SciMedCentral

International Journal of Clinical Anesthesiology

Research Article

Comparison of a Novel and Conventional Pentothal Dosing Regimens for Pediatric Sedation during Radiological Examinations

Ji Young Min, Jeong Rim Lee, Hye Mi Lee, Hyun Il Kim, and Hyo-Jin Byon*

Department of Anesthesiology and Pain Medicine, Yonsei University College of Medicine, Republic of Korea

***Corresponding author**

Hyo Jin Byon, Department of Anesthesiology and Pain Medicine, Severance Hospital, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Postal code: 03722, Republic of Korea

Submitted: 24 December 2018

Accepted: 18 January 2019

Published: 20 January 2019

ISSN: 2333-6641

Keywords

- Sedation; Thiopental; Children; Radiological examination

Abstract

Objective: An equation to calculate an induction dose of thiopental sodium for pediatric sedation during radiological examination has been proposed based on the results of retrospective regression analysis in a previous study (-8.153 + 0.799 × age [months] + 153.844 × body surface area). The purpose of the present study was to compare the dose of thiopental using this equation and a conventional dosing strategy in children undergoing radiological examinations.

Methods: A total of 94 children scheduled to undergo elective computed tomography (CT) or magnetic resonance imaging (MRI) were randomly assigned to control and experimental groups. Children in the control group received an initial dose of thiopental sodium, calculated using the equation, while those in the experimental group received an initial dose of 2 mg/kg of thiopental, followed by 1 mg/kg of thiopental sodium until Ramsay sedation score was 4–5. A rescue injection of thiopental sodium 2 mg/kg was administered when the children awakened or moved during the imaging scans.

Results: All sedations were achieved and successfully maintained during the scans in both groups. Induction and total doses of thiopental sodium in the experimental group were significantly greater than those of the control group, while the dose and number of rescue injections in the experimental group were significantly lower compared with the control group. There was no difference in the duration of sedation, CT or MRI scans, or length of stay in the post-anesthetic care unit between the two groups. There were no complications related to thiopental sodium in either group.

Conclusions: The equation for induction dose of thiopental sodium proposed in a previous study can prevent additional injection of thiopental sodium during radiological examination. However, caution is needed when using the equation because the overall dose of thiopental is greater compared with the conventional dosing strategy.

ABBREVIATIONS

BSA: Basal Surface Area; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; ASA: American Society of Anesthesiologists

INTRODUCTION

Thiopental sodium is a type of barbiturate used as a sedative drug, not only for general anesthesia, but also for procedural sedation in children [1-6]. However, pediatric sedation using thiopental is not successful in all cases. The overall success rate of procedural sedation has been reported to be 94–98% in children [7,8]. Paradoxical reactions have been observed in 1.2% of children who receive thiopental for procedural sedation, while other side effects related to thiopental sodium have been reported in 6% of children [9,10]. For success and prevention of complications in pediatric sedation, therefore, an adequate dose of sedative drug is essential [11]. If the dose of sedative drug is insufficient to achieve the desired level of sedation, the procedure is unlikely to be successful. In contrast, however, side effects, such as hypotension, hypopnea or apnea, related to sedative drugs can occur if the dose of sedative drug is too high for children [12]. Some clinical guidelines have been proposed for successful pediatric sedation [13-15]. However, the recommended dose of sedative drugs in these guidelines have a wide range, regardless of procedure type [16]. The dose of sedative drugs was determined based solely on body weight of the children, although other characteristics, such as age, height, or body surface area (BSA), can impact the effect of sedative drugs [17-19]. For these reasons, calculation of the proper dose of sedative drug for pediatric sedation has been a challenge for clinicians. In a previous study, we performed regression analysis using medical records of successful sedation in children undergoing radiological examination using computed tomography (CT) or magnetic resonance imaging (MRI) [20]. The relationship between the dose of thiopental sodium used in successful cases of pediatric sedation and characteristics of the children was defined. Based on the results of the regression analysis, an equation (-8.15 + 0.80 × age [months] + 153.84 ×

BSA) was proposed for calculation of the dose of thiopental sodium for pediatric sedation. At the time, however, a formal clinical study was not performed to evaluate the effect and safety of using the dose calculated by the equation. The aim of present study, therefore, was to compare the dose of thiopental sodium calculated using the equation proposed in the previous study with a conventionally calculated dose of thiopental sodium in children undergoing radiological examinations [21,22].

