

Pediatric characteristics and the dose of propofol for sedation during radiological examinations: a retrospective analysis

Ji Young Min¹, Jeong-Rim Lee³,
Yhen Seoung Kang², Jung Hwan Ho² and
Hyo Jin Byon³ 

Abstract

Objective: The present study aimed to investigate patients' characteristics that can affect the dose of propofol required to sedate children undergoing imaging.

Methods: In this retrospective, observational study, we reviewed medical records of children aged 0 to 18 years who were classified as having American Society of Anesthesiologists status I or 2 and they underwent imaging under propofol sedation between January 2011 and August 2016. Collected data included patients' demographics, propofol doses, duration of sedation, and complications. Regression analysis was performed to determine patients' characteristics that may affect the dose of propofol required to induce sedation.

Results: A total of 925 patients were included. Simple linear regression showed that the dose of propofol was correlated with age, height, weight, and body surface area. Using the results of multiple linear regression, the following formula was used to estimate the dose of propofol (mg) for sedation: $0.75 + 0.14 \times \text{age (months)} + 45.82 \times \text{body surface area (m}^2\text{)}$.

Conclusion: A child's age, height, and body surface area should be considered when deciding the induction dose of propofol. Additionally, the formula that we have proposed can be used to estimate the dose of propofol required to induce sedation in children undergoing imaging.

¹Department of Anesthesiology and Pain Medicine, Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

²Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, National Insurance Service Ilsan Hospital, Ilsan, Republic of Korea

³Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Republic of Korea

Corresponding author:

Hyo Jin Byon, Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul 03722, Republic of Korea.

Email: JINOBEN@yuhs.ac



Keywords

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Introduction

Pediatric patients often undergo radiological examinations, such as computed tomography (CT) or magnetic resonance imaging (MRI). Children must remain motionless during such examinations so that accurate imaging can be obtained. The long duration of some imaging procedures, noise of the machines, and anxiety caused by being alone in a confined space can cause difficulty for pediatric patients in remaining still. Therefore, many children need to be sedated during radiological examinations.^{1,2}

When sedating children, determining the optimal dose of sedative medications is essential.^{3,4} If the sedative dose is too low, children may wake up or move during the radiological examination, which can interrupt the procedure and impede the ability to obtain accurate imaging. Inadequately sedated children can also fall from the machine and become injured. Conversely, if the sedative dose is too high, it can lead to complications, such as hypotension, apnea, and airway obstruction. Because of anatomical and physiological differences, children are more prone to these complications of sedation than adults.^{5,6} For these reasons, physicians often struggle to determine the most appropriate sedative doses for pediatric patients.

Sedative dosing strategies in children should consider the condition of the child, the type of examination or procedure, and the predicted degree of pain. Propofol is widely used for pediatric sedation owing to its rapid onset and rapid recovery.^{7,8} However, there is no definitive guideline

regarding the dosage of propofol for children undergoing radiological examinations.^{9–11} Furthermore, the current guideline suggests a range of propofol doses for pediatric sedation based on only the child's body weight. The physician must then choose the propofol dose within the suggested range, depending on his or her experience, preference, and the medical condition of the child. Therefore, understanding which patients' characteristics can affect the sedative effect of propofol in children undergoing sedation for radiological examinations would be helpful.

The present study used regression analysis of retrospectively collected data from pediatric patients who successfully underwent sedation for radiological examinations without complications. This study aimed to identify patients' characteristics that may affect the sedative effect of propofol. We also proposed a formula, which might be used as a reference to determine the propofol dose required to induce sedation in children undergoing radiological examinations.

Materials and Methods

Study population

In this retrospective, observational study, we analyzed medical records of children aged 0 to 18 years. These children were classified as having American Society of Anesthesiologist physical status 1 or 2 without complications and underwent propofol sedation for either a CT or MRI scan at a single tertiary medical center from 1

January 2011 to 31 August 2016. Patients were excluded from the analysis if they received any sedatives other than propofol before or during the examination, if there was evidence of a respiratory infection or uncorrected heart disease, or if there was incomplete documentation regarding demographic data or propofol dosing. The study protocol was approved by the ethics committee of Severance Hospital Yonsei University (IRB no.: 4-2016-0733). Informed consent was not required because this was a retrospective study.

