



Sedation of hypercyanotic spells in a neonate with tetralogy of Fallot using dexmedetomidine

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Abstract

Objective: Sedation is an important step in the management of patients with hypercyanotic spells associated with tetralogy of Fallot (TOF) to ameliorate and prevent recurrence of cyanosis. This case report illustrates the effectiveness of dexmedetomidine-induced sedation in the management of hypercyanotic spells in a neonate with TOF.

Description: An 8-day-old term newborn patient with TOF showed hypercyanotic spells, as indicated by an abrupt decrease in arterial saturation (SpO₂) level measured by a pulse oximeter from 80% to as low as 50%, when the patient became irritable and agitated. We started continuous infusion of dexmedetomidine at a dose of 0.2 µg/kg/min without a loading bolus injection. About half an hour after commencement of dexmedetomidine infusion, the patient reached an acceptable level of sedation, together with a drop in heart rate by approximately 20 beats/min. There was no apparent respiratory depression or marked change in blood pressure. SpO₂ was also stable during dexmedetomidine infusion. The patient underwent a successful Blalock-Taussig shunt operation on the next day of admission.

Comments: Dexmedetomidine may be useful for the management of hypercyanotic spells in pediatric patients with TOF.

J Pediatr (Rio J). 2008;84(4):377-380: Hypercyanotic spell, sedation, tetralogy of Fallot.

Introduction

Patients with tetralogy of Fallot (TOF) often develop paroxysmal exacerbations of cyanosis, so-called hypercyanotic spells. Sedation of patients is an important aspect of the management of such episodes to ameliorate cyanosis and to prevent recurrence,¹ because agitation could increase sympathetic stimulation on the right ventricular (RV) infundibular muscle, thereby causing subpulmonic obstruction.² Morphine has been recommended primarily as a seda-

tive for the treatment of TOF patients with hypercyanotic spells.^{1,2} However, morphine causes significant vasodilation in both venous and arterial beds, resulting in significant reduction of cardiac preload and systemic vascular resistance. This can occasionally cause paradoxical exacerbation of cyanosis by increasing right-to-left shunting.³ In addition, morphine could potentially cause ventilatory depression, particularly in small infants and newborns, which could further worsen the cyanotic condition.²

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Dexmedetomidine is a highly selective α_2 -adrenergic agonist with sedative, analgesic, and anxiolytic properties.⁴ In contrast to other hypnotic sedatives, sedation with α_2 -agonists causes minimal respiratory depression.^{4,5} In addition, activation of α_2 receptors in peripheral blood vessels causes vasoconstriction and, in the autonomic ganglia, stimulation of the receptor inhibits release of catecholamines.^{4,6} These features of dexmedetomidine make it a better fit for sedation of TOF patients (particularly small infants) with hypercyanotic spells. We report an 8-day-old patient with TOF in whom dexmedetomidine produced effective sedation and management of hypercyanotic spells.

Case report

An 8-day-old term newborn patient (body weight = 3,020 g) was transferred to our hospital due to apparent cyanosis without any symptoms of respiratory distress. Echocardiography revealed TOF with a long narrowing segment of RV outflow tract. Arterial saturation (SpO_2) level measured by a pulse oximeter ranged from 80 to 83% during quiet breathing at rest. However, SpO_2 decreased abruptly to as low as 50% when the patient became irritable and agitated, indicative of hypercyanotic spells (we did not perform blood gas analysis, and thus did not have data showing acidemia). Phenobarbital suppository (2.5 mg/kg) was used upon admission, but this treatment failed to produce full sedation and prevent cyanotic spells. After receiving approval of the ethics review committee of our hospital and a signed consent form from the parents, we started continuous infusion of dexmedetomidine at a dose of 0.2 $\mu\text{g}/\text{kg}/\text{min}$ without a loading bolus injection. Figure 1 shows the time course of sedation level, heart rate, SpO_2 , blood pressure and respiratory rate before and after dexmedetomidine infusion.

About 30 minutes after commencement of dexmedetomidine infusion, the patient reached an acceptable level of sedation, together with a drop in heart rate by approximately 20 beats/min. There was no apparent respiratory depression or marked change in blood pressure. Clinical assessment of the sedation level using Ramsay scale indicated scores > 4 (score 4 = patient is sleeping and shows brisk response to loud noise or glabellar tap; score 5 = patient is sleeping and shows sluggish responses to the stimuli; score 6 = no response to the stimuli) after use of dexmedetomidine. SpO_2 , respiratory rate and blood pressure were also stable during dexmedetomidine infusion, except for the time of milk feeding through a nasogastric tube, which was provided for fear that hunger-induced agitation might cause cyanotic spells (4 hours after admission). At that occasion, SpO_2 fell down to about 60 to 63%, and phenylephrine infusion (0.005 mg/kg) restored SpO_2 rapidly to 80s levels. The dose of dexmedetomidine was increased to 0.3 $\mu\text{g}/\text{kg}/\text{min}$. The patient maintained a stable condition thereafter until a Blalock-Taussig shunt operation was successfully performed on the next day of admission (16 hours after admission).

