Dexmedetomidine for Pediatric Sedation for Computed Tomography Imaging Studies

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Dexmedetomidine is a sedative with limited experience in the pediatric population. This is the first study that prospectively evaluates the sedation profile of a dexmedetomidine pilot program for pediatric sedation for radiological imaging studies. In March 2005, our hospital sedation committee approved the replacement of IV pentobarbital with dexmedetomidine as the standard of care for CT imaging. Detailed Quality Assurance (QA) data sheets collect relevant information on each patient, which is then logged into a computerized sedation database. After IRB approval, all QA data was accessed. Sixty-two patients with a mean age of 2.8 years (SD = 1.8, range 0.5–9.7) received IV (IV) dexmedetomidine administered as a 2 mcg/kg loading dose over 10 minutes, followed by repeat boluses of 2 mcg/kg over 10 minutes until target of Ramsay Sedation Score 4 (RSS) achieved. Patients were then maintained on 1 mcg/kg/hr infusion until imaging is completed. Repeated-measures ANOVA indicated that compared to pre-sedation values, the heart rate and mean arterial blood pressure decreased an average of 15% during bolus, infusion and recovery ($P < 0.01$). No significant changes were observed in respiratory rate or end-tidal CO2. Mean recovery time was 32 ± 18 minutes. Based on our pilot results, dexmedetomidine may provide a reliable and effective method of providing sedation.

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Neonates and infants undergoing radiological imaging studies often require sedation to minimize motion artifact. Historically, chloral hydrate and pentobarbital have been the drug of choice for pediatric sedation in radiology departments (1–4). Rates of successful sedation with this medication range from 85–98% (5,6). Both pentobarbital and chloral hydrate are medications which each have almost 100 years of clinical experience. Because of their extended half-life, they have been associated with prolonged recovery times and sedation-related morbidity (7–10).

Since 1993, pentobarbital has been the mainstay of our pediatric sedation program for diagnostic imaging in radiology. In an effort to decrease our rate of failed sedations, reduce our recovery room time and improve our adverse event rate, the Radiology Sedation Committee established a pilot program using dexmedetomidine (Precedex; Hospira, Lake Forest, IL) as a sedation replacement to pentobarbital for CT imaging. Dexmedetomidine is a highly selective α2 adrenoceptor agonist that has sedative and analgesic effects (11). It has limited experience in the pediatric population. There has not been a prospective study evaluating its use for pediatric sedation for diagnostic imaging studies. Following approval by the Radiology and Hospital Sedation Committee, we established a pilot protocol to replace pentobarbital with dexmedetomidine. This study was designed to evaluate the efficacy and adverse event profile of dexmedetomidine. To our knowledge, we are the only institution which has established a dexmedetomidine sedation program for CT imaging.

METHODS

Database

In December 1993, the Children’s Hospital Radiology Sedation Committee was established to create sedation guidelines for the department of Radiology and to monitor staff credentialing and quality assurance. The radiology nursing staff collects and records specific information on each sedation. This information is transcribed to a computerized database (FileMakerPro, version 2.1; Claris, Cupertino, CA) by a single designated staff member. The database contains information on patient demographics, medical diagnosis, time of examination, duration of fasting status, type of examination performed as well as the date of
the study, medications and dosages (micrograms per kilogram body weight) administered, patient’s American Society of Anesthesiologists (ASA) physical status classification, (12) adverse and paradoxical events, time required to sedate and recover, and failed sedations.

Within 24 hours of the sedation, a radiology nurse attempts to contact all patients (or their parents) who were sedated. Satisfaction and delayed adverse events are recorded at this time. All adverse events are reviewed at monthly meetings of the Radiology Sedation Committee. Current protocols are routinely reviewed and modified and new protocols are frequently piloted in efforts to improve sedation practice.

**Definition of Terms**

All adverse events and specific demographics related to the patient and the sedation are entered into the computerized database. Adverse events are classified according to acuity and placed in different categories: A, B and C. Category A encompasses the most serious events which include need for resuscitation, cardiovascular complications, decrease in oxygen saturation, aspiration, allergic reaction, and the use of reversal agent. Grade B: prolonged sedation (greater than 3 hours recovery time), vomiting, unplanned admission, and paradoxic reaction. Grade C: failed sedation, awakens before procedure over, greater than 3 IV attempts.