MATERIALS AND METHODS

This prospective, randomized controlled study was performed in single tertiary hospital. After obtaining approval from the Institutional Ethics Committee, informed consent was obtained from parents of the children and from the children if they were > 7 years of age. The study included children between 1 and 12 years of age, with American Society of Anesthesiologists (ASA) physical status I or II, undergoing sedation for CT or MRI with an expected duration of < 20 minutes. Patients with known severe respiratory or cardiac disease, neurological deficits, upper respiratory infection, anomaly of airway, and those who received analgesics or sedatives within the previous 24 h were excluded from this study. According to hospital policy, all children fasted for > 6 h before CT or MRI, and no premedication was administered before the scan. Before arrival to the CT or MRI room, a 24-gauge cannula was inserted in the dorsum of the child's hand, and dextrose or saline was infused at flow rate determined by the child's weight. All children were monitored using electrocardiogram, pulse oximeter, noninvasive blood pressure, and capnography on arrival to the CT or MRI room. Vital signs, including arterial blood pressure, heart rate and end-tidal CO_2, were recorded at 5 minutes intervals through the entire study period. The children were randomly assigned into either a control group or the experimental group using a computerized randomization table. In children assigned to the control group, an initial dose of thiopental sodium 2 mg/kg was injected over a period of 30 s. In children assigned to the experimental group, an initial dose of thiopental sodium was calculated using the following equation: -8.15 + 0.80 × age (months) + 153.84 × BSA. After the initial dose of thiopental sodium was administered in both groups, 1 mg/kg of thiopental sodium was followed until Ramsay sedation score was 4–5. If children awakened or moved during the CT or MRI scan, a rescue injection of thiopental sodium 2 mg/kg was administered, and the cumulative rescue dose was restricted to < 10 mg/kg. The children and sedation providers were blinded to the patient group allocation, and an independent researcher prepared and administered the initial dose of thiopental sodium. Unsuccessful sedation was defined as an interruption or failure of CT or MRI due to the child's awakening or movement during the scan. The occurrence of the most frequently reported complications of pediatric sedation using thiopental sodium, such as hypotension, bradycardia, hypoxia, apnea, and airway obstruction, were assessed during the study period. After CT or MRI scan, the children were moved to the recovery room, and were then discharged when Aldrete score was > 8 points.

STATISTICAL ANALYSIS

Sample size estimation was performed in accordance with the results of a previous study investigating pediatric sedation with thiopental sodium reporting a mean (± standard deviation [SD]) 109 ± 35 minutes of recovery time [4]. A sample size of 47 in each group was calculated to detect a 20% difference in recovery time between the two groups, with an alpha of 5% (confidence interval, 95%), a power of 80%, and an anticipated dropout rate of 10%. All data are expressed as mean (SD), or number (%), or median (interquartile range [IQR]). Data between the groups were compared using Pearson's chi-squared, Fisher's exact, independent t, or Mann-Whitney U tests, as appropriate. Statistical significance was defined at $P < 0.05$.

RESULTS AND DISCUSSION

Results

A total of 94 children undergoing radiological examination were enrolled in this study. Sedations in all children were achieved and successfully maintained during the CT or MRI scans. There was no significant difference in the characteristics of the children or type of radiological examination between the two groups (Table 1). CT/MRI scans were performed in 4/43 and 3/44 children in the control and experimental groups, respectively. The median age of the children was 52 months in the experimental group and 39 months in the control group; the difference, however, was not statistically significant. Preexisting disease necessitating CT or MRI scans were not different between the groups, although CT or MRI was performed most frequently for neurological diseases (Table 2). The induction dose of thiopental sodium, as defined by dose administered until Ramsay sedation score was 4–5, of the experimental group was significantly greater than that of the experimental group (Table 3). The rescue dose of thiopental sodium to maintain the level of sedation was significantly greater in the control group than

Table 1: Characteristics of children undergoing pediatric sedation for radiological examination.

