Original Article

Efficacy and safety of intravenous thiopental for sedation during magnetic resonance imaging in pediatric patients: A retrospective analysis

ABSTRACT

Introduction: Although the administration of rectal thiopental for sedation during magnetic resonance imaging (MRI) has been well described, there are limited data regarding its intravenous (IV) use in this clinical scenario. The aim of this study was to investigate the efficiency of IV thiopental for sedation during MRI in the pediatric population.

Methods: A retrospective review was conducted over a 12-month period of pediatric patients who received IV thiopental for sedation during MRI. Data collected included the procedure length, the induction dose, the time to sedation, recovery time, total sedation time, and adverse events. The parents were telephoned and questioned regarding any adverse effect after discharge and their satisfaction (yes = satisfied; no = not satisfied) regarding the sedation process.

Results: A total of 300 (American Society of Anesthesiology I–II status) pediatric patients received IV thiopental for sedation during MRI. The average age of the patients was 4.7 ± 3 years. Thiopental was administered as an initial IV bolus dose of 3 mg/kg, followed by additional bolus doses of thiopental (1 mg/kg) as needed to achieve a Ramsay sedation score of 4. The average procedure length was 20.7 ± 11.9 min. The average total dose of thiopental during the procedure was 5.6 ± 0.9 mg/kg. Patients recovered in an average time of 11 ± 5.6 min after a total sedation time of 31.7 ± 14.2 min. None of the patients had oxygen desaturation, adverse effects before or after discharge, and no patient required unplanned hospital admission. All parents were satisfied with the sedation process.

Conclusion: IV thiopental is an effective, safe, and inexpensive medication for the sedation of children undergoing MRI.

Key words: Magnetic resonance imaging; pediatric anesthesiology; sedation; thiopental

Introduction

With its narrow confines and noisy environment, magnetic resonance imaging (MRI) generally necessitates sedation or general anesthesia for children. Sedation is meant not only to control anxiety but also to maintain immobility and ensure optimal image acquisition.[1,2] In addition to controlling movement, the medication used for sedation must ensure patient safety and allow for rapid recovery and hospital discharge.[1] Given limited access to the sedated child, agents that provide sedation and yet maintain hemodynamic and respiratory stability are preferable.[3]

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Among the variety of medications that have been used for sedation, the barbiturates have been used safely in various clinical scenarios for many years.[4,5] With the advent of newer agents such as propofol and dexmedetomidine, the use of barbiturates such as thiopental has decreased. However, it remains a core medication on the World Health Organization's essential drug list.[6]

For sedation during radiologic procedures, thiopental is generally administered through the rectal route.[7-13] Although the data concerning rectal thiopental demonstrate its efficacy, onset and recovery times may be somewhat prolonged with limited ability to titrate the dose to achieve the desired effect. Although intravenous (IV) thiopental has been commonly used in the operating room for the induction of anesthesia, there is limited knowledge regarding its IV administration for procedural sedation while maintaining spontaneous ventilation.[14,15] The current study provides data regarding dosing requirements, efficacy, and safety of IV thiopental for sedation during MRI in pediatric-aged patients.

Methods

Ethical approval for this study (Ethical Committee No. KAEK 2016/54) was provided by the Clinical Research Ethical Committee of Ondokuz Mayis University, Samsun, Turkey. Verbal consent was obtained from the parents. This retrospective study included pediatric patients who received IV thiopental for sedation during MRI over a 12-month period. We excluded patients who had received rectal thiopental or other anesthetic agents, those who had incomplete anesthesia records, and those who had premedication with any other sedative medication before the procedure. Data collected from the patients' records included age, gender, weight, procedure length, time in minutes from the initial administration of the sedative to a Ramsay sedation score of 4 (time to sedation), total thiopental dose, time elapsed from the end of the procedure to meeting the discharge criteria (recovery time), time from adequate sedation (Ramsay sedation score of 4) to meeting the discharge criteria (total sedation time), and adverse effects. The parents were telephoned the day following the procedure and questioned regarding adverse effects (nausea/vomiting, drowsiness, confusion, dizziness, headache, or any unanticipated hospital admission) after discharge and their satisfaction (yes/no) concerning the sedation process.

