Original Article

Efficacy and safety of rectal thiopental, intramuscular cocktail and rectal midazolam for sedation in children undergoing neuroimaging

HANDAN ALP, ZERRIN ORBAK, IBRAHIM GÜLER AND SEVIN ALTINKAYNAK Department of Pediatrics, Atatürk University Faculty of Medicine, Erzurum, Turkey

AbstractBackground: This study was designed to investigate the overall usefulness of rectal thiopental, rectal
midazolam and i.m. modified cocktail (meperidine-chlorpromazine hydrochloride-feniramin maleat) in 70
children undergoing computed tomography (CT) and magnetic resonance imaging (MRI).
Methods: The dosage of thiopental was 50 mg per kg for infants under 6 months of age, 35 mg per kg between

six and 12 months, and 25 mg per kg for older children. The maximal dose did not exceed 700 mg in this study. The dosage of midazolam was 1 mg per kg for all children. A modified cocktail was described as a formulation including 11 mg/mL of meperidine, 2.8 mg/mL of chlorpromazine and 2.8 mg/mL of pheniramine maleat. The dosage of modified cocktail was 0.1 mL per kg for all children.

Results: The mean induction time for the i.m. cocktail was significantly longer than that for rectal thiopental (P < 0.001). The mean <u>duration</u> of <u>deep</u> sedation was <u>60.79</u> ± 27.00 min with rectal thiopental and 58.74 ± 39.70 min with i.m. cocktail (P > 0.05). Although the mean duration of sleep for rectal thiopental and i.m. cocktail was similar, the mean discharge duration for i.m. cocktail was significantly longer than that for rectal thiopental (P < 0.05). Children sedated with the cocktail therapy also required a longer period of observation in the department. Significant decreases in heart rate, systolic blood pressure and oxygen saturation occurred in three groups (P < 0.001). The effect of rectal midazolam was minimal. **Conclusions**: Rectal thiopental may be the drug of choice for pediatric sedation because it has a more rapid onset and offset of action. It is also safe and effective at the dosage studied in children undergoing MRI.

Rectal midazolam also may be used in children undergoing CT imaging because of minimal side-effects.

Key words intramuscular modified cocktail, neuroimaging, pediatric sedation, rectal midazolam, rectal thiopental.

Computed tomography (CT) and magnetic resonance imaging (MRI) are now accepted as a major diagnostic advance. Total examination times of CT scan and MRI are approximately 10–15 min for unenhanced studies and 30 min for studies undertaken without contrast enhancement, respectively.¹ The whole procedures require the patient to remain immobile during the scan. As any movement results in significant artifacts and a non-diagnostic scan, sedation usually is required.² For this reason several different sedatives have been used. The ideal pediatric sedating agent should be safe, efficacious, painless to administer, rapid in onset and offset of action, and have a minimum of adverse

Correspondence: Zerrin Orbak MD, Atatürk Üniversitesi, Dis Hekimligi Fakültesi, Periodontoloji Anabilim Dali, 25240 Erzurum, Turkey. Email: zerrinobak@yahoo.com

Received 12 June 2000; revised 6 February 2002; accepted 11 April 2002.

effects. Orally administered chloral hydrate is the most frequently used first-line drug. Combined demerolphenergan-thorazine is the second most commonly used sedation preparation. The third most commonly used sedation preparations are barbiturates.^{3,4} Except for the short-acting barbiturates, these drugs have a long period of post-sedation drowsiness.^{1,4}

This study was designed to investigate the overall usefulness of rectal thiopental, rectal midazolam and i.m. modified cocktail (meperidine-chlorpromazine hydrochloridefeniramin maleat), using onset of action, duration of sedation and side-effects in 70 children undergoing CT and MRI.

Methods

A total of 70 children were evaluated before CT and MRI scans took place. Sedation was required for 42 (60%) CT and

28 (40%) magnetic resonance studies. All of the patients were less than 7 years old (mean age: 23.98 ± 17.54 months, range: 2–78 months). The mean ages of three groups were similar (P > 0.05). Thirty-eight children were males and 32 were females. Demographic description are shown in Table 1. Of the 70 children, 30 children received rectal thiopental, 20 received rectal midazolam and 20 received i.m. cocktail. Informed parental consent was obtained for all infants.

