Procedural Sedation by Pediatric Hospitalists: Analysis of the Nature and Incidence of Complications During Ketamine and Nitrous Oxide Sedation

abstract

OBJECTIVE: The goal of this study was to determine the nature and rate of complications during procedural sedation by pediatric hospitalists (PH) using ketamine and nitrous oxide (N₂O).

METHODS: This study was a retrospective review and analysis of a quality improvement database for sedations performed by PH at St Louis Children’s Hospital from February 2007 to February 2013. Information was obtained on sedations performed and reported in the quality improvement database by PH over this time period using ketamine and N₂O.

RESULTS: PH performed 8870 sedations from 2007 to 2013, 60.2% using ketamine and 39.8% using N₂O. Procedural completion rates were >99%; 0.12% of sedations were not completed due to inadequate sedation, and sedation level was not achieved in 1.71% of sedations. There were no occurrences of death, need for cardiopulmonary resuscitation, unplanned intubation, or emergency anesthesia consultation. The only major complications were 4 unplanned admissions, 2 each with ketamine and N₂O. With ketamine, the 2 highest rates of complications were airway repositioning (3.99%) and nausea and/or vomiting (2.98%). With N₂O, the 2 highest complication rates were nausea and/or vomiting (8.50%) and airway repositioning (1.10%). Respiratory and cardiovascular events were more frequently encountered with ketamine, whereas nausea/vomiting, sedation level not achieved, and inadequate sedation resulting in procedure not completed occurred more frequently with N₂O.

CONCLUSIONS: PH at St Louis Children’s Hospital successfully provided sedation by using ketamine and N₂O with low rates of complications for a variety of procedures.

Every day, children of all ages undergo painful procedures and radiologic imaging in hospitals across the nation. Procedural sedation (PS) is often needed to alleviate the pain, anxiety, and distress associated with these procedures and to facilitate the safe completion of the procedure itself. Appropriate analgesia/sedation for procedures is critical to a child’s emotional well-being as well as to obtain better outcomes. Weisman et al reported that inadequate analgesia for initial procedures in young children may diminish the effectiveness of adequate analgesia in subsequent procedures.

There is wide variability in the provision of PS and analgesia at different institutions, and this variability is due in part to the availability of sedation providers.
Anesthesiologists have been unable to meet the growing demands of PS, and nonanesthesiologists are increasingly providing PS for children. Several studies have demonstrated the safety of procedural sedation using ketamine and nitrous oxide (N₂O) by emergency physicians and intensivists. Pediatric intensivists and emergency physicians have been the primary nonanesthesiologist sedation providers because they have the greatest experience managing the pediatric airway in patients in the emergency department (ED) and ICU. However, pediatric hospitalists (PH) are increasingly providing sedation for various painful procedures and for radiologic imaging of children across the nation. It is important to establish that PH can provide safe and effective PS even though many of them lack the training in airway management provided during fellowship training of emergency physicians and intensivists.

The hospitalist sedation program at St Louis Children’s Hospital (SLCH) consists of 50 PH who provide procedural sedation at multiple settings in the hospital, including the ED, Ambulatory Procedure Center (APC), and Pediatric Acute Wound Service (PAWS). A variety of sedation agents are used by PH based on their training and sedation credentialing. A tiered system of sedation providers exists, ranging from PH who provide sedation only in the ED (tier 1) to providers who are trained to use propofol in the APC (tier 3). The sedation service follows safety standards established by the American Academy of Pediatrics and the American Society of Anesthesiologists, as well as institutional standards. Adverse events during sedation are tracked by using a quality improvement (QI) sedation database in which all sedation-related adverse events are manually entered.

We previously analyzed the complication rates of propofol sedations performed by PH at SLCH, and we found that the propofol sedation program was effective, with low rates of major complications (0.18%). However, sedation with propofol is provided by the more experienced tier 3 PH who have had specialized training in the operating room to manage the pediatric airway. The primary sedation agents used by all PH sedation providers (tiers 1, 2, and 3) are ketamine and N₂O. To determine the effectiveness and safety of PS performed by all PH at SLCH, we measured rates of complications that occurred during sedations performed by PH at SLCH using ketamine and N₂O. These rates were determined from a retrospective review and analysis of a QI database. To the best of our knowledge, there are no previous studies reporting the safety of procedural sedation performed by PH using ketamine and N₂O.

