Case Report

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Dexmedetomidine and Pulmonary Hypertension: A Case Report and Review of the Literature

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Abstract

Given its favorable effects on respiratory and hemodynamic function, dexmedetomidine remains a commonly used agent for procedural sedation in various scenarios in infants and children. Procedural sedation may be particularly problematic in patients with co-morbid conditions such as pulmonary arterial hypertension (PAH). To date, there are limited data regarding the administration of dexmedetomidine in the setting of PAH. We report the use of dexmedetomidine at part of a sedative regimen for procedural sedation during incision and drainage of an abscess and bone marrow biopsy in an adolescent with PAH. Previous reports regarding the use of dexmedetomidine in patients with PAH are reviewed and its applications in this scenario are discussed.

Keywords: Dexmedetomidine; Pulmonary hypertension; Procedural sedation

Introduction

Since its introduction into clinical practice, the applications of dexmedetomidine (Precedex®, Hospira Worldwide Inc, Lake Forest, Illinois) in the fields of intensive care medicine and anesthesiology have continued to increase. The current FDA-approved indications for dexmedetomidine include the provision of short term sedation (less than 24 hours) of adult patients in the ICU setting and for monitored anesthesia care (MAC) in adults in the operating room setting. To date, although it does not hold FDA-approval in the pediatric population, there is significant clinical experience in many scenarios including intraoperative use as part of a balanced anesthetic technique, the provision of sedation during mechanical ventilation, sedation and anxiolysis in the non-intubated Pediatric ICU patient, the prevention of emergence delirium, and as an agent for procedural sedation [1]. Given its favorable effects on respiratory function when compared with opioids, benzodiazepines and propofol, dexmedetomidine is being used more frequently for procedural sedation including patients with co-morbid conditions including congenital heart disease (CHD) [2-7]. When considering patients with co-morbid cardiac disease, one particularly difficult population includes those patients with pulmonary arterial hypertension (PAH). To date, there are limited data regarding the use of dexmedetomidine in the setting of PAH. We report the use of dexmedetomidine as part of a sedative regimen for procedural sedation during incision & drainage of an abscess and bone marrow biopsy in an adolescent with PAH. Previous reports regarding the use of dexmedetomidine in patients with PAH are reviewed and its applications in this scenario are discussed.

Case Report

Institutional Review Board approval is not required at Nationwide Children's Hospital (Columbus, Ohio) for the presentation of single case reports. A 15-year-old, 63.5 kilogram, adolescent with a history of Milroy disease and pulmonary hypertension who was status post pulmonary embolism presented with pancytopenia and a left axillary abscess. Previous cardiology evaluation had revealed pulmonary artery pressure equal to systemic pressure. The patient had history of a right axillary abscess, 5 months prior, after which he had developed multiple pulmonary emboli. Home medications included tadalafil 20 mg every day and coumadin 5 mg every day. Two doses of vitamin K were administered prior to the procedure to normalize coagulation function. The patient was transported to the operating room and standard American Society of Anesthesiologists' monitors were placed. Oxygen was administered at 3 liters per min-

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Table 1. Anecdotal Reports of Dexmedetomidine for Procedural Sedation in Patients With Pulmonary Hypertension

Author and references	Clinical situation	Dexmedetomidine dosing and outcome
Nathan AT et al [16]	16-year-old with impending respiratory failure due to pneumonia. PAH due to chronic lung disease since infancy.	Dexmedetomidine used to provide anxiolysis during increased work of breathing. The dexmedetomidine infusion was started at 0.5 µg/kg/hour and continued for 48 hours with effective pain control and anxiolysis.
Munro HM et al [17]	12-year-old with idiopathic PAH undergoing cardiac catheterization for reactivity to guided therapeutic options.	Ketamine 15 mg bolus times two followed by dexmedetomidine (loading dose of 1 µg/kg followed by an infusion of 1 µg/kg/hr). The dexmedetomidine infusion was continued at 0.5 µg/kg/hr for 2 hours postoperatively to provide sedation due to behavioral concerns. Hemodynamic stability maintained throughout.
Toyama H et al [18]	30-year-old with severe PAH for caesarean section at 32 weeks under general anesthesia.	Dexmedetomidine (0.4 µg/kg/hour) was used to provide postoperative anxiolysis and prevent emergence agitation following general anesthesia and during tracheal extubation.
Shinohara H et al [19]	21-year-old requiring monitored anesthesia care during regional anesthesia for inguinal hernia repair	Dexmedetomidine at 0.2 - 0.3 µg/kg/hour used to provide sedation and anxiolysis during Ilioinguinal-iliohypogastric block and subsequent surgical procedural.

