Journal of Clinical Anesthesia and Pain Medicine

Research Article

The Potential Consequences of Fluid Fasting Time on Hypotension During Pediatric Sedation While Using Propofol

This article was published in the following Scient Open Access Journal:
Journal of Clinical Anesthesia and Pain Medicine
Received October 20, 2017; **Accepted** November 01, 2017; **Published** November 08, 2017

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

[1]Department of Pediatrics, Pediatric Critical Care, Florida Hospital for Children, Section of Critical Care Medicine, University of Central Florida College of Medicine, USA

[2]Department of Pediatrics, St. Christopher's Hospital for Children, Drexel College University College of Medicine, Philadelphia, PA, USA

Abstract

Background: There are concerns that fluid abstinence prior to a given procedure may put patients at risk for hypotension during sedation.This hazard may be magnified in children since they less likely tolerate the similar length of fluid abstinence as adults due to smaller circulating volumes and greater fluid loss. The objective of this study was to show whether the duration of fluid abstinence contributes to worsening of arterial blood pressure changes during sedation with propofol.

Materials and Methods: This study is a retrospective chart review of 263 children who received intravenous (IV) propofol by bolus then continuous infusion to complete magnetic resonance imaging from June 2011 through May 2013. All patients were instructed to take nothing by mouth as directed by the American Society of Anesthesiologists preoperative fasting guideline. Actual time of abstinence was documented prior to initiation of sedation. Study data included patient characteristics (gender, age, and weight), propofol bolus dose, and infusion rate. Hemodynamic parameters were measured at baseline and 5 minute intervals for the sedation duration which were routine per policy. IV fluid received was also recorded. Total and percent maximum decrease in systolic blood pressure (SBP) and mean arterial pressure (MAP) relative to baseline were calculated. Associations of hemodynamic changes with fluid abstinence and other patient characteristics were explored with linear correlation and regression analyses.

Result: Mean fluid abstinence time was 538.4 +/- 294.0 minutes, propofol bolus dose 2.4 +/- 0.9 mg/kg, propofol infusion rate dose 160.1 +/- 29.3 g/kg/min, and duration 51.6 +/- 24.8 minutes. Duration of procedure, baseline SBP, and MAP were significantly correlated with blood pressure decreases but not with fluid abstinences time. Fluid abstinence time was not significantly correlated with maximum SBP decrease ($r = 0.02$, $p = .727$) or maximum percent MAP decrease ($r = 0.08$, $p = .20$).

Conclusion: In our study, duration of fluid abstinence prior to sedation with propofol is not independently associated with hemodynamic changes in children.

Keywords: Propofol, Sedation, Hypotension, Preoperative Fasting, Children

Introduction

In 1999, the American Society of Anesthesiologists (ASA) adopted preoperative fasting guidelines to enhance the quality and safety of patient care. The guidelines suggest that a healthy, non-pregnant patient should fast six hours from solid and two hours from liquids [1] (Table 1). Although these guidelines are available, studies suggest that providers are still using the blanket statement "NPO after midnight" [1]. This makes it particularly difficult for the medical team to control fasting duration in the non-hospitalized preoperative infant and child. The importance of this is emphasized by evidence in the literature citing that prolonged fasting time is associated with a significantly larger decrease in blood pressure during halothane anesthesia in infants

Table 1: Preoperative and sedation Fasting Guidelines.

Ingested material Minimum fasting duration (h)
Clear liquids 2
Breast milk 4
Infant formula 6
Nonhuman milk 6
Light meal 6

From the American Society of Anesthesiologists [9].

***Corresponding Author:** Ramin Nazari, Department of Pediatrics, Pediatric Critical Care, Florida Hospital for Children, Section of Critical Care Medicine, University of Central Florida College of Medicine, 2501 N. Orange Avenue Suite 301 Orlando, FL 32804 USA, Tel: 215.255.7866 , Office: 407-303-2888, Fax: 407-303-2869, Email: raminnazari@yahoo.com, ramin.nazari.md@FLhosp.org

[2,3].

Hypotension during induction of general anesthesia and procedural sedation with propofol is very common and well reported [4-8] with multiple factors having been implicated [7]. Prolonged preoperative fluid abstinence might be expected to exacerbate this complication, as it does during inhaled induction in infants [2,3]. In a study with healthy adults younger than 65 years, the duration of preoperative fluid abstinence did not appear to affect mean arterial pressure (MAP) when propofol was infused rapidly for induction of anesthesia [8]. However, no studies have addressed the impact of duration of fluid abstinence on propofol-induced hypotension in children.

