Prolonged Recovery and Delayed Side Effects of Sedation for Diagnostic Imaging Studies in Children

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ABSTRACT. Objective. Although sedation-related adverse events in children in the hospital setting have been extensively reported, limited data are available regarding adverse events after discharge home. Despite nationally recommended discharge criteria, in busy outpatient settings, children may be sent home into the care of their parents after a brief recovery from sedation, placing them at risk for adverse events in an unmonitored setting. Previous studies have not addressed issues such as requirement for escalation of care after discharge (ie, emergency department visits or hospitalization), or parental satisfaction with their child’s sedation experience. This study was undertaken to evaluate the recovery and delayed adverse events after discharge of children who received sedation for magnetic resonance imaging or computed tomography.

Methods. With approval from the institutional review board and written informed consent from a parent, children (<18 years old) sedated for magnetic resonance imaging or computerized tomography were studied. Sedative drugs were ordered at the discretion of the radiologist responsible for the procedure in accordance with institutional sedation guidelines and in consideration of the child’s health status. Pediatric nurses in the diagnostic areas administered the sedative agent(s) and monitored children according to preestablished institutional guidelines. Demographics, sedative(s) administered, and adverse events including hypoxemia (decrease in $\text{SpO}_2$ by >10% of baseline) and sedation events such as inadequate, failed, or excessive sedation, were documented on the institutional quality assurance tool. Children were discharged from the hospital when they met the following preestablished discharge criteria: return to baseline vital signs, level of consciousness close to baseline, and the ability to maintain a patent airway. The following day, parents were telephoned and questioned regarding the child’s alertness, side effects, and whether medical follow-up had been sought. Parents also rated their overall satisfaction with the sedation experience.

Results. Three hundred seventy six children comprised the sample. Eighty nine percent of children received chloral hydrate (CH; 64 ± 13 mg/kg), and 11% midazolam (.15 ± .13 mg/kg) as the primary sedative. There was an 8% incidence of failed sedation, and a 1.6% incidence of hypoxemia during the procedure. Three children required prolonged monitoring in the postanesthesia care unit before discharge; 1 child attributable to an allergic reaction, a second attributable to wheezing and oxygen desaturation, and the third attributable to prolonged sedation from CH and midazolam. These children were discharged home from the postanesthesia care unit without additional sequelae.

Side effects after discharge included: motor imbalance (31%), gastrointestinal effects (23%), agitation (19%), and restlessness (14%). Agitation and restlessness lasted greater than 6 hours in more than one third of children who experienced these effects. CH was more commonly associated with imbalance compared with midazolam, and restlessness and prolonged imbalance were associated with younger age. Medical advice was sought after discharge for 15 (4%) children, 3 of whom required a visit to the emergency department for excessive or prolonged sedation. Each of these children had received CH as a sole sedative in recommended doses (61–77 mg/kg). In 1 of these cases, the procedure had been aborted because of inadequate sedation in the hospital, yet the child became difficult to arouse at home.

Only 48% of children returned to baseline activity and behavior within 8 hours of the procedure; however, 89% were back to baseline status within 24 hours. Notably, 5% of all children did not return to baseline activity until the second day after the procedure. Although not statistically significant, infants <12 months old experienced delayed recovery (ie, ≥24 hours) more frequently compared with older children. Sixteen percent of parents were dissatisfied with the sedation experience. Inadequate/failed sedation and agitation after discharge contributed to parent dissatisfaction.

Conclusions. Our data demonstrate that children may experience prolonged recovery as well as a significant incidence of delayed side effects after sedation for a diagnostic procedure. Specifically, we found a high incidence of motor imbalance, agitation, gastrointestinal effects, and restlessness after discharge. Factors related to these side effects included younger age (restlessness and prolonged imbalance) and use of CH (agitation and motor imbalance). Failed sedation and agitation contributed significantly to parental dissatisfaction with the child’s sedation experience. These findings highlight the importance of careful premedication education and preparation of the patient/family regarding the potential for delayed recovery, anticipated side effects, and how to obtain medical follow-up if necessary. Future studies should focus on sedation methods that reduce sedation-related adverse events and promote the safety of sedated children. Pediatrics 2000;105(3). URL: http://www.pediatrics.org/cgi/content/full/105/3/e42; sedation, recovery, adverse effects, age group, pediatric.

**ABBREVIATIONS.** MRI, magnetic resonance imaging; CT, computed tomography; CH, chloral hydrate; ED, emergency department; ASA, American Society of Anesthesiologists.
Children frequently require sedation to facilitate outpatient diagnostic imaging procedures such as magnetic resonance imaging (MRI) or computed tomography (CT). Limitations in health care resources and personnel have made it difficult to monitor these children for prolonged periods. In many instances, the nurse in charge of monitoring recovery of 1 child is also responsible for sedating and monitoring the next child. Therefore, despite nationally recommended discharge criteria,1 children are often sent home into the care of their parents after a brief recovery.

