RESEARCH ARTICLE

Use of Intranasal Dexmedetomidine as a Solo Sedative for MRI of Infants

Gokhan Olgun, MD,[a,b] Mir Hyder Ali, MD[a,b]

ABSTRACT

BACKGROUND: Dexmedetomidine, a selective α-2 receptor agonist, can be delivered via the intranasal (IN) route and be used for procedural sedation. The drug's favorable hemodynamic profile and relative ease of application make it a promising agent for sedation during radiologic procedures, although there are few studies on its efficacy for MRI studies.

METHODS: A retrospective chart review was performed between June 2014 and December 2016. Outpatients between 1 and 12 months of age who received 4 μg/kg of IN dexmedetomidine for MRI were included in the analysis. Our aim with this study was to determine the rate of successful completion of the sedation procedure without the need for a rescue drug (other than repeat IN dexmedetomidine).

RESULTS: A total of 52 subjects were included in our study. Median (interquartile range) patient age was 7 (5–8) months. Median (interquartile range) procedure length was 40 (35–50) minutes. Overall success rate (including first dose and any rescue dose IN) of dexmedetomidine was 96.2%. None of the patients had significant adverse effects related to dexmedetomidine.

CONCLUSIONS: IN dexmedetomidine is an effective solo sedative agent for MRI in infants.

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Dexmedetomidine, a selective α-2 agonist, is commonly used to sedate critically ill children and adults. After being approved by the Food and Drug Administration in 2008 for use outside of ICUs, dexmedetomidine has started to be used for imaging and procedural sedation.[1–4] Dexmedetomidine is available intravenously, but it can also be administered via buccal, intranasal (IN), and intramuscular routes.[5] The IN route has been found to be effective for sedated computed tomography imaging in children[6–8] and for sedated auditory brainstem response exams and EEGs.[9] IN dexmedetomidine can be administered via an atomizer or drops. Both forms have been found to be equally successful methods of sedation in children.[10] An additional advantage of dexmedetomidine as a sedative is that it may have a less harmful impact on the developing brain compared with other sedative agents.[11–13]

One important advantage of the IN route is that intravenous (IV) placement, which can be challenging and traumatic for children, can be avoided. Because of its safety and its easy application, IN dexmedetomidine is now being used as a solo drug for sedation.[7,14,15] In the current study, we sought to determine the efficacy of IN atomized dexmedetomidine for sedated pediatric MRI studies.

METHODS

In our outpatient sedation suite, we use 4 μg/kg per dose of IN dexmedetomidine with an atomizer device for infants presenting for noncontrast MRI, with an anticipated study duration of $<$1 hour. If patients fail sedation with IN dexmedetomidine, then either an additional 2 μg/kg dose of IN dexmedetomidine is given or an IV line is placed and followed with propofol administration per the physician's discretion.

In this retrospective study, patients between 1 and 12 months of age presenting for sedation between June 2014 and October 2016 for noncontrast MRI studies with an anticipated study duration of $<$1 hour were included. Patients receiving initial sedatives other than IN dexmedetomidine alone and patients on assisted ventilation were excluded from the analysis.

We collected data on the following: patient age, sex, weight, and type and length of the procedure; the dexmedetomidine initial dose; and the number and amount of any additional doses. Adverse events were defined as the following: a $>$20% change in baseline heart rate or blood pressure, an apnea lasting more than 20 seconds, oxygen desaturations to $<$90%, and any seizures. MRI reports were examined for language that would suggest lack of quality or motion artifact.

Our aim with this study was to determine the rate of successful completion of the sedation procedure with IN dexmedetomidine alone. Failure of IN dexmedetomidine was defined as requiring propofol to complete the sedated MRI.

Statistical analyses were performed by using SPSS software version 15 (SPSS Inc, Chicago, IL). The variables were investigated by using visual (histograms and probability plots) and analytical methods (Kolmogorov-Smirnov or Shapiro-Wilk tests) to determine if they were normally distributed. Descriptive variables were presented by using medians and interquartile ranges (IQRs) for nonnormally distributed variables and frequencies and proportions for ordinal variables. The institutional review board approved the study and the need for informed consent was waived.

RESULTS

We identified 79 subjects between 1 and 12 months of age who presented for outpatient, noncontrast MRI. Twenty-seven patients were on assisted ventilation (including patients with tracheostomy and home ventilation, home bilevel positive airway pressure, and continuous positive airway pressure) and were excluded from the study. All 52 of the remaining subjects received IN dexmedetomidine (ie, no patients received an initial alternative regimen). Demographics of the 52 study subjects are presented in Table 1. The subjects were predominantly boys, with a median age of 7 months.

