Comparison of Dexmedetomidine With Pentobarbital for Pediatric MRI Sedation

abstract

BACKGROUND AND OBJECTIVE: Intravenous pentobarbital has been used in the past to sedate pediatric patients in preparation for MRI; however, the drug has unpredictable sedation time. Dexmedetomidine, because of its short half-life, is gaining popularity for pediatric MRI sedation in settings where the use of propofol is restricted for nonanesthesiologists. The objective was to compare induction time, recovery time, total sedation time, sedation failure rate, and adverse outcomes of patients sedated with pentobarbital and dexmedetomidine in preparation for pediatric MRI.

METHODS: We reviewed a sedation database that contains clinical data for all children undergoing MRI studies while sedated with pentobarbital or dexmedetomidine between May 15, 2008, and October 30, 2010.

RESULTS: During the study period, 281 sedations were induced in preparation for MRI (160 with pentobarbital, and 121 with dexmedetomidine). The 2 groups were comparable with regard to age, weight, gender, and American Society of Anesthesiologists status. The dexmedetomidine group had a significantly shorter recovery time (39 ± 21 vs 49 ± 27 minutes [P = .002]) and total sedation time (107 ± 28 vs 157 ± 44 minutes [P = .0001]). Induction time was similar between the groups. The adverse event rate for the study population was 3%.

CONCLUSIONS: Dexmedetomidine and pentobarbital can both be used successfully for MRI sedation in children. However, dexmedetomidine had a significantly shorter recovery time and total sedation time in our population.

MRI studies require maintenance of a motionless state for a prolonged time. Pediatric patients often need to be sedated to achieve a motionless state, which, in turn, ensures completion of the study and the acquisition of images of diagnostic quality.

Intravenous pentobarbital (Nembutal; Abbott, Rockville, MD) has been used successfully in the past for procedural sedation in children and was the drug most commonly used to prepare children for MRI sedation. Pentobarbital is a long-acting barbiturate with a terminal half-life of 26 hours. Compared with other drugs, including those in the barbiturate family, pentobarbital has required frequent redosing to achieve an adequate level of sedation. Therefore, its sedation time is unpredictable, it presents an increased risk of significant adverse events, and it requires a longer time to full awakening after completion of the procedure. Prolonged recovery time correlates with increased patient monitoring time, bed occupancy, and parental anxiety.

Recent efforts have been directed toward finding an alternative to pentobarbital with more predictable onset and recovery. Dexmedetomidine (Precedex; Hospira, Inc., Lake Forest, IL) is a centrally acting alpha-2 agonist approved for use in adults for the treatment of hypotension and sedation during intubation, mechanical ventilation, and anesthesia. The objectives of this study were to compare induction time, recovery time, total sedation time, sedation failure rate, and adverse outcomes of patients sedated with pentobarbital and dexmedetomidine in preparation for pediatric MRI.

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sedation, MRI, pentobarbital, dexmedetomidine

ABBREVIATIONS
ASA: American Society of Anesthesiologists
CT: computerized tomography
RSS: Ramsay Sedation Scale

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Lake Forest, IL) is a potent, highly selective α-2 adrenoceptor agonist with a distribution half-life of ~8 minutes and a terminal half-life of 3.5 hours. It provides an adequate level of sedation while maintaining cardiorespiratory stability. Because of its pharmacokinetic properties, it has been gaining popularity for pediatric MRI sedation.4–6

Propofol is often used to sedate children in preparation for MRI because of its predictability, rapid onset, and offset of action.6–7 In many institutions, only anesthesiologists can administer propofol. In these restricted-use settings, dexmedetomidine might be an alternative for sedation.8–10

A previous study demonstrated dexmedetomidine to be a safe and effective alternative to pentobarbital for pediatric computed tomography (CT) scans. Its role in MRI sedation has not been compared with pentobarbital.11 The purpose of this study was to compare induction time, recovery time, total sedation time, sedation failure rate, and adverse outcomes among pediatric patients sedated with pentobarbital or dexmedetomidine in preparation for pediatric MRI sedation.