The definition of each adverse event and demographic data-point is defined below (7):

**A Failed Sedation:** Inadequate sedation subsequent to receiving the maximum allowable dosages per the sedation protocol or inability to complete the planned procedure secondary to unacceptable motion artifact.

**A Prolonged Sedation:** Inability to meet discharge criteria 3 hours following ingestion of the sedative or failure to return to baseline mental and behavioral status within 24 hours of receiving sedation.

**Decrease in Oxygen Saturation:** Sustained decrease in oxygen saturation of greater than 5% from baseline for more than 1 minute, despite facemask oxygen delivery of 6 L/minute, head repositioning, suctioning and physical stimulation.

**A Need for Resuscitation:** Decline in the patient’s respiratory rate and oxygen saturation that requires resuscitative efforts which include positive pressure ventilation, cardiopulmonary resuscitation or the use of medications which reverse the sedation.

**A Cardiovascular Complication:** Sustained (>5 minute) decrease (≥20%) in the patient’s mean arterial pressure with or without a decrease in heart rate below the lower limit of the normal range for the patient’s age.

**An Unplanned Admission:** An unexpected admission to the hospital overnight as a direct result of an adverse event directly related to the sedation.

**A Gastrointestinal Side Effect:** Vomiting, aspiration or diarrhea occurring within 24 hours of the administration of sedation.

**An Allergic Reaction:** Unexplained rash or allergic symptoms that develop within 24 hours of receiving sedation.

**The Time To Achieve Sedation:** Time in minutes from initial administration of sedative to achievement of adequate sedation of the patient.

**Paradoxical Reaction:** a rage, irritability or agitation that was not present prior to sedation.

**Duration of Sedation:** Total duration of sedation defined as the time from which the initial sedative is administered to the point at which the last dose of sedation is received.

**Imaging Time:** Time duration of entire imaging study from initiation of scan to radiologist confirming completion of successful CT study. Sounds awkward.

**Recovery Time:** Time in minutes from last dose of sedation to point at which patient meets discharge criteria from the recovery room.

**Sedation Protocol**

Prior to administering sedation, all sedation candidates are evaluated by a radiology nurse in order to determine whether the child has any medical conditions that would disqualify this patient from sedation. Specifically, in its Sedation Policies and Guidelines, the Radiology sedation committee has established a list of medical conditions that would contraindicate a child from receiving dexmedetomidine sedation (Table 1). Our Sedation Policies and Guidelines incorporate and expound on those recommended by the American Academy of Pediatrics (13,14). The nurse collects and documents the patient’s past medical, surgical, sedation and anesthetic history. A physical examination, review of systems and review of pertinent laboratory data is recorded along with the current medications, allergies and fasting status. The supervising anesthesiologist confirms the findings prior to obtaining informed consent for the sedation.

Although all pentobarbital sedation at our institution has been administered by a radiology nurse with physician (radiologist or anesthesiologist) oversight, for this pilot program all dexmedetomidine was administered by an anesthesiologist. Although dexmedetomidine is considered a sedative and theoretically only requires a pulse oximeter and blood pressure
monitor as required by American Academy of Pediatrics, we elected to do full monitoring, as if the child was undergoing a general anesthetic.

After evaluating different dosage regimens, the Radiology Sedation Committee established by consensus a protocol for dexmedetomidine administration. The protocol specifies that all children have a baseline set of vital signs prior to sedation which include MAP, oxygen saturation, heart rate and respiratory rate. An initial loading dose of 2 mcg/kg IV dexmedetomidine is administered over a 10 minute period. Patients are monitored initially with pulse oximetry. As the level of sedation increases, additional monitors are added in conjunction with the patient’s tolerance. Typically, the child does not tolerate nasal prong capnography and insufflation of the non-invasive blood pressure cuff until there is a Ramsay Sedation Score (RSS) 4 (15). A RSS 4 or RSS 5 is a clinically derived scoring system that is generally accepted as an adequate sedation depth to tolerate diagnostic imaging studies. After the initial loading dose, the sedation score is assessed, usually by confirming tolerance of blood pressure measurement or nasal prongs. If RSS 4 has been achieved, and the CT scan is not yet completed, the maintenance infusion of 1 mcg/kg/hr is initiated until completion of study. However, if RSS 4 has not been achieved with the initial load, a repeat bolus of 2 mcg/kg over 10 minutes is administered. If the RSS 4 is achieved following this 2nd bolus, an infusion of 1 mcg/kg/hr is immediately started. At a RSS 4, all patients are fully monitored as if undergoing a general anesthetic. Specifically, pulse oximetry, capnometry, respiratory rate, blood pressure, heart rate and electrocardiogram are followed and documented at 5-minute intervals throughout the procedure. Regardless of sedation level, all children complete the initial loading dose. The CT imaging study is initiated as soon as the desired level of sedation has been achieved, sometimes even during the initial or repeat loading dose.