**METHODS**

**Study Design**

Since 2007, sedation providers at SLCH have completed a QI form at the end of each procedure. The QI form collects information on patient age range (patient gender is not recorded), hospital setting where the sedation is performed, nature of the procedure, patient risk factors or active medical problems, sedation plan, agents used, and complications. The data are entered into a QI database by an administrative assistant. The database was analyzed for all the sedations performed by PH using ketamine and N₂O from February 2007 to February 2013.

The QI form was revised and expanded in September 2011 to gather more specific information about each episode of sedation. The expanded form included additional data elements about the procedures performed, concentration of N₂O used for sedation, and an expanded complication section including queries for emergency anesthesia consultation and occurrence of rash, hives, stridor, laryngospasm, and seizures. Elements that are present only in the new QI form are noted in Table 1, and percentages of these elements are calculated by using the number of sedations performed using N₂O and ketamine since September 2011. Thus, rates for major complications include “emergency anesthesia consultation” only since 2011. The new QI form also has queries for the concentration of N₂O used. The QI form only queries for inadequate sedation resulting in a procedure not being completed. The percentage of patients with procedures completed successfully is thus derived by subtracting those with procedures not completed due to inadequate sedation from the total number of patients sedated. There is no query in the QI data form regarding patient distress during a procedure.

**Sedation Protocol**

Presedation assessment is completed by the sedation provider before all sedations. Patients are monitored according to guidelines of the American Academy of Pediatrics and American Society of Anesthesiologists. Children being sedated for painful procedures are generally premedicated with 0.2 to 0.3 mg/kg of oxycodone (maximum dose: 10 mg) and 15 mg/kg of acetaminophen (maximum dose: 650 mg). N₂O is administered via a face mask at a concentration of 70% for ∼5 minutes and then N₂O is decreased to 50% for a total duration of ∼15 minutes. After sedation, 100% oxygen is administered for 2 minutes.
to prevent diffusion hypoxia as well as to improve the scavenging of exhaled N\textsubscript{2}O. Ketamine is generally administered at an initial dose of 0.5 to 1 mg/kg. Additional doses are administered at a dose of 0.5 to 1 mg/kg. Vital signs and depth of sedation according to the University of Michigan sedation scale\textsuperscript{13} are monitored continuously and recorded every 5 minutes in the chart. The QI form records inadequate sedation and sedation level not achieved or exceeded. Pain scores are recorded in the sedation forms by using the Face, Legs, Activity, Cry, Consolability scale or the Wong-Baker Faces Pain Rating Scale based on the age of the patient.\textsuperscript{14,15} Only scores >6 are recorded in the QI form.

### Statistical Analysis

$P$ values for the comparison of characteristics and proportions of complications between patients sedated by using ketamine or N\textsubscript{2}O were calculated by using Pearson’s $\chi^2$ test for large cell counts and Fisher’s exact test for cell counts $\leq 5$. Confidence intervals for proportions of complications were calculated by using exact methods when the number of complications was small ($\leq 5$) and according to Woolf’s method when the number of complications was larger.

Institutional review board approval was obtained for the study.
RESULTS

PH performed 8870 sedations from 2007 to 2013, 60.2% using ketamine and 39.8% using N\textsubscript{2}O. At least 46% and 73% of children sedated with ketamine and N\textsubscript{2}O, respectively, were premedicated with a sedative or opioid. Although the QI form queries did not distinguish between a sedative or an opioid, the general practice of the PH at SLCH was to use oxycodone as a premedication. The old QI forms did not have a query for the concentration of N\textsubscript{2}O used; however, data from the new QI forms (901 N\textsubscript{2}O sedations) showed that 99.1% of N\textsubscript{2}O sedations were performed by using 70% N\textsubscript{2}O.

The age range of patients sedated, procedure for which patients were sedated, and the hospital setting for the sedation are presented in Table 2. Children aged between 7 months and 4 years were sedated more frequently with ketamine, whereas children >4 years of age were more often sedated by using N\textsubscript{2}O. Ketamine was used more frequently in all sites except for the PAWS unit and unknown location. Almost 81% of N\textsubscript{2}O sedations performed by PH were provided in the PAWS unit. The old QI forms did not have a detailed query for procedures; however, data from the new QI forms that included detailed queries for procedures revealed that most of the N\textsubscript{2}O sedations in the PAWS unit were provided for abscess incision and drainage (32.3%), abscess and postoperative dressing changes (34.2%), and burn debridement and dressing changes (19.6%). Most ketamine sedations (96.2%) were performed at 3 locations: PAWS (43.7%), ED (35.7%), and the APC (16.8%). A detailed query of procedures for ketamine sedations in the new QI form (1181 ketamine sedations) demonstrated that in the PAWS unit, the range of procedures using ketamine sedation was similar to those listed earlier for N\textsubscript{2}O sedations. Most sedations in the ED were provided for abscess incision and drainage (38.8%), fracture reduction and casting (29.5%), and laceration repair (14.4%). In the APC, ketamine was used primarily for placement of peripherally inserted central catheters (68.2%).