We have previously reported 3 incidents of delayed oxygen desaturation in hospitalized children who had received chloral hydrate (CH) for brief diagnostic procedures.2 Although adverse events from sedation in the hospital setting have been extensively reported,2,4,5 limited data are available regarding adverse events after discharge home.6–8 Furthermore, no previous studies have evaluated whether sedation-related adverse events after discharge result in escalation of care such as emergency department (ED) visits or hospital admission. Lastly, parental satisfaction from sedation experiences of their children has not been addressed in previous reports. Therefore, this study was designed with the following specific aims in mind: 1) to describe the recovery after discharge of children who receive sedation for MRI or CT; 2) to determine the incidence of delayed adverse events and need for medical follow-up in this population; and 3) to evaluate parent satisfaction with their child's sedation experience.

METHODS

With approval from the institutional review board and written informed consent from a parent, all children (>18 years old) who received sedation for outpatient MRI or CT procedures from May 1998 through November 1998 were studied. Sedative drugs were ordered at the discretion of the radiologist responsible for the procedure in accordance with institutional sedation guidelines and in consideration of the child's health status. Pediatric nurses in the diagnostic areas administered the sedative agent(s) and monitored children according to preestablished institutional guidelines. Monitoring included continuous pulse oximetry in every case. Blood pressure was measured before and after the procedure and more frequently at the discretion of the caregiver. The nurse completed a sedation documentation record and quality assurance tool during the procedure. In addition to patient demographics and medication(s) administered, the quality assurance tool captured adverse events which included: respiratory (eg, hypoxemia [decrease in Spo2 by ≥10% of baseline]) and sedation events. Sedation events included: 1) inadequate sedation, defined as difficulty completing the procedure because of the child's anxiety or inability to cooperate; and 2) sedation failure, defined as an aborted procedure related to inadequate sedation or paradoxical reaction. The time to onset of sedation, procedure duration, and time from the end of the procedure to patient discharge were recorded. Children were discharged from the hospital when they met the following discharge criteria: return to baseline vital signs, level of consciousness close to baseline, and the ability to maintain a patent airway.

Before discharge, parents were given a brief survey containing questions related to their child's behavior and recovery at home. This survey was to be completed at home over the next 24 hours. Parents were telephoned the next day and the following information included on the survey was obtained: the degree of the child's wakefulness (ie, 1 = asleep, 2 = asleep but arousable, 3 = awake but drowsy, 4 = awake/alert); the presence of side effects including restlessness, hyperactivity and agitation, motor imbalance (ie, ataxia or inability to support head), respiratory difficulties, and gastrointestinal upset; time to return of baseline behavior and activity; and whether medical follow-up or advice from a health care provider was sought after discharge. Restlessness was defined as the inability to settle down. Agitation was defined as severe motor restlessness, associated with anxiety, hyperactivity, or aggressive behavior. Lastly, parents were asked to rate their overall satisfaction with the sedation experience using a 4-point scale (ie, 1 = very dissatisfied, 2 = somewhat dissatisfied, 3 = somewhat satisfied, and 4 = very satisfied).

Data were analyzed using descriptive statistics and are reported as mean ± standard deviation where applicable. χ2 analyses with Fisher's exact test were used to compare nonparametric data, such as adverse events, return to baseline activity, and parent satisfaction. Unpaired t tests were used to compare continuous data, such as age. P values of <.05 were considered statistically significant.

RESULTS

Four hundred twenty-nine families were approached to consider participation in this study. Thirty parents (7%) refused participation, and 23 (5%) of the remaining could not be reached for follow-up within the first week of discharge. Therefore, data from 376 children (3.8 ± 3.4 years old; 53% male and 47% female) who underwent MRI (n = 276) or CT (n = 100) were included in the final analysis. Seventy-two percent were classified as American Society of Anesthesiologists (ASA) physical status 1, 27% as ASA 2, and 1% as ASA 3. Oral CH (64 ± 13 mg/kg) was the most frequently administered primary sedative (336/89%), and in 34 (10%) of these cases, intravenous midazolam was added to augment the level of sedation. Midazolam (.15 ± .13 mg/kg) was used as a sole sedative in 40 children (11%). Children who received CH as a sole sedative were significantly younger than those who received midazolam in combination or as a sole agent (2.9 ± 2.5 years vs 4.5 ± 2.7 and 10 ± 3.3, respectively; P < .0004). The mean time to onset of sedation was 26 ± 16 minutes and the mean duration of the procedure was 35 ± 23 minutes.