Following the procedure, the patient is transported to the radiology recovery room where a nurse monitors and records the identical vital signs every 5 minutes until discharge criteria are met.

Record Review
After Institutional Review Board approval, the prospectively gathered data was reviewed to compare outcome variables for all children who underwent CT imaging and received as standard of care dexmedetomidine per established protocol outlined above. All patients (parents) signed written, informed consent for the sedation. A total of 62 patients were sedated between March 15 and June 1, 2005. Outcome data were acquired from Quality Assurance forms which included time to sedation, recovery time, amount of medication (mcg/kg) administered, vital signs, failed sedations and adverse events.

Statistical Analysis
Continuous variables including age, weight, dose, heart rate, respiratory rate, mean arterial pressure, end-tidal carbon dioxide, as well as the times to sedation and discharge were tested to assess whether they followed a Gaussian-shaped distribution and no significant skewness or non-normality was detected. Therefore, these variables are expressed in terms of the mean and standard deviation and changes in the vital measurements from baseline were evaluated using repeated-measures analysis of variance (ANOVA) (16). Adverse events are reported as percentages with 95% confidence intervals as determined by the normal approximation. A power analysis indicated that a minimum sample size of 60 patients would provide estimation of the true adverse event rate to within 5% with a confidence level of 95% (version 5.0, nQuery Advisor, Statistical Solutions, Cork, Ireland). Finally, multiple logistic regression analysis was applied to determine if any demographic or procedural variables were associated with adverse events during sedation (17). Statistical analysis was performed using the SPSS software package (version 12.0, SPSS Inc., Chicago, IL). Two-tailed values of P < 0.05 were considered statistically significant.

RESULTS
Sixty-two children received dexmedetomidine per above delineated protocol for CT imaging (34 males and 28 females) with a mean age of 2.8 years (SD = 1.8, range 6 months–9.7). Patients’ weight averaged 14.6 ± 5.1 kg. The majority of examinations consisted of imaging the head and/or neck (66%), abdomen (18%), and thorax or spine (13%). 32% were ASA I and 58% were ASA II. The demographics of the study group are presented in Table 2.

Among the 62 patients, the mean loading dose of dexmedetomidine was 2.2 mcg/kg. Per protocol, all patients completed the 2 mcg/kg loading dose over 10 minutes. 52 patients sedated to RSS4 with the loading

<table>
<thead>
<tr>
<th>Table 1. Medical Conditions That Contraindicate Dexmedetomidine</th>
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<td>Active, uncontrolled gastroesophageal reflux</td>
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<td>Active, uncontrolled vomiting</td>
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<tr>
<td>Current (or within the past 3 mo) history of apnea requiring an apnea monitor</td>
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<td>Active, current respiratory issues that are different from the baseline status (pneumonia, exacerbation of asthma, bronchiolitis, respiratory syncitial virus)</td>
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<td>Unstable cardiac status (life-threatening arrhythmias, abnormal cardiac anatomy, significant cardiac dysfunction)</td>
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<td>Craniofacial anomaly, which could make it difficult to effectively establish a mask airway for positive pressure ventilation if needed</td>
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<td>Current use of digoxin, beta blockers, or calcium channel blockers</td>
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<tr>
<td>Moya Moya disease</td>
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<td>Non-onset stroke</td>
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Children’s Hospital, Boston, Radiology sedation guidelines, 2005.
Of these patients, 6 children were able to complete the CT imaging study during the loading dose. Ten patients (16%) required a second bolus (1–2 mcg/kg). A total of 56 patients (90%) required the maintenance infusion of 1 mcg/kg/hr following the loading dose (± 2nd bolus).

Pre-sedation mean values of heart rate and respiratory rate for the entire cohort were 115 ± 19 (range 80–164) and 24 ± 4 (range 16–34), respectively. Repeated-measures ANOVA indicated that compared to pre-sedation, heart rate decreased during bolus, infusion, and in recovery (P < 0.01). Mean decline in HR from baseline (pre-sedation) to recovery was 15% (SD = 10%). 70% of the patients exhibited a decrease in heart rate of between 5–25%. As shown in Table 3, ten patients (16%) developed sinus arrhythmias (SA) during either the bolus or infusion. Despite the sinus arrhythmia, all patients demonstrated hemodynamic stability. All SA resolved prior to completion of the study and lasted for no longer than 2–3 minutes. There were no incidences of SA in the recovery room. No significant changes were observed in respiratory rate (Fig. 1).