METHODS
For the purpose of continuous quality improvement, we established a patient sedation database. Demographics and sedation-related variables are entered into the database daily. After receiving approval from the institutional human research review board, we reviewed the sedation database to identify the records for children who underwent MRI studies under sedation by using either pentobarbital or dexmedetomidine between May 15, 2008, and October 30, 2010. The following data were extracted: age, gender, weight, body part imaged, physical status classification as defined by the American Society of Anesthesiologists (ASA),12 and medications administered, as well as dosage and route, induction time (time from initial administration of the drug to achievement of sufficient sedation to perform MRI), procedure initiation time, procedure end time, discharge time, and adverse events. Adverse events were defined as failed sedation (inability to achieve an adequate level of sedation to perform the procedure and premature arousal/movement before completion of study), abnormal oxygen saturation level (≤95%), apnea (cessation of breathing for more than 20 seconds), emergence delirium (a state of consciousness in which the child was inconsolable, irritable, uncompromising, or uncooperative, typically thrashing, crying, moaning, or incoherent),13 or any other event that could have endangered the patient and was felt to be associated with the sedatives. Patients with any missing data element in the database were excluded from the study.

All participants had been electively scheduled for MRI and advised to stay nil per os (nothing by mouth) based on recommendation from the American Academy of Pediatrics and ASA.14 In accordance with hospital policy for sedation, respiratory rate, heart rate, blood pressure, pulse oximetry, and nasal capnography were monitored continuously from the time of induction to discharge. The MRI area was equipped with airway management devices (including oxygen, masks, laryngoscopes, endotracheal tubes of various sizes, and suction devices) and the area was staffed with personnel competent in pediatric sedation and airway management.

Sedation level was measured by using the Ramsay Sedation Scale (RSS). This scale assigns a score of 1 to 6 based on clinical assessment of the level of sedation. A score of 4 was accepted as an adequate level of sedation for the procedure.15

Patients were determined to be eligible for discharge when they achieved a score of 10 according to the Aldrete criteria.16

Based on institutional guidelines, pentobarbital was administered intravenously at an initial dose of 2 mg/kg and repeated as 1 to 2 mg/kg every 3 minutes to a maximum dose of 7 mg/kg until the patient reached an RSS score of 4. Intravenous midazolam was administered as a 1-mg dose (maximum of 2 doses) until sufficient sedation was achieved to perform the MRI.

During the study period, our sedation protocol also called for an intravenous bolus of 2 µg/kg of dexmedetomidine administered over 10 minutes, followed by a maintenance infusion of 1 µg/kg, which was discontinued 10 minutes before the end of the MRI session. After the initial intravenous bolus of dexmedetomidine, the RSS score was assessed; if a score of 4 had not been achieved before initiation of the maintenance infusion, the bolus was repeated at 1 to 2 µg/kg over 10 minutes.17 Intravenous midazolam also was administered as needed until sufficient sedation was achieved to perform the MRI. Our patients were sedated in a room adjacent to the MRI suite. Once adequate sedation was achieved, they were transferred into the MRI suite.

The primary outcome variable was recovery time (the length of time after...
completion of the procedure to the time the patient met discharge criteria). Secondary outcome variables were induction time, total sedation time (the time from the end of induction to recovery), adverse events, and failed sedation.

Data were analyzed by using the SPSS 20.0 statistical package (IBM SPSS Statistics, IBM Corporation, Chicago, IL). Age and weight are expressed as medians (interquartile range).

Difference in gender, ASA status, and body parts imaged were compared by using the Pearson χ² test. A 2-sample independent t-test was used to compare differences in recovery time, induction time, and total sedation time between the pentobarbital and dexmedetomidine groups. The relative contributions of different body parts imaged on recovery and total sedation time were assessed with a sensitivity analysis, and results were compared by using an independent t-test. A P < .05 was considered significant.

RESULTS

The database held records for 281 sedations for MRI during the study period. Documentation was incomplete for 10 patients, and the level of sedation needed for the procedure was not achieved in 5 patients. There was no difference in the rate of incomplete documentation or sedation failure between the groups (Table 1). MRI was completed successfully in 266 patients; 154 (58%) were sedated with pentobarbital and 112 (42%) with dexmedetomidine.