Table 1 lists the rates of complications occurring during ketamine and N\textsubscript{2}O sedation. Procedural completion rates were >99%, and 0.12% of sedations were not completed due to inadequate sedation; sedation level was not achieved in 1.71% of sedations. There were no occurrences of death, need for cardiopulmonary resuscitation, unplanned intubation, or emergency anesthesia consultation. The only major complications were 4 unplanned admissions, 2 each with ketamine and N\textsubscript{2}O. With ketamine, the 2 highest rates of complications were airway repositioning (3.99%) and nausea and/or vomiting (2.98%). With N\textsubscript{2}O, the 2 highest complication rates were nausea and/or vomiting (8.50%) and airway repositioning (1.10%). Sedation level was not achieved in 1.20% of ketamine sedations and 2.49% of N\textsubscript{2}O sedations. A comparison of complications associated with each agent found that respiratory and cardiovascular events were more frequently encountered with ketamine, whereas nausea/vomiting, sedation level not achieved, and inadequate sedation resulting in procedure not completed occurred more frequently with N\textsubscript{2}O.

DISCUSSION

The sedation program at SLCH evidenced >99% successful sedations, with low rates of major complications when performing sedation using ketamine or N\textsubscript{2}O (0.04% and 0.06%, respectively). Indeed, among the major

---

**TABLE 2 Characteristics of Sedations Performed by PH**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Ketamine (n = 5339)</th>
<th>N\textsubscript{2}O (n = 3531)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age range</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–6 mo</td>
<td>103 (1.93)</td>
<td>56 (1.59)</td>
<td>.26</td>
</tr>
<tr>
<td>7–12 mo</td>
<td>392 (7.34)</td>
<td>147 (4.06)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>1–4 y</td>
<td>2573 (48.19)</td>
<td>1216 (34.44)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>5–12 y</td>
<td>1521 (28.49)</td>
<td>1110 (31.44)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>13–18 y</td>
<td>704 (13.19)</td>
<td>925 (26.20)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>&gt;18 y</td>
<td>25 (0.47)</td>
<td>59 (1.67)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Unknown age</td>
<td>21 (0.39)</td>
<td>18 (0.51)</td>
<td>.399</td>
</tr>
<tr>
<td>Hospital setting for the sedation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APC</td>
<td>897 (16.8)</td>
<td>263 (74.5)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>PAWS</td>
<td>2334 (43.72)</td>
<td>2841 (80.46)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>ED</td>
<td>1904 (35.66)</td>
<td>379 (10.73)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Radiology</td>
<td>90 (1.69)</td>
<td>11 (0.31)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Other location</td>
<td>90 (1.69)</td>
<td>30 (0.85)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Unknown location</td>
<td>24 (0.45)</td>
<td>7 (0.20)</td>
<td>.053</td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dressing change</td>
<td>2033 (38.08)</td>
<td>2195 (62.16)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Wound debridement/laceration repair</td>
<td>1118 (20.94)</td>
<td>597 (16.91)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Fracture reduction/casting</td>
<td>523 (9.80)</td>
<td>58 (1.64)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>LP/bone marrow biopsy</td>
<td>98 (1.84)</td>
<td>11 (0.31)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Radiologic imaging</td>
<td>218 (4.08)</td>
<td>5 (0.14)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Other*</td>
<td>1564 (29.29)</td>
<td>827 (23.42)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Unknown procedure</td>
<td>11 (0.21)</td>
<td>3 (0.08)</td>
<td>.27</td>
</tr>
</tbody>
</table>

Data are presented as n (%). LP, lumbar puncture.