All adverse events that occurred are presented in Tables 1 and 2. Children who experienced inadequate sedation were older than those whose sedation was adequate (4.8 ± 3.2 vs 2.7 ± 3.4 years, respectively; P = .03). Twenty-eight procedures (MRI: 25 [9.3%] vs CT: 3 [3%]; P = .05) had to be aborted because of inadequate sedation. The mean time from the procedure end to discharge home was 26 ± 15 minutes. Three children were admitted to the post anesthesia care unit for prolonged monitoring after their procedure. One of these children required di-

<table>
<thead>
<tr>
<th>TABLE 1.</th>
<th>Adverse Events in the Hospital and After Discharge [n (%)]</th>
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<tbody>
<tr>
<td></td>
<td>In Hospital</td>
</tr>
<tr>
<td>Oxygen desaturation</td>
<td>6 (1.6)</td>
</tr>
<tr>
<td>Inadequate/failed sedation</td>
<td>43 (12)</td>
</tr>
<tr>
<td>Gastrointestinal effects</td>
<td>9 (2)</td>
</tr>
<tr>
<td>Agitation</td>
<td>9 (2)</td>
</tr>
<tr>
<td>Motor imbalance</td>
<td>NA</td>
</tr>
<tr>
<td>Restlessness</td>
<td>NA</td>
</tr>
<tr>
<td>Escalation of care/parent seeks</td>
<td>3 (&lt;1)</td>
</tr>
</tbody>
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NA indicates not applicable.
* Includes 3 admissions to emergency department for excessive sedation.

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phenytoin for an allergic reaction (hives) after CH. Another child with a history of asthma experienced oxygen desaturation to 85% and required a nebulized metered treatment with albuterol and supplemental oxygen, and the last child experienced prolonged sedation after CH and midazolam administration. These children were discharged home from the post anesthesia care unit without further adverse sequelae.

Fifty three percent of children were asleep during the trip home and 31% continued to sleep for at least 6 hours after discharge. Motor imbalance was the side effect most frequently reported by parents (Table 1). In 1 case, motor imbalance led to a fall; however, this did not result in injury. In another child, imbalance persisted throughout the next day while the child was attending day care. Motor imbalance was more common in children who received CH (31%) compared with those who received midazolam alone (18%; P = .05). Furthermore, in 66% of infants <12 months old who experienced gross motor imbalance, this effect lasted greater than 6 hours (P < .05 compared with older age groups).

Agitation or aggressive behavior occurred in 19% of children and persisted for greater than 6 hours in 36% of these cases. Eighteen percent of children who received CH as a sole sedative experienced agitation compared with only 8% of those who received midazolam as a sole agent (P = not significant). Lastly, 14% of parents reported restlessness in their children, which was prolonged (> 6 hours) in 33%, and lasted for 2 days in 1 case. Restlessness was significantly related to younger age (2.9 ± 2.5 vs 5 ± 3.5 years; P < .05).

Other side effects reported by parents included nausea and vomiting (13%) and diarrhea (11%) which did not require treatment and resolved within 6 hours in the majority of children. Furthermore, 2 parents reported that their children experienced breathing difficulty at home. One of these incidents was described as a “choking” episode with labored breathing for several minutes followed by an irregular sleep pattern. The parents did not seek medical intervention and the episode resolved spontaneously. The other child was evaluated in the ED the following day for respiratory distress and was diagnosed with an upper respiratory infection. Notably, 3 children returned to the ED within a few hours of discharge because of excessive/prolonged sedation requiring observation for 2 to 4 hours. Each child had received CH as a sole sedative in recommended doses (61–77 mg/kg). Interestingly, in 1 of these cases the procedure had been aborted because of inadequate sedation in the hospital. After discharge, this child became difficult to arouse and was unable to support his head resulting in the return visit to the ED. A week later, this child’s diagnostic procedure was completed uneventfully with a general anesthetic.

Only 48% of children returned to baseline activity and behavior within 8 hours of the procedure; however, 89% were back to baseline status within 24 hours. Notably, 5% of all children did not return to baseline activity until the second day after the procedure. Although not statistically significant, infants <12 months old experienced delayed recovery (ie, ≥24 hours) more frequently compared with older children (Fig 1).

The majority of parents (84%) were somewhat to very satisfied with their child’s sedation experience, while 9% were somewhat dissatisfied and 7% were very dissatisfied. Not surprisingly, parents of children who experienced inadequate sedation or failed procedures were more likely to be dissatisfied (51% and 60%, respectively) than those with adequate or successful sedation (11% and 12%, respectively; P < .0001). In addition, parents whose children experienced agitation at home were more likely to be dissatisfied compared with parents of children without this side effect (29% vs 12%; P = .0005).