Pediatric sedation protocol

Oxygen saturation by pulse oximetry, an electrocardiogram, non-invasive blood pressure, and end-tidal carbon dioxide were monitored throughout the radiological examinations. Patients received an intravenous injection of 0.004 mg/kg of glycopyrrolate followed by 1.5 mg/kg of propofol.

Loss of consciousness was defined as the absence of the eye lash reflex or the ability to apply a face mask without the child resisting. The sedation level was maintained at 4 to 6 points using the Modified Ramsay Sedation Scale. If the patient remained conscious, an additional 0.5 to 1.0 mg/kg of propofol was administered every minute until loss of consciousness was achieved. For examinations lasting longer than 20 minutes, a continuous infusion of propofol was administered at a rate of 25 to 100 μ g/kg/minute. An additional dose of propofol was administered if the patient regained consciousness or moved during the examination.

Patients were transferred to the post-anesthesia recovery room after the radiological examinations. They were discharged when their hemodynamic values remained at 20% of baseline, their modified Aldrete recovery score was at least 9 points, they were fully conscious, and they could consume water without nausea or vomiting.

Data collection

Collected medical record data included demographic information (sex, age, weight, height, and body surface area [BSA]), diagnosis, type of procedure, total duration of the radiological examination, initial dose of propofol, additional doses of propofol and injection times, and total dose of propofol administered. Information on the incidence of complications, such as respiratory depression, airway obstruction, hypotension, bradycardia, and aspiration, was also collected. In this study, BSA was defined as follows: $\sqrt{\text{weight (kg)} \times \text{height (cm)}}/3600$.

Successful sedation was defined as the loss of consciousness after injection of propofol, as well as no recovery of consciousness, considerable movement, or complications during the examination. The dose of propofol required to induce sedation was defined as the total dose administered until the patient lost consciousness. Respiratory depression was defined as the occurrence of desaturation (oxygen saturation by pulse oximetry < 90%), hypercapnia (end-tidal carbon dioxide > 50 mmHg), or apnea. Hypotension and bradycardia were diagnosed on the basis of normal values of blood pressure and pulse rate for the patient's age. Children who experienced sedation-related complications were excluded from the regression analysis.

Statistical analysis

Linear regression analysis was used to determine the relationships between the patient's sex, age, weight, height, BSA and the dose of propofol required to induce sedation. The results of regression analysis were then used to determine a formula that can estimate the dose of propofol required to induce sedation in children undergoing radiological examinations. The variance inflation factor (VIF) was checked for

multiple collinearity before performing multiple linear regression. Multiple collinearity among independent variables, as indicated by a VIF value > 10 , indicated that these variables could not be analyzed simultaneously using a single model. Therefore, these variables were analyzed using different models. Each model was visually inspected for linearity, heteroscedasticity, and normality of the residuals. Residual analysis was also performed using a studentized residual to verify normal distribution and isodispersion. A probability–probability plot was used to evaluate the skewness of the distribution. All analyses were performed using SAS version 9.4 (SAS Inc., Cary, NC, USA).

Results

After reviewing the medical records, 925 cases of successful sedation were included in the regression analysis. Table 1 shows the demographic data of the included patients. The median dose of propofol required to induce sedation was 2 mg/kg (interquartile ratio, 2–2.8 mg/kg).

Simple linear regression analysis was performed to investigate the relationships between the dose of propofol required to induce sedation and sex, age, weight, height, and BSA (Table 2). There were significant associations between the dose of propofol required to induce sedation and age, weight, height, and BSA (all $p < 0.001$). Figure 1 shows scatter plots of the relationships between the dose of propofol required to induce sedation and the patients' characteristics. The scatter plots show a tendency for the slope of the propofol dose to increase with increasing age, weight, height, and BSA.

Multiple linear regression analysis was performed to determine the relationships between the dose of propofol required to induce sedation and two or more characteristics of children other than sex. The VIF of

Table 1. Characteristics of the 925 children included in present study

Characteristics	n = 925
Sex	
Boys	618 (66.8)
Girls	307 (33.2)
Median age, months	28.2 (12.6–52.8)
Median weight, kg	12 (9–16)
Median height, cm	89 (74.6–103)
Median BSA, m ²	0.6 (0.5–0.7)
ASA class	
I	120 (13.0)
II	805 (87.0)
Examination	
CT	218 (23.6)
MRI	700 (75.7)
CT + MRI	7 (0.7)
Imaging site	
Brain	476 (51.4)
Head and neck	142 (15.4)
Chest	22 (2.4)
Abdomen	72 (7.8)
Spine	182 (19.6)
Extremity	31 (3.4)

Values are median (interquartile range) or number (%). BSA, body surface area; ASA, American Society of Anesthesiologists; CT, computed tomography; MRI, magnetic resonance imaging.