Demographic characteristics of the 266 patients in the study are presented in Table 1. No statistically significant differences were noted between the pentobarbital and dexmedetomidine groups. Most patients in each group had an ASA physical status classification of II (Table 1).

The induction time was similar for both groups. The recovery time for patients sedated with dexmedetomidine was significantly shorter than that of the pentobarbital group (39 ± 21 vs 49 ± 27 minutes [P = .002]). Total sedation times were 107 ± 28 minutes for patients sedated with dexmedetomidine and 157.47 ± 44.00 minutes for the pentobarbital group (P = .0001) (Fig 1).

The body part most frequently imaged in both groups was the brain. The spine was imaged in 19 patients (7%) in the entire study population, in 16 patients (84%) of the pentobarbital group, and in 3 patients (16%) in the dexmedetomidine group (P = .01) (Table 2). Because of the higher number of patients requiring spine MRIs in the pentobarbital group, the influence of spine MRI on total sedation time and recovery time was evaluated by using a 1-way sensitivity analysis. Sensitivity analyses that excluded spine MRI (outliers) showed that the difference in recovery and total sedation time in the dexmedetomidine group was still significantly shorter than that of the pentobarbital group (Table 3).

Among the 154 patients sedated with pentobarbital, 66 (43%) were sedated successfully after a bolus dose of 4 mg/kg, 41 (27%) required 5 mg/kg, 18 (12%) received 3 mg/kg, 17 (11%) received 6 mg/kg, 8 (5%) received 2 mg/kg, and 4 (2%) received the maximum dose of 7 mg/kg. Among the 112 patients sedated with dexmedetomidine, 72 (64%) received a total of 2 µg/kg, 12 (11%) received 3 µg/kg, and 22 (20%) required 4 µg/kg. Sixty-nine (45%) patients in the pentobarbital group and 45 (40%) from the dexmedetomidine group received an additional 1 to 2 mg per dose of intravenous midazolam.

Adverse events during sedation were noted in 8 (3%) of our patients: 7 (4.5%) in the pentobarbital group and 1 (0.9%) who received dexmedetomidine. The difference was not statistically significant (P = .08). The most common adverse event in the pentobarbital group was emergence delirium on awakening, which occurred in 4 patients. Other adverse events included 2 patients with oxygen desaturation and 1 patient with transient apnea. The adverse event in the dexmedetomidine group was oxygen desaturation.

DISCUSSION

Pentobarbital and dexmedetomidine were both associated with successful sedation in preparation for MRI, but patients who received dexmedetomidine

<table>
<thead>
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<th>TABLE 1 Patient Characteristics</th>
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<tr>
<td>Pentobarbital, n = 154</td>
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<tr>
<td>Median age, y (IQR)</td>
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<tr>
<td>Male gender, n (%)</td>
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<td>Weight, kg (IQR)</td>
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<td>ASA status, n (%)</td>
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<td>ASA I</td>
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<td>Failed sedation, n (%)</td>
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IQR, interquartile range.
had a shorter recovery (39 vs 49 minutes) and total sedation time (107 vs 157 minutes) than those who received pentobarbital. Siddappa et al\textsuperscript{18} reported recovery times ranging from 19.5 to 35.2 minutes, depending on the dexmedetomidine dose, and Lubisch et al\textsuperscript{19} reported a recovery time of 47 minutes with dexmedetomidine. Recovery time after pentobarbital sedation has been reported as 54 ± 43 to 95 ± 28 minutes.\textsuperscript{2,11} The difference in recovery and total sedation time between the 2 sedatives may have significant impact on patient flow, physician and nurse productivities.

Pentobarbital has been used as a sedative for many years in patients undergoing radiologic studies.\textsuperscript{20} Although it has an established record of safety and effectiveness and has been demonstrated to be superior to sedatives such as chloral hydrate and midazolam,\textsuperscript{21–23} its sedation time is long (80–100 minutes).\textsuperscript{22} This length of time might be related to the relatively large dose of the drug needed to induce an immobile state. It is usually longer than the time needed for most radiologic procedures, including MRI. It is reasonable to be concerned that excess or deep sedation might be associated with an increased risk of adverse events (which was not demonstrated in this study).

