Intranasal Dexmedetomidine Use in Pediatric Patients for Anxiolysis in the Emergency Department

Allison Kenneally, PharmD, Megan Cummins, PharmD, MPH,* Abby Bailey, PharmD, BCCCP,**
Katelyn Yackey, MD,† Landon Jones, MD,† Craig Carter, DO,†
*Adam Dugan, PhD,‡ and Regan A. Baum, PharmD, BCCCP**

Objectives: In recent years, dexmedetomidine has gained traction as a treatment for anxiolysis in the emergency department (ED). When used with an atomizer, it may also be given intranasally for anxiolysis. The primary objective was to determine the level of ED provider satisfaction and comfort with intranasal (IN) dexmedetomidine for anxiolysis in pediatric patients with behavioral agitation and/or acute psychosis. The secondary objectives included determining safety, rates of therapy failure, and ED length of stay compared with oral midazolam. The efficacy of IN dexmedetomidine versus oral midazolam in patients with autism spectrum disorder (ASD) was also evaluated.

Methods: This was a single-center, prospective study in a pediatric ED from March 1 to December 31, 2021. Patients were included in the study if the ED provider requested IN dexmedetomidine anxiolysis and completed a postadministration survey. Safety and efficacy outcomes were assessed by chart review and compared with patients who received oral midazolam during the same study period. Efficacy was defined as the rate of treatment failure, as the need for procedural termination, progression to procedural sedation, or the requirement of additional medications for anxiolysis.

Results: Sixty-two patients received IN dexmedetomidine {median dose [interquartile range (IQR)] of 3.05 [2.04–4.00] μg/kg/dose} compared with 58 who received oral midazolam [median (IQR) dose of 0.29 (0.25–0.48) mg/kg/dose). Providers reported high comfort and satisfaction scores, with median (IQR) scores of 90 (75–100) and 88 (60–100) of 100. Twenty-nine percent of patients experienced treatment failure, most commonly because of the need for additional medications. Those who received IN dexmedetomidine had a longer ED length of stay (6.0 vs 4.4 hours, $P = 0.010$). Among the patients with ASD, those who received IN dexmedetomidine had a lower rate of treatment failure compared with oral midazolam (21.2% vs 66.7%, $P = 0.039$).

Conclusions: This study demonstrates that IN dexmedetomidine has high levels of provider comfort and satisfaction, moderately high success rate, and a promising safety profile. In addition, IN dexmedetomidine may be superior to oral midazolam in patients with ASD for anxiolysis, but additional studies are needed.

Key Words: dexmedetomidine, anxiolysis, intransal

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In the United States, approximately 20% of all emergency department (ED) visits are patients aged younger than 18 years.[1] Acute injury is one of the leading causes of visits for pediatric patients aged older than 5 years and is the second leading cause of admission secondary only to respiratory illness.[1] For pediatric patients, acute injury and ED visits are significant contributors to patient stress. This stress may be especially severe in patients with an underlying behavioral or psychiatric disorder. On presentation to the ED, patients may require urgent medical evaluation, which may include a physical examination, diagnostic imaging, phlebotomy, or invasive procedures. Ultimately, these patients may require treatment of anxiety to facilitate their care in a safe and effective manner.

When selecting an agent for chemical anxiolysis, the characteristics of the drug need to be considered. The ideal medication for chemical anxiolysis will be a rapid-acting medication with minimal to no risk and a short duration of action.[2] The goal is for patients to remain alert, be adequately calm, but avoid prolonged length of stay (LOS) due to oversedation. In addition, the agent should have minimal adverse effects, with multiple routes of administration.[3] Medications administered via the intranasal (IN) route may be particularly beneficial in the pediatric population because they are not associated with the pain of intravenous (IV) or intramuscular administration. This is especially important for pediatric patients because establishing IV access may be a significant cause of stress.[3] Currently, there are no consensus or guideline recommendations for the preferred chemical treatment of anxiolysis. The pharmaceutical class with the most literature and historical use is benzodiazepines, specifically midazolam, which can be given IV, IN, and orally. However, benzodiazepines may cause respiratory depression and are known to have negative sequela with long-term exposure in pediatric patients.[4] Ketamine can also be used for analgesia or anxiolysis in pediatric patients, and respiratory depression is relatively uncommon.[5] However, ketamine may cause nausea and vomiting, and at high doses may cause a dissociative reaction, adding to distress in an agitated patient.