The success rate for an initial dose of 4 μg/kg of IN dexmedetomidine was 94.2% (95% confidence interval [CI], 84%–98.8%) and for IN dexmedetomidine alone was 96.2% (95% CI, 86.7%–99.5%). One patient received an additional 2 μg/kg dose of IN dexmedetomidine. Two patients (3.8%) could not be sedated with IN dexmedetomidine and required propofol. These patients were 4 and 6 months of age and were undergoing a brain MRI. Both patients awoke during the scan, and a second dose of IN dexmedetomidine was not given per physician discretion; the scans were completed with propofol. On the basis of the wording of the MRI reports, we found no evidence of motion artifact or poor image quality.

TABLE 1 Baseline Clinical Parameters of Subjects Undergoing Sedation With IN Dexmedetomidine for MRI

Parameters	
Boys, *n* (%)	33 (64)
Age, mo, median (IQR)	7 (5–8)
Wt, kg, median (IQR)	8 (7–10)
Type of MRI imaging, *n* (%)	
Brain MRI	44 (84)
Spine MRI	6 (12)
Extremity MRI	2 (4)
Procedure length, min, median (IQR)	40 (35–50)

There were no documented episodes of oxygen desaturation or apnea. Sixteen patients had a documented $>$20% decrease from their baseline heart rate after receiving IN dexmedetomidine. Of these 16, the average decrease in heart rate was 25% (95% CI, 21%–32%). Two patients had a $>$20% decrease in mean arterial blood pressure. No patients received interventions for these vital sign changes.

DISCUSSION

In this retrospective investigation of infants undergoing sedated outpatient MRI, we demonstrate that a dose of 4 μg/kg of IN dexmedetomidine is highly effective and appears to be safe. Dexmedetomidine is commonly used as an IV sedative agent for imaging procedures, but the IN route is gaining popularity. Sulton et al[16] demonstrated that a dose of 3 μg/kg of IN dexmedetomidine in combination with IN midazolam was effective for MRI of children. All 224 procedures were completed and

there were no adverse effects. In contrast, Baier et al[9] reported abandoning the combination of 3 μg/kg IN dexmedetomidine even when oral midazolam was added because of unacceptably low success rates. In a randomized study, Tug et al[17] evaluated usage of IN dexmedetomidine for pediatric MRI and compared 4 μg/kg per dose to 3 μg/kg per dose. The authors concluded that subjects receiving the higher dose had better parental separation scores and more effective sedation. The need for rescue drug administration was 70% in the 3 μg/kg per dose group and 30% in the 4 μg/kg per dose group. In our study, we support the notion that the 4 μg/kg per dose is effective. The mean age in our study was lower than in the Tug et al[17] study, which may indicate increased sedative effects of dexmedetomidine with younger age. Potts et al[18] have shown decreased clearance of dexmedetomidine in neonates and infants compared with older children, which may translate into a longer duration of activity. In accordance with this, in a recent study it was demonstrated that the effective dose 50 of IN dexmedetomidine was higher in children with noncyanotic cardiac disease between 13 and 36 months of age compared with 1 to 6 and 7 to 12 months of age.[19]

There is increasing recognition that sedatives and anesthetics may cause neurotoxicity in the developing brain.[11] Even short-term use of sedatives like ketamine has been shown to have deleterious effects in some animal models.[12] Dexmedetomidine emerges as a promising agent in the sedation of infants and neurologically injured children. Dexmedetomidine may ameliorate developmental neurotoxicity associated with other sedatives and has neuroprotective properties.[13,20]

IV access can be difficult to obtain in infants and requires skills and expertise. In contrast, IN medications are easy to administer and are associated with less pain and anxiety. These advantages make them very valuable in pediatric procedural sedation.

The safety of dexmedetomidine has been evaluated in children and infants with critical disease and congenital heart disease and has been found to be safe, with a minimal side effect profile,[21,22] although in general it has been associated with bradycardia and hypotension and can trigger seizures and arrhythmias.[23,24]

Our study has several limitations. First, our sample size is relatively small and originates from a single center, making generalizability difficult. Additionally, we did not have sufficient power to ensure that rare but serious safety events do not occur with this sedative regimen. The limited age range (1–12 months) precludes making a generalization about IN dexmedetomidine effectiveness beyond infancy. Additional studies are needed to clarify the dosage and safety profile in older populations.

CONCLUSIONS

In our study, we add support to recent findings that IN dexmedetomidine can be used successfully in procedural sedation for noncontrast MRI in infants.