* Includes insertion of peripherally placed central catheter, chest tube removal, joint aspiration, voiding cystourethrogram, and Botox injection.
complications, only 4 unplanned admissions (2 for each agent) were recorded in the QI database for 8870 sedations performed over a 6-year time period. The QI database did not have queries for emergency anesthesiologist consultation until September 2011, and there were none recorded since then. Previous studies reported similar low major complication rates when using propofol for sedation.12

The overall rate of respiratory events was 2.15% for ketamine sedations. This finding is comparable to the incidence of respiratory adverse events (3.9%) reported in a meta-analysis by Green et al of 8282 pediatric ketamine sedations performed in 32 EDs. Respiratory events were defined in the study by Green et al as any of the following: upper airway obstruction, apnea, oxygen desaturation to ≤90%, or laryngospasm. The QI database at SLCH did not have queries for apnea and laryngospasm until September 2011. There were no episodes of apnea, stridor, or laryngospasm recorded since September 2011 during ketamine or N₂O sedations.

For N₂O sedations, the rate of respiratory events was 0.91%. In a prospective study, Zier et al reported an incidence of 0.1% for respiratory events with N₂O sedations. However, that study used a dental nasal mask, which likely entrained room air and diluted the concentration of N₂O that was administered to patients. At SLCH, a full face mask was used for N₂O sedations, which minimized entrainment of room air. Furthermore, 99% of N₂O sedations used 70% N₂O, and 73% of the children were premedicated with a sedative or opioid, likely resulting in a deeper level of sedation compared with the study results of Zier et al.

Among the airway interventions occurring with ketamine and N₂O sedations (3.76% and 1.10%, respectively) (Table 1), the vast majority (89%) were airway repositioning. This is not considered an adverse event but rather an expected intervention necessary to relieve airway obstruction commonly noted during deep sedation of children. As expected, the rate of airway repositioning was some threefold higher with ketamine compared with N₂O, consistent with the generally deeper level of sedation obtained with ketamine.

The rate of major complications observed in the 8870 ketamine and N₂O sedations performed by PH at SLCH was 0.05%. This rate is comparable to that observed by Coullores et al in their study of the impact of provider specialty on the major complication rates. Their analysis included 133,941 procedural sedation records submitted to the Pediatric Sedation Research Consortium by 38 participating institutions. Major complications were defined as aspiration, death, cardiac arrest, unplanned hospital admissions, or emergency anesthesia consultation. Rates of major complication during sedation by pediatricians in their group were 0.12% (95% confidence interval: 0.07–0.2) in 12,113 sedations. They did not report the agents used by the pediatricians in their study.

The current study did have limitations, primarily involving the accuracy of the data. The QI database at SLCH relies on a voluntary reporting system, and some providers do not fill out forms at the end of each sedation. Providers may also not report transient desaturations or obstruction that are self-resolving and of no clinical significance. Errors in entering the information both onto the form and into the database also occur; manual entry into the database is performed by an administrative assistant rather than the sedation provider. For instance, among the 8870 sedations, 12 were recorded as occurring at hospital locations at which PH do not administer sedation. Likewise, 13 procedures were recorded for which PH at SLCH do not provide sedation. It is likely that there are errors/omissions resulting in both underestimation and overestimation of various complication rates. The QI form does not include queries regarding the state of the patient (eg, if the patient was in pain or was crying during the procedure). Thus, it is possible that the procedure was completed, but the patient might not have been adequately sedated. Finally, the study reflects the sedation experience of 1 hospitalist group at a single institution.

CONCLUSIONS
The current study documents that PH at SLCH provide safe and effective sedation using ketamine and N₂O. This finding is important because there are barriers in many institutions for PH to provide deep sedation. These barriers result in procedures (eg, incision and drainage of abscesses) being performed in the operating room by anesthesiologists, which not only raises costs significantly but also exposes patients to the unnecessary risks of general anesthesia. There have been many studies illustrating the safe use of ketamine and N₂O for procedural sedation by ED physicians and intensivists.3–7 This is the first study demonstrating the safe and effective use of ketamine and N₂O by PH. It is important to note that a comprehensive sedation training program with anesthesia oversight and close collaboration with anesthesiologists is a key element of the PH sedation program at SLCH. Use of
ketamine and N₂O by PH across the nation, with similar sedation training models in collaboration with anesthesiologists, can help provide safe and effective sedation for a variety of procedures, which will improve the overall care for patients undergoing painful procedures.

ACKNOWLEDGMENT
Statistical analysis was provided by the Washington University Institute of Clinical and Translational Sciences which is supported by grant UL1 TR000448 from the National Center for Advancing Translational Sciences of the National Institutes of Health.

REFERENCES