An application to the American Academy of Pediatrics for guidelines on the use of these depressant agents in children was granted.⁵ Equipment was suitable for children of all ages and sizes being treated. As sedation of pediatric patients has serious associated risks such as hypoventilation, apnea and cardiopulmonary impairment, the risks should be avoided or accurately, rapidly diagnosed and appropriately treated.

Patients were admitted to the sedation clinic 1 h prior to the scheduled imaging and evaluated by the same pediatrician. Intake of food and liquids was offered as follows: (i) infants 0–5 months, no milk or solids for 4 h before the scheduled procedure; (ii) infants 6–36 months, no milk or solids for 6 h before the scheduled procedure; and (iii) children older than 36 months, no milk or solids for 8 h before the scheduled procedure.⁵ A brief history was taken and physical examination was carried out to exclude significant infection, cardiorespiratory risk factors, hepatic function, medications and drug allergies. Before administration of the sedative medication, a baseline determination of vital signs were documented and sedatives were then given.

After administration of the sedative, continuous quantitative monitoring of oxygen saturation (Ohmeda 3700 pulse oximeter; Datex-Ohmeda Division, Instrumentarium Corp, Finland); heart rate, respiratory rate and blood pressure were recorded every 20 min during the imaging procedure, and then every 20 min until discharge.

Once the child became sleepy the child was transferred to the imaging table. Monitoring continued during CT examination. This procedure terminated during MR imaging because of the special technical problems (i.e. the powerful magnetic field, the generation of radiofrequency). The child's head position was checked frequently to ensure airway patency. The same pediatrician remained present until the patient had recovered from sedation and was responsible for the patient during the period of sedation. Failure to fall asleep within 30 min after administration of thiopental and modified cocktail were recorded. The onset and duration of deep sleep from which the infant was not arousable by light touch and imaging time were recorded. For rectal midazolam, sedation was judged to be a failure if the CT and MR imaging could not be completed or fewer than 95% of the images were considered acceptable. All episodes of desaturation or cardiac dysfunction were recorded, and any measures taken to maintain or restore baseline cardiorespiratory function were

Table 1 Demographic description of 70 Turkish children in astudy examining the effiacy and safety of rectal thiopental, i.m.cocktail and rectal midazolam for sedation in children undergoingneuroimaging

| | Thiopental | Cocktail | Midazolam |
|---------------|---------------|---|---------------|
| Male (n, (%)) | 17 (56.7) | $\begin{array}{c} 10\ (50.0)\\ 10\ (50.0)\\ 24.5\pm 18.08\end{array}$ | 11 (55.0) |
| Female | 13 (43.3) | | 9 (45.0) |
| Age (months)† | 22.67 ± 18.24 | | 23.95 ± 15.97 |

†Mean ± SD.

noted. Respiratory depression was defined as a drop in arterial oxygen saturation below 90%.

Sedation was evaluated on a five-grade scale according to Karl *et al.* as follows: grade 1 being agitated, grade 2 anxious, grade 3 calm, grade 4 drowsy and grade 5 asleep.⁶ Duration of sedation was the time from onset until the child was fully alert again. After the examination, patients were observed by their parents and pediatrician in the waiting room until their level of consciousness was such that they could be safely discharged. We used discharge criteria that were recommended by the American Academy of Pediatrics.⁵

Patient information and sedative regimen were recorded. Although children were asleep, sedation was judged to be a failure if the CT scan and MR imaging could not be completed. Sedation was judged to be a failure if the MR study could not be completed, additional sedation for completion of the study was required, or fewer than 95% of the images were considered acceptable. If the patient was not arousable at the end of the procedure, the patient was transferred to a waiting room until the patient could be aroused. Thereafter, the patient was sent home. The patient was arousable when he responded to a simple command or answered a question. Prolonged drowsiness was defined as not being fully awake 2 h after drug administration.

Thiopental is short-acting pentobarbital derivate. Thiopental when given intravenously, induces unconsciousness within 20-30 s due to its high lipid solubility and can cause a profound dose-related depression of respiration.⁴ This problem is not encountered when thiopental is given rectally. Because the drug has to be absorbed by the rectal mucosa, more distribution takes place in the body than with i.v. administration.⁴ The dosage of thiopental was 50 mg per kg for infants under 6 months of age, 35 mg per kg between six and 12 months, and 25 mg per kg for older children.¹ The maximal dose did not exceed 700 mg in this study. Thiopen-5% tal sodium (500 mg) was dissolved in 10 mL of water in a syringe to which an 8-Fr feeding catheter was attached, which was then advanced with a turning motion into the rectum to insure adequate delivery. After the appropriate dose had been administered, and the feeding catheter had

been withdrawn, the parent was asked to keep the buttocks pressed closely together for 5 min to prevent leakage and/or defecation.

Midazolam is a short-acting benzodiazepine. Midazolam is well absorbed after rectal administration.⁷ The dosage of midazolam was 1 mg per kg for all children. For this reason, a dormicum (5 mg/mL) formulation of midazolam was used. The drug was administered as a thiopental.

Original lytic cocktail (cardiac mixture) descriptions refer to a formulation including 25 mg/mL of meperidine, 6.5 mg/mL of promethazine and 6.5 mg/mL of chlorpromazine, with a recommended dose of 0.1 mL/kg of bodyweight (a maximum dose of 1.5 mL). The most satisfactory ratio was the 2:1:1 ratio. Intramuscular injection has been the most common route of administration; however, i.v. administration (without dosage modification) has become more popular.⁸ As promethazine hydrochloride are not available in Turkey, pheniramine maleat was used to replace promethazine. Meperidine is a synthetic opioid with an analgesic potency approximately 10% of that of morphine. Chlorpromazine is a phenothiazine antipsychotic agent with a relatively low potency. Pheniramine maleat has antihistaminic activity.8 A modified cocktail was described as a formulation including 11 mg/mL of meperidine, 2.8 mg/mL of chlorpromazine and 2.8 mg/mL of pheniramine maleat. No proprietary mixtures were available, so the solution was prepared locally. The dosage of the modified cocktail was 0.1 mL per kg for all children. The drug was administered i.m.

Data are presented as the mean \pm standard deviation (SD). Data were compared by Student's *t*-test and ANOVA variance analysis. Findings were also evaluated by percentage and tested for the difference between two group proportions.

Results

Sleep occurred after midazolam sedation in two (10%) out of 20 cases. Other patients who were sedated with midazolam were calm (30%) or drowsy (60%). Sleep induction time of rectal thiopental was compared with that of i.m. cocktail. The mean induction time for i.m. cocktail (22.10 ± 16.21 min, range 5–56 min) was statistically significant longer than that

for rectal thiopental $(7.31 \pm 2.77 \text{ min}, \text{ range } 4-15 \text{ min})$ (*P* < 0.001).

The mean duration of deep sedation was 60.79 ± 27.00 min with rectal thiopental and 58.74 ± 39.70 min with i.m. cocktail (*P* > 0.05).

All successfully sedated patients were asleep within 15 min in the rectal thiopental group and within 20 min in the rectal midazolam group. Sedation was continued for at least 30 min in these two groups. Sleep was achieved within 15 min of administration of i.m. cocktail in five patients (25%) and sedation was continued for at least 30 min in four patients (20%).

A complete return duration to the presedation level of consciousness is shown in Table 2. Although the mean duration of sleep for rectal thiopental and i.m. cocktail was similar, the mean discharge duration for i.m. cocktail was statistically significant longer than that for rectal thiopental (P < 0.05). Children sedated with the cocktail mixture also required a longer period of observation in the department.

In each of the three drug groups, distribution of patients according to type of sedation are shown in Table 3. The type of sedative drug significantly affected grade of sedation (P < 0.01).

In each of the three groups, the baseline values of decreases in heart rate, systolic blood pressure and temperature are shown in Table 4. Baseline vital signs did not differ in groups (P > 0.05). Minimal heart rate, systolic and diastolic blood pressure of groups were also similar.

