Because of the high incidence and untoward effects of emergence delirium in the pediatric population, investigating pharmacologic measures for preventing this phenomenon is important to the anesthesia provider. Dexmedetomidine, a highly selective α₂ agonist, has been shown to prevent emergence delirium in the perioperative setting; however, recommendations for best practice regarding use of this medication are not widely available. Barriers to the use of dexmedetomidine may include side effects such as bradycardia and delayed emergence, as well as limited evidence for the best practice of timing, method, and dosing of dexmedetomidine. This review of the evidence included 2,142 study participants ranging in age from 1 to 15 years. The findings suggest that administering an intravenous bolus dose of 0.5 μg/kg of body weight in the intraoperative phase demonstrated a significant reduction in the incidence of emergence delirium with minimal side effects. Administration of dexmedetomidine immediately following induction of anesthesia revealed benefit in these patients without a delay in emergence from anesthesia. Along with the benefit of preventing emergence delirium in pediatric patients, the evidence also suggests that dexmedetomidine may lower volatile-agent and analgesic requirements.

Keywords: Bolus, dexmedetomidine, emergence delirium, pediatric, prevention.

Emergence delirium (ED) occurs frequently in the pediatric population, with a reported incidence ranging from 20% to 80%.¹⁻⁴ Emergence delirium has been described as a mental disturbance, dissociated state of consciousness, and a confusion state without recognition of the surrounding environment; and it is accompanied by agitation behaviors such as kicking, screaming, thrashing, or involuntary physical activity.¹⁻⁶ These movements are nonpurposeful, and affected patients are less likely to be consolable by caregivers.¹⁻⁶ Emergence delirium is distressing for the parents and may lead to patient injury.¹⁻⁴,⁶ Emergence delirium occurs within a mean of 14 minutes (SD = 11 minutes) after recovery from anesthesia but can be delayed up to 45 minutes following emergence.¹⁻⁶ Risk factors for ED include the use of fast-acting volatile agents such as desflurane or sevoflurane; preschool age; male gender; ear, nose, and throat surgery; patient’s preoperative anxiety; parental anxiety; few siblings; poor sociability; poor social adaptive capability; and poor quality of previous medical experience.¹⁻⁶

Although there are many theories regarding the development of ED, the exact pathophysiology is unknown.¹⁻²,⁴,⁶ Therefore, identifying key interventions that prevent ED has proved difficult. Alpha-2 agonists, such as dexmedetomidine and clonidine, have been shown to prevent ED.¹⁻⁶ Intraoperative bolus dosing may be the preferred method of delivery because of the simplicity of administration. For this review, the researchers investigated the efficacy of various intraoperative bolus dosages of dexmedetomidine in reducing the incidence of ED in the pediatric surgical patient.

Review of the Literature

• History. Emergence delirium can cause a patient to have involuntary nonpurposeful movements, which can lead to patient injury in the form of falls, catheter removal necessitating replacement, surgical wound dehiscence, or other injury.¹⁻²,⁴,⁶ These involuntary movements may also cause caretaker injury.⁶ Witnessing ED is a difficult experience for the family, patient, and provider; and ED has been shown to reduce patient satisfaction scores.¹,³ In open postanesthesia care unit (PACU) environments, the effects of ED may also affect surrounding patients.³ Emergence delirium can extend length of stay and increase costs to the institution.¹,³,⁴,⁶ These potential problems warrant further investigation into preventive strategies.

• Dexmedetomidine. Dexmedetomidine, a selective α₂ agonist, has several pharmacodynamic properties that have demonstrated its usefulness in preventing ED.¹,⁷,⁸ This agent exhibits anxiolytic, analgesic, antisialagogue, and volatile agent–sparing properties.¹,⁷,⁸ The evidence
supporting dexmedetomidine as a preventive agent for ED led to this review to identify effective intraoperative bolus dosing of this agent.

**Materials and Methods**

- **PICO Question.** The PICO (population, intervention, context, and outcome) question was as follows: “In pediatric patients aged 1 to 15 years at risk of emergence delirium (P), what is the optimal bolus dose of dexmedetomidine (I) during general anesthesia for surgical procedures (C) to decrease the incidence of emergence delirium with minimal side effects (O)”?

