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Does IV Fluid Administration Prevent Hypotension in Pediatrics During Propofol Induced General Anesthesia?

Ramin Nazari[1*], Sharon Calaman[2], Ajit Mammen[2], Bruce Bernstein[2], Vean Tan[2], Maria Bergel[2], Carlos A. Carmona[3] and Shonola Da-Silva[2]

[1]*Department of Pediatrics, Florida Hospital for Children, Section of Critical Care Medicine, University of Central Florida College of Medicine, Orlando, USA*
[2]*Department of Pediatrics, Section of Critical Care Medicine, St. Christopher`s Hospital for Children, Drexel University College of Medicine, Philadelphia, USA*
[3]*Department of Pediatrics, Florida Hospital for Children, Orlando, USA*

Abstract

Background: Hypotension during sedation and general anesthesia with propofol is very common and well reported. The hypotension that results often leads to major interventions, which may prolong the anesthetic time and sometimes force the procedure to be aborted. Prevention of hypotension would be helpful in avoiding these complications. In this study, we hypothesized that intravenous fluid (IVF) administration at 2X maintenance (2XMIVF) during the sedation with general anesthetic doses of propofol would reduce the incidence of significant decreases in arterial blood pressure.

Methods: The study was a retrospective chart review comparing a cohort of children undergoing sedation with general anesthetic doses of propofol receiving 2XMIVF (Group 2, n=100) with a prior cohort not acquiring IVF (Group 1, n=100). Study data included patient characteristics (gender, age, and weight), propofol bolus dose and infusion rate, and hemodynamic parameters measured at baseline and at 5-minute intervals for the procedure duration as dictated by the sedation monitoring guidelines. Total and percent maximum decrease in systolic blood pressure (SBP) and mean arterial pressure (MAP) relative to baseline were calculated. Max SBP and MAP decreases were also dichotomized at 25 SBP units (SBPdrop25) and 20% MAP (pctMAPdrop20). Group differences in baseline and blood pressure changes during the procedure were explored with Chi square analyses, t-tests, and linear correlations. Interventions such as adjusting propofol infusion rate or administration of fluid boluses were also recorded.

Results: Small but significant differences between groups were noted in procedure duration, propofol infusion, and bolus. Differences in the rates of SBPdrop25 and pctMAPdrop20 were not significant comparing the groups 1 and group 2 in bivariate analyses (46% versus 42% and 86% versus 83%, respectively). Logistic regression models adjusting for covariates that were significantly different between groups also found no significant group differences in SBPdrop25. (A.O.R. 1.18, 95% CI 0.67—2.08) or pct MAP drop20 (A.O.R. 1.12, 95% CI 0.51—2.45). A total of 22 interventions, in response to decreases in arterial blood pressure and other indications were recorded in the No IVF group compared to 6 in the IVF group. This difference was statistically significant (p = .001).

Conclusion: The use of 2XMIVF during sedation with propofol at general anesthetic doses did not show a statistically significant difference in SBP and MAP changes. The patients in group 2; however, had less procedure interrupting interventions including adjusting the propofol infusion rate and the need to give fluid boluses. The use of IVF during propofol administration especial at higher doses experienced for general anesthesia may be justified because it results in a more efficient sedation process.

Keywords: Propofol; Hypotension; General Anesthesia; Fluid; Intravenous Infusions; Blood Pressure; Children;

Abbreviations

IVF - intravenous fluid

2X MIVF - 2X maintenance fluids

SBP - systolic blood pressure

MAP – Mean arterial pressure

ED – Emergency Department

IRB - Investigational Review Board

PPPSS- Painless Pediatric Procedure and Sedation Service

ASA - American Society of Anesthesiologist

MRI - Magnetic Resonance Imaging

NS – Normal Saline

ETCO2 – End-Tidal CO2

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***Corresponding Author:** : Ramin Nazari, Department of Pediatrics, Florida Hospital for Children, Section of Critical Care Medicine, University of Central Florida College of Medicine, 2501 N Orange Ave, Suite 301, Orlando, FL, USA 32804, E-mail: ramin.nazari.md@FLhosp.org

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Introduction

Attractive pharmacologic properties of propofol (2,6 diisopropylphenol) as a deep sedation agent including its rapid onset of action, predictable level of sedation, and rapid recovery with minimal adverse effects [1-5] account for its migration outside of the operating room to a variety of sedation venues. Some of these include the radiology, emergency department (ED), intensive care, and specific sedation units [6, 7].

The induction of general anesthesia with propofol or use as a sedative agent; however, has been associated with a decrease in systolic arterial pressure [8]. The mechanism of this hypotension is not well understood, but has been attributed to a decrease in systemic vascular resistance caused by a combination of venous and arterial vasodilatation [9]. Depression of

myocardial contractility and an impaired baroreflex mechanism may also play a role [10, 11].