In recent years, dexmedetomidine has gained traction as a treatment for anxiolysis. In treating anxiety, the goal is for the patient to remain calm, awake, and cooperative. This differs from sedation or procedural sedation, where a moderate to deep level of sedation is desired to facilitate diagnostic or therapeutic interventions. Dexmedetomidine is an alpha$_2$-adrenergic agonist with anesthetic and sedative properties due to the activation of G-proteins inhibiting norepinephrine release.[6] It is not FDA-approved for use in pediatric patients; however, it is most commonly used off-label as an IV sedative in the intensive care unit for mechanically ventilated patients. When used with an atomizer, it may also be given IN for anxiolysis, where it has been studied in a variety of settings to facilitate diagnostic and therapeutic interventions. In 2008, Yuen et al[7] established that IN dexmedetomidine was similar to oral midazolam in reducing anxiety during parental separation and improving cooperation before anesthesia. Subsequently, Neville et al[8] compared IN dexmedetomidine to IN midazolam during laceration repair and found they performed similarly. Behrle et al[9] also used IN dexmedetomidine for noninvasive procedural sedation with starting doses of 3 μg/kg/dose and found 92% of patients were successfully sedated, and there were no significant differences in the rate of observed adverse events or interventions when compared with a cohort that did not receive dexmedetomidine. Yuen et al[10] concluded in a later study that starting doses of 2 μg/kg/dose IN

From the*Department of Pharmacy, University of Kentucky HealthCare, Lexington, KY.; †Department of Emergency Medicine, University of Kentucky HealthCare, Lexington, KY.; and ‡Department of Biostatistics, University of Kentucky, Lexington, KY.
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Reprints: Abby M. Bailey, PharmD, 800 Rose St, H110, Lexington, KY 40536 (e-mail: ammyna3@uky.edu).

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were sufficient to achieve satisfactory anxiolysis before laceration repair. Several studies have used IN dexmedetomidine for sedation to facilitate computerized tomography (CT) imaging. They concluded that IN dexmedetomidine was suitable for pediatric patients undergoing noninvasive studies such as CT imaging and was a safe therapy in this patient population.[11,12]

Available literature has yet to evaluate provider satisfaction and comfort surrounding IN dexmedetomidine use in pediatric patients in the ED setting. In addition, much of the available literature looks at the use of IN dexmedetomine outside of the ED in procedural units. Therefore, the aim of this study was to determine provider satisfaction with IN dexmedetomidine as an anxiolytic in pediatric patients with acute behavioral agitation or psychosis in the ED. Additional outcomes evaluated included any associated adverse events, LOS, and compared the IN dexmedetomidine results with oral midazolam.

METHODS

The University of Kentucky Chandler Medical Center has 21 dedicated pediatric ED beds with an annual volume of approximately 25,000 patients per year. This study was a prospective provider survey followed by a retrospective chart review of IN dexmedetomidine use in a pediatric ED at a single, tertiary referral center. This was followed by a retrospective chart review of patients who had received oral midazolam as the comparator group. The study was approved by the institutional review board before patient enrollment. Intranasal dexmedetomidine was given in accordance with institutional policy, which allowed for a dose of 1 to 5 μg/kg (200 μg maximum) using a 200 μg/2 mL formulation administered by an IN mucosal atomization device.

Patients were identified for inclusion if an order was placed in the electronic medical record for IN dexmedetomidine in the ED between March 1 and December 31, 2021. Patients were excluded if they had an allergy or sensitivity to dexmedetomidine, nasal obstruction or trauma, rhinitis, epistaxis, were younger than 6 months, older than 18 years, or had a medical condition affecting ciliary function. At the time of ordering, the provider was given a survey wherein prospective data collection was done on the indication for use as well as the provider's perceived satisfaction with the intended effect (Fig. 1). Patient's baseline level of agitation/distress was scored on a scale of 1 (crying or resisting) to 8 (asleep and not responding to gentle shaking or prodding). This was evaluated at 3 time points: at the time of administration (assumed to be baseline), 30 minutes after administration, and at recovery. This scale was selected based on previous literature evaluating the effects of IN dexmedetomidine as part of premedication for anesthesia.[7,10] This scale was determined to be easy to use across providers when informally surveyed for feedback on study design. Within this survey, providers were asked if the patient experienced any adverse drug reactions attributed to IN dexmedetomidine and if the patient experienced therapy failure. Provider comfort was scored on a scale of 1 (none) to 100 (completely) along with perceived time to onset and duration of affect. The surveys were collected after completion and data were entered into a REDCap database.[13,14]