  - **Search Strategy.** The search for evidence (2010-2018) examined PubMed, the Cumulative Index to Nursing & Allied Health Literature (CINAHL), and the Cochrane Database of Systematic Reviews. The search terms applied both individually and in combination were *emergence delirium*, *pediatric*, and *dexmedetomidine*. Inclusion criteria included research studies, systematic reviews, and case reports involving human participants published in English in a full-text form in peer-reviewed journals addressing the PICO question. All sources that did not meet inclusion criteria were excluded.

  We focused our search of the evidence on the use of dexmedetomidine administered intraoperatively as an intravenous bolus with the primary purpose of ED prevention rather than as a rescue agent administered in the PACU. All sources that indicated dexmedetomidine administration via infusion or rescue dose administration were excluded. Limiting the search to intraoperative intravenous bolus dosing further increased homogeneity and provided a practical method of preventing ED perioperatively.

  Individual studies included in an appraised systematic review were not individually reviewed. Reference lists of the included evidence were examined for other evidence sources. Sources were included based on reviewing the title, abstract, and full text. The evidence was critically appraised using the methods described by Melnyk and Fineout-Overholt. Attributes such as inclusion criteria and appraisal method were noted for systematic reviews and randomization and sample size determination were noted for clinical trials. Evidence levels range from Level I (systematic review of randomized controlled trials [RCTs]) to Level VII (expert opinion).

**Results**

A total of 166 potential sources were identified through a systematic search (Figure). Much of the current literature evaluates continuous infusion dosing of dexmedetomidine rather than bolus administration. Seven sources met inclusion criteria. The evidence reviewed consisted of 5 RCTs and 2 meta-analyses (Table 1). All sources were high-level evidence (level I) and level II. The sources of evidence were of global origin and included studies from India, Korea, Greece, and China. Methods for blinding included having a separate clinician prepare and label the medications to be administered or wrapping the intervention and control medication syringes in foil.

The participants evaluated ranged in age from 1 to 15 years old. The difference in age between the intervention and control groups was not statistically significant. Both male and female gender were included, and several sources identified homogeneous distribution of genders between groups. The ASA physical status of participants ranged from 1 to 3. Surgical procedures in which the use of dexmedetomidine was evaluated included tonsillectomy and adenoidectomy, ophthalmic operations, laparoscopic inguinal hernia repair, and infraumbilical procedures. General anesthesia was maintained by sevoflurane or desflurane with or without nitrous oxide, total intravenous anesthetic with propofol and remifentanil, or it was unreported.

The evidence evaluated the use of dexmedetomidine administered intraoperatively by intravenous bolus. Dexmedetomidine dosing ranged from 0.15 to 2 μg/kg. The timing of administration occurred shortly after induction or before emergence. Additionally, the included sources investigated ED as either a primary or secondary outcome.

Emergence delirium was most commonly assessed using the Pediatric Anesthesia Emergence Delirium (PAED) score (Table 2). The PAED score assesses for ED by observation of the patient and assigning a numeric score from 0 to 4 in 5 categories: eye contact, purposeful action, awareness of surroundings, restlessness, and inconsolability. A higher total score is correlated with the degree of ED. Other tools that were used in the evidence included the Watcha scale and the 5-point scale. The PAED score demonstrated reliability of 0.84 (95% CI = 0.76-0.90) and internal consistency of 0.89, and the Watcha scale is mentioned as having a high correlation with the PAED score. Although descriptions of the 5-point scale did not present reliability or validity, the scale follows measurements similar to the PAED score and the Watcha scale.

Other dependent variables studied included time to extubation, time to emergence (or awakening), PACU length of stay, postoperative nausea and vomiting (PONV), pain scores, analgesic requirements, incidence of bradycardia, and incidence of hypotension.