We therefore conducted this retrospective study to explore whether the fluid fasting time (FFT) may independently contribute to arterial blood pressure changes during sedation with propofol in children.

Methods

Study design

This institutional review board (IRB) approved retrospective analysis used data from patients undergoing procedural sedation by our Painless Pediatric Procedural Sedation Service (PPPSS) from June 1, 2011 to March 31, 2013. Informed consent was waived for this study. Our sedation chart contained a pre-sedation evaluation record, physician sedation record, and nursing sedation record. The pre-sedation evaluation record contained the initial physician evaluation, diagnoses, a special notation if a procedural sedation was performed, and the final disposition for every patient. The physician sedation record contained the indication for the procedural sedation, patient weight, a pre-sedation assessment, the doses and routes of administration of all medication used, notation of any interventions, complications, and a post sedation assessment. The nursing sedation record contained the indication for the procedural sedation, patient weight, a pre-sedation nursing assessment, the doses, routes, and times of administration of all medications used. Additionally, there was a record of pulse rate, respiratory rate, blood pressure, and pulse oximetry readings throughout the entire duration of the procedural sedation. This was accompanied by notation of any interventions, complications, and a post sedation nursing assessment. As per protocol, patient vital signs were recorded every 5 minutes. Subjects were eligible for the study if propofol was the sole agent used for procedural sedation.

Setting

This study was conducted at St. Christopher`s Hospital for Children (SCHC), a 189-bed free standing academic children hospital, located in the North East of Philadelphia, Pennsylvania. SCHC established a PPPSS in 2008 that is operated by fellowship trained and board certified pediatric critical care physicians. The program is responsible for all children undergoing procedural sedation who fall into the American Society of Anesthesiologists' guidelines for sedation outside of the operating room. The procedures included MRI studies using predominantly propofol as the sole agent for sedation.

Data collection and outcome measures

All sedations that were performed with propofol in the SCHC MRI department from June 1, 2011 to March 31, 2013 were identified by querying the PPPSS records. Patients were eligible if they were between 1-18 years old, had an ASA-PS category I or II, and received propofol as the sole agent for the procedure. Patients were excluded from the study if they were younger than 1 year old or greater than 18 years old, if they had any hemodynamic instability, or unstable cardiac conditions as documented prior to initiation of sedation. Patients were also excluded if they received any adjunct medication for sedation. The study investigators reviewed each of the identified procedural sedations performed with propofol for the following 10 data points: patient age, patient weight, indication for procedural sedation, bolus and infusion dose of propofol administered, use of any additional medication, multiple vital sign records throughout the procedural sedation, notation of the occurrence of an adverse event in any record, nature of the adverse event, intervention performed in response to an adverse event, and final patient disposition. An adverse event was defined as any occurrence of hypotension {defined as a systolic blood pressure (SBP) drop >25 point or mean arterial pressure (MAP) drop more than 20% from pre-sedation baseline SBP and MAP}. All the data points from each of the identified records were compiled in a Microsoft Excel spreadsheet and analyzed with SPSS version 20.0 on a secure computer system in compliance with institutional requirements of Protected Health Information.

Statistical Analysis

Two multivariate linear regression models were developed to test the independent associations of fluid fasting time with blood pressure changes. The outcomes for these were maximum systolic blood pressure drop (SBPdropMax) and maximum percent mean arterial pressure drop (pctMAPdropMax), relative to baseline measures. SBPdropMax indicates the maximum absolute decrease in systolic blood pressure while pctMAPdropMax captures the proportional decrease in MAP.

First, significant relationships of patient characteristics and sedation procedure variables with blood pressure changes were explored with bivariate analyses. These included t-tests for differences associated with categorical variables (patient gender, use of IV fluid infusion and intervention during sedation) and linear correlations of continuous variables (age, weight, and duration of the sedation, propofol bolus and infusion doses, baseline SBP, MAP and heart rate) with blood pressure decreases.

Variables that were significantly associated with SBPdropMax or pctMAPdropMax were included with fluid fasting time in subsequent multivariate models. Hierarchical regression strategies were utilized in which the selected covariates were entered first as a set into the regression and then FFT was added to a second regression, adjusted for the first set of covariates.

This analysis calculates the R^2 change associated with FFT following adjustment for other covariates. The integrity of these models was assessed by analysis of residuals (visual inspection of normality plots, identification of outliers and Kolgomorov-Smirnow tests of normal distribution) and exploration of collinearity (tolerance statistics).