To date, various strategies have been attempted to prevent hypotension, but they have yielded inconclusive results. Preloading with fluids (colloids and crystalloids) [12], the use of vasopressors including ephedrine, dopamine, dobutamine, and metaraminol [13, 14], as well as intravenous (IV) atropine [15] are strategies that have been tried with differing results.

In this study, we hypothesized that administration of a significant amount of IV fluid during the general anesthetic doses of propofol would minimize significant decreases in arterial blood pressure especially with doses that more in lines with general anesthetic doses.

Materials and Methods

This study is a retrospective chart review comparing two cohorts of children. Group 1 was a prior cohort (n =100) of children not obtaining intravenous fluid (IVF) administration during general anesthesia for MRI imaging. Group 2 was a cohort (n = 100) undergoing general anesthesia with propofol while receiving intravenous fluid at twice normal daily maintenance rate (2XMIVF) for MRI imaging. Approval was obtained from the investigational review board (IRB) of Drexel University College of Medicine/St. Christopher's Hospital for Children in Philadelphia, PA. Informed consent was waived for this observational study.

The section of critical care medicine at St. Christopher's Hospital for Children operates a physician directed Painless Pediatric Procedure and Sedation Service (PPPSS) that provides sedation to American Society of Anesthesiologist (ASA) category I- II patients to complete procedures such as Magnetic Resonance Imaging (MRI) that require immobility.

All patients undergoing procedural general anesthesia through the program were monitored as per a defined policy. For years, sedation agents were administered without accompanying intravenous fluid. In April 2012, the section and PPPSS adopted a change in the sedation policy. Intravenous fluids, typically normal saline (NS), were administered concomitantly at 2 times maintenance for the weight of each patient using the Holliday-Segar nomogram. The infusion of intravenous fluid was changed from keep vein open (KVO) to 2 times maintenance right before propofol was given. No fluid boluses were given prior to giving propofol.

All patients between 1 year old to 18 years of age who received anesthesia with propofol as a sole sedative agent for diagnostic studies through the PPPSS in the 12-month interval from June 2012 through May 2013 were reviewed for the study. These patients were compared to a cohort from before June 2012, representing the pre- IVF era.

Patients were excluded if they were younger than 1 year old or greater than 18 years of age. Additionally, patients were excluded if they had any hemodynamic instability or unstable cardiac conditions as documented prior to initiation of sedation in the chart. Patients were also excluded if they received any adjunct medication for sedation.

The venues were equipped with cardio respiratory monitoring, pulse oximetry, oxygen, suction and a pediatric cardiopulmonary resuscitation cart. End-tidal carbon dioxide (ETCO2) monitoring via nasal cannula was performed routinely for all patients undergoing MRI or other imaging and as needed when risk factors were present.

Patient's vital signs were recorded by the nurse at baseline in the admit room, prior to propofol bolus and initiation of propofol infusion, and every 5 minutes during anesthesia per our hospital sedation policy. Blood pressure was obtained by an MRI compatible automated pneumatic system with an appropriate size cuff manufactured by Invivo Corp, Gainesville, Florida.

Every intervention performed during the procedure in response to either hemodynamic changes or patient depth of anesthesia was recorded as per our policy. Early termination of the procedure, need for administration of IVF in response to hypotension, or adjusting the rate of infusion were identified as an event.

Statistical Analysis

Systolic and mean arterial blood pressure changes from baseline were calculated for each 5-minute measurement period during the procedure. Primary outcomes for these analyses included systolic hypotension and mean arterial hypotension. We defined systolic hypotension as a drop of systolic BP of ≥ 25 mm Hg from baseline [16] recorded at any time for the duration of the sedation. Mean arterial pressure hypotension was defined as a ≥ 20% reduction of MAP relative to baseline.

Differences between groups in patient characteristics (gender, age, weight, NPO time, hemodynamic parameters, propofol bolus and infusion dose, sedation duration and interventions) were explored with bivariate analyses (chi square and t-tests) (Table 2). Variables found to be significantly different between groups were included as covariates with Group 2 (Group 2 versus Group 1) in multinomial logistic regression models exploring associations with SBP and MAP hypotension.

Results

Baseline data and primary outcomes are presented in Table 1. Groups were significantly different in mean NPO solid and liquid (clears) time, propofol bolus dose, and duration of the overall anesthesia time. Overall, 44% of the sample had an SBP drop greater than 25 mmHg during sedation, while the MAP 20% drop rate was 84.5%. In the bivariate analysis (analysis of two variables for determining the empirical relationship between them), these rates were not statistically different comparing groups (Table 2).