In contrast to other sedative agents, dexmedetomidine has sedative properties that mimic natural sleep, without significant respiratory depression.\textsuperscript{24} Electroencephalograms obtained from children during dexmedetomidine sedation resemble those portraying non–rapid-eye-movement sleep.\textsuperscript{25} Even in relatively high doses, dexmedetomidine has little effect on airway caliber in children.\textsuperscript{26} In a variety of clinical settings, including cardiac catheterization suites, radiology departments, and ICUs, dexmedetomidine has been used as the sole sedative agent, providing reliable, effective, and hemodynamically stable sedation.\textsuperscript{27} In 2011, Mason et al\textsuperscript{11} concluded that dexmedetomidine was a suitable alternative to pentobarbital for the sedation of children before computerized axial tomography (CT), and the agent has subsequently gained popularity for noninvasive procedural sedation. However, MRI sessions last longer that CT scans, so more prolonged sedation is required. It is therefore important to consider the half-life of dexmedetomidine, the need for and frequency of redosing, and the adverse effect profile for MRI procedures. Our data show that, despite the need for redosing when using dexmedetomidine, it could be a safe alternative to pentobarbital, because of its shorter recovery time, the shorter duration of exposure to a sedative agent, and a decreased risk of cardiopulmonary side effects.\textsuperscript{12}

Adverse events were unusual in our study, but were more often associated with pentobarbital than with dexmedetomidine. The most significant adverse reaction occurred in 4 patients.
sedated with pentobarbital, who exhibited emergence delirium when awakening. Kienstra et al28 and Greenberg et al29 reported an incidence of emergence delirium ranging from 7% to 11% of patients sedated with pentobarbital, resulting in delayed discharge and prolonged total sedation time. Although other adverse events have been described with both agents, they were not seen in our study. The low incidence of adverse events might be secondary to actions taken by the sedation team that we did not extract from the database, such as administration of intravenous fluids.

Several studies have compared the use of propofol, pentobarbital, and dexmedetomidine for MRI sedation.7,8,30 Propofol appears to be more efficient because it results in fewer inadequate sedations and allows patients a much shorter recovery time. However, the use of propofol for sedation outside the operating room is controversial, because of the drug’s potential for rapid, profound changes in sedation/depth of anesthesia, respiratory depression, transient apnea, and hypotension, as well as the lack of antagonist medications. Therefore, in many institutions, the use of propofol is limited to anesthesiologists.5,10,31 In settings in which propofol use is restricted or contraindicated, dexmedetomidine and pentobarbital can be used as alternatives for MRI sedation.

The limitations of our study include its retrospective nature and associated limitations in accuracy of data collection. Although the sedation protocols were identical, use of dexmedetomidine sedation after a decade of pentobarbital use may have been positively affected by the sedation team’s experience in sedating children. In addition to the new agent used, practitioner’s confidence with sedation and non-pharmacologic interactions may have had an effect. These were not systematically collected. The time required for an MRI scan depends on the body parts being imaged and the sedation protocol used for the scan. We did not control for the length of the MRI sessions. Table time also can be affected by changes in MRI protocols and machine upgrades. Software upgrades to improve image quality were made during our study period, but the same MRI machines were used, without any reported change in testing times. We are not aware of changes in the protocol that could have affected our results. Adverse events associated with procedural sedation are rare. Even though we found fewer such events with dexmedetomidine, our sample size is not powered enough to allow us to state that they were “infrequent.”

CONCLUSIONS

Both dexmedetomidine and pentobarbital can be used for MRI sedation in children. In this study, recovery time and total sedation time after administration of dexmedetomidine was shorter than that after pentobarbital. Considering restrictions on the use of propofol in many institutions, coupled with the possibility of drug shortages, pentobarbital remains an alternative agent for MRI sedation in children. Among these 2 sedatives, dexmedetomidine is more attractive because it offers reliable and efficient sedation, even for prolonged studies such as MRI.

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REFERENCES

7. Mallory MD, Baxter AL, Kost S. Pediatric Sedation Research Consortium. Propofol vs pentobarbital for sedation of children undergoing magnetic resonance imaging:


