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ORIGINAL ARTICLE

High-dose dexmedetomidine sedation for pediatric MRI

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Summary

Objectives: To test the hypothesis that high-dose dexmedetomidine can be successfully used for pediatric magnetic resonance imaging (MRI) sedation without significant hemodynamic compromise.
Background: The dexmedetomidine dose required to achieve optimal sedation is often higher than its recommended dose. High doses of dexmedetomidine can lead to significant hemodynamic side effects.
Methods: Dexmedetomidine use for pediatric MRI over a 1-year period was retrospectively reviewed. A dexmedetomidine bolus of 2 $\mu g \cdot kg^{-1}$ intravenous followed by 1 $\mu g \cdot kg^{-1} \cdot h^{-1}$ infusion was used. Dexmedetomidine efficacy, side effects, timing of side effects, and additional use of medications were analyzed. Data were compared by *t*-test, Mann–Whitney rank-sum test, Fisher's exact test, and ANOVA.
Results: High-dose dexmedetomidine was used in 77 patients, and MRI was completed in 76 (99%) patients. A second bolus of dexmedetomidine was required in 28 (36%) patients, and 22 (29%) patients required additional medications (midazolam, fentanyl, or ketamine) for adequate sedation. A 25% decrease in blood pressure (BP) was observed in 10.5%, a transient increase in BP in 3.9%, and a heart rate $< 60\ min^{-1}$ in 7.9% of cases. These side effects resolved spontaneously. There were no apneas or respiratory depression. Vital sign changes, recovery time, and discharge time were not significantly different in subgroups of patients receiving one or two boluses of dexmedetomidine with or without additional medications. Transient hypertension was more common in patients receiving two boluses of dexmedetomidine ($P = 0.048$).
Conclusions: High-dose dexmedetomidine can be successfully used for pediatric MRI sedation, but a significant number of children require additional medications for optimal control. Hemodynamic side effects resolved spontaneously. High-dose dexmedetomidine did not result in respiratory depression.

Introduction

The use of dexmedetomidine in pediatric sedation for neuroimaging has been reported in the past few years (1–5). Dexmedetomidine exerts its action through activation of pre- and postsynaptic alpha 1 adrenoreceptors, with a short redistribution half-life of 9 min and elimination half-life of 110 min(6). The increasing popularity of dexmedetomidine use in children stems from its ability to provide adequate procedural sedation with a relatively low risk of respiratory depression (7). In addition, dexmedetomidine is associated with a significantly lower need for artificial airway support during sedation for magnetic resonance imaging (MRI) in children with obstructive sleep apnea, compared to propofol (8).

The success of dexmedetomidine as a sedative agent varies greatly depending on the dose employed and the clinical situation (5). This agent has been found to be very effective in some studies (3,4,9); however, a recent report noted that the use of dexmedetomidine as a single agent was not as effective as anticipated (2). Dexmedetomidine appears to be very effective as a sole agent for procedural sedation when used at higher doses (3,4), but this can increase the risk of side effects, including hypotension, bradycardia, or transient hypertension with the loading dose.

Dexmedetomidine is currently the drug of choice for pediatric patients requiring sedation for MRI at our institution. This report describes our experience with dexmedetomidine as the main agent for children requiring sedation for MRI, focusing on its efficacy and side effects.

Materials and methods

After approval by the Institutional Review Board, we performed a retrospective chart review of all patients who received sedation for MRI between July 1, 2007, and June 30, 2008.

During the study period, our sedation protocol consisted of an intravenous (IV) bolus of 2 $\mu g \cdot kg^{-1}$ of dexmedetomidine administered over 10 min, followed by a maintenance infusion of 1 $\mu g \cdot kg^{-1} \cdot h^{-1}$. A second bolus of 2 $\mu g \cdot kg^{-1}$ of dexmedetomidine was administered to patients who were not adequately sedated prior to initiation of the maintenance infusion. Additional medications, such as midazolam or fentanyl, were also used during the procedure to achieve optimal sedation in patients exhibiting movement that could interfere with image acquisition.

Data obtained for analysis included age, weight, gender and primary diagnosis, dexmedetomidine dose (bolus and continuous infusion), additional medications given, level of sedation reached, and medical interventions. In accordance with hospital policy for procedural sedation, heart rate (HR), respiratory rate (RR), and blood pressure (BP) were recorded every 5 min. Oxygen saturation was monitored continuously via pulse oximetry throughout the procedure. Level of sedation was assessed by the following scale: 1 = awake, 2 = drowsy and easy to arouse, 3 = drowsy and drifts off to sleep, and 4 = somnolent and minimal response to physical stimuli. Monitoring and assessment of sedation were performed by a trained nurse practitioner under direct supervision of a pediatric intensivist or anesthesiologist. Patients were monitored until they were awake, drinking fluids, and had a minimum Aldrete score of 9 points (10). Upon discharge home, a direct phone number was provided to parents for reporting of any adverse effects or in case further advice or assistance was needed.

Data are presented as means and standard deviations, unless otherwise noted. Dexmedetomidine-induced vital sign changes from baseline for entire study cohort were compared using *t*-test and Mann–Whitney rank-sum test. Patients were divided into four subgroups depending on dexmedetomidine bolus and additional medications received. Dex1 group received one bolus of dexmedetomidine, Dex2 group received two boluses of dexmedetomidine, Dex1A group received one bolus of dexmedetomidine and additional medications, and Dex2A group received two boluses of dexmedetomidine and additional medications. These four sedation groups were compared with respect to age, weight, BP, HR, procedure time, and recovery time using ANOVA. Incidence of bradycardia and hypotension was analyzed with Fisher's exact test. Recovery time of bradycardia and hypotensive patients was compared with normal cohorts using *t*-test. Data were analyzed using dedicated statistical software (SIGMASTAT version 2.03; SPSS Inc, Chicago, IL, USA). A $P < 0.05$ was considered statistically significant.

Results

Seventy-seven patients received dexmedetomidine for MRI, and the procedure was satisfactorily completed in 76 (99%) patients. There were 49 boys and 27 girls, ranging in age from 1 to 20 years (5 ± 3.5 years) and in weight from 8.5 to 68.5 kg (20.7 ± 12 kg). The most prevalent primary diagnoses included seizure disorder ($n = 20$), developmental delay and behavioral disorder ($n = 16$), autism ($n = 7$), and neoplasia ($n = 6$).

Dexmedetomidine bolus was used once in 48 (63%) patients, of which 12 received additional medications during the procedure. A second bolus of dexmedetomidine was required in 28 (36%) patients, and 10 of these patients required additional medications during the procedure. A total of 22 (29%) patients required additional medications for spontaneous movements affecting quality of MRI.

Dexmedetomidine-induced vital sign changes from baseline for whole group are shown in Figure 1. Hypotension (systolic BP decrease of >25%) and transient hypertension (systolic BP increase of >25%) were observed in eight (10.5%) and three (3.9%) patients, respectively. Bradycardia (HR < 60 min^{-1}) was observed in six (7.9%) patients. Despite a statistically significant decrease in respiratory rate from baseline, no apnea events were observed in our cohort. One

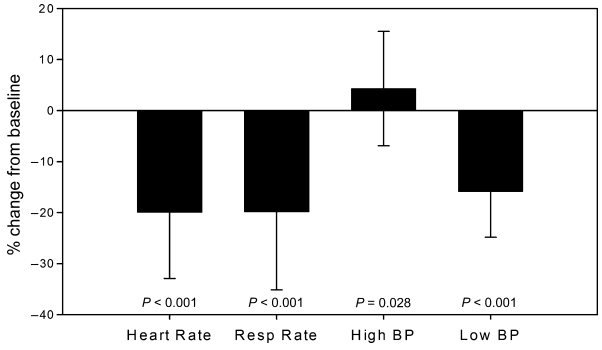

Figure 1 Maximal change in vital signs from baseline.

patient with a history of obstructive sleep apnea required repositioning of the neck for a transient drop in oxygen saturation. Most patients received prophylactic supplemental oxygen through nasal cannula and maintained oxygen saturations >95%, so the true incidence of desaturation while breathing room air could not be determined.

Patients are divided into four subgroups depending on dexmedetomidine bolus and additional medications received. Comparison of BP, HR, procedure time, and recovery time between these subgroups of patients are shown in Table 1. None of the variables attained statistical significance between groups even though HR trended toward being lower in the group that received two boluses of dexmedetomidine.

Characteristics of hypotensive patients are shown in Table 2. According to Pediatric Advanced Life Support (PALS) guidelines, the lower limit of acceptable systolic BP is 70 mmHg + 2 × age in children 1–10 years, or 90 mmHg if older than age 10 years (11). Following these criteria (as opposed to the 25% decrease from baseline criteria), six of the eight hypotensive patients in Table 2 were hypotensive. Only one patient had

Table 1 Comparison of vital signs and recovery time between sedation groups

Characteristics	Dex1 (n = 36)	Dex2 (n = 18)	Dex1A (n = 12)	Dex2A (n = 10)	P-value
Age, months	64 ± 52	59 ± 32	47 ± 29	48 ± 30	0.58
Weight, kg	22 ± 14	20 ± 8	20 ± 16	16 ± 5	0.62
Lowest BP, mmHg					
Systolic	91 ± 9	87 ± 11	89 ± 13	92 ± 7	0.67
Diastolic	49 ± 9	46 ± 8	45 ± 12	52 ± 7	0.24
Lowest heart rate min^{-1}	72 ± 10	69 ± 13	79 ± 15	76 ± 7	0.08
Procedure time, min	42 ± 22	52 ± 25	52 ± 26	49 ± 27	0.37
Recovery time, min	69 ± 27	77 ± 30	71 ± 33	69 ± 26	0.78

Values are mean ± SD.