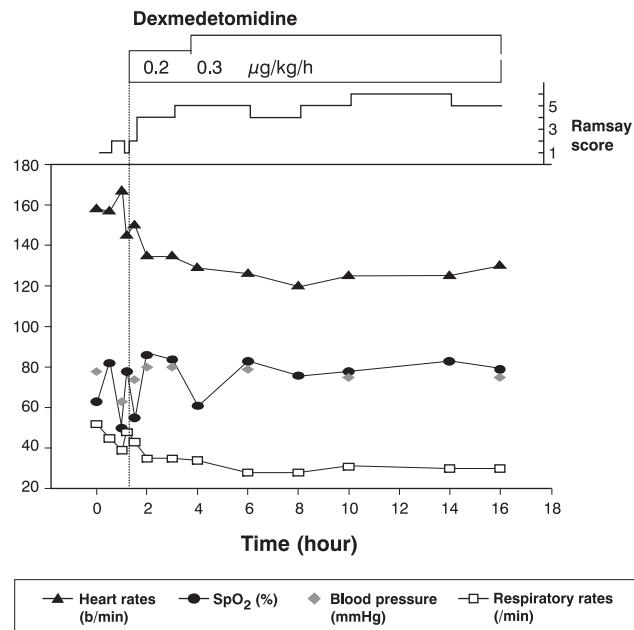


Figure 1 - Time course of sedation level, heart rate, SpO_2 , blood pressure and respiration after hospital admission

Discussion

Dexmedetomidine is currently approved only for intubated and mechanically ventilated adults in the intensive care unit. However, its use and efficacy has been reported in several other clinical situations in the pediatric population, including sedation for noninvasive radiological procedures,⁷ mechanical ventilation,⁸ prevention of emergence of delirium after general anesthesia, and treatment of withdrawal following prolonged administration of opioids and benzodiazepines.⁹ In addition to these conditions, the present report suggests that dexmedetomidine may be useful for the management of hypercyanotic spells in pediatric patients with TOF.

Hypercyanotic spells are mediated by an increase in degree of subpulmonic obstruction, which is caused by changes in myocardial contractility through sympathetic nerve stimulation, and is exacerbated by a decrease in cardiac preload or systemic arterial afterload.¹⁻³ Respiratory instability further exacerbates cyanosis.² Thus, ideal sedation for the management of TOF patients who are at risk of hypercyanotic spells includes well-exerted sympatholytic effect, maintained systemic vascular and venous resistance, and minimal effects on respiration. A highly selective α_2 -adrenergic agonist, dexmedetomidine, potentially meets these criteria and is potentially useful for the management of hypercyanotic spells in TOF patients as suggested by the present report.

Activation of α_2 -adrenoreceptors in the central nervous system, particularly in the locus ceruleus, is involved in the sedative action of dexmedetomidine by reducing central sympathetic flow.¹⁰ Because the α_2 -agonist should have little direct effect on respiration, based on receptor binding studies, the effects of dexmedetomidine on respiratory function can be minimal.^{10,11} Previous reports on the clinical use of this agent in pediatric patients are generally consistent with these pharmacologic profiles, demonstrating that dexmedetomidine provided profound sedation levels without significant adverse effects on ventilation.¹² In adult cases, however, respiratory complications have been reported, which are mostly associated with large and rapid initial loading doses.¹³ Therefore, in the present case, we started dexmedetomidine at a relatively low dose of continuous infusion (0.20 $\mu\text{g}/\text{kg}/\text{h}$) without a bolus loading dose. With this dosing regimen, the patient was sedated well, enough to prevent recurrence of agitation-induced hypercyanotic spells, and the respiratory state was stable throughout. To the best of our knowledge, the present patient (8-day-old) is the youngest among the reports describing the use of dexmedetomidine in children. Because newborn patients are themselves at risk of respiratory instability with or even without use of sedatives, minimal effects of dexmedetomidine on respiratory function would be of particular benefit for TOF patients in this age group.

The effects of dexmedetomidine on peripheral vessel are also important in considering the management of tetralogy spells, since lowering the vascular tone can induce hypercyanotic spells. Activation of α_2 receptor in peripheral blood vessels can potentially cause vasoconstriction, and several clinical studies indeed reported hypertensive responses after bolus injection of relatively larger doses of dexmedetomidine. Paradoxically, hypotension can also occur after large dosing administration of dexmedetomidine,^{4,14} presumably due to inhibition of sympathetic outflow that overrides its direct effects on the vasculature. Thus, to maximize the potential benefits of peripheral dexmedetomidine actions in the management of cyanotic spells, it is important to balance the direct effects on the vasculature with the sympatholytic actions by titration of the dose by continuous but not bolus infusion.

To date, morphine is recommended for sedating TOF patients with hypercyanotic spells.¹⁻³ However, morphine often causes both arterial and venodilation, resulting in paradoxical exacerbation of cyanosis. Morphine is also known to increase the risk of repetitive apneas or delayed ventilatory suppression. Ketamine may be an alternative to morphine due to its vasoconstrictive effects.² However, ketamine has relatively high incidence of airway complications (e.g., laryngospasm, partial airway obstruction and apnea) and gastrointestinal complications that could potentially have adverse effects on respiration under nonintubated and sedated conditions (e.g., emesis and excessive salivation).¹⁵

Dexmedetomidine may be useful to circumvent these untoward effects of morphine and ketamine in the management of tetralogy spells. Prospective studies comparing the

sedative, hemodynamic, and respiratory effects of dexmedetomidine with and without other agents (including morphine or ketamine) for the treatment of TOF-associated hypercyanotic spells are warranted.

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