For the comparator group, patients were identified retrospectively in the electronic medical record if they received oral midazolam between June 1, 2020 and December 31, 2021. Patients were excluded if they were older than 18 years or midazolam was used for an indication other than agitation or anxiety. Data points collected, retrospectively, for both groups included the following: age, weight, medical history, medication dose, race, presentation and discharge time in the ED, ED disposition, vital signs, treatment failures including termination of examination or inability to complete examination without progression to procedural sedation (requiring IV medications) or if additional medications were required. Lastly, any documented adverse events including rates of hypotension, bradycardia, and respiratory depression were collected. The survey responses also included documentation of adverse events, but retrospective chart review was also conducted on all patients.

The primary study outcome was to determine the level of provider satisfaction and comfort surrounding the efficacy and ease of use of IN dexmedetomidine for anxiolysis in pediatric patients with behavioral agitation and/or acute psychosis. Secondary outcomes included determining the efficacy of IN dexmedetomidine compared with oral midazolam. Efficacy was determined by treatment failure including termination of examination or inability to complete examination without progression to procedural sedation or if additional medications were required. In addition, quantifying the rate of adverse events was included in the secondary outcomes. Bradycardia, hypotension, and respiratory events were defined as heart rate, systolic blood pressure, and respiratory rate below normal for age, respectively. Finally, LOS was evaluated as a secondary outcome and was defined by hospital stay (from ED presentation to discharge order) in hours. A preplanned post hoc analysis was done to determine the efficacy and safety of IN dexmedetomidine in patients with autism spectrum disorder (ASD) versus without ASD and to determine the efficacy and safety of IN dexmedetomidine based on the dose provided.

Descriptive statistics were used to analyze data and were completed in R programming language, version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria). Categorical variables were reported using frequencies and column percentages (%), and P values were calculated using χ^2 and Fisher exact tests, as appropriate. Continuous variables were assessed for normality using histograms. Normally distributed continuous variables were reported using means and standard deviations (SD), and P values were calculated using Welch t tests; otherwise, medians and first/third quartiles were reported, and P values were calculated using Mann-Whitney U tests.

RESULTS

Sixty-two patients were included in the IN dexmedetomidine group—53 had completed provider surveys—and 58 patients were included in the oral midazolam comparator group. Baseline demographics can be found in Table 1. Those who received IN dexmedetomidine were significantly older (6.4 vs 3.5 years, $P = 0.001$) and more likely to have a medical history significant for ASD (54.8% vs 10.3%, $P < 0.001$). Patients who received IN dexmedetomidine were found to have a median (IQR) dose of 3.05 (2.04–4.00) μg/kg, whereas those in the oral midazolam group had a median (IQR) dose of 0.29 (0.25–0.48) mg/kg. The most common indication for IN dexmedetomidine was for facilitation of a physical examination or laboratory draws, whereas oral midazolam was used more frequently for laceration repairs or facilitation of imaging. There was no significant difference in the percentage of patients that required hospital admission (29.0% vs 17.2%, $P = 0.190$).

Overall, there was high provider comfort and satisfaction with the use of IN dexmedetomidine, with median scores of 90 (75–100) and 88 (60–100), respectively (Table 2). The median perceived onset was 25 (15–30) minutes and duration was 60 (30–83) minutes. Additional secondary outcomes can be found in Table 2. There was no difference in the overall rate of therapy failure between those who received IN dexmedetomidine versus oral midazolam (29.0% vs 20.7%, $P = 0.399$), with the most common reason for therapy failure being the need for additional medications. Those who received IN dexmedetomidine had a longer ED LOS than those who received oral midazolam (6.0 vs 4.4 hours, $P = 0.010$). The patient's behavior scores did improve after receiving IN dexmedetomidine (Table 2). The median (IQR) behavior score before administration was 1 (1–3), which

Patient sticker including:

MRN _____

Name (last, first) _____

DOB: _____

Provider Satisfaction Survey

Procedure information:

Please select **indication** for medication use *(circle any appropriate):*

Diagnostic Imaging | Facilitation of exam or lab draws | Incision & drainage | Laceration repair | NG tube placement | Other: _____

Please select **rationale** for choice of this medication *(check any that apply)*:

□ Known behavioral difficulty *(circle any that apply)*:

ADHD | Acute Agitation | Anxiety | Autism / spectrum disorder | Depression | Other: _____

□ Longer duration of action desired

□ Previous failure to other agent - If so identify agent: _____

Rate the **level of patient comfort** *(mark in appropriate box)*:

Behavior scores / Sedation scores	Prior to admin *(enter time given):* (HH:MM)	30 min after admin of IN Dexmedetomidine	At recovery *(enter time):* (HH:MM)	At discharge
1. Crying or resisting				
2. Anxious and not reassurable				
3. Anxious but reassurable				
4. Calm and cooperative				
5. Alert & Awake				
6. Drowsy, sleepy & lethargic				
7. Asleep but responds only to mild prodding or shaking				
8. Asleep & not responding to mild prodding or shaking				

Provider Perceived time to: Onset _____ (min) and **Duration** _____ (min)

Adverse Events *(check any that apply):*

□ **NONE**

□ **Hypotension:** □ increased observation □ IVF □ Vasopressors □ Other_____

□ **Bradycardia:** □ increased observation □ IVF □ Atropine / Vasopressors □ Other_____

□ **Respiratory depression:** □ increased observation □ Administered O2 □ Intubation □ Other_____

Therapy failure *(check any that apply):* □ **NONE** □ Procedure terminated □ PSAA □ Additional meds required

□ Other: _____

Provider *(rate 0-100 with number)*: 0 (none) 50 (undecided) 100 (completely)

1. Rate your **level of comfort** using IN dexmedetomidine *(rate comfort with number)*: _____
2. Rate your **level of satisfaction** with the effect of IN dexmedetomidine *(rate comfort with number)*: _____
3. **Type of provider** *(check one):* □ Attending □ Resident □ Midlevel / APP

Please return to ED Pharmacy

FIGURE 1. Sample survey provided to ED providers following administration of dexmedetomidine.

correlates with "crying and resisting". It improved to a median (IQR) score 30 minutes after administration to 6 (3.5–7), which correlates with "drowsy, sleepy, and lethargic", and finally it recovered with a median (IQR) score of 4.5 (3–5), which is between "calm and cooperative" and "alert and awake".

Only 1 individual experienced an adverse event in either group; a 7-year-old boy with ASD who received 4 μg/kg of IN dexmedetomidine for placement of IV access and then proceeded to procedural sedation with IV ketamine for a laceration repair. Approximately 60 minutes after receiving IN dexmedetomidine

TABLE 1. Baseline Demographics

	IN Dexmedetomidine (n = 62)	PO Midazolam (n = 58)	*P*
Age (y), median (IQR)	6.4 (3.0–8.8)	3.5 (1.9–8.3)	0.001
Weight (kg), median (IQR)	23.8 (18.6–41.9)	16.7 (12.7–30.0)	0.126
Female, n (%)	15 (24.2%)	25 (43.1%)	0.045
Medical history includes ASD, n (%)	34 (69.4%)	6 (10.3%)	<0.001
Race			
White, n (%)	49 (79.0%)	55 (94.8%)	N/A
Hispanic, n (%)	1 (1.6%)	0 (0.0%)	
African American, n (%)	10 (16.1%)	3 (5.2%)	
Other, n (%)	2 (3.2%)	0 (0.0%)	
Dose (μg/kg; mg/kg), n (%)	3.05 (2.04–4.00)	0.29 (0.25–0.48)	N/A
Indication for medication			
Diagnostic imaging, n (%)	15 (24.2%)	8 (13.8%)	0.225
Facilitation of examination or laboratory draw, n (%)	31 (50.0%)	15 (25.9%)	0.011
Incision and drainage, n (%)	0 (0.0%)	21 (36.2%)	0.052
Laceration repair, n (%)	10 (16.1%)	1 (1.7%)	0.021
Nasogastric tube placement, n (%)	1 (1.6%)	4 (6.9%)	1.000
Other, n (%)	16 (25.8%)	5 (8.6%)	0.011
Rationale for medication			
Longer duration of action desired, n (%)	7 (11.3%)	—	N/A
Previous failure of other agents, n (%)	15 (24.2%)	—	N/A
ADHD, n (%)	6 (9.7%)	—	N/A
Acute agitation, n (%)	6 (9.7%)	—	N/A
Anxiety, n (%)	11 (17.7%)	—	N/A
ASD, n (%)	34 (54.8%)	—	N/A
Depression, n (%)	1 (1.6%)	—	N/A
Other, n (%)	4 (6.5%)	—	N/A
Admitted to hospital, n (%)	18 (29.0%)	10 (17.2%)	0.190