Results

A total of 263 patients who received sedations with propofol in the MRI department and met the inclusion criteria were identified

and analyzed. Demographic details and baseline characteristics are presented in Table 2. Patients underwent sedation most often for brain (74.5 %), spinal column (8.8%), abdomen and pelvic area (4.2 %) and joint (2.6 %). Propofol was the sole medication in these cases. The average bolus dose was 2.35 mg/kg (SD, 0.87 mg/kg), infusion rate was 160.1 microgram/kg/minute (SD, 29.2 microgram/kg/ minute) and mean duration time was 51.6 minutes (SD, 24.7 minutes).

No significant differences in mean SBPdropMax or pctMAPdropMax were found in association with gender, infusion group, or whether interventions were undertaken during the sedation (Table 3). Baseline SBP, MAP, and HR were significantly correlated with both SBPdropMax and pctMAPdropMax. Duration of the sedation was also correlated with SBPdropMax, but not pctMAPdropMax (Table 4). Fluid fasting time was not significantly correlated with either SBPDropMax or pctMAPdropMax. These relationships are depicted graphically in Figures 1 and 2. Since baseline SBP and MAP were strongly correlated (r = 0.813), baseline SBP but not baseline MAP was included in the SBPdropMax model and baseline MAP. The baseline SBP was not included in the pctMAPdropMax model. Table 5 provides a summary of the multivariate regression analyses. In the model predicting SBPDropMax, baseline SBP, HR and duration of the sedation were each strongly significant predictors of SBP

Table 2: Characteristics of the Study Population (n = 263).

Characteristic Value
Gender Male 114 (43.3) Female 149 (56.7)
Continuous variables Age, months 71 (42.6, 12-216) Weight, kg 25.97 (15.8, 7-104) Fluid abstinence time, minutes 538 (294, 91-1140) Baseline SBP, mm Hg 104 (13, 54-150) Baseline MAP, mm Hg 75 (11.3, 43-106) Baseline HR, beats/min 100 (18.8, 61–163)

SBP= Systolic Blood Pressure; MAP= mean arterial blood pressure; HR= heart rate. Values are number (%) or mean (SD, range).

Table 3: Mean blood pressure changes by patient and sedation characteristics.

	SBPDropMax (SD)	P value	pctMAPdropMax (SD)	P value
Female	-23.5 (15.4)	0.69	-31.8 (12.5)	0.42
Male	-22.8 (13.8)		-30.6 (11.3)	
Fluid Infusion	-24.3 (15.5)	0.28	-31.8 (12.6)	0.47
No Fluid Infusion	-22.4 (13.8)		-30.7 (11.4)	
Intervention	-26.4 (15.8)	0.26	-34.0 (12.7)	0.18
No Intervention	-23.0 (14.5)		-30.6 (12.0)	

Table 4: Correlations of baseline variables with blood pressure changes.

	SBPDropMax		pctMAPdropMax	
	r	P value	r	p value
Age (months)	0.009	0.89	0.098	0.11
Weight (kg)	- 0.039	0.52	0.046	0.46
NPO to Clear (minutes)	0.022	0.73	0.080	0.20
Sedation Duration (minutes)	- 0.125	0.04	- 0.085	0.17
Propofol bolus Dose	0.050	0.42	0.064	0.30
Propofol infusion dose	- 0.61	0.33	- 0.105	0.09
Baseline SBP	- 0.770	< 0.001	- 0.601	< 0.001
Baseline MAP	- 0.609	<0.001	-.719	< 0.001
Baseline HR	- 0.179	0.004	- 0.234	< 0.001

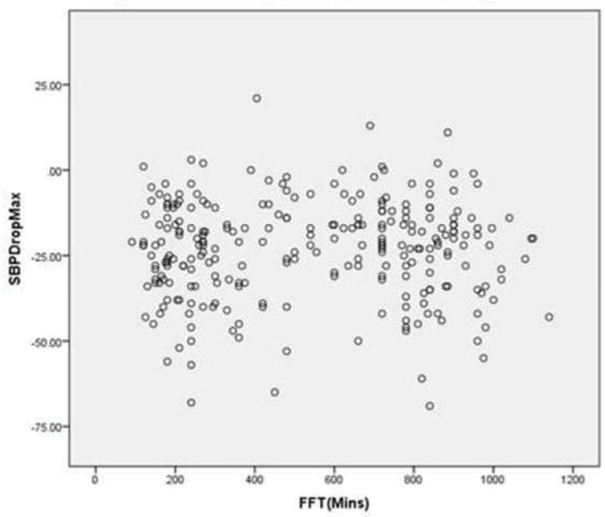

Figure 1: Fluid Fasting Time and Maximum SBP Drop.