**Discussion of the State of the Art**

The evidence demonstrates that bolus-dose dexmedetomidine is an effective agent to reduce the occurrence of ED (odds ratio [OR] = 0.28; 95% CI, 0.21-0.36; I² = 41%). The evidence also proposed effective dosages to administer dexmedetomidine, as well as ap-
appropriate timing of administration, and secondary effects on patient hemodynamics.10-16

- **Effective Dose Range.** This review revealed that dexmedetomidine as an intraoperative intravenous bolus dose ranging from 0.5 to 2 μg/kg was shown to reliably decrease the incidence of ED (OR = 0.28; 95% CI, 0.21-0.36; I² = 41%). In one study, the ED incidence was 9.4% in the dexmedetomidine group (95% CI, 25.52-57.7), 13.9% in the propofol group (95% CI, 6.5-28.7), and 40.6% in the control group (95% CI, 25.5-57.7; P = .004).14 In other studies, the ED incidence in the control group was 60% vs 21% in the dexmedetomidine group (P = .005).10-16 Doses less than 0.5 μg/kg did not consistently prevent ED (P < .5511 to P = .00111,13). It was also noted that although a dose of 0.5 μg/kg was more effective at preventing ED (P = .001)13 than a dose of 0.25 μg/kg (P < .001),13 it remains unclear whether a dose greater than 0.5 μg/kg has additional benefit in reducing ED.10,12,13,15 The administration of lower doses of dexmedetomidine was associated with higher PAED scores, indicating an elevated level of agitation and ED.11 Patients who received a lower dose of 0.15 μg/kg (11% ED incidence) compared with 0.3 μg/kg (0% ED incidence)11 often had higher PAED scores (P < .05).11

- **Timing of Administration.** Dexmedetomidine was most commonly administered following induction of anesthesia.10-13,15,16 Dexmedetomidine was given as a bolus over 5 minutes11,12 or over 10 minutes,13-15 as recommended by the manufacturer.17 Delays in emergence or extubation were not recorded across all sources. However, when dexmedetomidine was administered following induction, it was not shown to increase time to extubation (95% CI, −0.98 to 1.39).12 PACU length of stay (standard mean difference [SMD] = −0.37; 95% CI, −1.02-0.28; I² = 94%),10 or time to discharge (P = .071).10-12 When dexmedetomidine was administered in the time just before emergence, the time to awakening and the incidence of sedation in the PACU were higher compared with the control group.14 The median time to awakening was as follows: dexmedetomidine group = 10.0 minutes (95% CI, 10.14-17.35 minutes) vs propofol group = 5.0 minutes (95% CI, 4.37-9.50 minutes) vs control group = 0.0 minutes (95% CI, 0.0-2.77 minutes).14 The incidence of sedation in the PACU was 62.5%, 44.4%, 12.5%, respectively, in the dexmedetomidine, propofol, and control groups; P = .010.14
### Table 1. Meta-analyses and Randomized Studies Examining Use of Dexmedetomidine to Prevent Pediatric Emergence Delirium 10-16