Dexmedetomidine had a mean time to sedation of approximately 10 ± 2 minutes and a sedation duration, which averaged 21 minutes (range 10–37 minutes). Duration of CT imaging averaged just over 8 to pre-sedation, MAP decreased during infusion and recovery (P < 0.01). Similar to the change in HR, the average decline in MAP from baseline to recovery was 15% (SD = 15%) with about 70% of patients showing a decline between 1–30%. No significant changes were observed in end-tidal CO2 levels (Fig. 2). No supplemental oxygen was delivered during the sedation. There were no significant drops (≥5%) in oxygen saturation. Despite the drop in blood pressure and heart rate, all changes were still within the clinical range of normal (≥5 percentile for age).

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**Table 2. Demographics of the Patients Undergoing Sedation for Computed Tomography Imaging (n = 62)**

| Age (yr) | 2.8 ± 1.8 (0.5–9.7) |
| Weight (kg) | 14.6 ± 5.1 (8.0–32.9) |
| Male | 34 (55%) |
| Female | 28 (45%) |
| Type of examination |  |
| Head or neck | 41 (66%) |
| Thorax or spine | 8 (13%) |
| Abdomen | 11 (18%) |
| Hip | 2 (3%) |
| ASA physical status |  |
| I | 20 (32%) |
| II | 36 (58%) |
| III | 6 (10%) |
| Total loading dose (µg/kg)* | 2.2 ± 0.6 (2–4) |

Values are mean ± sd (range) or number (%).

Loading dose: initial dose (2 µg/kg) + second bolus (if needed) to achieve Ramsey sedation score = 4. Ten patients had a second bolus of 2 µg/kg.

**Table 3. Performance Characteristics of Dexmedetomidine, Electrocardiogram Findings, and Adverse Events During Sedation and in the Recovery Room**

| Performance results (min) |  |
| Time to achieve sedation | 9.9 ± 2.4 (6–20) |
| Duration of sedation | 21.0 ± 5.5 (10–37) |
| CT imaging time | 8.1 ± 4.3 (2–20) |
| Recovery Time | 31.8 ± 18.0 (5–75) |
| ECG findings* |  |
| Duration sedation | 10 (16.1) |
| Adverse events | 5 (8.1) |
| Duration recovery | 3 (4.8) |
| Delayed (24 h) | 2 (3.2) |

Values are mean ± sd (range) or number (%).

*All sinus arrhythmia occurred during initial loading bolus or maintenance infusion.

**Figure 1. Heart rate and respiratory rate throughout the sedation time course in all patients.** Repeated-measures ANOVA revealed a statistically significant change (P < 0.01) in heart rate but no change in respiratory rate after baseline. Asterisks denote significant changes relative to pre-sedation levels.

**Figure 2. MAP and end-tidal carbon dioxide at various time points from pre-sedation to recovery.** End-tidal CO2 was not measured prior to sedation. Repeated-measures ANOVA indicated that relative to pre-sedation baseline levels, mean BP declined significantly during infusion and continued to be lower than baseline during recovery (P < 0.01). However patients remained within the normal range. No significant changes were observed from bolus to infusion and recovery with respect to end-tidal CO2. Asterisks denote significant changes relative to pre-sedation levels.
minutes (range 2–20 minutes). Mean recovery time was nearly 32 ± 18 minutes (Table 2). Performance characteristics of dexmedetomidine for the study group are shown in Table 2.

There were no Type A adverse events in this study. All adverse events were Type B and occurred during sedation \(\left(n = 5\right)\) or in the recovery room \(\left(n = 3\right)\). Irritability, agitation, and vomiting were the most common Type B occurrences (Table 3). Two children became increasingly agitated during the loading dose. After more than 5 minutes of extreme agitation during the loading dose, at the anesthesiologist’s discretion, an alternate means of sedation was chosen (propofol for one child and pentobarbital for another). A total adverse event rate of 8.1% was observed during sedation and 4.8% during recovery. Only two delayed events occurred at 24 hours (event rate = 3.2%) and these were both irritability.