REFERENCES

1. Mahmoud M, Mason KP. Dexmedetomidine: review, update, and future considerations of paediatric perioperative and periprocedural applications and limitations. *Br J Anaesth*. 2015;115(2):171–182
2. Mason KP, Fontaine PJ, Robinson F, Zgleszewski S. Pediatric sedation in a community hospital-based outpatient MRI center. *AJR Am J Roentgenol*. 2012; 198(2):448–452
3. Mason KP, Zgleszewski SE, Prescilla R, Fontaine PJ, Zurakowski D. Hemodynamic effects of dexmedetomidine sedation for CT imaging studies. *Paediatr Anaesth*. 2008;18(5):393–402
4. Mason KP, Zurakowski D, Zgleszewski SE, et al. High dose dexmedetomidine as the sole sedative for pediatric MRI. *Paediatr Anaesth*. 2008;18(5):403–411
5. Takemoto CK, Hodding JH, Kraus DM. *Pediatric & Neonatal Dosage Handbook*. 21st ed. Hudson, OH: Lexi-Comp, Inc; 2014:365–366
6. Yoo H, Iirola T, Vilo S, et al. Mechanism-based population pharmacokinetic and pharmacodynamic modeling of intravenous and intranasal dexmedetomidine in healthy subjects. *Eur J Clin Pharmacol*. 2015;71(10): 1197–1207
7. Mekitarian Filho E, Robinson F, de Carvalho WB, Gilio AE, Mason KP. Intranasal dexmedetomidine for sedation for pediatric computed tomography imaging. *J Pediatr*. 2015; 166(5):1313–1315.e1
8. Iirola T, Vilo S, Manner T, et al. Bioavailability of dexmedetomidine after intranasal administration. *Eur J Clin Pharmacol*. 2011;67(8):825–831
9. Baier NM, Mendez SS, Kimm D, Velazquez AE, Schroeder AR. Intranasal dexmedetomidine: an effective sedative agent for electroencephalogram and auditory brain response testing. *Paediatr Anaesth*. 2016;26(3): 280–285
10. Li BL, Zhang N, Huang JX, et al. A comparison of intranasal dexmedetomidine for sedation in children administered either by atomiser or by drops. *Anaesthesia*. 2016; 71(5):522–528
11. Loepke AW. Developmental neurotoxicity of sedatives and anesthetics: a concern for neonatal and pediatric critical care medicine? *Pediatr Crit Care Med*. 2010; 11(2):217–226
12. Paule MG, Li M, Allen RR, et al. Ketamine anesthesia during the first week of life can cause long-lasting cognitive deficits in rhesus monkeys. *Neurotoxicol Teratol*. 2011;33(2):220–230
13. Schoeler M, Loetscher PD, Rossaint R, et al. Dexmedetomidine is neuroprotective in an in vitro model for traumatic brain injury. *BMC Neurol*. 2012;12:20
14. Reynolds J, Rogers A, Capehart S, Manyang P, Watcha MF. Retrospective comparison of intranasal dexmedetomidine and oral chloral hydrate for sedated auditory brainstem response exams. *Hosp Pediatr*. 2016;6(3): 166–171
15. Reynolds J, Rogers A, Medellin E, Guzman JA, Watcha MF. A prospective,

randomized, double-blind trial of intranasal dexmedetomidine and oral chloral hydrate for sedated auditory brainstem response (ABR) testing. *Paediatr Anaesth*. 2016;26(3):286–293

16. Sulton C, Kamat P, Mallory M, Reynolds J. The use of intranasal dexmedetomidine and midazolam for sedated magnetic resonance imaging in children: a report from the Pediatric Sedation Research Consortium [published online ahead of print June 12, 2017]. *Pediatr Emerg Care*. doi:10.1097/PEC.0000000000001199
17. Tug A, Hanci A, Turk HS, et al. Comparison of two different intranasal doses of dexmedetomidine in children for magnetic resonance imaging sedation. *Paediatr Drugs*. 2015;17(6):479–485
18. Potts AL, Warman GR, Anderson BJ. Dexmedetomidine disposition in children: a population analysis. *Paediatr Anaesth*. 2008;18(8):722–730
19. Yu Q, Liu Y, Sun M, et al. Median effective dose of intranasal dexmedetomidine sedation for transthoracic echocardiography in pediatric patients with noncyanotic congenital heart disease: an up-and-down sequential allocation trial. *Paediatr Anaesth*. 2017; 27(11):1108–1114
20. Sanders RD, Sun P, Patel S, Li M, Maze M, Ma D. Dexmedetomidine provides cortical neuroprotection: impact on anaesthetic-induced neuroapoptosis in the rat developing brain. *Acta Anaesthesiol Scand*. 2010;54(6):710–716
21. Whalen LD, Di Gennaro JL, Irby GA, Yanay O, Zimmerman JJ. Long-term dexmedetomidine use and safety profile among critically ill children and neonates. *Pediatr Crit Care Med*. 2014;15(8):706–714
22. Lam F, Bhutta AT, Tobias JD, Gossett JM, Morales L, Gupta P. Hemodynamic effects of dexmedetomidine in critically ill neonates and infants with heart disease. *Pediatr Cardiol*. 2012;33(7):1069–1077
23. Kubota T, Fukasawa T, Kitamura E, et al. Epileptic seizures induced by dexmedetomidine in a neonate. *Brain Dev*. 2013;35(4):360–362
24. Burns KM, Greene EA. Long QT syndrome unmasked by dexmedetomidine: a case report. *Congenit Heart Dis*. 2014; 9(1):E11–E15

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