<table>
<thead>
<tr>
<th>Author, year, country/evidence type and level</th>
<th>N</th>
<th>Surgical procedure/primary anesthetic agent</th>
<th>ED scoring tool used</th>
<th>Dexmedetomidine bolus dose, μg/kg</th>
<th>Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cho et al, 2018, China Meta-analysis; Level I</td>
<td>1,097 (9 RCTs)</td>
<td>Tonsillectomy/anesthesia not described</td>
<td>PAED score and 5-point scale</td>
<td>0.3-2</td>
<td>ED scores and incidence of ED lower in dexmedetomidine group vs control group</td>
<td>Pain scores and total dose of analgesics in recovery were lower in dexmedetomidine group</td>
</tr>
<tr>
<td>Jain et al, 2018, India Prospective double-blinded randomized study; Level II</td>
<td>53</td>
<td>Cataract removal/desflurane with sub-Tenon block</td>
<td>PAED score</td>
<td>Group 1: 0.15 Group 2: 0.3</td>
<td>PAE score reduction in group 2 vs group 1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Dexmedetomidine administered following induction over 5 min Defined ED as PAED score &gt; 12</td>
</tr>
<tr>
<td>Tsiotou et al, 2018, Greece RCT; Level II</td>
<td>60</td>
<td>Tonsillectomy ± adenoidectomy/propofol</td>
<td>Watcha scale</td>
<td>1</td>
<td>ED incidence of 16.1% in study group vs 48.3% in control group</td>
<td>Dexmedetomidine administered following induction over 10 min Defined ED as Watcha scale ≥ 3</td>
</tr>
<tr>
<td>Sun et al, 2017, China RCT; Level II</td>
<td>100</td>
<td>Laparoscopic inguinal hernia repair/sevoflurane</td>
<td>5-point scale</td>
<td>Group 1: 0.25 Group 2: 0.5 Group 3: 1</td>
<td>45.8% frequency of ED in control group 30.4%, 12%, and 4% frequency of ED in groups 1, 2, and 3, respectively</td>
<td>Dexmedetomidine administered following induction and within 10 min before surgery Defined ED as score ≥ 4 on 5-point scale No bradycardia or hypotension reported</td>
</tr>
<tr>
<td>Makkar et al, 2016, India RCT; Level II</td>
<td>100</td>
<td>Infraumbilical surgical/desflurane with caudal block</td>
<td>PAED score</td>
<td>0.3</td>
<td>9.4% frequency of ED vs 40.6% in control group 13.9% frequency of ED in propofol group</td>
<td>Dexmedetomidine administered 15 min before end of surgery over 5 min Defined ED as PAED score ≥ 10</td>
</tr>
<tr>
<td>Song et al, 2016, Korea RCT; Level II</td>
<td>112</td>
<td>Strabismus repair/desflurane</td>
<td>PAED score and 5-point scale</td>
<td>Group 1: 0.25 Group 2: 0.5 Group 3: 1</td>
<td>60% frequency of ED in control group 48%, 44%, and 21% frequency of ED in groups 1, 2, and 3, respectively</td>
<td>Dexmedetomidine administered with induction over 10 min Defined ED as PAED score ≥ 10 or ≥ 3 on 5-point scale</td>
</tr>
<tr>
<td>Zhu et al, 2015, China Meta-analysis; Level I</td>
<td>620 (5 RCTs)</td>
<td>Multiple procedures/sevoflurane</td>
<td>PAED score</td>
<td>0.15-1</td>
<td>Incidence of ED lower in dexmedetomidine group vs control group&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Increased time to discharge in dexmedetomidine group Lower incidence of PONV in dexmedetomidine group</td>
</tr>
</tbody>
</table>

**Abbreviations:** ±, with or without; ED, emergence delirium; OR, odds ratio; PAED, Pediatric Anesthesia Emergence Delirium; PONV, postoperative nausea and vomiting; RCT, randomized controlled trial; RR, risk ratio.

<sup>a</sup> PAED score is measured continuously and recorded every 5 min, up to 30 min postoperatively. The 5-point scale is measured every 5 min, up to 2 hours postoperatively. Watcha scale is measured at 20 min postoperatively; study also measured ED at 10- and 30-min points.<sup>12</sup>

<sup>b</sup> ED score standard mean deviation = −0.79; 95% CI = −1.16 to −0.43; ED incidence odds ratio = 0.28; 95% CI = 0.21-0.36.

<sup>c</sup> Pain score standard mean deviation = −1.82; 95% CI = −2.50 to −1.13; analgesic dosage standard mean deviation = −0.59; 95% CI = −0.89 to −0.30.

<sup>d</sup> Standard mean deviation = 0.37; 95% CI = −1.02 to 0.28.

<sup>e</sup> P < .05, measured at 0, 10, 20, 30, 40, 50, and 60 min postoperatively.
One benefit of giving dexmedetomidine immediately following induction of anesthesia may be its volatile agent-sparing (P < .05) and analgesic effects (SMD = −0.59; 95% CI, −2.24 to 1.06; I² = 71%). Postoperative pain scores in recovery were notably lower in patients receiving dexmedetomidine (SMD = −1.82; 95% CI, −2.50 to −1.13; I² = 89%). They required less administration of analgesic agents (SMD = −0.59; 95% CI, −0.89 to −0.30; I² = 71%). In addition to these effects, dexmedetomidine possesses anxiolytic properties that may contribute to the reduction in the incidence of ED. The peak effect of dexmedetomidine occurs within 15 minutes and the half-life is 1.8 hours. Although the surgical procedures in this review were relatively brief, it should be considered that because of these pharmacokinetic traits, early administration of dexmedetomidine in a case lasting several hours may be less efficacious in preventing ED.

