Post-sedation Events in Children Sedated for Dental Care

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Moderate oral sedation is used in pediatric dentistry for safe delivery of dental care to children. However, there is a paucity of data on the effects of pediatric dental sedations after discharge of children from the dental office. The purpose of this study was to evaluate and compare the incidence of adverse events occurring with meperidine and hydroxyzine versus midazolam alone 8 and 24 hours after sedation in pediatric dental patients. In this prospective study, a convenience sample of 46 healthy children presenting to a private pediatric dental practice for dental treatment needs was selected. A telephone survey of the parents of children sedated with either meperidine and hydroxyzine or midazolam alone was conducted 8 and 24 hours after the administration of sedation medications. Data analysis included descriptive statistics, frequency and proportion analysis, and Fisher exact test. Forty children were sedated with meperidine and hydroxyzine, and 6 who were sedated with midazolam. In both groups, 50% of the children slept in the car on the way home. Three children in the meperidine and hydroxyzine group vomited in the car. A significantly larger proportion of children in the meperidine and hydroxyzine group experienced prolonged sleep at home ($P = .015$). More children in the midazolam group exhibited irritability in the first 8 hours ($P = .07$). There were no statistical differences between the 2 groups with respect to incidence of pain, fever, vomiting, sleeping in the car, snoring, and difficulty in waking up. The lingering effects of orally administered sedation medications can lead to prolonged sleep, irritability, and vomiting in children after they have been discharged from the dental clinic. Most of these events occurred within the first 8 hours, but in some children the effects were seen up to 24 hours later.

Key Words: Sedation; Children; Adverse events.

Moderate oral sedation is utilized by pediatric dentists to provide dental care for children who are unable to cooperate during in-office dental procedures.¹ Studies have evaluated the intraoperative safety and effectiveness of sedation medications commonly used in pediatric

dentistry by investigating patient parameters such as oxygen saturation, respiratory rate, blood pressure, and patient behavior during the course of the sedation.²⁻⁷ However, little is known about the effects of sedation medications used in pediatric dentistry after the discharge of the child.⁸ The elimination half-life of sedation medications often exceeds the duration of the dental appointment, and opportunities exist for the occurrence of adverse events after patient discharge either during

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the drive home or even at home. Upon reviewing adverse outcomes in children sedated for medical procedures, authors have suggested that sedated children are prematurely discharged from hospitals.^{9–12} The risk for adverse events after discharge may be similar to the risk for adverse events during and shortly after the sedation. It is critical to know the effects of these medications beyond the time spent by the child in the dental office, so that parents can be appropriately cautioned about the expected effects and how to distinguish them from any potential emergencies that may lead to airway obstruction.

In a pilot study comparing the effects of a triple combination sedation regimen (meperidine, chloral hydrate, and hydroxyzine) with midazolam alone in pediatric dental patients, prolonged sleep and difficulty in waking up children was identified as a cause for concern.⁸ However, other regimens were not evaluated and the full spectrum of adverse events after the discharge of pediatric patients following sedation for dental care is not known.

The purpose of this prospective study was to evaluate and compare the incidence of postsedation events in pediatric dental patients who received oral administration of either meperidine and hydroxyzine or midazolam to facilitate delivery of dental care.

METHODS

This prospective study of adverse events after moderate oral sedation of children receiving dental treatment was approved by the LSUHSC International Review Board. The parents of children who were sedated for dental treatment in the dental office of a pediatric dentist, who is a diplomate of the American Board of Pediatric Dentistry, were invited to participate in a telephone survey assessing their child's disposition 8 and 24 hours after the sedation. It was a convenience sample of consecutively scheduled children over a 3-month period. Consenting parents were given printed copies of the questionnaires to take home.

The sedation regimen and the dose of medications used were determined by the treating dentist. The patient selection for sedation and monitoring were based on the guidelines set forth by the American Academy of Pediatric Dentistry.¹³ In summary, the children who were sedated needed dental treatment but exhibited acute situational anxiety. They had a health history that classified them as ASA I or ASA II. They did not have a history of snoring and tonsils occluded less than 50% of the oropharynx. Their weight was less than the 75th percentile as determined for their age and gender per the growth charts by the American Academy of Pediatrics.¹⁴

During the sedation, intraoperative monitoring was performed using a precordial stethoscope and a pulse oximeter to measure oxygen saturation and pulse rate.

The treating dentist administered 1 of 2 sedation regimens orally, namely meperidine with hydroxyzine pamoate or midazolam alone. Doses were calculated based on each child's weight. The doses of the medications used are listed in Table 1. The parents received verbal and printed discharge instructions about observing their child for rhythmicity of breathing, prolonged sleep, nausea, vomiting, allergic reactions, and fever.

