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Intranasal Dexmedetomidine Administration Precipitates Respiratory Failure in Child With Croup and Asthma

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ABSTRACT

Intranasal dexmedetomidine administration in clinically recommended doses has a small but important risk of causing catastrophic respiratory failure in the setting of preexisting severe respiratory workloads.

JEL Classification: Critical Care Medicine, Paediatrics and Adolescent Medicine, Respiratory Medicine

1 | Introduction

Dexmedetomidine is an agent that has limited, potential respiratory depressant effects [1]. We report the sudden emergence of ventilatory failure in a child with croup and asthma who was treated with intranasal (IN) dexmedetomidine to facilitate intravenous (IV) access placement and improve tolerance of facemask aerosolized medication delivery. Cardiopulmonary monitoring and preparation of adjunctive respiratory support measures may help to ensure safe use of dexmedetomidine in the setting of pre-existing respiratory distress.

2 | Case History and Examination

This 4-year-old boy was diagnosed with recurrent croup and moderate persistent asthma. At night, snoring without obvious apnea occurred. Outpatient medications included nebulized budesonide 0.5 mg twice/day, albuterol 90 μg/actuation 4 puffs q4 hours PRN, and montelukast 4 mg PO daily.

After 1 day of croupy cough, inspiratory stridor, wheezing, clear rhinorrhea, and fever, this child presented to an outlying hospital emergency department and was treated with oral dexamethasone and five epinephrine aerosols. Eight hours later, on admission to the pediatric intensive care unit (PICU) his weight was 26.4 kg (> 95th isobar), body mass index 21 (> 95th isobar), temperature of 98.1°F, respiratory rate 20 breaths/min, pulse oximeter saturation 99% on room air, heart rate 150/min with good perfusion, and blood pressure 145/95 Torr. Air exchange was diffusely diminished. Cognition was intact and full sentences were spoken with a hoarse voice. Biphasic stridor and wheezing were present. Moderate labored breathing was present. Treatments included aerosolized epinephrine, continuous nebulized albuterol, ipratropium, and helium/oxygen 60/40. Facial respiratory devices were continually being removed by the child. Attempts to place an IV were unsuccessful.

3 | Differential Diagnosis, Investigations, and Treatment

After 4 h in the PICU, IN dexmedetomidine 2 μg/kg was administered to provide sufficient sedation that would allow for insertion of an IV. No other pre-medications that may have reduced ventilatory sufficiency were administered.

Abbreviations: ETT, endotracheal tube; IN, intranasal; IV, intravenous; OD, outer diameter; PICU, pediatric intensive care unit.

Within 10 min of dexmedetomidine, an IV was placed. Twenty minutes following IN dexmedetomidine, somnolence replaced his vigorous interactivity with his mother and staff. Markedly decreased auscultated breath sounds and acute onset see-saw breathing were simultaneously apparent. Active expiratory efforts ceased. Bag-mask ventilation became necessary and then a 3.5-mm outer diameter (OD) endotracheal tube (ETT) was placed.

While stridor resolved, marked biphasic wheezing persisted. Polymerase chain reactions were positive for *parainfluenza* III (nose) and group A *Streptococcus* (throat). A chest radiograph revealed a hazy left-sided opacity. Copious secretions grew *Moraxella catarrhalis* 4+. A 7-day course of ceftriaxone 2 g IV daily was started. After 2 days of methylprednisolone 1 mg/kg IV q 6 h, the ETT was upsized (5.0 mm OD). Extubation was accomplished on PICU Day 4. After 10 days of PICU care, the child was discharged on the same medications prescribed at admission. At follow-up, a sedated bronchoscopy of the subglottic airway was normal.

Multiple respiratory disease processes were present on admission. Each pathology contributed to impairment of respiratory system compliance and/or resistance (Table 1). Administration of IN dexmedetomidine was rapidly followed by onset of respiratory failure.

4 | Conclusion and Results

Dexmedetomidine has been successfully used to ease work of breathing in croup and asthma. However, when multiple respiratory pathologies are simultaneously present, as were in our child, the administration of IN dexmedetomidine is fraught with risk of causing respiratory decompensation. If used at all, it should be used with caution. For procedural sedation, administer the minimally effective dose, and plan preemptively for immediate additional emergent respiratory support.

In this report, IN dexmedetomidine 2 μg/kg was used for procedural sedation and appeared to precipitate respiratory failure in a child manifesting moderate respiratory distress associated with croup, asthma/bronchiolitis, and evolving pneumonia. In a clinical scenario complicated by the presence of increased respiratory workloads, if used at all, IN dexmedetomidine, should be administered in the lowest effective dose.

5 | Discussion

Dexmedetomidine is a sedative that has been reported to reduce agitation and improve acceptance of respiratory support equipment in severe croup [2] and asthma [3]. This report describes a child who simultaneously presented with both disease processes and was treated with IN dexmedetomidine to induce sedation. He quickly developed hypoventilatory respiratory failure. Several factors likely contributed to labored-breathing at presentation (Table 1). We speculate that adverse effects associated with dexmedetomidine administration hindered essential physiologic adaptations and may have actually increased respiratory workloads. Acute increased upper airway obstruction

TABLE 1 | Potential extra respiratory workloads at presentation.