Characteristic	Control group (n=47)	Experimental group (n=47)	*p* value
Male sex	25 (52)	22 (48)	0.68
Age, months	39 (23–55)	52 (27–60)	0.25
Weight, kg	15.1 (69–140)	16 (12.5–19.8)	0.19
Height, cm	94.5 (10–106)	100 (88.5–107)	0.20
Body surface area, m^2	0.61 (0.5–0.73)	0.68 (0.56–0.77)	0.17
Data presented as n (%) or median (interquartile range)			

Table 2: Underlying disease of children undergoing radiological examination.

Disease	Control group (n=47)	Experimental group (n=47)
Neurological disorder	17	20
Endocrine disorder	2	4
Anatomical defect	9	5
Vascular disorder	2	2
Tumor	11	12
Others	6	4
Data presented as n.		

Table 3: Outcome measures of children undergoing pediatric sedation during radiological examination.

Measure	Control group (n=47)	Experimental group (n=47)
Induction dose, mg/kg	5.1 (1.99)	7.6 (1.04)*
Additional dose, mg/kg	1.6 (2.13)	0.5 (1.59)*
Total dose, mg/kg	6.9 (2.96)	8.2 (1.83)*
Rescue injections, n	22	8*
Duration of sedation, minutes	39.3 (15.58)	43.9 (14.55)
Duration of radiological examination, minutes	25.4 (13.75)	23.8 (8.99)
Recovery time, minutes	13.2 (9.62)	17.6 (10.18)
PACU length of stay, minutes	31.1 (3.73)	33.7 (6.11)

Data presented as mean (standard deviation) unless otherwise indicated. *Statistically significant difference ($p< 0.05$).
PACU: Post Anesthesia Care Unit

in the experimental group. The total dose of thiopental sodium administered during CT or MRI scan was significantly greater in the experimental group compared with that in the control group. Duration of sedation, duration of CT or MRI scans, recovery time, and length of stay in the post anesthesia care unit were not different between two groups. The number of rescue injections of thiopental sodium was significantly higher in the control group than in the experimental group. No complications related to thiopental injection, such as hypotension, bradycardia, hypoxia, apnea or airway obstruction, occurred during the study period.

Discussion

In this study, we compared the use of a previously reported equation (i.e., -8.15 + 0.80 × age [months] + 153.84 × BSA) to calculate the dose of thiopental sodium with the conventional dosing strategy for pediatric sedation. The induction and total dose of thiopental were greater when using the equation to calculate the dose of thiopental sodium compared with the conventional dosing strategy. However, the additional injections and rescue dose of thiopental sodium was greater when using conventional dosing strategy compared with the equation. There were no complications due to thiopental sodium injection during CT or MRI scans in either group.

The proper dose of sedative drug (s) is essential to achieve sedation without complications during CT or MRI scans in children. Calculation of the dose of thiopental sodium for pediatric sedation has been a challenge for clinicians. The equation used to calculate the dose of thiopental sodium in this study was proposed in our previous study, which performed a retrospective regression analysis of medical records of pediatric sedation for CT or MRI scans. Although the equation was developed using data from medical records only when the pediatric sedation was successful and without complications, a formal clinical study was not performed to validate the equation.

In this study, the number of rescue injections and the rescue dose of thiopental sodium were greater when the conventional dosing strategy was applied compared with those when the equation was used? Thiopental sodium was administered additionally when Ramsay sedation score was not maintained at 4–5 after induction of sedation was achieved once. Considering the short duration of CT or MRI scans in this study, the need for rescue injection of thiopental sodium may mean that the initial dose of thiopental sodium was insufficient to maintain the desired level of sedation. Injection of thiopental sodium during CT or MRI scans requires the efforts of sedation providers, and interrupts the process of CT or MRI scans, which in turn can interfere with acquiring good-quality scans. Furthermore, improper provision of rescue injection (s) of thiopental sodium when the level of sedation is not maintained can threaten the safety of children.