Dex1, initial dexmedetomidine bolus of 2 $\mu g \cdot kg^{-1}$, once. Dex2, initial dexmedetomidine bolus of 2 $\mu g \cdot kg^{-1}$, twice. Dex 1A, Initial dexmedetomidine bolus of 2 $\mu g \cdot kg^{-1}$, once and received additional sedative medications during dexmedetomidine infusion. Dex 2A, initial dexmedetomidine bolus of 2 $\mu g \cdot kg^{-1}$, twice and received additional sedative medications during the procedure.

Table 2 Characteristics of hypotensive patients

Patients characteristics	1	2	3	4	5	6	7	8
Age, months	44	15	126	108	57	54	243	42
Weight, kg	15	8.5	44.5	31.5	16.5	20.5	61	16.5
Sedation group	Dex1	Dex2	Dex1	Dex2	Dex2	Dex2	Dex1	Dex2
Basal BP, mmHg								
Systolic	138	112	113	114	120	106	131	112
Diastolic	90	48	69	67	73	75	83	65
Lowest BP, mmHg								
Systolic	90	71	81	78	85	64	101	78
Diastolic	51	34	42	51	49	42	75	41
Hypotension duration, min	10	30	10	5	15	5	10	5
Lowest HR	65	86	74	56	63	81	61	75
Procedure time, min	35	75	117	27	63	56	28	51
Recovery time, min	130	107	75	60	60	51	75	121

HR, heart rate.

bradycardia associated with hypotension. The incidence of hypotension between the groups that received one or two boluses of dexmedetomidine was not statistically significant ($P = 0.24$). Comparison of systolic blood pressure (SBP), diastolic blood pressure (DBP), and HR changes at 5-min interval among all four sedation subgroups during dexmedetomidine sedation is shown in Figure 2.

Although a drop in BP was commonly observed during dexmedetomidine sedation, fluids or medications were not used to correct it during this study period. Hypotension was more often observed toward the end of procedure or immediately after stopping the dexmedetomidine infusion. Mean procedure time was 48 ± 24 min. Hypotension was observed at the 49 ± 24 min time point after the dexmedetomidine bolus. Hypotension lasted for 30 min in one patient and was limited to < 15 min in all other hypotensive patients.

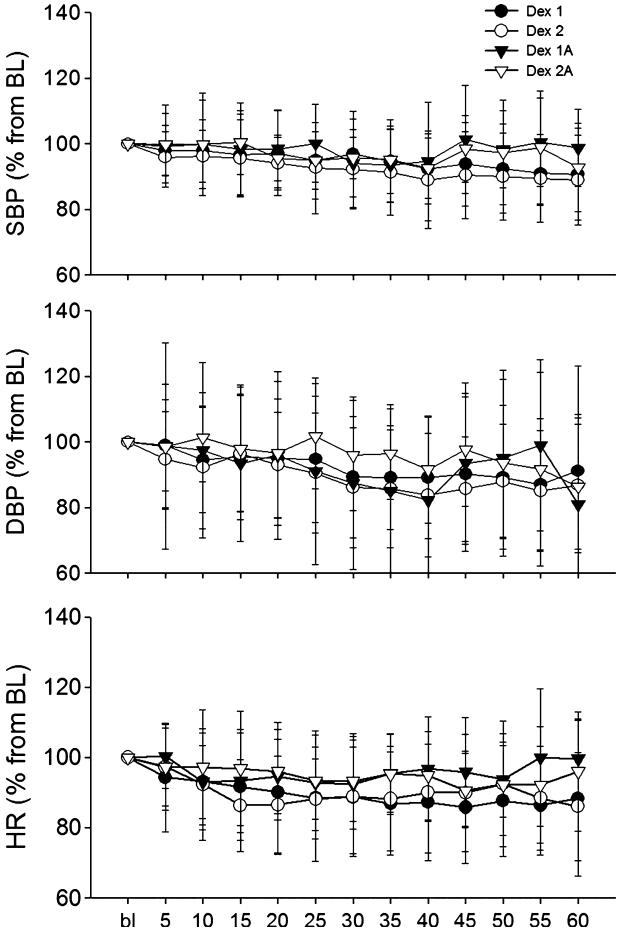

Figure 2 Percentage changes of BP and HR from baseline over time for the four sedation subgroups. SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

