CASE REPORT

Monitored anesthesia care with dexmedetomidine and remifentanil during cardiac catheterization in a patient with Duchenne muscular dystrophy and malignant hyperthermia susceptibility

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ABSTRACT

Sedation during invasive procedures is frequently required not only to provide appropriate humanitarian care, but also to facilitate the completion of invasive procedures. Although the current sedative agents are 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 remifentanil to provide sedation (monitored anesthesia care) during cardiac catheterization and coronary angiography in an 11 years old patient with Duchenne muscular dystrophy. Co-morbid conditions included depressed myocardial function, a recent concern of coronary artery insufficiency, a family history of malignant hyperthermia, and impaired respiratory function. Dexmedetomidine was administered as an infusion starting at 0.7 μg/kg/hour without a loading dose, while remifentanil was administered as an infusion of 0.1 μg/kg/min. There was no patient response to local infiltration of the groin or placement of the arterial catheter for coronary angiography. The patient tolerated the procedure well without adverse effects. The combination of dexmedetomidine and remifentanil for monitored anesthesia care in the pediatric patient is discussed and the potential efficacy of this combination for procedural sedation is reviewed.

Key words: Dexmedetomidine; Remifentanil; Sedation; Monitored anesthesia care; Duchenne muscular dystrophy; Malignant hyperthermia; Co-morbid diseases

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INTRODUCTION

General anesthesia is generally required for cardiac catheterization in the pediatric population although sedation or monitored anesthesia care (MAC) may also be used.[1,2] The use of effective sedation or general anesthesia not only allows the control of hemodynamic parameters, but also ensures a motionless patient thereby facilitating the timely completion of the procedure. During procedural sedation, the incidence of adverse effects has been reported to be higher in patients with underlying co-morbid conditions especially those involving the cardiac or respiratory system.[3]

Duchenne muscular dystrophy (DMD), an x-linked disorder with an incidence of 1 in 3,300 male births, generally presents as weakness between 4 and 8 years of age. This genetic defect results in a deficiency of the dystrophin protein in skeletal, cardiac, and smooth muscle. Skeletal muscle involvement predominates as the major clinical feature of this disorder during the first decade of life. However, as these patients enter the 2nd and the 3rd decade of life, progressive myocardial involvement leads to impaired myocardial contractility, conduction disturbances, and arrhythmias. Given the involvement of both cardiac and respiratory function, there is a significantly increased risk during anesthetic care of these patients.[4,5] When endotracheal intubation is necessary for anesthetic care, postoperative mechanical ventilation may be required.[6,7]

Although general anesthesia may be required for specific surgical procedures, sedation or MAC with the maintenance of spontaneous ventilation may be chosen for even moderately painful procedures such as cardiac catheterization. In such cases, there are many options although frequently used agents such as propofol may result in respiratory depression.[8-10] We report our novel experience with a combination of dexmedetomidine and remifentanil for sedation during cardiac catheterization and coronary angiography in an 11-year-old patient with Duchenne muscular dystrophy, co-morbid respiratory and cardiac involvement, a family history of malignant hyperthermia (MH), and suspected coronary artery ischemia. The potential applications of this combination in procedural sedation are discussed and previous reports from the literature reviewed.

CASE REPORT

Institutional Review Board approval is not required at Nationwide Children's Hospital (Columbus, Ohio) for the presentation of single patient case reports. The patient was an 11-year-old, 31 kilogram boy who presented to the cardiac catheterization laboratory for a diagnostic coronary angiography. He had a history of Duchenne muscular dystrophy and dilated cardiomyopathy. There was also a strong family history of MH in first degree relatives. He had presented to the hospital with a one day history of substernal chest pain radiating down his left arm. Further workup revealed an elevated serum troponin level and an electrocardiogram with ST segment elevation in the inferior leads. An echocardiogram performed that day showed worsening left ventricular function with an ejection fraction of 42% and new areas of dyskinesis of the basilar and inferior wall. Therapy included a dose of acetylsalicylic acid, supplemental oxygen via nasal cannula, a heparin infusion at 12 units/kg/hr, and a nitroglycerin infusion at 1 μg/kg/min. The anesthesia machine was flushed with high flow oxygen, the soda lime canister was replaced, and the anesthesia vaporizers were removed per the departmental MH protocol. The patient was held *nil per os* for 6 hours and transported to the cardiac catheterization suite. Premedication included 2 mg of intravenous midazolam. Standard American Society of Anesthesiologists' monitors were placed including a nasal cannula with end tidal carbon dioxide ($EtCO_2$) monitoring capability. A second peripheral intravenous cannula was inserted. Dexmedetomidine and remifentanil were started at 0.7 μg/kg/hr and 0.1 μg/kg/min, respectively. After ensuring an adequate depth of sedation, the groin was infiltrated with 1% lidocaine. There was no patient response to the injection of the local anesthetic agent. The right femoral artery was also cannulated without response. The patient's heart rate and respiratory rate remained within 20% of baseline. His pulse oximetry reading remained above 96% on 3 lit/min of oxygen with an $EtCO_2$ of 36-44 mmHg. There was an initial drop in systolic blood pressure of 20% when the infusions were started. After discussion with the cardiologist, it was determined that the nitroglycerin could be discontinued as his chest pain had resolved. With the discontinuation of the nitroglycerin infusion and a 10 ml/kg bolus of lactated ringer's solution, his systolic blood pressure promptly returned to baseline. An arterial blood gas obtained during the procedure revealed: pH 7.33, CO_2 47.9 mmHg, PaO_2 218 mmHg, HCO_3^- 25.4 mEq/lit with an SpO_2 of 100% on 3 lit/min of oxygen. During the procedure, it was necessary to upsize the femoral artery catheter. Prior to this, the remifentanil infusion was increased to 0.15 μg/kg/min. There was no patient response to the catheter change. Coronary angiography did not reveal any occlusive disease of the coronary arteries and the procedure was completed in 45 minutes. The femoral artery catheter was removed and adequate hemostasis was achieved. The dexmedetomidine and remifentanil infusions were discontinued. The patient was awake and conversing within 5 minutes. He was transported to the Cardiothoracic Intensive Care Unit with standard monitors and supplemental oxygen at 3 liters/minute via nasal cannula. The ST elevation which had occurred prior to the procedure resolved during the case. In the immediate post-procedure period, the patient complained of pain in the right groin which was treated with hydromorphone 10 μg/kg. There were no other complications during the hospital stay. The patient was discharged home on postoperative day 2 with planned follow-up with his cardiologist in the outpatient setting.