**Hemodynamic Effects.** The hemodynamic effects of dexmedetomidine may pose concern for the anesthetist when electing to include this agent in the plan of care. Dexmedetomidine possesses biphasic hemodynamic effects resulting in a transient increase in blood pressure, followed by a decrease in heart rate and blood pressure. However, in studies of adult and pediatric patients, doses up to 2 μg/kg have been used without a clinically significant mean difference in the heart rate per minute (P > .05) or in blood pressure (P > .05). The evidence suggests that even in the presence of decreased heart rate and blood pressure, no hemodynamic interventions were indicated because the variations were within normal limits (P = .05), even when dexmedetomidine was administered in procedures that are likely to trigger vagal reflexes.

**Conclusion**

Maximizing the benefits ofdexmedetomidine is dependent on the dosage and timing of administration. Higher doses of dexmedetomidine appear to decrease both the incidence and severity of ED. However, doses greater than 0.5 μg/kg may not provide additional protection against the occurrence of ED and may delay recovery from anesthesia. Therefore, a total dose of 0.5 μg/kg appears appropriate for preventing ED in the pediatric population (Table 3). The anesthetist should consider administering dexmedetomidine immediately following the induction of anesthesia. Administering dexmedetomidine at this time has been shown to reduce the minimum alveolar concentration (MAC) requirement of the volatile agent and may prevent delays in postanesthesia recovery.

Future studies that aim to quantify the contribution of dexmedetomidine to the MAC level would help the anesthetist to appropriately reduce the volatile agent, assisting in a more expeditious emergence time and decreased side effects. Further investigation into the use of dexmedetomidine for preventing ED in the pediatric population is necessary. The use of this medication should be evaluated in longer and more complex procedures. It should be considered that the pharmacokinetic profile of dexmedetomidine may warrant administration as an infusion or repeated bolus dose in longer procedures to achieve a reduction in ED.

A secondary outcome in one study reported a decreased risk of PONV, and this desirable outcome should also be further investigated. Furthermore, as the opioid-free anesthetic trend continues, studies that evaluate the optimal amount of dexmedetomidine that both prevents ED and reliably provides pain relief in the absence of opioids would be of great interest to the anesthetist.

**REFERENCES**

8. Bedirli N, Akcabay M, Emik U. Tramadol vs dexmedetomidine
Table 2. Pediatric Anesthesia Emergence Delirium (PAED) Scale

<table>
<thead>
<tr>
<th>Point value</th>
<th>Item description</th>
<th>Not at all</th>
<th>Just a little</th>
<th>Quite a bit</th>
<th>Very much</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The child makes eye contact with the caregiver</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>The child’s actions are purposeful</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>The child is aware of his/her surroundings</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>The child is restless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>The child is inconsolable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 3. Recommendations for Timing and Dosage of Dexmedetomidine to Reduce Incidence of Emergence Delirium

Abbreviations: ED, emergence delirium; PACU, postanesthesia care unit.


AUTHORS

Alexander N. Manning, MSNA, CRNA, is a nurse anesthetist at Robert Wood Johnson University Hospital. He was a student in the Master of Science in Nurse Anesthesia program at the Wake Forest School of Medicine at the time this article was written.

Leah K. Bezzo, MSNA, CRNA, is a nurse anesthetist at Seattle Children’s. She was a student in the Master of Science in Nurse Anesthesia program at the Wake Forest School of Medicine at the time this article was written.

Jamie K. Hobson, MSNA, CRNA, is a nurse anesthetist at Novant Health Forsyth Medical Women’s Center. She was a student in the Master of Science in Nurse Anesthesia program at the Wake Forest School of Medicine at the time this article was written.

Justine E. Zoeller, MSNA, CRNA, is a nurse anesthetist at Montefiore Medical Center. She was a student in the Master of Science in Nurse Anesthesia program at the Wake Forest School of Medicine at the time this article was written.

Courtney A. Brown, PhD, CRNA, CHSE, is an assistant professor of anesthesiology in the Wake Forest School of Medicine Nurse Anesthesia Program.

Kristin J. Henderson, DNAP, CRNA, CHSE, is an assistant professor of anesthesiology in the Wake Forest School of Medicine Nurse Anesthesia Program and director of simulation at Bowman Gray Center for Experiential and Applied Learning.

DISCLOSURES

The authors have declared no financial relationships with any commercial entity related to the content of this article. The authors did not discuss off-label use within the article.