The questionnaires were administered by the same investigator (not the treating dentist) 8 hours and 24 hours after the sedation medications were administered. The questionnaire items were developed by consensus of the investigators and expounded on the items investigated by Martinez and Wilson.⁸ The 8-hour postsedation survey consisted of questions regarding the child's:

- complaint of pain
- body temperature (fever was recorded if the body temperature was greater than 37.8°C [100°F]),
- vomiting,
- snoring and sleeping in the car on the way back home,
- sleeping at home and subsequent arousability,
- irritability,
- ability to eat and drink,
- need for medications at home, and
- need for medical care after the sedation appointment.

The 24-hour postsedation questionnaire had similar questions with the exception of those eliciting the incidence of sleep and snoring in the car. The parents' responses were dichotomized as "yes" or "no." The need to use medications and the need to seek medical care were the only questions that permitted open-ended responses to elicit the nature of the problem.

The data were transferred into an Excel spreadsheet. Descriptive statistics were performed to enumerate patient characteristics. Frequency and proportions were calculated to evaluate the incidence of adverse events after discharge. Fisher exact test was performed to compare the proportion of subjects experiencing adverse events in the 2 sedation regimens. The significance level was set a priori at .05.

RESULTS

The parents of 52 children consented to participate in the study, but parents of only 46 children completed the 8-hour and 24-hour surveys. There were no adverse events during the sedation appointment in the dental office. Forty children were sedated with meperidine and

Table 1. Dose of Orally Administered Medications Used for Sedation of Children for Dental Care

	Medication	Range	Maximum
Regimen 1	Meperidine	1–2 mg/kg	50 mg
	Hydroxyzine	1–2 mg/kg	25 mg
Regimen 2	Midazolam	0.5–0.7 mg/kg	15 mg
Common to regimens 1 and 2	Nitrous oxide and oxygen (inhalation)	30–40%	40%
	Lidocaine with 1 : 100,000 epinephrine	3–4 mg/kg	4 mg/kg

hydroxyzine combination, and 6 children were sedated with midazolam. The number of boys and girls was comparable with a male to female ratio of 1 : 1.1. The patient characteristics of the 2 regimens are listed in Table 2.

The parental responses to the 8- and 24-hour surveys are summarized in Table 3. Sixteen children (35%) reported pain in the first 8 hours in the meperidine and hydroxyzine group, and 1 child in the midazolam group reported pain the first 8 hours. Almost half of these 16 children ($n = 7$) in the meperidine and hydroxyzine group also reported pain in 24 hours. Two children in the meperidine and hydroxyzine group and 1 in the midazolam group had fever in the first 8 hours ($P = .04$), but none had fever in the 8- to 24-hour period. Overall, there was no statistical difference between the 2 sedation regimens in terms of the proportion of subjects experiencing pain ($P = .647$) and fever ($P = .349$). Nine children were given acetaminophen for pain and fever and 7 children were given ibuprofen by their parents. One child was given diphenhydramine (Benadryl). Three children vomited within the first 8 hours of sedation, and another child vomited in the 8- to 24-hour period. All children who vomited had been sedated with meperidine/hydroxyzine. None of the children sedated with midazolam vomited, but the difference between the groups was not significant ($P = 1.000$).

Fifty percent of the children in both drug regimens slept in the car on the way home. Of those sleeping in the car, 43.5% were also snoring. There was no statistical difference in sleeping or snoring in the car between the 2 drug regimens ($P = 1.000$). Of the 20 children in the meperidine and hydroxyzine group who slept in the car, 25.0% were difficult to wake up. None of the parents in the midazolam group reported difficulty in waking up their children. Of the children who slept in the car, 13 children in the meperidine and hydroxyzine group and 1 in the midazolam group had a car ride of

less than 30 minutes to reach home, and 5 children in the meperidine and hydroxyzine group and 2 in the midazolam group were driven in the car for more than 30 minutes.

Of the children in the meperidine and hydroxyzine group, 5.0% were irritable in the first 8 hours, whereas 32% of children in the midazolam group were irritable in the first 8 hours after sedation ($P = .07$). However, in the 8- to 24-hour period, 15.0% of the children in the meperidine and hydroxyzine group were irritable and only 1 child (16.7%) in the midazolam group was irritable.