Table 1: Patient Characteristics

	Group 1	Group 2 (IVF + Propofol)	Total	P value
Gender				0.57
Female	43 (43%)	39 (39%)	82 (41%)	
Male	57 (57%)	61 (61%)	118 (59%)	
Age (months)	69.8 (40.0)	76.5 (43.4)	73.14 (41.7)	0.25
Weight (kg)	25.6 (14.7)	27.1 (16.8)	26.4 (15.8)	0.48
NPO Solids (min)	835.8 (152.9)	756.2 (161.7)	796.0(169.9)	<0.001
NPO Clear (min)	567.3 (308.6)	482.1 (267.9)	524.7(291.4)	0.04
Sedation Duration (min)	46.80 (19.05)	54.50 (25.03)	50.65(22.51)	0.02

Propofol Bolus (mg/kg)	2.53 (0.94)	2.12 (0.67)	2.33(0.84)	<0.001
Propofol Infusion (mcg/kg/min)	157.45 (30.11)	162.21 (31.96)	159.83(31.06)	0.28
Baseline SBP	104.20 (20.32)	103.67 (13.60)	103.9(13.01)	0.77
Baseline MAP	75.25 (11.11)	75.53 (17.31)	75.39(11.00)	0.86
Baseline HR	100.43 (20.32)	98.81 (17.31)	99.62(18.84)	0.55
SBP=systolic blood pressure, MAP=mean arterial blood pressure, HR=heart rate. Values are number (%) or mean (SD)				

Table 2: SBP and MAP Drop Categories, by Infusion Groups

	Group 1	Group 2	Total	P value
SBP Hypotension	42 (42%)	46 (46%)	88 (44%)	0.57
MAP Hypotension	83 (83%)	86 (86%)	169 (84.5%)	0.56

Table 3 summarizes the logistic regression analyses for SBP hypotension and MAP hypotension. The analyses generate odds ratios for likelihood of a SBP 25-point drop and a MAP drop of 20% in group 1 relative to group 2 while adjusting for other covariates which were found to be different between the two groups. Both 95% confidence intervals and p values are provided for covariates and the primary predictor – Group 2. After adjusting for covariates, group 1 is not significantly more or less likely to experience an SBP drop of ≥ 25 points or more (adjusted OR = 0.779, 95% C.I. = 0.421, 1.440) or a MAP drop of ≥ 20% (adjusted OR = 0.694, 95% CI = 0.297, 1.623).

Interventions applied during procedure time with propofol were primarily reductions in propofol infusion rate or administration of IV fluids as a bolus (10-20 ml/kg). A total of 22 interventions were recorded in the group 1 compared to 6 interventions in group 2. This difference was statistically significant (p = .001).

Table 3: Multinomial Logistic Regression Analysis: Association of Hypotension with Infusion Groups, Adjusting for Covariates

	SBP Hypotension AOR (95% C.I.)	P value	MAP Hypotension AOR (95% C.I.)	P value
Covariates				
NPO Solids	1.002 (1.000--1.004)	0.072	1.003 (1.000-- 1.006)	0.027
NPO Clear	0.999 (0.998--1.000)	0.25	0.999 (0.998--1.001)	0.374
Duration	1.000 (0.987--1.013)	0.97	1.018 (0.996--1.040)	0.108
Propofol Bolus	0.992 (0.698--1.410)	0.96	1.154 (0.690--1.929)	0.586
Study Groups				
Group 1 Vs Group 2	0.779 (0.421--1.440)	0.43	0.694 (0.297--1.623)	0.399

Discussion

Hypotension after induction of anesthesia with propofol is well recognized. The mechanism of propofol- induced hypotension is unresolved. While many studies have demonstrated a significant decrease in systemic vascular resistance [17, 18] that would account for the decrease in arterial blood pressure, the mechanism of propofol induced hypotension is controversial. Some studies suggest that propofol causes a significant reduction in contractility [19] while others demonstrate only minimal depression of contractility [20]. Other studies attribute the decrease in blood pressure to a decrease in myocardial contractility [8, 21].

During the past two decades, many strategies have been explored to reduce these hemodynamic changes. These efforts have been aimed at reducing complications or prolongation in sedation or general anesthesia time. Some interventions attempted have consisted of administrating vasoactive medications. They include giving ephedrine before starting propofol infusion [22], using IV atropine to prevent bradycardia and hypotension during sedation [15], adding ketamine in combination with propofol [23, 24], and maximizing preload with extra intravenous fluid before induction with propofol [12]. They have all ended up with varying success, and almost all those studies were done in adults.

To our knowledge and based on a literature search, there are limited studies that have been done solely in children to show how this blood pressure change can be minimized. It is only recently in 2015, that Jager et al published results of a prospective, randomized, controlled, non-blinded study exploring if preloading children with crystalloids could decrease hypotension [25]. They preloaded a group of patients with a 20ml/kg bolus prior to sedation and then to any patients showing signs of hypo-perfusion or non- responsive to decreases in propofol infusion rate. Their results concluded that there was no effect from the pre-induction isotonic fluid bolus. More interestingly, they found that only decreasing the propofol infusion rate by 0.5 to 1mg/kg per hr resulted in immediate blood pressure improvement [25].