Table 2 Mean discharge duration of sedative drugs in a studywith 70 Turkish children examining the effiacy and safety of rectalthiopental, i.m. cocktail and rectal midazolam for sedation inchildren undergoing neuroimaging

| Drug | Discharge duration (min) | Range (min) |
|------------|--------------------------|-------------|
| Thiopental | 94.04 ± 33.30 | 60–180 |
| Cocktail | 118.00 ± 41.80 | 65-210 |
| Midazolam | 65.90 ± 10.36 | 60-100 |
| P-value | T-C <i>P</i> < 0.05 | |
| | T-M <i>P</i> < 0.001 | |
| | C-M <i>P</i> < 0.001 | |

C, cocktail; M, midazolam; T, thiopental.

 Table 3
 In each three groups distribution of patients according to type of sedation in a study with 70 Turkish children examining the effiacy and safety of rectal thiopental, i.m. cocktail and rectal midazolam for sedation in children undergoing neuroimaging

| Drug | Grade I <i>n</i> (%) | Grade II n (%) | Grade III n (%) | Grade IV n (%) | Grade V n (%) |
|------------|-------------------------|-------------------|--------------------|-------------------|------------------|
| Thiopental | 0 (0) | 0 (0) | 1 (3.3) | 0 (0) | 29 (96.6)*, ** |
| Cocktail | 0 (0) | 1 (5) | 0 (0) | 2(10) | 17 (85) |
| Midazolam | 0 (0) | 0 (0) | 6 (30) | 12 (60) | 2 (10) |

*P < 0.01 for thiopental versus cocktail; **P < 0.001 for thiopental versus midazolam.

| Drug | H | eart rate (beats/min | (| Systolic | blood pressure (r | nmHg) | Diastolic blood p | ressure (mmHg) | Temperature (°C |
|-----------------|------------------|----------------------|----------------|--------------------|-------------------|------------------|-------------------|-----------------|-----------------------|
| | Baseline | Minimum | Decrease (%) | Baseline | Minimum | Decrease (%) | Baseline | Minimum | Decrease (%) |
| Thiopental | 119.8 ± 17.8 | 107.6 ± 21.0 | 10.4 ± 9.3 | 89.7 ± 14.6 | 85.7 ± 13.4 | <mark>4.9</mark> | 53.1 ± 12.3 | 49.0 ± 12.2 | $0.39 \pm 0.32^{**}$ |
| Cocktail | 116.7 ± 15.6 | 108.1 ± 16.3 | 7.4 ± 6.5 | 88.5 ± 6.6 | 83.2 ± 5.4 | 5.8* | 53.9 ± 9.2 | 48.9 ± 9.4 | $0.47 \pm 0.39^{***}$ |
| Midazolam | 122.0 ± 16.0 | 113.0 ± 18.0 | 7.3 ± 8.5 | 89.7 ± 11.3 | 88.2 ± 9.6 | 2.0 | 53.8 ± 11.9 | 50.2 ± 9.1 | 0.11 ± 0.16 |
| <i>P</i> -value | > 0.05 | > 0.05 | > 0.05 | > 0.05 | > 0.05 | < 0.05 | > 0.05 | > 0.05 | < 0.01 |
| | | | | | | | | | |

Table 4Baseline values and decreases in heart rate. systolic blood pressure and temperature of 70 Turkish children

*P < 0.05 for cocktail versus midazolam; **P < 0.05 for thiopental versus midazolam; ***P < 0.01 for cocktail versus midazolam

Statistically significant decreases in heart rates occurred in all groups (P < 0.001), however, percent of decreases did not differ among groups (Table 4). Bradycardia was observed in two patients after rectal thiopental and one patients after i.m. cocktail. Statistically significant decreases in systolic blood pressure occurred in three groups (P < 0.001).

Body temperature was decreased approximately 1°C in four patients of the thiopental group and in two patients of the cocktail group. Hypotermia (less than 36.5°C rectally) was not observed during sedation in any of the patients. Although statistically significant decreases in body temperature occurred after rectal thiopental and i.m. cocktail (P < 0.01), the effect of rectal midazolam was minimal (Table 4).

