extracorporeal shock wave lithotripsy.[5] Patients received either dexmedetomidine (1 μg/kg over 10 min) followed by ketamine (1 mg/kg) or midazolam (0.05 mg/kg) followed by ketamine (1 mg/kg). Sedation was equally effective in both groups without clinically significant changes in the hemodynamic and respiratory parameters. Although there was no difference in the time to achieve an Aldrete score of 8, the time for eye-opening, verbal response, and cooperation was decreased in the dexmedetomidine-ketamine group. Additionally, the incidence of nausea and vomiting was significantly lower with dexmedetomidine-ketamine compared with midazolam-ketamine (4.7% versus 32%).

Additional anecdotal experience in small case series or individual case reports have consistently demonstrated the utility of dexmedetomidine in conjunction with ketamine for procedures in which a deep level of sedation is required while maintaining spontaneous respiration [Table 1].[6-11] This anecdotal experience demonstrates the efficacy of the dexmedetomidine-ketamine combination in achieving the desired level of sedation while minimizing the incidence of adverse effects. Dexmedetomidine can be expected to prevent the tachycardia, hypertension, salivation, and emergence phenomena associated with ketamine. While ketamine may prevent the bradycardia and hypotension which has been reported with dexmedetomidine.[12]

Table 1: Small case series and isolated case reports regarding dexmedetomidine-ketamine for procedural sedation

Authors and reference number	Type of study and cohort size	Outcomes
McVey JD and Tobias JD [6]	Retrospective case series using dexmedetomidine and ketamine for sedation during lumbar puncture for spinal anesthesia in 12 children ranging in age from 2–9 years	The lumbar puncture for the performance of spinal anesthesia was tolerated in all patients. Dexmedetomidine infusion was reduced for associated bradycardia in one patient. One patient required fluid bolus to treat hypotension (BP = 68/38 mmHg). Two patients had upper airway obstruction, which resolved with repositioning of the airway.
Bozdogan *et al.*[7]	Case series of 3 infants (5-10 months of age) with congenital heart disease who required sedation during caudal block for surgical repair of incarcerated hernia	Bolus of ketamine (1 mg/kg) and dexmedetomidine (1 μg/kg) administered over 10 min to achieve a Ramsey sedation score of 4. The bolus dose of both agents was repeated in all 3 patients. This was followed by a dexmedetomidine infusion (0.7-1 μg/kg/h during the procedure). The procedure was completed without complications.
Barton *et al.*[8]	Procedural sedation in 6 infants (3 days to 29 months) with congenital heart disease	Dexmedetomidine was started at 2 μg/kg/h. Three of the six patients required ketamine (0.3-0.5 mg/kg) because of movement during the procedure. Effective sedation was achieved.
Luscri N and Tobias JD[9]	Case series of 3 children with trisomy 21 who sedation during an MRI scan for evaluation of sleep apnea	While these patients required sedation, the nature of the disease required that their airway remain unintubated during the scan. Effective sedation was achieved with no significant respiratory or hemodynamic effects, although one patient required additional dexmedetomidine and ketamine.
Irvani M and Wald M[10]	Single patient case report	Effective sedation for fiberoptic intubation in a 6-year-old girl with Treacher Collins syndrome and severe micrognathia.
Mahmoud *et al.*[11]	Single patient case report	Dexmedetomidine infusion with ketamine boluses to provide procedural sedation to a 4-year-old boy for the biopsy of a large anterior mediastinal mass, lumbar puncture and bone marrow aspiration. A 1 mg/kg dose of propofol was used to facilitate LMA placement.

Additionally, ketamine as part of the sedation induction may speed the onset of sedation and eliminate the slow onset time when dexmedetomidine is used as the sole agent.

The co-morbidities of DMD placed our patient at high risk for adverse effects during procedural sedation as there was both decreased myocardial function and limited respiratory reserve. In our patient, maintenance of spontaneous respiration was a priority as his neuromuscular disease placed him at risk for postoperative respiratory failure should the need arise for general anesthesia, endotracheal intubation, and controlled ventilation. Additionally, his level of anxiety was high, so preventing movement and providing adequate sedation and anxiolysis might have also been a challenge. A dexmedetomidine loading dose of 1 μg kg administered over 5 min followed by an infusion was effective in providing sedation and anxiolysis while ketamine was necessary as in the previously published reports to provide analgesia. No significant increase in HR from baseline was noted with the initial bolus dose while no bradycardia was noted with the infusion. Additionally, the patient denied any recall of the procedure and the recovery was uneventful without evidence of emergency phenomena such as hallucinations.

Although anecdotal, our case report illustrates the potential utility of the combination of ketamine and dexmedetomidine for procedural sedation, especially in patients with compromised respiratory or cardiac function. When compared with other agents used for procedural sedation, these two agents should have limited effects on the ventilatory function while their hemodynamic effects should negate each other. Our patient maintained hemodynamic and respiratory stability with sedation that was adequate to allow for successful completion of the procedure. Applications to other clinical scenarios may be warranted.

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