Procedural technique

On the day of the procedure, the patients were held nil *per os* for 4–6 h before MRI. A peripheral IV cannula was placed in the awake state. Thiopental was administered as an initial bolus dose of 3 mg/kg over 30–60 s, followed by incremental doses of 1 mg/kg at 2 min intervals to achieve the desired level of sedation which was a Ramsay sedation score of 4 (deeply sedated, responds to a nonpainful stimulus).[16] All patients breathed spontaneously without an artificial airway. The patients were monitored with pulse oximetry, capnography from a nasal cannula, and continuous electrocardiogram (heart rate). Respiratory rate, peripheral oxygen saturation, end-tidal carbon dioxide (CO_2), and heart rate were recorded at 5-min intervals throughout sedation process.

Statistical analysis

Statistical analyses were performed with SPSS 18.0 (IBM, Armonk, New York, USA) for Windows. Data are presented as the mean ± standard deviation, median (minimum–maximum), and frequency (%). The Shapiro–Wilk test was used to analyze normal distribution assumptions of the quantitative outcomes. Data were analyzed by Mann–Whitney U-test for nonnormal data. To compare two dependent groups, we used the Wilcoxon-signed ranks test for nonnormal data. A $P < 0.05$ was considered statistically significant.

Results

Over a 12-month period, 300 patients (128 girls and 172 boys) received IV thiopental for sedation for MRI. Sedation was effective in all patients and allowed for completion of the MRI. All of the patients breathed spontaneously through without an artificial airway. There was no apnea or respiratory problems that required airway/ventilation interventions throughout any of the procedures. The most common procedure was a cranial MRI. The distribution of procedures is listed in Table 1. The demographics of the study group are listed in Table 2. The average age of the patients was 4.7 ± 3 years, and the average weight was 17.6 ± 8.2 kg. A total of 152 patients (50.6%) were American Society of Anesthesiology (ASA) I status and 148 patients (49.4%) were ASA II status. The average length of the procedures was 20.7 ± 11.9 min.

The median dose of thiopental for the induction of sedation was 5.0 mg/kg. The average total dose of thiopental during the procedure was 5.6 ± 0.9 mg/kg. When

Table 1: Type of magnetic resonance imaging procedures

Type	*n* (%)
Cranial	194 (64.7)
Abdominal	53 (17.7)
Lumbar	33 (11)
Spinal	16 (5.3)
Cardiac	3 (1)
Thoracic	1 (0.3)

Table 2: Demographic and sedation data of the patients (*n*=300)

	n (%)	Mean±SD	Median (minimum-maximum)
Gender			
Male	172 (57.3)		
Female	128 (42.7)		
ASA			
I	152 (50.6)		
II	148 (49.4)		
Age (years)		4.7±3.0	4.5 (0.1-17)
Weight (kg)		17.6±8.2	16 (2-60)
Procedure length (min)		20.7±11.9	18 (10-95)
Total dose (mg/kg), (min)*		5.6±0.9	5.2 (3.0-10)
0-15	150 (50)	5.1±0.4	5 (3.0-6.6)$^{+}$
16-30	118 (39)	5.6±0.7	5.6 (3.8-7.5)
31-45	23 (7.6)	6.8±0.9	6.6 (4.8-8.5)
≥46	9 (3)	8.8±0.7	8.7 (7.8-10)
Time to sedation[a] (s)		29.5±39	15 (7.0-240)
Time to recovery[b] (min)		11±5.6	10 (0-40)
Total sedation time[c] (min)		31.7±14.2	30 (11-105)
Respiratory rate (breaths/min)**		21.9±4.4	22 (17-35)
End-tidal CO_2 (mmHg)**		31.2±3.2	31 (20-42)
Oxygen saturation (%)**		98.8±0.5	99 (97-100)

*Total cumulative dose of thiopental during the procedure. **Average values from vital signs obtained at 5 min intervals. $^{+}P<0.001$ when comparing various 15 min epochs. aTime in min from initial administration of the thiopental to a Ramsay sedation score of 4. [b]Time elapsed from the end of the procedure to meeting the discharge criteria. [c]Time from adequate sedation (Ramsay sedation score of 4) to meeting the discharge criteria. ASA: American Society of Anesthesiologists; SD: Standard deviation

comparing the thiopental dose for the procedures lasting 15 min, 16–30 min, 31–45 min, and longer than 45 min, there was a significant increase in the thiopental dose (median, range) as the time increased (5 mg/kg [3.0–6.6], 5.6 mg/kg [3.8–7.5], 6.6 mg/kg [4.8–8.5], and 8.7 mg/kg [7.8–10] mg/kg, respectively, for the four time epochs, $P < 0.001$). Heart rate at the beginning of the sedation, at the 5th min, and at the 10th min was 101 ± 12.5, 100 ± 12.4, 100 ± 12.2 beats/min, respectively [Table 2].

The recovery time was 11 ± 5.6 min with a total sedation time of 31.7 ± 14.2 min. None of the patients had oxygen desaturation (oxygen saturation <90%), adverse effects, or unanticipated hospital admissions, and all of the parents were satisfied with the sedation process. The demographic characteristics as well as sedation and recovery times are presented in Table 2.

Discussion

The current retrospective study evaluated the efficacy and safety of IV thiopental for procedural sedation during MRI in the pediatric-aged patient. Results of the present study demonstrate that IV thiopental provided effective and safe sedation in children undergoing MRIs. The use of thiopental for procedural sedation was first reported in 1979 reporting that it produced sedation as effective as the "cardiac cocktail" which included a combination of intramuscular (IM) meperidine (Demerol), promethazine, and chlorpromazine (Thorazine) otherwise known as the DPT.[17] They reported easier administration, more rapid onset, and shorter duration of sedation. Although the authors noted no complications, they suggested careful observation for respiratory depression.[17] The same authors provided additional data in a prospective randomized trial in 72 pediatric patients undergoing computed tomography (CT) imaging.[18] The patients were randomly assigned to receive either the IM cocktail (2.0 mg/kg of meperidine, 1.0 mg/kg of both chlorpromazine and promethazine) or 25–45 mg/kg of rectal thiopental. Sedation was not achieved in 3% of the thiopental group or in 14% of the IM cocktail group. Additional sedatives were required by 8 patients in the thiopental group and by 5 patients in the cocktail group. The mean time for onset of sedation was 8 min with thiopental and 18 min with the cocktail. The mean duration of sedation was 7 h for the cocktail group and 2.75 h for the rectal thiopental group. All scans were acceptable in the rectal thiopental group, but 14% of those in the IM cocktail were not.

Glasier *et al*. outlined their experience with the use of rectal thiopental for sedation during either CT or myocardial infarct imaging in a cohort of 462 children.[7] The dosing scheme included an initial dose of 25 mg/kg followed by a second dose of 15 mg/kg if the child was awake 20 min later. The average time to sedation was 12.2 min with a recovery time of 71.1 min. Oxygen desaturation occurred in 11% of the patients and was easily treated with the administration of supplemental oxygen and varying the head position. Additional adverse effects included rectal irritation (34%), sleepiness, nausea/vomiting, and ataxia.

However, others have noted no respiratory depression or oxygen desaturation even in patients with congenital heart disease.[8] Beekman *et al*. noted that they chose the rectal route of administration because thiopental can cause dose-related respiratory depression when administered IV. The time to sedation was 30 min and the recovery time was approximately 90 min.[8] Alp *et al*. also evaluated the safety and efficiency of rectal thiopental in pediatric sedation for CT and MRI, again choosing the rectal route given the previously mentioned concerns of respiratory depression with IV administration.[10] They noted oxygen desaturation in 10% of the patients. This was immediately corrected by

repositioning the patients' head and neck. While the time to sedation was within 15 min in their study, there is no record of the discharge times. Others investigated a low dose rectal-thiopental regimen, using 15–25 mg/kg in a cohort of 90 children requiring sedation for CT imaging.[19] Oxygen desaturation occurred in 1 patient, vomiting in 2 patients, and fecal soiling in 14 patients.