Multiple logistic regression analysis was conducted to assess whether demographics, procedural, or sedation variables were associated with adverse events during sedation. Age, weight, gender, type of examination, and dose of dexmedetomidine were not found to be significant predictors of adverse events during sedation (all \(P > 0.10\)).

At 24 hour follow-up, all parents were contacted and given a scale of approval rating that included very satisfied, satisfied, neutral and dissatisfied. Most parents expressed a high degree of satisfaction with the use of dexmedetomidine: 98% indicated that they were either satisfied \(\left(n = 44\right)\) or very satisfied \(\left(n = 17\right)\). Only 1 parent was neutral and none indicated dissatisfaction.

**DISCUSSION**

In 1993, the Department of Radiology established a computerized database for all sedations. This database has enabled the Radiology Sedation Committee to perform quality assurance, review outcome data and evaluate modifications of the sedation protocols. By conducting pilot studies with alternative sedation techniques \((8,9)\) and analyzing the results efficiently with this database, we have been able to establish new protocols and improve existing ones \((18)\). The committee represents a collaboration between members of the Departments of Anesthesia and Radiology.

Recent literature looked at 16,467 sedations, and found a total of 58 cases of oxygen desaturation, representing an overall incidence of 0.35%. There were 2 cases of pulmonary aspiration (incidence of 0.01%), 10 sedations which required airway resuscitation (incidence of 0.06%) and a failed sedation rate of <1% \((10)\). Other authors report a 2.9% incidence of hypoxemia and a 7% failed sedation rate \((19)\). Clearly, some of the medications (fentanyl, pentobarbital, midazolam, droperidol, morphine, chloral hydrate) that are currently being used for sedation are long acting and potential respiratory depressants. There is a growing interest in \(\alpha_2\) agonists for sedation and analgesia.

Dexmedetomidine has a short half-life of 1.5–3 hours after IV dosing \((20,21)\). This is a significantly shorter half-life than that of pentobarbital and chloral hydrate. A short-half life could make dexmedetomidine easier to titrate, quicker to recover from and potentially associated with less prolonged sedation related adverse events.

Another significant advantage of dexmedetomidine is that in adults, it provides sedation and analgesia with no accompanying change in resting ventilation when administered within clinical dosing guidelines \((22–24)\). Some feel that dexmedetomidine actually mimics some aspects of natural sleep \((22)\). It has been shown to produce dose-dependent decreases in blood pressure and heart rate as a result of its \(\alpha_2\) agonist effect on the sympathetic ganglia with resulting sympatholytic effects \((25,26)\). An additional advantage of dexmedetomidine is that antagonists to \(\alpha_2\) agonists exist and could potentially provide for a quick reversal of the hemodynamic or sedative effects \((27)\).

There is limited prospective literature in children. The majority of publications are case reports and series describing dexmedetomidine for sedation of children who are ventilated, detoxifying from opioids and benzodiazepines, failing traditional sedation techniques for MRI imaging, or undergoing an awake craniotomy \((28–31)\). Dexmedetomidine has been found to cause potentially life threatening cardiovascular complications in some adults and children \((23,27,32–34)\). Currently, it is approved by the Food and Drug Administration (FDA) for use as a sedative for adults on ventilators. Under the FDA it is limited to use as a continuous IV infusion for no more than 24 hours. It does not have FDA approval in the pediatric population.

We have shown that dexmedetomidine may provide a reliable and effective method of providing sedation to children undergoing diagnostic imaging studies. We found no effect on baseline respiration as evidenced by respiratory rate and end-tidal CO2 values. The decreases in heart rate and blood pressure were still clinically acceptable for this pediatric population. However, until larger studies confirm hemodynamic stability of dexmedetomidine in the pediatric population, we would recommend full monitoring. Developing a standard protocol for dexmedetomidine administration that would guarantee high success with minimal adverse events will require further clinical trials. A limitation of this study is its small sample size of 62 patients. We powered the study to estimate the true adverse event rate to within 5% with a high level of statistical confidence (i.e., 95%). Greater precision regarding the true adverse event rate would have required considerably more patients. Therefore, our results need to be interpreted with caution regarding safety since data from a larger prospective study are needed to establish assurance of dexmedetomidine safety in pediatric CT imaging.
In conclusion, in the setting of an organized, appropriately staffed and monitored sedation program, dexmedetomidine may be an appropriate agent for sedation of infants undergoing CT imaging procedures.

REFERENCES