Three patients exhibited initial transient hypertension at the 19 ± 9 min time point after dexmedetomidine bolus. Hypertension lasted < 15 min in all three patients. Interestingly, all three patients received two boluses of dexmedetomidine and were < 10 years of age. One had HR of 52 and other two had HR between 60 and 70. The occurrence of initial transient hypertension was significantly more common in the patients who received two boluses vs one bolus of dexmedetomidine ($P = 0.046$).

Characteristics of patients with bradycardia are shown in Table 3. Only one of these patients had associated hypotension. In two patients, bradycardia was prolonged, lasting for approximately one hour. None of the patients required interventions to treat bradycardia. The incidence of bradycardia between patients who received one or two boluses of dexmedetomidine was not statistically significant ($P = 0.89$).

Time to discharge when dexmedetomidine was used alone was 72 ± 27 and 77 ± 32 min when additional medications were also used ($P = 0.5$). Discharge time was defined as the time from the end of the procedure to the actual time when patient left the recovery room. Recovery time of hypotensive patients (85 ± 30 min) and nonhypotensive patients (72 ± 27 min) was not statistically significant ($P = 0.25$). Recovery time of bradycardic patients (59 ± 24 min) vs nonbradycardic patients (72 ± 26 min) was also not statistically significant ($P = 0.26$).

Discussion

Dexmedetomidine was approved by the United States Food and Drug Administration (FDA) on December 24, 1999, for the sedation of adults receiving mechanical ventilation. In October 2008, the FDA approved dexmedetomidine for use in nonintubated patients requiring sedation prior to and during surgical and other procedures.

Table 3 Characteristics of patients with bradycardia

Patients characteristics	1	2	3	4	5	6
Age, months	121	15	95	108	69	105
Weight, kg	26	13.5	27.8	31.5	17.5	68.5
Sedation group	Dex2	Dex1	Dex2	Dex2	Dex2	Dex1A
Basal HR	68	92	95	72	80	75
Lowest HR	52	54	52	56	53	52
Bradycardia duration, min	15	5	60	10	15	50
Lowest SBP, mmHg	90	108	89	78	107	101
Procedure time, min	42	20	71	27	50	35
Recovery time, min	95	20	72	60	50	57

HR, heart rate; SBP, systolic blood pressure.

Tobias *et al.* (12–14) were the first to report the use of dexmedetomidine in children. In those studies, the dexmedetomidine dose was relatively low, consisting of a loading dose of 0.25–0.5 $\mu g \cdot kg^{-1}$ and an infusion rate of 0.25–0.5 $\mu g \cdot kg^{-1} \cdot h^{-1}$. A subsequent study by Berkenbosch *et al.* (15) reported the successful use of dexmedetomidine for pediatric procedural sedation by using a loading dose of 0.92 ± 0.36 $\mu g \cdot kg^{-1}$ over 10 min followed by infusion of 0.69 ± 32 $\mu g \cdot kg^{-1} \cdot h^{-1}$. This dose is lower than the one used in our study, but their reported success rate is similar to ours. Our patients received a higher initial dose (2 $\mu g \cdot kg^{-1}$) and yet 36% of children required second bolus of 2 $\mu g \cdot kg^{-1}$, which was well tolerated. Another study using a dexmedetomidine loading dose of 3 $\mu g \cdot kg^{-1}$ with an infusion rate of 1.5–2 $\mu g \cdot kg^{-1} \cdot h^{-1}$ found this regimen to be well tolerated with success rates of 97.6% (4). In our study, approximately one-third of the children (10 of 28) who received a second dose of dexmedetomidine required additional sedatives as well. Given the high failure rate of the second bolus dose of dexmedetomidine in achieving adequate sedation, it may have perhaps been preferable to administer additional sedatives rather than the second bolus dose. Previous investigators have reported a higher incidence of bradycardia (16%) with the use of higher doses of dexmedetomidine (3 $\mu g \cdot kg^{-1}$ bolus followed by 2 $\mu g \cdot kg^{-1} \cdot h^{-1}$) than those used in our study (4,16). Similar to our findings, previous investigators have also reported that hypertension is more likely to occur in children who receive more than one bolus of dexmedetomidine (17). Bradycardia and hypotension does not always occur together. Treating bradycardia with glycopyrrolate in children with normal BP can lead to hypertensive episodes (16).