When the equation was used, the total dose of thiopental sodium was greater compared with the conventional dosing strategy. This is because the induction dose calculated using the equation was approximately 25% greater than that in the conventional dosing strategy. This may be explained by the fact that the equation used in this study was developed using data from medical records of successful pediatric sedations without complication (s) related to thiopental sodium. If the dose of thiopental sodium is increased, the incidence of complications related to thiopental sodium may also increase; however, no complications related to thiopental sodium were recorded in this study. These findings correspond well with those of an earlier study, which reported the success of high-dose propofol and dexmedetomidine-induced pediatric sedation without an increase in complications [21,22]. The sample size in the present study may not have been sufficient to compare the incidence of complications related to thiopental sodium. A formal clinical investigation using a larger sample size should be performed to evaluate complication rates. It is, nevertheless, exceedingly difficult to prevent complications in every case of pediatric sedation. Sedation providers still need to be careful when using the equation to calculate the induction dose of thiopental sodium for pediatric sedation.

Recovery time from sedation was not different between the groups, regardless of whether the equation or the conventional strategy was used to determine the induction dose of thiopental sodium. We speculated that recovery from sedation could be delayed using the conventional dosing strategy compared with the equation because rescue injection of thiopental sodium may increase the total dose of thiopental sodium. Contrary to our expectation, however, the total dose of thiopental sodium when using the equation was greater than that calculated using the conventional dosing strategy. Nevertheless, the dose of thiopental sodium calculated using the equation did not delay recovery from sedation compared with the conventional dosing strategy.

Children in this study were included only when the duration of CT or MRI scan was expected to be < 20 minutes. This means there would have been no need to infuse sedative drugs to maintain the level of sedation for CT or MRI scan. This is because the equation used in this study was proposed only for calculating the induction dose of thiopental sodium for pediatric sedation. Thiopental sodium is not recommended as a sedative drug to infuse for pediatric sedation because of its long context-sensitive half-time. The longer thiopental sodium is infused, the longer recovery from sedation is delayed. Other sedative drugs with short context-sensitive half-time, such as propofol, are widely used for infusion in pediatric sedations. However, further research will be needed to evaluate infusion or rescue injection of thiopental sodium for CT or MRI scans exceeding 20 minutes in duration.

There were several limitations to this study. First, in control group, thiopental sodium 2 mg/kg was administered as the initial loading dose, followed by 1 mg/kg of thiopental sodium until sedation was achieved. If the dosing strategy for thiopental sodium was different, the results of the present study may have been different. Second, the age range of the children recruited for the present study (1 to 12 years) was relatively wide, and we did not have subgroups based on the age of the children. However, the aim of present study was to compare two dosing strategies of thiopental sodium, and there was no statistical difference in age between the control and experimental groups. Third, the health of the children recruited for the present study was ASA physical status I or II. Therefore, caution should be exercised when the results of the present study are applied to seriously ill children. In particular, in children with respiratory or cardiovascular disease or anatomical airway anomalies, the dose of thiopental sodium calculated using the equation may induce serious complications such as hypotension, airway obstruction, apnea, and shock.

CONCLUSION

In conclusion, when the equation proposed in the previous study was used to calculate the induction dose of thiopental sodium for pediatric sedation in the present study, the number of additional injections of thiopental sodium during radiological examination was decreased and there was no statistically significant increase of recovery time, although the total dose of thiopental sodium for sedation when using the equation is greater than that in the conventional dosing strategy. However, physicians should be aware of the possibility of complications due to the greater dose of thiopental sodium when the equation is used. Further clinical researches that focus on complications of thiopental sodium should be performed.

ACKNOWLEDGEMENTS

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI16C0793).