These reports all demonstrate the potential efficacy and safety of rectal thiopental for sedation during radiologic imaging. However, the importance of strict monitoring of respiratory status with pulse oximetry and end-tidal CO_2 monitoring is demonstrated by an incidence of oxygen desaturation in up to 10% of the patients. Despite its efficacy, the recovery time may be prolonged up to 2.5–3 h in some reports. Although generally effective, the absorption and pharmacokinetics of rectal medications may be erratic, affected by the level of placement in the rectal vault given the differential venous drainage of the high and low rectal veins and the effects of first-pass hepatic metabolism.[20,21] In addition, there are barriers (patient, cultural, and traditional) concerning the use of the rectal route, especially for patients older than 6 years of age.[22] There are also different sociocultural norms, attitudes, and preferences between various countries. While it is favored in certain countries, it is unthinkable to others. The acceptability of rectal drug administrations among older children is generally poor, with the IV route being preferable to many older patients.[20]

To date, there remains a paucity of reports regarding the use of IV thiopental for sedation during MRI. IV thiopental in doses similar to what we used in the current study (initial 3 mg/kg bolus dose with rescue doses of 1 mg/kg) compared favorably in efficacy to the sedative effects of a midazolam-ketamine combination in children undergoing MRI.[14] The authors found thiopental to be safe and effective with shorter total sedation and recovery times than the midazolam-ketamine combination. They further recommended thiopental as a safe alternative to a midazolam-ketamine combination for procedural sedation during MRI in children.[14]

In a prospective trial, a combination of propofol and ketamine was compared with thiopental and ketamine in 50 children, ranging in age from 3 to 5 years during MRI.[15] All of the children were premedicated with IV glycopyrrolate (0.01 mg/kg) and midazolam (0.05 mg/kg). Ketamine (1 mg/kg) was administered just before moving to the MR scanner. After positioning, either propofol (PK group) or thiopental (TK group) was administered at a dose of 1 mg/kg. The need to repeat the dose of medication (propofol or thiopental) was higher in the PK group compared to TK group (40% vs. 8%; *P* 0.0081). The incidence of oxygen desaturation was comparable whereas recovery time was significantly shorter for the PK group.

In recent years, there has been a shift to the use of newer medications such as propofol or dexmedetomidine for sedation during MRI in children. In comparative studies, onset and recovery times are generally slower with dexmedetomidine although its effects on airway function and respiratory parameters are less.[3,23] However, others have suggested that the failure rate may be unacceptably high when dexmedetomidine is used as the sole agent.[24] Although its efficacy may be increased by the use of higher dosing regimens, the potential for adverse effects may also increase.[23,24] An additional concern with dexmedetomidine is the cost which is generally significantly higher than propofol or thiopental.

Given the wide spectrum of patients presenting for MR imaging, it is likely that several alternative medications may be useful to provide effective sedation in this unique clinical setting. In our practice, we have found IV thiopental to be effective and safe with a rapid induction time, brief recovery time, and lack of adverse effects. However, given the potential of all sedative medication to affect hemodynamic and respiratory function, appropriate presedation evaluation and monitoring are required for all patients.[25] One limitation of our study is its retrospective nature, and hence, adverse effects may have been missed or not recorded. We do not have real-time parental feedback, but rather information based on a phone call. Furthermore, IV thiopental is not available in some countries. In addition, we do not have blood pressure data as we did not measure blood pressure during the procedure based on our usual clinical practice. We believe that the intermittent inflation of the blood pressure cuff may disturb lightly sedated patients, which may cause the patient to move and disrupt the MRI procedure. Such a practice is not recommended in patients with comorbid cardiovascular diseases. All of the patients in our current cohort were ASA status I or II. As with propofol, the barbiturates, especially in bolus dosing, can have dose-related cardiovascular effects. We these caveats in mind, we believe that IV thiopental provides effective sedation during MRI. It is a cost-effective alternative to other commonly used agents. Prospective, comparative studies with these agents may help to determine the optimal agent for procedural sedation during MRI.

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Conflicts of interest
There are no conflicts of interest.

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