All children in the meperidine and hydroxyzine group exhibited prolonged sleep at home in the 8- to 24-hour period. Five children (12.5%) were difficult to wake up in this time period. In the midazolam group, 66.7% of the children exhibited prolonged sleep, and 1 child was difficult to wake up. Prolonged sleep at home was significantly higher in the meperidine and hydroxyzine group ($P = .015$).

While all children had ingested liquids within the first 8 hours, 11 children (20.0%) did not eat during the first 8 hours. There was no difference based on the sedation regimens used. There were no medical emergencies that necessitated a visit to the emergency department or the children's pediatrician.

DISCUSSION

The results of this parental survey highlight the lingering effects of orally administered sedation medications in the postsedation period. There appears to be a residual effect of the sedation medications in the first 8 hours after administration of the medications, and in some cases, up to 24 hours later. Half of the sedated children in both drug regimens slept in the car during the ride back home. This has the potential for airway obstruction,

Table 2. Summary of Patient Characteristics in the 2 Sedation Regimens

	Meperidine + Hydroxyzine ($n = 40$)	Midazolam ($n = 6$)
Age range (mo)	34–113	29–116
Mean age $\pm$ SD (mo)	67.79 $\pm$ 21.71	74 $\pm$ 37.86
Weight range (kg)	13.6–35.5	12.7–21.0
Mean weight $\pm$ SD (kg)	21.3 $\pm$ 5.25	16.8 $\pm$ 3.14

Table 3. Summary of Adverse Events 8 and 24 Hours After Sedation

	8 Hours Post Sedation		24 Hours Post Sedation	
	Meperidine N (%)	Midazolam N (%)	Meperidine N (%)	Midazolam N (%)
Pain	14 (35)	1 (16.7)	7 (17.5)	1 (16.7)
Fever	2 (5)	1 (16.7)	0	0
Vomiting	3 (7.5)	0	1 (2.5)	0
Sleep in car	20 (50)	3 (50)		
Snoring in car	9 (22.5)	1 (16.7)		
Sleep at home			40 (100)	4 (66.7)
Difficulty in waking up	5 (12.5)	0	5 (12.5)	1 (16.7)
Irritable	2 (5)	2 (32)	6 (15)	1 (16.7)

since children may tilt their head down to their chest while sleeping in a car seat. It has been found that children and infants sleeping in car safety seats have a significantly lower oxygen saturation.^{15,16} If a responsible adult is not accompanying the child, the guardian driving the car will be unable to reposition the child's head and maintain a patent airway. It is, therefore, important to ask parents to bring another responsible adult to accompany their child in the car when planning sedations for pediatric patients. Similar concerns regarding the drive back home were identified by Martinez and Wilson.⁸ In their pilot study evaluating the effects of sedation with a triple combination regimen (meperidine, chloral hydrate and hydroxyzine) and midazolam alone, the authors found that prolonged sleep and difficulty in arousing the child were more commonly seen in the triple combination group.⁸ This is different from the results of our study, where 50% children in both groups (meperidine/hydroxyzine and midazolam) slept on the way home. This may be attributable to the time points at which we conducted the survey. While Martinez and Wilson conducted the survey only at 24 hours, we interviewed the parents at 8 and 24 hours. It is likely that parents were able to report the events more accurately at the 8-hour interview.

The pharmacologic effects of the medications used also influence the incidence of outcomes after discharge. The triple combination used by Martinez and Wilson incorporated a narcotic, a sedative-hypnotic, and an anti-anxiety agent, respectively.⁸ The effects, therefore, may have been more profound than just with the narcotic and the anti-anxiety agent used in our protocol. This difference highlights the potential for all sedation regimens to cause prolonged somnolence in children; this in turn is a reason for concern in discharging sedated children. The incidence of sleeping in the car did not correlate with the duration of the car ride to reach home, implying that sleeping after discharge was a pharmacologic effect.

Midazolam is considered a short-acting benzodiazepine with an elimination half-life of 1.4 to 2.4 hours.¹⁷ It is the shortest acting oral sedative agent available for use

in children.¹⁸ It is the most popularly used benzodiazepine for the sedation of children.¹⁸ Meperidine has an elimination half-life of 3–4 hours, and chloral hydrate has an elimination half-life of 8 to 10 hours.¹⁷ When 50% of children sedated with midazolam are somnolent, the effects of meperidine and chloral hydrate and their combination can only be expected to be more profound.