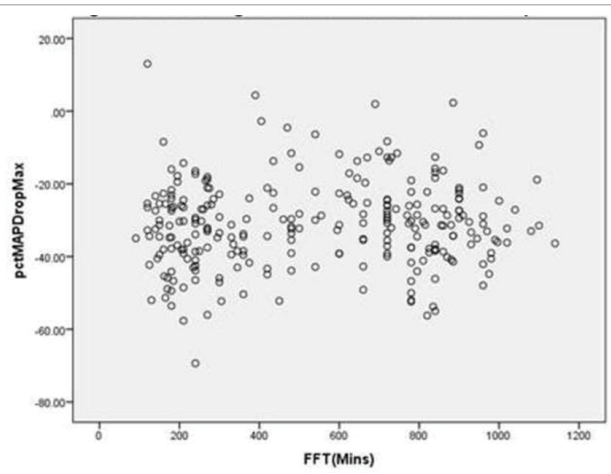

Figure 2: Fluid Fasting Time and Maximum Percent MAP Drop.

Table 5: Multiple Regression Models Predicting Blood Pressure Changes.

Predictors	Unstandardized β	95% C.I. Lower, Upper	P value	R^2 Change
Maximum SBP Drop				
Baseline SBP	-0.826	-0.905, -0.746	<0.001	
Baseline HR	-0.122	-0.179, -0.064	<0.001	
Duration	-0.092	-0.136, -0.049	<0.001	0.637 [a]
FFT (min)	0.001	-0.002, 0 .005	0.503	0.001[b]
Maximum pct MAP Drop				
Baseline MAP	-0.735	-0.823, -0.646	<0.001	
Baseline HR	-0.088	-0.141, -0.036	0.001	0.537[c]
FFT (min)	0.001	-0.002, 0.005	0.416	0.001 [d]

a. Cumulative R^2 for Baseline SBP, Baseline HR and Duration
b. R^2 change associated with FFT
c. Cumulative R^2 for Baseline SBP, Baseline HR
d. R^2 change associated with FFT

changes. The R^2 for this set of covariates was 0.637. FFT, adjusted for these predictors, was not significant (β = 0.001, 95% C.I. -0.002 – 0.005, p 0.50, R^2 change =0.001). For pctMAPdropMax, baseline MAP and HR were significant predictors (R^2=0.537) while FFT time was not (β = -0.001, 95% C.I. -0.002 – 0.005.

p=0.42, R^2 change =0.001). In both regression models, tolerance values for all predictors were > 0.9, indicating no collinearity issues. Kolmogorov-Smirnov tests indicated no departure from normal distribution of unstandardized residuals in both full models (SBPdropMax p = 0.33, pctMAPdropMax p=0.11). Five outliers with standardized residuals < -3 or >3 were identified in the SBPdropMax model and 3 in the pctMAPdropMax model. Recalculation of regression models removing these outliers showed negligible change in regression coefficients p values. NPO time remained a non-significant predictor.

Discussion

The American Society of Anesthesiologists adopted practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration in 1998 [9]. It is widely assumed that prolonged preoperative fasting can cause a decrease in circulating blood volume because of ongoing urine production and insensible losses [10]. The autonomic and hormonal effects of dehydration on the cardiovascular system are well known and might be expected to exacerbate propofol-induced hypotension, which is itself partly mediated by the sympathetic nervous system [11]. Studies addressing prolonged fasting and the hemodynamic responses to induction of anesthesia have been limited to the anesthetic inhalation gases in the pediatric population [2,3]. Friesen, et al. found limited evidence for an effect of fasting time on hypotension during halothane induction in infants [3]. Findings of a previous study in young healthy adults receiving a rapid propofol infusion for induction of anesthesia, failed to demonstrate significant relationships between fasting time and changes in MAP [8].