ADHD indicates attention deficit hyperactivity disorder; PO, oral.

and 2 minutes after receiving 0.46 mg/kg IV ketamine for procedural sedation, he experienced bradycardia with a lowest documented heart rate of 65 beats per minute and respiratory depression with lowest documented respiratory rate of 12 breaths per minute. This required only increased observation and was self-limited.

In those patients with ASD who received IN dexmedetomidine versus oral midazolam, there was a lower rate of therapy failure in those who received IN dexmedetomidine (21.2% vs 66.7%, $P = 0.039$). In comparing those with ASD versus those without ASD who received IN dexmedetomidine, there was no difference in the provider comfort scores (80 vs 92.5, $P = 0.117$), provider satisfaction (90 vs 84, $P = 0.865$), or rates of therapy failure due to any cause (23.5% vs 35.7%, $P = 0.457$). Finally, safety and efficacy outcomes were compared based on the dose of IN dexmedetomidine; those who received less than 3 μg/kg (n = 20) and those who received 3 μg/kg or greater (n = 42). There were no significant differences in the patient comfort before administration ($P = 0.944$), 30 minutes after administration ($P = 0.620$), or at time of recovery ($P = 0.835$); median provider comfort scores (85 vs 90, $P = 0.605$); median provider satisfaction scores (95 vs 77.5, $P = 0.521$), and rates of therapy failure (20% vs 28.6%, $P = 0.681$).

DISCUSSION

Overall, providers expressed a high degree of satisfaction with using IN dexmedetomidine, with a median (IQR) score of 88 (60–100) of 100. In addition, they reported a high degree of comfort with IN dexmedetomidine, with a median (IQR) score of 90 (75–100) of 100. The median (IQR) dose of IN dexmedetomidine in this study was 3.05 (2.04–4.00) μg/kg/dose, aligning with dosing of IN dexmedetomidine cited to be effective in current literature.[8,9,15] There was an overall treatment failure rate of 29% in those who received IN dexmedetomidine, with most deemed a failure due to the requirement of additional medications. This is higher than previously reported studies. Behrle et al[9] reported only 8% of patients were unsuccessfully sedated with 3 μg/kg/dose of IN dexmedetomidine for noninvasive procedures; however, 39% of patients also received IN midazolam but were not deemed treatment failures as they would have been in our study. Li et al[16] reported a 13% treatment failure rate for those who received 3 μg/kg/dose of IN dexmedetomidine for sedation during transthoracic echocardiography examination. The authors note, however, with the various definitions of treatment failure, it is difficult to compare these rates across studies.

The perceived onset of action and duration of action was 25 (15–30) minutes and 60 (30–83) minutes, respectively. This onset and duration of action is within the reported range from other studies; however, this may be subject to recall bias because it is a perceived outcome. In one pharmacokinetic analysis of IN dexmedetomidine completed in 50 pediatric patients by Uusalo et al,[17] it was found that the time to reach peak serum concentration after a 2- to 3-μg/kg dose of IN dexmedetomidine was 37 minutes, and the maximal reduction in comfort scores was achieved 45 minutes after administration. Similarly, Li et al reported a mean onset of action of 16.7 minutes and a wake-up (ie, recovery) time of

TABLE 2. Provider Survey Results and Secondary Outcomes

			IN Dexmedetomidine (n = 53)
Type of provider			
Attending physician, n (%)			12 (22.6%)
Resident physician, n (%)			38 (71.7%)
APRN or PA, n (%)			3 (5.7%)
Patient behavior score before administration			
1 – crying or resisting, n (%)			27 (50.9%)
2 – anxious and not reassurable, n (%)			12 (22.6%)
3 – anxious but reassurable, n (%)			11 (20.8%)
4 – calm and cooperative, n (%)			2 (3.8%)
5 – alert and awake, n (%)			1 (1.9%)
6 – drowsy, sleepy, and lethargic, n (%)			0 (0.0%)
7 – asleep but responds only to mild prodding or shaking, n (%)			0 (0.0%)
8 – asleep and does not respond to mild prodding or shaking, n (%)			0 (0.0%)
Patient behavior score 30 min after administration			
1 – crying or resisting, n (%)			6 (11.3%)
2 – anxious and not reassurable, n (%)			3 (5.7%)
3 – anxious but reassurable, n (%)			5 (7.5%)
4 – calm and cooperative, n (%)			20 (18.9%)
5 – alert and awake, n (%)			2 (3.8%)
6 – drowsy, sleepy, and lethargic, n (%)			14 (26.4%)
7 – asleep but responds only to mild prodding or shaking, n (%)			13 (24.5%)
8 – asleep and does not respond to mild prodding or shaking, n (%)			1 (1.9%)
Patient behavior score at recovery			
1 – crying or resisting, n (%)			3 (5.7%)
2 – anxious and not reassurable, n (%)			3 (5.7%)
3 – anxious but reassurable, n (%)			5 (9.4%)
4 – calm and cooperative, n (%)			9 (17.0%)
5 – alert and awake, n (%)			12 (22.6%)
6 – drowsy, sleepy, and lethargic, n (%)			7 (13.2%)
7 – asleep but responds only to mild prodding or shaking, n (%)			1 (1.9%)
8 – asleep and does not respond to mild prodding or shaking, n (%)			0 (0.0%)
Provider comfort, median (IQR)			90 (75–100)
Provider satisfaction, median (IQR)			88 (60–100)
Provider-perceived onset of action (min), median (IQR)			25 (15–30)
Provider-perceived duration of action (min), median (IQR)			60 (30–83)
Rationale for medication			
Longer duration of action desired, n (%)			7 (11.3%)
Previous failure of other agents, n (%)			15 (24.2%)
ADHD, n (%)			6 (9.7%)
Acute agitation, n (%)			6 (9.7%)
Anxiety, n (%)			11 (17.7%)
ASD, n (%)			34 (54.8%)
Depression, n (%)			1 (1.6%)
Other, n (%)			4 (6.5%)
Secondary outcomes	IN Dexmedetomidine (n = 62)	PO Midazolam (n = 58)	*P*
Adverse event (hypotension, bradycardia, or respiratory depression), n (%)	1 (1.7%)	0 (0.0%)	1.000
Therapy failure due to any reason, n (%)	18 (29.0%)	12 (20.7%)	0.399
Therapy failure reason			
Procedure termination, n (%)	2 (3.2%)	0 (0.0%)	0.496
Progression to procedural sedation, n (%)	5 (8.1%)	5 (8.6%)	1.000
Additional medications required, n (%)	11 (17.7%)	12 (20.7%)	0.859
Other, n (%)	4 (6.5%)	0 (0.0%)	0.120
ED LOS (h), median (IQR)	6.0 (4.1–7.6)	4.4 (3.2–6.6)	0.010

APRN indicates advanced practice registered nurse; PA, physician's assistant.

44.3 minutes.[16] In our study, behavior scores were initially highest before the IN dexmedetomidine was given, with 50.9% of patients scored as "crying or resisting". Most patients, however, had their lowest behavior score 30 minutes after dosing because 26.4% were "drowsy, sleepy, and lethargic" and 24.5% were "asleep but only responds to mild prodding or shaking" at this time point. This decline in the behavior scores around the 30-minute time point further aligns with the currently published literature and this study's reported onset of action.