Our study despite being retrospective, adds to the literature of propofol induced hypotension in children. We demonstrate that the infusion of 2x MIVF when started at the same time as the propofol bolus does not prevent or attenuate the decrease in blood pressure after the bolus and even the continued propofol infusion. Our work and that of Jager et al

strongly suggest that fluid may not be the answer to correcting this type of hypotension. From their work and ours, it is seen that neither fluid preload [25] nor fluid maintenance given at the start of bolus dose/continued infusion will resolve hypotension. The answer for the pediatric population may be to simply start decreasing the propofol infusion as Jager et al showed [25]. In addition, the question still lies whether a bolus amount of IVF >20cc/kg and/or continued IVF after that bolus would have possibly maintained blood pressures after the propofol bolus and drip were started.

For this study, we defined clinically significant hypotension as a decrease in SBP of greater than 25 points below the baseline or decrease in MAP greater than 20% below base line measurement. There were some differences in demographic data between the two groups but by adjusting for covariates, we did not find significant differences between groups regarding the incidence of hypotension.

In other words, the mean of propofol bolus dose [Group 1: 2.53 mg/kg (0.94) versus in Group 2: 2.12 mg/kg (0.67) and infusion rate in Group 1: 157.45 mcg/kg/min (30.11) versus Group 2: 162.21 mcg/kg/min (31.96)] in both groups as well as NPO time for clear fluids were slightly different. After statistically adjusting these covariates, data did not demonstrate efficacy for adding IVF to prevent a decrease in BP change during propofol administration. The NPO time to clear fluid and propofol bolus dose in group 2 was less than group 1, so the natural expectation would be that there should be less hypotension in group 2. Despite this, our data showed that the rate of hypotension even by giving 2XMIVF in group 2 was not significantly different between the two groups.

The use of intravenous fluid to prevent propofol induced hypotension has not been extensively evaluated in children. It would seem rather intuitive, given some of the postulated mechanisms of propofol induced hypotension, that a “full tank” in the systemic circulation would attenuate the degree of hypotension with propofol. Several mechanisms may be postulated to explain the failure of fluid administration to attenuate hypotension after the induction of sedation and general anesthesia with propofol [12,14]. The crystalloid fluid administered may be rapidly distributed into the interstitial and intracellular spaces with only a fraction remaining in the systemic circulation. The other reason could be that the volume of fluid that we administered during the high doses of propofol in a sedation typesetting to achieve procedure completion were simply not enough to prevent hypotension.

The pharmacodynamic effects of propofol may be an alternative explanation. Propofol has negative inotropic properties and is a potent vasodilator; therefore, we probably would need a much higher volume-like-bolus dose to prevent this hypotension. In a previous study done by Turner RJ and colleagues, administration of crystalloids as preload in adults did not attenuate the decrease in systolic arterial pressure after induction of anesthesia with propofol [12].

Although our study did not demonstrate any significant differences between the two groups with regards to the incidence of hypotension during propofol infusion, there was some surprising difference in the number of intra sedation interventions between two groups. While these interventions were only categorized as fluid bolus requirements, decrease in propofol infusion rate, or premature termination of the procedure, the difference between the two groups reached statistical significance (22 vs. 6, p=0.001). While we did not do a cost analysis involved with administration of saline during the procedure, the number of interventions may significantly impact the efficacy of the process and patient dissatisfaction associated with an incomplete study. The jury is out within our group as to if these findings justify the use of 2XMIVF during propofol administration for procedural general anesthesia.

There are several limitations of this study. The principal limitation is that this study is a retrospective chart review analysis. This made it impossible to drill down deeper in to the specificity of the adverse events and identify the frequency of each category. Another limitation of this study was a lack of a standard protocol for propofol bolus and infusion rate. The other consideration as well is the topic of dosing of propofol. In relation to other papers reviewing pediatric sedation, the doses used in our study were higher for what consists sedation. The doses were more in line for what consist general anesthesia. Since this study is retrospective, it is difficult to say if the higher doses were used due to the specific patients requiring that that high of doses or if there were other reasons for doing so.

Conclusion

The use of 2XMIVF during general anesthetic doses with propofol did not show a statistically significant difference in SBP and MAP changes. However, the patients in the group 2 had less procedure interrupting interventions, including adjusting the propofol infusion rate, and the need to give fluid boluses. The use of IVF during propofol administration may be justified because it results in a more efficient process especially if higher amounts are given constitute general anesthesia, but more research would be necessary to prove justifying this benefit.

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