DISCUSSION

Our patient presented with multiple co-morbidities which might be expected to increase the risk for adverse events. Significant co-morbid conditions included cardiac and respiratory involvement related to DMD, a family history of MH, which excluded the use of volatile anesthetic agents for general anesthesia, and clinical evidence suggestive of coronary artery ischemia. In patients with MH, a total intravenous anesthetic technique using propofol is most commonly chosen for sedation or general anesthesia. Numerous studies have reported the efficacy of propofol for monitored anesthesia care for pediatric patients undergoing invasive and non-invasive procedures.[8-10] However, propofol can cause a significant decrease in cardiac contractility, mean arterial pressure, and systemic vascular resistance. Additional cardiovascular effects may be caused by augmentation of central vagal tone leading to bradycardia, conduction disturbances and asystole.[11,12] Given our patient's limited cardiovascular reserve and the potential coronary artery ischemia, there was the concern that propofol may decrease diastolic blood pressure and thereby impact myocardial oxygen supply and coronary perfusion pressure. An additional

concern was the potential for respiratory depression related to a direct inhibition of upper airway muscle activity and a centrally mediated inhibition of airway reflexes.

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 it 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.[13] Dexmedetomidine has also been used as a primary anesthetic agent in patients undergoing surgery who are susceptible to malignant hyperthermia.[14-16] Through its agonistic effects at central α_2-adrenergic receptors, dexmedetomidine exerts a negative chronotropic effect resulting in a decrease in heart rate and a reduction in central sympathetic outflow, both of which are ideal in patients at risk for coronary artery ischemia. When compared with propofol, the respiratory depressant effects of dexmedetomidine are limited.[10] Although generally effective for sedation during non-invasive procedures, its use as a sole agent has not been uniformly successful for invasive procedures.[17-19]

One potential option is to supplement sedation with ketamine. Ketamine has both analgesic and sympathomimetic properties, making it an ideal complement to dexmedetomidine.[20] This combination has been used successfully for MAC in pediatric patients undergoing cardiac catheterization.[21] Although dexmedetomidine has been shown to blunt the sympathetic response to ketamine, given our patient's clinical suspicion of coronary ischemia, we chose not to use ketamine given the potential for tachycardia and hypertension.

Analgesia is a key component of procedural sedation especially in patients with ischemia to prevent an increase in myocardial oxygen demand related to hypertension or tachycardia. We chose remifentanil for its intense analgesia, rapid onset, quick metabolism, and easy titration by continuous infusion. The latter may be particular relevant during cardiac catheterization when intense analgesia is required for brief periods such as during cannulae placement. Analgesia was further supplemented by the liberal use of local anesthetic infiltration at the insertion site. Additionally, remifentanil has limited direct myocardial depressant effects. One concern regarding remifentanil relates to its respiratory depressant effects which may be particularly problematic when the maintenance of spontaneous ventilation is desired.[22] However, given its rapid metabolism, its respiratory depressant effects would be readily reversible with discontinuation of the infusion. Additionally, albeit rare, a unique adverse effect noted with the synthetic opioids is chest wall rigidity.[23] This has been most commonly reported with bolus dosing, but may occur with infusions. To date, there are limited reports regarding the combination of dexmedetomidine and remifentanil for procedural sedation or general anesthesia. Burnett et al reported the use of these agents as the primary components of a general anesthesia in a patient with a mitochondrial myopathy.[24] Arpaci and Bozkirh described the successful use of a remifentanil-dexmedetomidine combination for sedation in adults undergoing cystoscopy.[25] However, to date there are no reports regarding this combination for monitored MAC or procedural sedation in pediatric patients.

In summary, our anecdotal experience highlights the effective use of a combination of dexmedetomidine and remifentanil for sedation in a pediatric patient with multiple co-morbid conditions including DMD, MH history, and clinical concerns of coronary ischemia. Effective sedation was provided by continuous infusions of both agents starting at 0.1 μg/kg/min for remifentanil and 0.7 μg/kg/hour for dexmedetomidine. We chose not to use a bolus infusion given the potential for adverse hemodynamic and respiratory effects in a patient with co-morbid conditions. Using this combination supplemented with local anesthetic infiltration, we noted minimal changes in hemodynamic parameters, oxygenation saturation, and ventilation. Emergence from sedation was rapid. Given the potential for adverse effects on hemodynamic and respiratory function with any sedation regimen, we would recommend adherence to the guidelines from the American Academy of Pediatrics for monitoring and care of the pediatric patient during procedural sedation.[26]

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