In this study, IN dexmedetomidine was compared with oral midazolam. This was chosen as the comparator because it was commonly used as a comparator in previous literature.[18,19] In addition, at our institution, oral midazolam was commonly used for anxiolysis and agitation for examination facilitation or procedures before introducing IN dexmedetomidine. Other medications, such as IN midazolam or IN ketamine, were not included as a comparator to avoid confounding indications (ie, pain or seizure management). There was no difference in the rate of treatment failures in those who received IN dexmedetomidine versus oral midazolam (29.0% vs 20.7%, $P = 0.399$). In 1 study comparing 2.5 μg/kg/dose of IN dexmedetomidine to 0.5 mg/kg/dose of oral midazolam in pediatric patients undergoing IV cannulation and CT scanning, a significantly high proportion of patients achieved appropriate sedation with IN dexmedetomidine (67% vs 24%, $P = 0.002$).[18]

Patients who received IN dexmedetomidine had a longer ED LOS as compared with those who received oral midazolam (6.0 vs 4.4 hours, $P = 0.010$). This rate is similar to that cited in other studies comparing IN dexmedetomidine with other agents. Behrle et al[9] reported a longer preprocedure, procedure, recovery, and total admit time in those who received IN dexmedetomidine. Although this longer duration of action may be beneficial in some patients where providers may anticipate a longer intervention, examination, or diagnostic procedure, its effect on LOS must also be considered. One confounding factor for ED LOS in our study was the number of patients requiring hospital admission. A higher percentage of patients who received IN dexmedetomidine was admitted to the hospital when compared with those who received oral midazolam (29% vs 17.2%, $P = 0.190$). Delays in transfer from the ED to the inpatient unit may have prolonged the ED LOS, whereas those patients who could be discharged did not require any further assessment, thus shortening their ED LOS.

Although there was a high degree of provider comfort with using IN dexmedetomidine, this drug is accompanied with potential adverse effects of bradycardia, hypotension, and respiratory depression. This study had only 1 physician-reported adverse event, where a child who received IN dexmedetomidine followed by IV ketamine experienced self-limited bradycardia and respiratory depression approximately 60 minutes after receiving IN dexmedetomidine and shortly after receiving the IV ketamine. This adverse event, although likely more attributable to the IV ketamine rather than the IN dexmedetomidine and may have also been precipitated by the use of 2 different medications for procedural sedation, highlights the need for appropriate patient monitoring after receiving a long–half-life medication like dexmedetomidine with other sedative agents. This low rate of adverse events is similar to other studies. Behrle et al[9] reported that of those patients who received IN dexmedetomidine, 3 required oxygen by mask, 1 required IV fluids, and 3 had oxygen desaturations. Similarly, Li et al[14] reported only 1 child required oxygen supplementation, and all others had an acceptable heart rate and blood pressure. Overall, this supports IN dexmedetomidine as a safe option for pediatric anxiolysis, with monitoring of patient's heart rate, respiratory rate, and oxygen saturations.

One interesting finding of this study is among those with ASD, IN dexmedetomidine had a lower rate of treatment failure as compared with those who received oral midazolam (21.2% vs 66.7%, $P = 0.039$). This is a significant finding because patients with ASD commonly require light sedation to cooperate with nonpainful diagnostic procedures, physical examinations, and placement of IV cannulas, but are commonly difficult to provide anxiolysis with currently used medications.[20] This study represents IN dexmedetomidine as a novel approach for light sedation and anxiolysis in patients with ASD and may be superior to oral midazolam; however, further research is needed to confirm this finding.

This study is the first to report provider satisfaction and comfort scores for the use of IN dexmedetomidine in pediatric ED patients who require anxiolysis. One limitation of this study is the small sample size at a single institution, and cohorts were unable to be matched when comparing outcomes. Another potential limitation of the study is biased survey responses because a variety of providers evaluated the patient and effects of IN dexmedetomidine and then relied on recall to complete each survey after medication administration, which could alter perception. Similarly, there was likely a higher rate of using IN dexmedetomidine in patients with ASD at this site due to positive anecdotal experiences from the physicians. This may have biased the results toward using IN dexmedetomidine at a higher rate in the ASD population instead of oral midazolam, thus benefiting IN dexmedetomidine. In addition, the use of IN dexmedetomidine may be limited in children of a heavier weight because the maximum dosage of 200 μg, which is required based on the formulation and maximum volume able to be instilled in the nasal cavity, may be a lower weight-based dose and then be less effective. Furthermore, because survey completion occurred after medication administration, perceived time to onset and duration of anxiolysis cannot be confirmed with objective data. Patient and guardian satisfaction were not evaluated in this study and represent an important factor in anxiolysis agent selection for patients with behavioral agitation. Finally, the behavioral scale used is subjective and not validated, although it was selected because it was easy to use and successfully used in previous published literature.[7]

This study overall demonstrates that the use of IN dexmedetomidine for anxiolysis in pediatric ED patients has high levels of provider comfort and satisfaction, a moderately high success rate, and a promising safety profile. In addition, IN dexmedetomidine may be superior to oral midazolam in patients with ASD. Future areas of exploration and research include patient and guardian satisfaction with IN dexmedetomidine as an agent for emergent anxiolysis.