Oxygen saturation at basal, 20, 40, 60 and 80 mins and minimal oxygen saturation of children undergoing CT scan are shown in Table 5. While the means of oxygen saturation at basal, 20, and 80 mins and minimal oxygen saturation were similar in three group (P > 0.05), the means of oxygen saturation at 40 and 60 mins were lower in i.m. cocktail group than the rectal thiopental and midazolam group (P < 0.05). However, the means of oxygen saturation had significantly dropped during sedation in three groups (P < 0.001). Oxygen saturation was less than 90% in two patients who received thiopental and four patients who received i.m. cocktail in children undergoing CT scan. This was transient and it was immediately corrected by repositioning the child's neck to open the upper airway.

In the midazolam group there was no patient who had respiratory depression (Table 6). Although none of the sedated patients required resuscitation, assisted ventilation, or intubation, continuous quantitative monitoring of oxygen saturation; and heart rate, respiratory rate and blood pressure is important during sedation, especially in i.m. cocktail sedation. Therefore, patients who underwent neuroimaging should be monitored by pulse oximeter. The use of MRIcompatible pulse oximeter during the MRI study is mandatory for the patients' safety.

When patients undergoing CT and MR imaging were grouped according to age, the study group included 39 infants who were young children up to 24 months old and 31 children who were 24 months to 78 months. The success rate for children less/more than 24 months old were 92.3/70.9%, respectively (P < 0.05). It was found that the children in whom sedation failed were older (Table 7).

The success of these sedatives for MRI was different from that for CT (Table 8). A better success rate for thiopental sedation in children undergoing MRI was observed. These data may suggest to use midazolam or thiopental sedation in children undergoing CT imaging.

The complications of drugs that occurred are summarized in Table 9. Respiratory depression was detected in six children (30%) who received i.m. cocktail and in three

| Drug | Basal | 20 min | 40 min | 60 min | 80 min | Min. SaO ₂ |
|------------|----------------|------------------------|----------------|----------------|----------------|-----------------------|
| Thiopental | 95.5 ± 1.3 | <mark>94.5</mark> ±1.9 | 95.4 ± 1.7 | 95.3 ± 1.6 | 95.8 ± 1.7 | 91.8 ± 2.2 |
| Cocktail | 95.9 ± 1.5 | 93.8 ± 2.1 | 93.7 ± 2.4 | 93.4 ± 2.1 | 94.1 ± 1.8 | 92.0 ± 3.0 |
| Midazolam | 95.4 ± 1.1 | 94.1 ± 2.0 | 94.5 ± 1.6 | 95.2 ± 0.9 | - | 92.6 ± 1.9 |
| P-value | > 0.05 | > 0.05 | < 0.05 | < 0.05 | > 0.05 | > 0.05 |

 Table 5
 Oxygen saturation at basal, 20, 40, 60 and 80 min and minimal oxygen saturation in children undergoing computed tomography scan

Min. SaO₂, minimal oxygen saturation. -, minimum oxygen saturation determined during imaging.

Table 6 Distribution of minimal oxygen saturation in children undergoing computed tomography scan

| | $\begin{array}{l} \text{Min. SaO}_2 \ge 95\\ n\left(\%\right) \end{array}$ | Min. $SaO_2 = 93-94$ <i>n</i> (%) | Min. $SaO_2 = 90-92$ n(%) | Min. SaO <mark>₂ ≤90</mark> n (%) |
|------------|--|--------------------------------------|------------------------------|--------------------------------------|
| Thiopental | 2 (12.5) | 4 (25.0) | 8 (50.0) | 2 (12.5) |
| Cocktail | 3 (30.0) | 2 (20.0) | 2 (20.0) | 4 (30.0) |
| Midazolam | 2 (12.5) | 8 (50.0) | 6 (37.5) | 0 (0.0) |
| P-value | $T^*-C^{**} > 0.05$ | T-C > 0.05 | T-C < 0.001 | T-C > 0.05 |
| | $T-M^{***} > 0.05$ | T-M < 0.01 | T-M > 0.05 | T-M > 0.05 |
| | C-M > 0.05 | C-M < 0.001 | C-M < 0.01 | C-M < 0.01 |

C, cocktail; M, midazolam; Min. SaO₂, minimal oxygen saturation; T, thiopental.