PAH = pulmonary artery hypertension

ute and end-tidal carbon dioxide ($ETCO_2$) monitored from a nasal cannula. Dexmedetomidine (50 µg) and ketamine (50 mg) were administered as a bolus dose over 1 - 2 minutes followed by an infusion of dexmedetomidine at 0.5 µg/kg/hr. The sedation was supplemented with fentanyl (50 µg). Initially, the bone marrow aspirate was started from the left anterior pelvic crest with the patient in the supine position. There was no change in the oxygen saturation (99-100%) or $ETCO_2$ (37 - 41 mmHg) from baseline. The mean arterial pressure (MAP) stayed at baseline values of 67 - 80 mmHg with a heart rate of 60 - 70 beats/minute. During transition to the second procedure (incision and drainage of the left axillary abscess), when there was no painful stimulus, there was a decrease of the mean arterial pressure (MAP) to 40 mmHg (71/43 mmHg) with a heart rate (HR) of 60 beats per minute. This was treated with a single bolus dose of phenylephrine (100 µg) which resulted in the return of the MAP to baseline. The dexmedetomidine was decreased to 0.3 µg/kg/hour. Incision and drainage of the abscess were completed without difficulty and with no response to the surgical incision. Total time for both procedures was 32 minutes. The patient was transported to the post-anesthesia care unit where he had an uneventful recovery. He was sleepy, but arousable and able to answer questions within 15 minutes. He denied memory of the procedure. He was discharged to the inpatient ward after 30 minutes.

Discussion

The presence of pulmonary arterial hypertension (PAH) is a significant risk factor for perioperative complications including cardiac arrest and death [8, 9]. Avoidance of pharmacologic agents and factors which precipitate an increase in pulmonary artery pressure (PAP) must be avoided to ensure a successful perioperative course for these patients. Procedural sedation can result in adverse effects on respiratory function as opioids, benzodiazepines, and propofol may result in respiratory depression that adversely affects PAP in spontaneously breathing patients [10]. Additionally, excessive effects on the systemic circulation with vasodilation are a significant concern in these patients who are dependent on a high systemic vascular resistance (SVR) for RV perfusion and maintenance of cardiac output.

There remains limited information regarding dexmedetomidine's effects on the pulmonary vasculature and pulmonary vascular resistance (PVR). The initial data from an animal investigation suggested that there may be reason for concern [11]. In 6 instrumented sheep, dexmedetomidine (2 µg/kg over 1 minute) transiently increased the mean PAP and PVR [11]. PVR increased from a baseline of 81 ± 16 dynes/s/cm^5 to a maximum of 141 ± 27 dynes/s/cm^5 and the mean PAP increased from 15 ± 1 to 18 ± 0 mmHg. There was a similar increase of both the MAP and SVR.

However, human data has demonstrated different and more reassuring results. Although transient pulmonary hemodynamic changes have been reported in healthy adult volunteers during a graded dexmedetomidine infusion, when compared to placebo; dexmedetomidine effectively attenuated the increase in MAP, PAP, and pulmonary capillary wedge pressure in adults with pulmonary hypertension undergoing mitral valve replacement [12, 13]. Similarly, no change in PAP or PVR were reported by Ishikawa et al when evaluating the hemodynamic effects of dexmedetomidine in adults following cardiac surgery [14].

More recently, the effects on dexmedetomidine on PAP and PVR were evaluated using echocardiographic analysis of tricuspid regurgitant velocity in a cohort of 22 pediatric patients following surgery for CHD [15]. Analysis was performed at 3 points: baseline, prior to dexmedetomidine (T0), 6 minutes after the loading dose (T1), and 1 hour after the initiation of the infusion (T2). Dexmedetomidine dosing included a loading dose of 0.62 µg/kg followed by an infusion of 0.5 µg/kg/hr. The pulmonary artery systolic pressure (mmHg) at the 3 points was 30 ± 13, 24 ± 10, and 26 ± 8 ($p = 0.001$ for T0 vs. T1 and $p < 0.001$ for T0 vs. T2). Additionally, the pulmonary artery systolic pressure to systemic systolic pressure ratio which was 33% at T0, decreased to 23% at T1 and 25% at T2 ($p = 0.002$). Additionally, anecdotal success has also been reported with the use of dexmedetomidine for sedation in high risk patients with pulmonary hypertension (Table 1) [16-19].

In our patient, we chose to use a combination of ketamine and dexmedetomidine. Although dexmedetomidine is generally effective for sedation and anxiolysis, additional agents may be required for painful invasive procedures. Recent experience has demonstrated that the addition of ketamine to dexmedetomidine may offer several benefits [20]. Dexmedetomidine may limit the tachycardia, hypertension, salivation, and emergence phenomena from ketamine while ketamine may prevent the bradycardia and hypotension which has been reported with dexmedetomidine. Additionally, the addition of ketamine to dexmedetomidine to initiate the sedation process speeds the onset of sedation and eliminates the slow onset time when dexmedetomidine is used as the sole agent with the loading dose is administered over 10 minutes. Although previously thought to be contraindicated in patients with pulmonary hypertension, more recent data suggest that ketamine has limited effects on the pulmonary vasculature [21, 22].

Dexmedetomidine along with ketamine provided adequate sedation with limited effects on respiratory function. Although dexmedetomidine may result in a decrease in SVR as was noted in our patient, this was easily treated with a single dose of phenylephrine. The reliance on dexmedetomidine and ketamine limited the need for supplemental opioid analgesia. PAH remains a rare disease with a high risk for morbidity and mortality following general anesthesia and procedural sedation. Further studies are needed to fully evaluate fully the effects of ketamine and dexmedetomidine (keto-dex) on the pulmonary vasculature and the role of these agents in procedural sedation. Regardless of the regimen chosen, close monitoring of respiratory status and hemodynamic function is mandatory in accordance with guidelines set forth by the American Academy of Pediatrics [23].

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