REFERENCES

1. McDermott KW, Stocks C, Freeman WJ. Overview of pediatric emergency department visits, 2015: Statistical brief #242. In: *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs*. Rockville, MD: Agency for Healthcare Research and Quality; 2006:1–17.
2. Tobias JD, Leder M. Procedural sedation: A review of sedative agents, monitoring, and management of complications. *Saudi J Anaesth*. 2011;5: 395–410.
3. Rech MA, Barbas B, Chaney W, et al. When to pick the nose: Out-of-hospital and emergency department intranasal administration of medications. *Ann Emerg Med*. 2017;70:203–211.
4. Mody K, Kaur S, Mauer EA, et al. Benzodiazepines and development of delirium in critically ill children: Estimating the causal effect. *Crit Care Med*. 2018;46:1486–1491.
5. Guthrie AM, Baum RA, Carter C, et al. Use of intranasal ketamine in pediatric patients in the emergency department. *Pediatr Emerg Care*. 2021; 37:e1001–e1007.
6. Dexmedetomidine. *Package Insert*. Lake Forest, IL: Hospira, Inc.; 2013.
7. Yuen VM, Hui TW, Irwin MG, et al. A comparison of intranasal dexmedetomidine and oral midazolam for premedication in pediatric

anesthesia: A double-blinded randomized controlled trial. *Anesth Analg*. 2008;106:1715–1721.

8. Neville DN, Hayes KR, Ivan Y, et al. Double-blind randomized controlled trial of intranasal dexmedetomidine versus intranasal midazolam as anxiolysis prior to pediatric laceration repair in the emergency department. *Acad Emerg Med*. 2016;23:910–917.
9. Behrle N, Birisci E, Anderson J, et al. Intranasal dexmedetomidine as a sedative for pediatric procedural sedation. *J Pediatr Pharmacol Ther*. 2017; 22:4–8.
10. Yuen VM, Hui TW, Irwin MG, et al. A randomised comparison of two intranasal dexmedetomidine doses for premedication in children. *Anaesthesia*. 2012;67:1210–1216.
11. Azizkhani R, Heydari F, Ghazavi M, et al. Comparing sedative effect of dexmedetomidine versus midazolam for sedation of children while undergoing computerized tomography imaging. *J Pediatr Neurosci*. 2020;15:245–251.
12. Mekitarian Filho E, Robinson F, de Carvalho WB, et al. Intranasal dexmedetomidine for sedation for pediatric computed tomography imaging. *J Pediatr*. 2015;166:1313–1315.e1.
13. Yuen VM, Hui TW, Irwin MG, et al. Optimal timing for the administration of intranasal dexmedetomidine for premedication in children. *Anesthesia*. 2010;65:922–929.
14. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42:377–381.
15. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform*. 2019;95:103208.
16. Li LQ, Wang C, Xu HY, et al. Effects of different doses of intranasal dexmedetomidine on preoperative sedation and postoperative agitation in pediatric with total intravenous anesthesia undergoing adenoidectomy with or without tonsillectomy. *Medicine (Baltimore)*. 2018; 97:e12140.
17. Li BL, Ni J, Huang JX, et al. Intranasal dexmedetomidine for sedation in children undergoing transthoracic echocardiography study—a prospective observational study. *Paediatr Anaesth*. 2015;25:891–896.
18. Uusalo P, Guillaume S, Siren S, et al. Pharmacokinetics and sedative effects of intranasal dexmedetomidine in ambulatory pediatric patients. *Anesth Analg*. 2020;130:949–957.
19. Ghai B, Jain K, Saxena AK, et al. Comparison of oral midazolam with intranasal dexmedetomidine premedication for children undergoing CT imaging: A randomized, double-blind, and controlled study. *Paediatr Anaesth*. 2017;27:37–44.
20. Brown JJ, Gray JM, Roback MG, et al. Procedural sedation in children with autism spectrum disorders in the emergency department. *Am J Emerg Med*. 2019;37:1404–1408.