 Table 7
 Age distribution and failure rates of sedatives in 70 Turkish children undergoing computed tomography and magnetic resonance imaging

| Drug | \leq 24 mont | hs (<i>n</i> , %) | > 24 mont | ths (<i>n</i> , %) | Total | (<i>n</i> , %) |
|------------|----------------|--------------------|-----------|---------------------|-----------|-----------------|
| | Success | Failure | Success | Failure | Success | Failure |
| Thiopental | 19(63.3) | 0 (0.0) | 10(33.3) | 1 (3.4) | 29 (96.6) | 1 (3.4) |
| Cocktail | 7 (35.0) | 2 (10.0) | 7 (35.0) | 4 (20.0) | 14(70.0) | 6 (30.0) |
| Midazolam | 10(50.0) | 1 (5.0) | 5 (25.0) | 4 (20.0) | 15(75.0) | 5 (25.0) |
| Total | 36(51.4) | 3 (4.3) | 22(31.4) | 9 (12.9) | 58 (82.9) | 12 (17.1) |

 Table 8
 The success rates of sedatives for magnetic resonance and computed tomography imaging

| Drug | Magnetic resonance | Magnetic resonance imaging $(n, \%)$ | | Computed tomography imaging $(n, \%)$ | |
|------------|--------------------|--------------------------------------|--------------------------|---------------------------------------|--|
| | Success | Failure | Success | Failure | |
| Thiopental | 13 (76.5) | 1 (9.1) | 16 (<mark>39.0</mark>) | 0 (0.0) | |
| Cocktail | 4 (23.5) | 6 (54.5) | 10 (24.4) | 0 (0.0) | |
| Midazolam | 0 (0.0) | 4 (36.4) | 15 (36.6) | 1 (100) | |
| Total | 17 (100) | 11 (100) | 41 (100) | 1 (100) | |
| P-value | T-C < 0.01 | | T-C < 0.05 | | |
| | T-M < 0.001 | | T-M > 0.05 | | |
| | C-M < 0.05 | | C-M > 0.05 | | |

C, cocktail; M, midazolam; T, thiopental.

children (10%) who received rectal thiopental. This complication was transient in all. Bradycardia occurred in one patient (5%) after i.m. cocktail and two patients (6.6%) after rectal thiopental. Prolonged sedation was observed in four children who received i.m. cocktail (10%) and rectal thiopental (6.6%); and they were arousable to physical stimulation and/or verbal command. No child required hospitalization because of any complication of these sedatives.

 Table 9
 Complications of sedatives used in a study examining the effiacy and safety of rectal thiopental, i.m. cocktail and rectal midazolam for sedation in children undergoing neuroimaging

| Side-effect | $\frac{\text{Thiopental}}{n (\%)}$ | Cocktail n (%) | Midazolam n (%) |
|--------------------|-------------------------------------|-------------------|--------------------|
| Bradycardia | 2 (6.6) | 1 (5.0) | 0 (0.0) |
| Desaturation | 3 (10.0) | 6 (30) | 0 (0.0) |
| Prolonged sedation | 2 (6.6) | 2 (10.0) | 0 (0.0) |
| Disquiet | 0 (0.0) | 4 (20.0) | 0 (0.0) |
| Hiccup | 1 (3.3) | 0 (0.0) | 1 (5.0) |
| Defecation | 2 (6.6) | 0 (0.0) | 0 (0.0) |
| Total | 10 (33.3) | 13 (65.0) | 1 (5.0) |

Discussion

Sedation is essential to obtaining quality MR and CT images in children. The ideal drug would allow optimal imaging with minimal side-effects. An ideal agent for pediatric sedation has yet to become available. The assessment of clarity of the scans provided a better, more objective comparison of the i.m. cocktail, rectal thiopental and midazolam.