REFERENCES

1. Greenberg SB, Adams RC, Aspinall CL. Initial experience with intravenous pentobarbital sedation for children undergoing MRI at a tertiary care pediatric hospital: the learning curve. Pediatr Radiol. 2000; 30: 689-691.
2. Malviya S, Voepel-Lewis T, Tait AR, Reynolds PI, Gujar SK, Gebarski SS, et al. Pentobarbital vs chloral hydrate for sedation of children undergoing MRI: efficacy and recovery characteristics. Paediatr Anaesth. 2004; 14: 589-595.
3. Mason KP, Sanborn P, Zurakowski D, Karian VE, Connor L, Fontaine PJ, et al. Superiority of pentobarbital versus chloral hydrate for sedation in infants during imaging. Radiology. 2004; 230: 537-542.
4. Mason KP, Zurakowski D, Connor L, Karian VE, Fontaine PJ, Sanborn PA, et al. Infant sedation for MR imaging and CT: oral versus intravenous pentobarbital. Radiology. 2004; 233: 723-728.
5. Strain JD, Campbell JB, Harvey LA, Foley LC. IV Nembutal: safe sedation for children undergoing CT. AJR Am J Roentgenol. 1988; 151: 975-979.
6. Strain JD, Harvey LA, Foley LC, Campbell JB. Intravenously administered pentobarbital sodium for sedation in pediatric CT. Radiology. 1986; 161: 105-108.
7. Frush DP, Bisset GS 3rd, Hall SC. Pediatric sedation in radiology: the practice of safe sleep. AJR Am J Roentgenol. 1996; 167: 1381-1377.
8. Slovis TL, Parks C, Reneau D, Becker CJ, Hersch J, Carver CD, et al. Pediatric sedation: short-term effects. Pediatr Radiol. 1993; 23: 345-348.
9. Egelhoff JC, Ball WS Jr, Koch BL, Parks TD. Safety and efficacy of sedation in children using a structured sedation program. AJR Am J Roentgenol. 1997; 168: 1259-1262.
10. Karian VE, Burrows PE, Zurakowski D, Connor L, Mason KP. Sedation for pediatric radiological procedures: analysis of potential causes of sedation failure and paradoxical reactions. Pediatr Radiol. 1999; 29: 869-873.
11. Mason KP, Green SM, Piacevoli Q, International Sedation Task F. Adverse event reporting tool to standardize the reporting and tracking of adverse events during procedural sedation: a consensus document from the World SIVA International Sedation Task Force. Br J Anaesth. 2012; 108: 13-20.
12. Pitetti RD, Singh S, Pierce MC. Safe and efficacious use of procedural sedation and analgesia by nonanesthesiologists in a pediatric emergency department. Arch Pediatr Adolesc Med. 2003; 157: 1090-1096.
13. Committee on Drugs. American Academy of P. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: addendum. Pediatrics. 2002; 110: 836-838.
14. American Society of Anesthesiologists Task Force on S, Analgesia by N-A. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology. 2002; 96: 1004-1017.
15. Godwin SA, Caro DA, Wolf SJ, Jagoda AS, Charles R, Marett BE, et al. Clinical policy: procedural sedation and analgesia in the emergency department. Ann Emerg Med. 2005; 45: 177-196.
16. Hansen TG. Sedative medications outside the operating room and the pharmacology of sedatives. Curr Opin Anaesthesiol. 2015; 28: 446-452.
17. Batchelor HK, Marriott JF. Paediatric pharmacokinetics: key considerations. Br J Clin Pharmacol. 2015; 79: 395-404.
18. Johnson TN. The problems in scaling adult drug doses to children. Arch Dis Child. 2008; 93: 207-211.
19. Cella M, Knibbe C, Danhof M, Della Pasqua O. What is the right dose for children? Br J Clin Pharmacol. 2010; 70: 597-603.
20. Min JY, Lee JR, Lee HM, Kim HI, Byon HJ. Induction dose of thiopental sodium for pediatric sedation during radiologic examination. Int J Clin Anesthesiol. 2018; 6: 1095.
21. Young TP, Lim JJ, Kim TY, Thorp AW, Brown L. Pediatric procedural sedation with propofol using a higher initial bolus dose. Pediatr Emerg Care. 2014; 30: 689-693.
22. Siddappa R, Riggins J, Kariyanna S, Calkins P, Rotta AT. High-dose dexmedetomidine sedation for pediatric MRI. Paediatr Anaesth. 2011; 21: 153-158.

Cite this article

Min JY, Lee JR, Lee HM, Kim HI, Byon HJ (2019) Comparison of a Novel and Conventional Pentothal Dosing Regimens for Pediatric Sedation during Radiological Examinations. Int J Clin Anesthesiol 7(1): 1097.