**DISCUSSION**

Our data demonstrate that children may experience prolonged recovery as well as a significant incidence of delayed side effects after sedation for a diagnostic procedure. Specifically, we found a high incidence of motor imbalance, agitation, gastrointestinal effects, and restlessness after discharge. Factors related to these side effects included younger age (restlessness and prolonged imbalance) and use of CH (agitation and motor imbalance). Failed sedation and agitation contributed significantly to parental dissatisfaction with the child’s sedation experience. These findings highlight the importance of careful presedation education and preparation of the patient/family regarding the potential for delayed recovery, anticipated side effects, and how to obtain medical follow-up if necessary.

CH remains the most commonly used sedative to facilitate diagnostic imaging studies at many institu-
and was, in fact, used in 89% of children included in the present study. Although its use resulted in a successful procedure in 95% of cases, CH was associated with a high incidence of side effects after discharge that lasted for greater than 6 hours in many children, particularly in those under 12 months old. Developmental differences in the metabolism of CH may be responsible for its prolonged hypnotic and side effects in infants.10 Mayers et al10 demonstrated a highly significant negative correlation between age and the half-life of trichloroethanol, an active metabolite believed to be primarily responsible for the hypnotic effects of CH. Furthermore, unlike adults, in neonates and infants, the parent drug itself (ie, CH) also may exert direct hypnotic effects.11

Motor imbalance was the most frequent side effect noted by parents after discharge and occurred more frequently in children who had received CH compared with those who had received midazolam. Staggering after discharge has similarly been reported in children sedated with rectal thiopental6 (4% incidence) or CH8 (18%) for diagnostic procedures. Such reports underscore the importance of careful discharge instructions regarding close observation of the children and their return to activities that require coordination.

Dysphoria, anxiety, and agitation have been associated with the use of several sedative/hypnotic agents including the phenothiazines, benzodiazepines, barbiturates, as well as ketamine.7,12–15 Slovis et al7 reported a higher incidence of hyperactivity with the use of pentobarbital (3%) compared with other sedatives. Depression of inhibitory centers in the central nervous system has been suggested as the mechanism for barbiturate induced paradoxical excitement.16 Such reactions have also been attributed to imbalance of neurotransmitters, such as serotonin, dopamine, and acetylcholine.17 Idiosyncratic reactions including disorientation, incoherence, and paranoid behavior have been described with the use of CH15; however, the precise mechanism by which this occurs remains unknown. Although not statistically significant, children in our study who had received CH experienced more than twice the incidence of agitation than those who received midazolam (20% vs 8%, respectively). Furthermore, agitation and aggressive behavior contributed significantly to parental dissatisfaction with the sedation experience. A variety of pharmacological agents have been used to treat such agitation without consistent success.12,18 Until effective treatment or alternative sedatives are available, parents should be prepared that their children may experience agitation and instructed regarding safe handling of their children to prevent injury. In children with a previous history of paradoxical reaction to CH or other sedatives, it may be prudent to select alternative agents.

In the present study, hypoxemia occurred in 1.6% of children during the procedure; however, the incidence of delayed hypoxemia is unknown because children were not monitored after discharge. Delayed hypoxemia has been reported in infants after sedation for diagnostic procedures.2 Discharge criteria have been established to avoid premature discharge of children into unmonitored settings thereby reducing the risk from sedation. However, the unpredictable onset of action and varied responses to current sedatives may place some children at risk for delayed effects. For example, 3 children in our sample who had met discharge criteria, later returned to the ED for delayed onset and/or excessive sedation. In addition to these, 14% of children in our sample were reported to be restless for several hours after discharge. It is uncertain whether the restlessness occurred because of prolonged extrapyramidal/neu-
rological effects of the sedative or was attributable to transient hypoxemic episodes. These data suggest that discharge criteria need to be reevaluated and that parents should be educated regarding the potential for delayed adverse events and need for continued observation during transportation and at home.

Appropriate monitoring of sedated children in accordance with the guidelines of the American Academy of Pediatrics and the mandates of the Joint Commission of Accreditation of Health Care Organizations has permitted early detection of adverse events and aversion of life-threatening sequelae from current sedation regimens. However, the ideal sedative drug with properties including rapid onset, consistency of effects, controllable duration of action, few side effects, minimal respiratory depression, and above all, safety remains to be identified. Although the intravenous anesthetic agent propofol possesses some of these properties, it can produce profound respiratory depression and loss of protective airway reflexes making it suitable for use only by persons trained in the administration of general anesthesia.

Therefore, future efforts toward enhancing the safety of sedated children must include development of newer sedation regimens, and scientific evaluation and comparison of such regimens to permit identification of the most effective sedation technique with the least side effects.

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