O'Brien et al. observed that the time from medication administration to suturing was 29 ± 12 min in the rectal thiopental group compared with 54 ± 33 min in the i.m. meperidine-promethazine-chlorpromazine group.9 Burckart et al. found that the onset of sedation averaged 8 min (range 3-15 min) for thiopental and onset of sedation with the cocktail used (meperidine, promethazine, chlorpromazine) averaged 18 min (range 5-40 min).¹⁰ In the present study the mean induction time for rectal thiopental was statistically significant shorter than that for the i.m. cocktail. All successfully sedated patients were asleep within 15 min and sedation was continued for at least 30 min in the rectal thiopental group. The rapid onset of action of rectal thiopental offers an advantage over the use of the i.m. cocktail. Thiopental can be given immediately prior to the scan. Burckart et al. found that the mean duration of sedation with the cocktail and rectal thiopental were 7 h (range 2–14 h) and 2.75 h (range 1–5 h) for a 25-mg/kg dose, 3.2 h for a 35-mg/kg dose, and 4.8 h for a 45-mg/kg dose.10 In another study it was observed that patients in the rectal thiopental group recovered more quickly and were discharged approximately 11/2 h earlier than those in the i.m. meperidine-promethazine-chlorpromazine group.9 Our results were similar to these results.

Latson *et al.* observed that the maximal decrease in oxygen saturation was less than 5% in 14 out of 15 infants where drugs were administered intranasally as nose drops.¹¹ Spear *et al.* found rectally administered midazolam (4.5 mg/kg) did not reliably produce unconsciousness (only one of 41 patients was asleep); and there were no statistically significant changes in arterial blood pressure, heart rate, oxyhemoglobin saturation (oxygen saturation (SaO₂) did not

decrease to less than 96%).¹² In a study of 225 children undergoing CT, Strain *et al.* found that 17 episodes (7.5%) of transient oxygen desaturation to 80% of baseline or less occurred after sedation.¹³ In a study by Glasier *et al.*, 11% of patients had desaturation and they were treated with oxygen and head positioning.¹⁴

Although none of the sedated patients required resuscitation, assisted ventilation, or intubation, the means of oxygen saturation were significantly dropped during sedation in three groups (P < 0.001) in our study. O'Brien *et al.* observed that at 15 and 30 min after administration, rectal thiopentaltreated patients were more deeply sedated than those receiving i.m. meperidine-promethazine-chlorpromazine, as evidenced by significantly lower Glasgow Coma Scores.9 In the present study in i.m. cocktail and rectal midazolam groups grade 5 sedation occurred in 85 and 10% patients, respectively. However, grade 5 sedation were found in 96.6% patients in rectal thiopental group. Deep sedation of pediatric patients has serious associated risks such as hypoventilation, apnea, airway obstruction and cardiopulmonary impairment.⁵ For this reason continuous quantitative monitoring of oxygen saturation (e.g. pulse oximetry), heart rate, respiratory rate and blood pressure should be monitored and recorded in a time-based record.

The higher failure rate in children more than 24 months old occurred. Greenberg *et al.* found the failure rate increased steadily for children more than 48 months old, and in infants who were older than 48 months was 81%.¹⁵ This condition may be concerned to motion artifact.

Burckart *et al.* and O'Brien *et al.* found that 14 and 36% patients in the i.m. cocktail group, and 3 and 20% patients in thiopental group were not sedated, respectively.^{9,10} Glasier *et al.* determined that rectal thiopentalsodium was a safe and effective drug for pediatric sedation.¹⁴ In the study by Glasier examinations were successfully completed in 96% of 325 patients and the average time from drug administration to sedation was 12.2 min. In another study this ratio was 95.2% for rectal thiopental.⁴

Cook *et al.* reported two deaths secondary to complications of combined demerol-phenergan-thorazine sedation in children with congenital heart disease undergoing cardiac catheterization.² In the study by O'Brien *et al.*, vital signs remained stable for all patients and no adverse reactions occurred.⁹ Burckart *et al.* observed that side-effects were minimal; two patients in the cocktail group experienced vomiting and four patients in the thiopental group developed gastrointestinal side-effects (two with vomiting, one with abdominal cramping, one with urinary and fecal incontinence).¹⁰ In our study serious complications were not observed for each of the three sedatives. Glasier *et al.* carried out 24-h telephone follow-up to assess delayed side-effects.¹⁴ They found a 34% incidence of minor rectal irritation and diarrhea, sleepiness, nausea and vomiting. Burckart *et al.* found that the CT scans following rectal thiopental sedation were diagnostic in all of the cases, whereas only 86% of the CT scans with the cocktail sedation were diagnostic (P < 0.05).¹⁰ In our study a better success rate was observed for thiopental sedation in children undergoing MRI; and midazolam was superior to thiopental for CT. It was suggested that the longer time required for MRI compared with that required for CT is also an important factor.