	Disease location	↑ Resistance	↓ Compliance
Asthma/bronchiolitis	Small lower airways	E + I	Over-distended, hyper-inflated lung
Croup	Subglottic region	I + E	(–)
Secretions ↑	Throughout airways	I + E	(–)
Pharyngitis	Pharyngeal airway	I + E	(–)
Pneumonia	Lung parenchyma	(–)	Infected, inflamed

Note: ↓ decreased, ↑ increased, (–) none.
Abbreviations: E = expiratory, I = inspiratory.

TABLE 2 | Adverse effects of intranasal dexmedetomidine in promoting emergence of hypoventilation-associated respiratory failure.

Possible adverse respiratory system effects from dexmedetomidine	Observations after Dexmedetomidine administration
↑ Inspiratory collapse of upper airway†	↑ WOB with ↓ air exchange
↓ Central ventilation drive resulting in elevated blood carbon dioxide concentration	↓ Arousal despite ↓ effective ventilation
↓ Dyspnea	↓ Ventilation and respiratory contractile effort
Exposure of nascent respiratory muscle fatigue	Child allowed bag-mask ventilation
↑ Accumulation of airway secretions	↑ Suctioning required
↓ Active expiratory phase	↓ Effective exhalation

Note: ↓ decreased, ↑ increased, dominant cause†.
Abbreviation: WOB = work of breathing.

was likely the dominant cause of hypoventilatory respiratory failure (Table 2).

Doses of IN dexmedetomidine used for pediatric procedural sedation have been reported to range from 1 to 3 μg/kg [4]. IN dexmedetomidine has been used to improve acceptance of venipuncture in children aged 2–5 years [5, 6]. Following administration, with 2 μg/kg, sedation onset-time has varied from 8.8 to 25 min [5, 6]. In this child, by 10 min after 2 μg/kg IN our child had permitted IV placement and after 20 min, he required bag-mask ventilation for hypoventilatory respiratory failure. Though 0.5 μg/kg IN is too small of a dose to induce sedation [7], perhaps a smaller dose of IN dexmedetomidine, maybe 1 μg/kg, would have avoided precipitation of hypoventilatory respiratory failure. Other sedatives that may have precipitated respiratory failure include intranasal fentanyl or intranasal midazolam. Intranasal naloxone may have been useful to reverse respiratory depression related to fentanyl administration. Inhaled nitrous oxide was not attempted but may have been preferable because of rapid onset and resolution of sedative effects.

Intravenous and intranasal dexmedetomidine have been widely used outside of the operating room by pediatric intensivists, pediatric hospitalists, and pediatric emergency department physicians. Airway obstruction after use of primarily IV dexmedetomidine was uncommon, occurring in only 0.27% of 13,072 pediatric cases; emergent airway intervention was needed in only 0.05%. Most of these children had no concomitant systemic disease [8]. In the presence of systemic disease, anticipatory monitoring and invasive respiratory support should be prioritized.

Even though airway tone is generally maintained after dexmedetomidine administration [9, 10]. Our patient displayed changes in work of breathing and air exchange that were unmistakable evidence of new onset, critically compromised, upper airway patency. Negative intraluminal airway pressure during the inspiratory phase of the respiratory cycle could have enhanced airway crowding in both the supraglottic pharynx and the subglottic extra thoracic trachea. Suppression of normal clearance of copious airway secretions could likewise have augmented upper (and lower) airway resistances. We suspect that worsening of inspiratory upper airway obstruction was the dominant cause of acute onset ventilator failure (Table 2). Undoubtedly, multiple severe and progressive disease processes preceded the sudden changes associated with dexmedetomidine administration (Table 1). These dynamic pathologies probably provided substantial contributions to the emergence of respiratory failure as well.

Ventilation is modulated to maintain blood carbon dioxide and oxygen levels in acceptable physiologic ranges. Lung ventilation is stimulated by hypoxia and hypercarbia. Dexmedetomidine may reduce acute ventilatory responses to hypercarbia [11] and hypoxia [12]. In our child, hypoxia was never clinically apparent. However, hypercarbia-associated "narcosis" may well have supervened and altered effective ventilatory drive. Also, the sedative effect of IN dexmedetomidine may have unmasked underlying nascent respiratory muscle fatigue.

Arguably, at presentation, the increased respiratory workloads were at least partially offset by dyspnea-associated increases of ventilatory contractile effort [13]. Dexmedetomidine has been reported in the intensive care [14] and palliative care [15] settings to reduce the experience of dyspnea. Initially, at presentation, our 4-year-old child may well have experienced dyspnea-associated, upregulated ventilatory contractile effort. Dexmedetomidine may have diminished this underlying adaptive physiologic mechanism.

Author Contributions

William E. Novotny: conceptualization, data curation, formal analysis, project administration, supervision, writing – original draft, writing – review and editing. **Pam Fox:** conceptualization, data curation, formal analysis, investigation, writing – original draft, writing – review and editing. **Dynita Haislip:** conceptualization, data curation, formal analysis, investigation, writing – original draft, writing – review and editing.

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The authors have nothing to report.

Ethics Statement

The Institutional Review Board of East Carolina University, Brody School of Medicine, and ECU Health (the Ethics Committee) does not require approval of a de-identified report of a single patient. Nonetheless, signed consent for this case report was obtained from the parent of this child. This study conforms to the US Federal Policy for the Protection of Human Subjects.

Consent

The authors of this manuscript confirm that a written patient consent has been signed and collected in accordance with the *Clinical Case Reports* patient consent policy.

Conflicts of Interest

The authors declare no conflicts of intrest.

Data Availability Statement

Data from this case report other than that reported in this manuscript cannot be shared in the interests of protecting patient confidentiality.

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