In our study, all children in the meperidine and hydroxyzine group exhibited prolonged sleep at home, with 5% of the children being difficult to awake. The proportion of children exhibiting prolonged sleep was significantly less in the midazolam group (66.7%), with 1 child being difficult to awake. This shows the prolonged effect of both sedation regimens several hours after the patients were discharged from the dental clinic, with greatest effects (eg, prolonged sleep and difficulty in awakening the child) seen in the meperidine and hydroxyzine group. Meperidine and hydroxyzine are both CNS depressants and therefore their synergistic effect may be the reason for prolonged sleep at home. Prolonged sleep after sedation for diagnostic imaging in children has also been reported by Malviya et al.¹¹ In their study, only 48% of sedated children returned to baseline activity at 8 hours, and 5% of the children did not return to baseline even on the second day after sedation with chloral hydrate.¹¹

Another finding of the pilot study by Martinez and Wilson⁸ was that none of their patients vomited. On the other hand, 3 of our patients vomited. All 3 of these patients were sedated with the meperidine and hydroxyzine combination. The dose range of the narcotic and hydroxyzine are similar between the 2 studies. However, in our study, the dose of hydroxyzine did not exceed 25 mg irrespective of the child's weight. It may be possible that increasing the dose of hydroxyzine can decrease the incidence of vomiting since hydroxyzine has an anti-emetic effect. The incidence of vomiting in our study is another postsedation event that should be an area of concern. In addition to being an unpleasant experience for the child and parent, it also carries the risk of aspiration in a somnolent child.

In our study, acetaminophen and ibuprofen were the medications of choice used by parents for the management of postoperative pain and fever. Therefore, it would be prudent practice to educate parents of children being sedated on the correct dose and frequency of both medications. One parent administered diphenhydramine to their child. Since diphenhydramine can cause sedation,¹⁷ it is a medication which parents of sedated children should be advised not to administer in the postsedation period. It also appears that some children do not wish to eat in the first 8 hours after sedation. Parents should be informed to anticipate this and encouraged to support their child to take liquids to maintain hydration in the first 8 hours after sedation.

Another interesting finding in our study is a statistical trend for children in the midazolam group to be irritable in the first 8 hours compared to the meperidine and hydroxyzine group ($P = .07$). This is anticipated because midazolam is known to cause paradoxical excitation in the postoperative period.¹⁷ Perhaps a larger sample size would have been able to establish this effect more definitively. It has been reported that combining hydroxyzine with midazolam can reduce the incidence of paradoxical excitation.⁶ In our study, midazolam was used alone. We also found that the number of irritable children in the meperidine and hydroxyzine group increased in the 8- to 24-hour period, while it declined in the midazolam group. The increase in the meperidine and hydroxyzine group may have occurred due to the delayed onset of excitation by hydroxyzine.¹⁷ Another explanation may be that this is an effect of normeperidine, an active metabolite of meperidine, which has a half-life of 12–16 hours and causes agitation and delirium.¹⁷

In our study, we looked at 2 time points to assess the adverse events after sedation, namely at 8 hours and at 24 hours. This enabled us to identify the adverse events, as well as the timeframe in which they are most likely to occur. Most of the postsedation events occurred within the first 8 hours post sedation, and, as anticipated, declined by 24 hours post sedation with the exception of prolonged sleep in the meperidine and hydroxyzine group.

This prospective survey of parents has several limitations. Although we gave printed copies of the surveys to the parents to make notes to facilitate accurate answers on the telephone, we were still reliant on parents' reports for accuracy. Direct observation of the children after discharge was not done by the investigators. We did not calibrate parents on assessment of prolonged sleep and irritability. These parameters were reported by parents based on their opinion of the difference between their children's behavior from an everyday nonsedated status. This study also did not

explore the association between the extent of dental procedures and sedation outcomes. It did not evaluate the association between sedation effectiveness and postsedation events. Although we had 2 regimens, the number of patients in the midazolam alone group was disproportionately low. This is because the intent of the study was to investigate the postsedation events and not dictate the treatment choices for the patients. Treatment decisions were made by the treating pediatric dentist irrespective of the study parameters. Therefore, the comparison between the 2 regimens should be made with caution.

CONCLUSIONS

- Adverse events following pediatric dental sedations can occur after discharge of the patient from the dental clinic. Most of these events are likely to occur within the first 8 hours, but may also occur up to 24 hours after sedation.
- Sleeping in the car during the ride back home was observed in half of the sedated children in this study. This has the risk of airway obstruction.
- Vomiting was seen in children sedated with meperidine and hydroxyzine but not in the children sedated with midazolam.
- Prolonged sleep at home was significantly higher in the children sedated with meperidine and hydroxyzine.

All authors declare that they do not have competing financial or nonfinancial interests in this manuscript.

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