Although it was seen that midazolam was superior to thiopental for CT, rectal thiopental may be used for pediatric sedation. It has a more rapid onset and offset of action and is safe and effective at the dosage studied in children undergoing neuroimaging, especially MRI. The rectal use of drug is an advantage. As oral agents tend to have slow, variable onset and depth of sedation, these factors may cause nausea; parenterally administered agents are painful, required skilled personnel, and may cause oversedation.

References

- Manuli MA, Davies L. Rectal methohexital for sedation of children during imaging procedures. *Am. J. Roentgenol.* 1993; 160: 577–80.
- 2 Cook BA, Bass JW, Nomizu S, Alexender ME. Sedation of children for technical procedures: Current standard of practice. *Clin. Pediatr.* 1992; **31**: 137–42.
- 3 Keeter S, Benator BM, Weinbeng SM, Hartenberg MA. Sedation in pediatric CT: national survey of current practice. *Radiology* 1990; **175**: 745–52.
- 4 Beekman RP, Hoorntje TM, Beek FJA, Kuijten RH. Sedation for children undergoing magnetic resonance imaging: efficacy and safety of rectal thiopental. *Eur. J. Pediatr.* 1996; **155**: 820–2.

- 5 American Academy of Pediatrics Committe on Drugs. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures. *Pediatrics* 1992; **89**: 1110–15.
- 6 Karl HW, Keifer AT, Rosenberg JL, Larach MG, Ruftle JM. Comparison of the safety and efficacy of intranasal midazolam or sufentanil for preinduction of anesthesia in pediatric patients. *Anesthesiology* 1992; **76**: 209–15.
- 7 Saint-Maurice C, Meistelman C, Rey E, Esteve C, DeLauture D, Olive G. The pharmacokinetics of rectal midazolam for premedication in children. *Anesthesiology* 1986; **65**: 536–8.
- 8 American Academy of Pediatrics Committe on Drugs. Reappraisal of lytic cocktail/demerol, phenergan, and thorazine (DPT) for the sedation of children. *Pediatrics* 1995; **95**: 598–602.
- 9 O'Brien JF, Falk JL, Carey BE, Malone LC. Rectal thiopental compared with intramuscular meperidine, promethazine, and chlorpromazine for pediatric sedation. *Ann. Emerg. Med.* 1991; 20: 644–7.
- 10 Burckart GJ, White TJ III, Siegle RL, Jabbour JT, Ramey DR. Rectal thiopental versus an intramuscular cocktail for sedating children before computerized tomography. *Am. J. Hosp. Pharm.* 1980; **37**: 222–4.
- 11 Latson LA, Cheatham JP, Gumbiner CH *et al.* Midazolam nose drops for outpatient echocardiography sedation in infants. *Am. Heart J.* 1991; **121**: 209–10.
- 12 Spear RM, Yaster M, Berkowitz ID *et al.* Preinduction of anesthesia in children with rectally administered midazolam. *Anesthesiology* 1991; 74: 670–4.
- 13 Strain JD, Campbell JB, Hervey LA, Foley LC. IV nembutal: safe sedation of children undergoing CT. Am. J. Roentgenol. 1996; 128: 573–6.
- 14 Glasier CM, Stark JE, Brown R, James CA, Allison JW. Rectal thiopental sodium for sedation of pediatric patients undergoing MR and other imaging studies. *Am. J. Neuroradiol.* 1995; 16: 111–14.
- 15 Greenberg SB, Faerber EN, Aspinall CL, Adams RC. Highdose chloral hydrate sedation for children undergoing MR imaging: safety and efficacy in relation to age. Am. J. Roentgenol. 1993; 161: 639–41.