Table 2. Simple linear regression analysis between demographic data and the dose of propofol required to induce sedation for children during radiological examinations

	Dose of propofol required to induce sedation	
	β (SE)	p value
Sex	0.083 (1.044)	0.937
Age (months)	0.421 (0.013)	< 0.001
Height (cm)	0.512 (0.020)	< 0.001
Weight (kg)	1.805 (0.052)	< 0.001
BSA (m ²)	63.867 (1.838)	< 0.001

SE, standard error; BSA, body surface area.

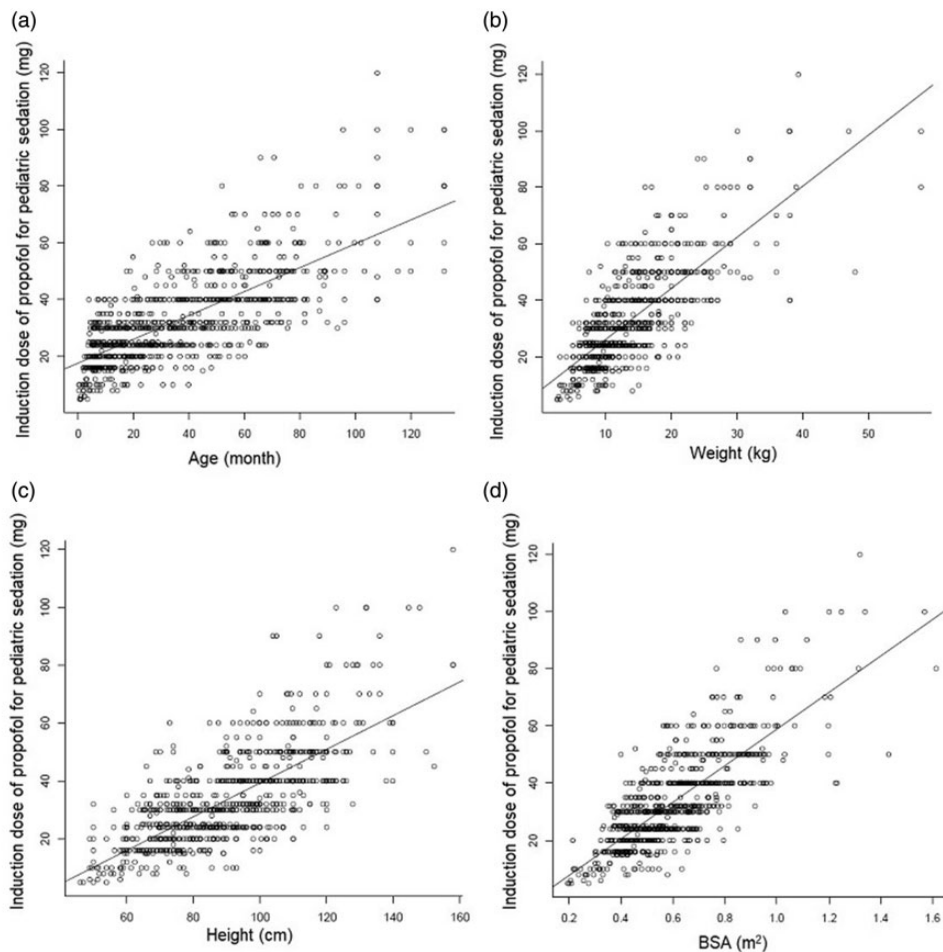


Figure 1. Simple linear regression between demographic characteristics and the dose of propofol required to induce sedation in children undergoing radiological examinations. (A) Age, (B) weight, (C) height, and (D) BSA
BSA, body surface area.

age, weight, height, and BSA was 5.7, 147.9, 43.9, and 318.8, respectively. The VIF of weight, height, and BSA showed multiple collinearity. Therefore, we were not able to simultaneously analyze these variables using the same model. Consequently, we used three models of age and weight together, age and height together, and age and BSA together (Table 3). Among the three models, the model of age and BSA had the highest adjusted R^2 value (0.612).

Therefore, this model was selected as the best formula for estimating the dose of propofol required to induce sedation in children undergoing radiological examinations. The formula for estimating the propofol induction dose (mg) is as follows: $0.75 + 0.14 \times \text{age (months)} + 45.82 \times \text{BSA (m}^2\text{)}$.

As shown in Figure 2, the data points appeared to be random with no particular tendency centering around zero.

Table 3. Regression equations describing the dose of propofol required to induce sedation taking into account age and other demographics (height, weight, and BSA)

Variables	Equation	Adjusted R ²
Age, height	$1.88 + 0.28 \times \text{age (months)} + 0.236 \times \text{height (cm)}$	0.571
Age, weight	$10.70 + 0.19 \times \text{age (months)} + 1.13 \times \text{weight (kg)}$	0.596
Age, BSA	$0.75 + 0.14 \times \text{age (months)} + 45.82 \times \text{BSA (m}^2\text{)}$	0.612

BSA, body surface area.

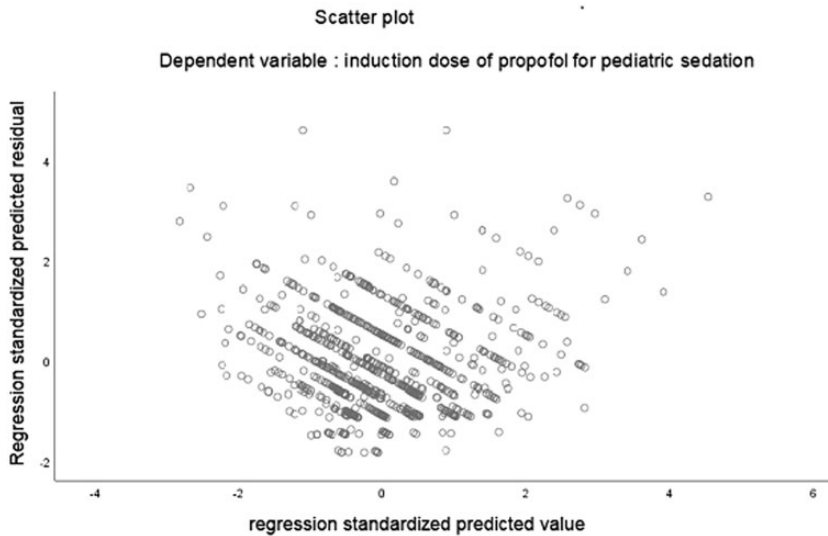


Figure 2. Residual plot between standardized and predicted values. The dependent variable was the induction dose of propofol for pediatric sedation

In addition, the probability–probability plot showed a nearly linear pattern, which indicated that normal distribution was an appropriate model for this data set (Figure 3).

Discussion

Several studies have evaluated the dose of propofol required for pediatric sedation.¹² However, these studies were performed in children who underwent various types of examinations and procedures. Unlike other types of examinations or procedures, children undergoing radiological

examinations, such as CT or MRI, do not require an analgesic effect, but remaining motionless during the examination is crucial. Therefore, in this investigation, we focused on determining the propofol dose required to induce sedation in children undergoing radiological examinations.

To determine the propofol dose required to induce sedation in children undergoing radiological examinations, we performed regression analysis of data from the medical records of children who underwent successful sedation for radiological examinations. We found that, in addition to weight, age, height, and BSA affected the dose of

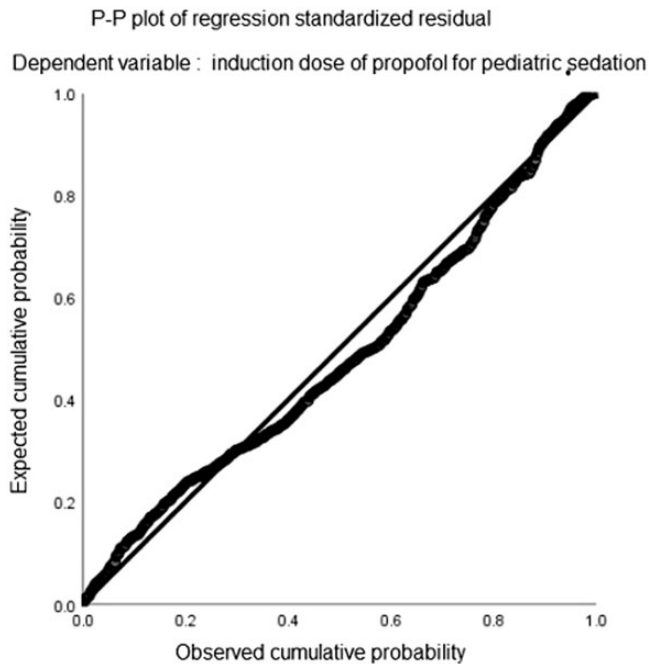


Figure 3. Probability–probability plot for the induction dose of propofol in children undergoing radiological examinations. The dependent variable was the induction dose of propofol for pediatric sedation

propofol required to induce sedation in children. Using the results of the regression analysis, we found that the following formula can be used to estimate the dose of propofol required to induce sedation in children undergoing a radiological examination: $0.75 + 0.14 \times \text{age (months)} + 45.82 \times \text{BSA (m}^2\text{)}$.

Current guidelines suggest that the dose of propofol required to induce pediatric sedation should be based only on the patient's weight.^{12,13} However, weight does not represent all aspects of a child's growth and development. The present study suggests that age and BSA should be considered together when determining the dose of propofol required to induce sedation in pediatric patients undergoing radiological examinations. The results of the present study are consistent with those of a previous study by Karalea et al.¹⁴ However, in

the present study, we reviewed more medical records of successfully sedated children than in Karalea et al.'s study¹⁴, and the children in our study only underwent radiological examinations.

Pharmacokinetic characteristics of propofol, such as volume of distribution and clearance, are affected by body composition, maturation of organ function, altered protein binding, and underlying disease. Children have a relatively larger volume of distribution and clearance than adults, and these characteristics change as the child grows.¹⁵ Therefore, unsurprisingly, age was a significant factor in the regression model in our study.

In the present study, we also found that BSA should be included in the regression formula to estimate the propofol dose required to induce sedation in children undergoing radiological examinations.

There may be several reasons that including the child's BSA in the formula shows a higher R^2 value than only including the child's weight. BSA is correlated with metabolic rate, which is proportional to drug redistribution and metabolism. Furthermore, the volume of drug distribution is closely associated with extracellular fluid volume, which is more closely correlated with BSA than weight. Therefore, BSA should be considered when deciding the dose of propofol required to sedate children for radiological examinations.¹⁶⁻¹⁹

In our study, the initial propofol dose administered was 1.5 mg/kg, which was followed by an additional 0.5 to 1.0 mg/kg every minute until loss of consciousness was achieved. Because the recorded dose of propofol might exceed the minimal dose required to induce sedation, we only included data from patients with no sedation-related complications. Therefore, the formula proposed in the present study may help physicians choose the optimal dose of propofol required to sedate children for radiological procedures.

Importantly, the present study only included children who underwent imaging studies, such as CT or MRI scans. There is generally no pain during such imaging studies, but children should remain motionless so that accurate imaging can be obtained. Other types of procedures for which children require sedation, such as reduction of fractures and laceration repair, require an analgesic effect and may require the child's cooperation. Therefore, caution should be used when applying the formula proposed in this study to children undergoing sedation for non-radiological procedures.

The present study has several limitations. First, the data were retrospectively obtained from medical records. However, these data were recorded in detail as part of a quality improvement effort regarding pediatric sedation. Second, the data were recorded

by pediatric sedation providers, which may have affected the results. Third, only healthy children classified as having American Society of Anesthesiologist physical status 1 or 2 were included in this analysis. Therefore, caution should be used when applying the results of this study to children who may be more susceptible to propofol-related complications. Finally, we did not take into account the effects of other medications that children were taking on the sedative effect of propofol.

Conclusions

In addition to weight, age, height, and BSA should be considered when deciding the dose of propofol required to sedate children for radiological examinations. Additionally, we have proposed a formula that can be used to estimate the dose of propofol required to induce sedation in children undergoing radiological examinations. However, further clinical investigations are required to validate this formula.

Author contributions

Yhen Seoung Kang and Jung Hwan Ho participated in collecting the patients' data. Ji Young Min, Jeong-Rim Lee, and Hyo Jin Byon participated in organizing the materials and the design of the study, and performed statistical analysis. All authors read and approved the final manuscript.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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ORCID iD

Hyo Jin Byon  <https://orcid.org/0000-0002-5400-6155>

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