Heard *et al.* (2) reported that the response to dexmedetomidine for MRI sedation can be somewhat unpredictable. In their series, when dexmedetomidine alone was used in the first eight patients, the success rate was only 37%. Those patients received a lower dexmedetomidine bolus dose (0.5–1.5 $\mu g \cdot kg^{-1}$) than ours, but comparable to the study by Berkenbosch *et al.* (15). Subsequently, when midazolam (0.1 $\mu g \cdot kg^{-1}$ bolus) was administered in conjunction with dexmedetomidine, the procedure was successfully completed in 12 of 13 children (92%) (2). In our study, despite higher doses of dexmedetomidine, 22 (29%) patients still required additional medications like midazolam, fentanyl, or ketamine to minimize movements during the MRI procedure, suggesting that adjunct agents are an important part of the sedation strategy for a sizeable minority of patients.

Despite the high doses of dexmedetomidine used in our series, the incidence of side effects was acceptable and well tolerated. The incidence of hypotension was 10.5% and did not require any intervention, which is consistent with the observations of others (4,15). The incidence of bradycardia in our study was 7.9%, which is considerably lower than the 16% reported by Mason *et al.* (4,16), while using higher dexmedetomidine doses (3 $\mu g \cdot kg^{-1}$ bolus followed by 2 $\mu g \cdot kg^{-1} \cdot h^{-1}$ of infusion). We speculate that higher doses of dexmedetomidine could translate into a greater likelihood of hemodynamic side effects. In ours and in several other studies (2–4,7), the effect of dexmedetomidine on respiration was negligible, reinforcing the notion that the risk of respiratory depression is minimal with careful dexmedetomidine sedation.

A recent review by Shukry and Miller (18) discussed the use of very high doses of dexmedetomidine (2–5 $\mu g \cdot kg^{-1}$ bolus, followed by infusions of up to 10 $\mu g \cdot kg^{-1} \cdot h^{-1}$) for airway procedures. The authors reasoned that patients tolerated such high doses of dexmedetomidine relatively well because airway surgeries were highly stimulating, thus resulting in acceptable heart rates and blood pressures. For noninvasive procedures, however, such high doses of dexmedetomidine can result in significant hemodynamic instability, so a dose 1 $\mu g \cdot kg^{-1}$ over 10 min followed by a continuous infusion of 0.2–0.7 $\mu g \cdot kg^{-1} \cdot h^{-1}$ has been recommended (18). As noted by Heard *et al.* (2), many clinicians find this range inadequate for sedation. Despite a higher dose of dexmedetomidine used in our study, a significant number of children required additional medications. Dexmedetomidine alone does not seem to achieve optimal sedation in all patients; therefore, it is difficult to determine the optimal dose of dexmedetomidine for adequate sedation without risking side effects. A higher dose of dexmedetomidine can have a higher incidence of hypertension, bradycardia, and hypotension (4,16,17).

In our study, the mean time to discharge after dexmedetomidine sedation was 72 min, shorter than the 90 min reported by Heard *et al.* (2). Mason *et al.* (4) observed recovery times ranging from 19.5 to 35.2 min, depending on the dexmedetomidine dose used, and Lubisch *et al.* (19) reported a recovery time of 47 min. These recovery times are shorter than our discharge time, but it is important to highlight the difference between recovery and discharge times. Some studies report the time when the patient met discharge criteria (recovery time), while we and others (2) report the actual time to leaving the recovery room (discharge time). Recovery time of hypotensive and bradycardic patients compared to normal cohorts was not statistically significant. The limitation of our current study is that with only eight hypotensive and six bradycardic patients, it is underpowered (< 0.5) to detect the true

difference. A larger study with more than 30 hypotensive and bradycardic patients will have enough power (>0.8) to identify the true difference in recovery time. Recovery time following propofol sedation for MRI in children has been shown to be even shorter (17 ± 8 min) (20). The fast recovery time of propofol must be weighed against the fact that it generally induces deeper sedation with more significant hemodynamic and respiratory side effects. When used in adequate doses, dexmedetomidine does not induce significant respiratory depression or hemodynamic compromise and still provides adequate sedation, making it an attractive choice to propofol and other IV sedatives.

Conclusion

High-dose dexmedetomidine can be successfully used for MRI sedation in children, but a sizeable minority of patients (29%) requires additional agents for optimal sedation. Hypotension (10.5%) is the most common side effect followed by bradycardia (7.9%) and transient hypertension (3.9%), but all have spontaneous resolution without interventions. Hypertension was observed in children receiving two boluses of dexmedetomidine. Respiratory depression was not observed with high-dose dexmedetomidine sedation in this study.

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