The objective of our study was to explore the association of fluid fasting time with the blood pressure decrease routinely observed in children during sedation with propofol. In multivariate linear regression models, we found no statistically significant relationships between FFT and either the largest systolic blood pressure drop or percent MAP drop from levels immediately prior to sedation administration. In our sample, FFT ranged from 91 to 1140 minutes. Morley et al. reported similar non-significant results for maximum MAP drop in their study with young, healthy adults [8]. They noted that their sample size (130) was adequate to detect an R^2 of 0.13 (a small association) with > 90% power. Our sample size (263) is twice that of the Morley study [8] and post hoc analysis indicates 90% power to detect an R^2 of .01 for a single independent variable (e.g. FFT) when controlling for 3 other variables with an R^2 equivalent to the 0.637 observed in our study. [That is, if the additional R^2 explained by FFT after adjusting for baseline SBP, baseline HR and duration of the sedation was as small as .01, there was a 90% chance that we would have found this relationship in our data]. Although FFT was not a significant predictor of SBP and MAP changes, baseline MAP and baseline HR, remained impressive predictors of pctMAPdropMax with β values of -0.736 and .091 respectively. In the SBPdropMax model, sedation duration, baseline SBP, and baseline HR were all significant independent predictors. While the effect of these patients' characteristics on blood pressure changes was not the object of this study, it is apparent that further investigation of these effects is warranted.

In our study the last 100 patients received intravenous fluid (Normal Saline at twice daily maintenance rate for weight) during sedation with propofol according to a change in practice of the PPPSS. However, our finding did not demonstrate any correlation between FFT and two other outcomes: hypotension and intravenous fluid administration.

Like previous studies in adults [12], we did not measure anxiety scores. It is possible that the more anxious patients had higher baseline MAP and HR. An acutely raised baseline MAP, consequent on anxiety, might conceivably exacerbate the hypotensive effect of bolus propofol at start. However, the study by Morley A. et al. failed to demonstrate an independent effect of anxiety on pctMAPdropMax during propofol induction [12]. Despite the finding of a previous study in adults [4] that showed a significant correlation between fasting time and 2 other predictors (weight and MAP), our findings did not demonstrate any correlation between those factors.

There are several limitations of this study. The principal limitation is that this study is a retrospective chart review analysis. Moreover, the patient population is not homogeneous and one third of the patients received intravenous fluid administered during their procedure. The other limitation was a lack of standard protocol for propofol bolus and infusion rate during sedation.

Conclusion

In our single site retrospective analysis of 263 healthy ASA I and II patients undergoing procedural sedation with propofol, we were not able to demonstrate any significant relationship between Fluid Fasting Time (FFT) and change in blood pressures. Thus, the routine practice of Nil- Per -oral (NPO) after midnight did not appear to have a negative effect on patient`s hemodynamics during procedural sedation.

Acknowledgements

We would like to thank all hospital staff, the patients, and their families for allowing this manuscript to be put together. There was no external funding necessary for this study. We also would like to thank the editing staff for reviewing our manuscript.

References

1. Anderson M, Comrie R. Adopting Preoperative Fasting Guidelines. *AORN J*. 2009;90(1):73-80.
2. Diaz JH. Halothane Anesthesia in Infancy: Identification and Correlation of Preoperative Risk Factors with Intraoperative Arterial Hypotension and Postoperative Recovery. *J Pediatr Surg*. 1985;20:502-507.
3. Friesen RH, Wurl JL, Friesen RM. Duration of Preoperative Fast Correlates with Arterial Blood Pressure Response to Halothane in Infants. *Anesth Analg*. 2002;95(6):1572-1576.
4. Claeys MA, Gepts E, Camu F. Haemodynamic Changes During Anaesthesia Induced and Maintained with Propofol. *Br J Anaesth*. 1988;6(1):3-9.
5. Grounds RM, Twigley AJ, Carli F, Whitwam JG, Morgan M. The Haemodynamic Effects of Intravenous Induction. Comparison of the Effects of Thiopentone and Propofol. *Anaesthesia*. 1985;40(8):735-740.
6. Holte K, Kehlet H. Compensatory Fluid Administration for Preoperative Dehydration--Does It Improve Outcome?. *Acta Anaesthesiol Scand*. 2002;46(9):1089-1093.
7. Mackenzie N, Grant IS. Comparison of the New Emulsion Formulation of Propofol with Methohexitone and Thiopentone for Induction of Anaesthesia in Day Cases. *Br J Anaesth*. 1985;57(8):725-731.
8. Morley AP, Nalla BP, Vamadevan S, et al. The Influence of Duration of Fluid Abstinence on Hypotension During Propofol Induction. Anesth Analg.

2010;111(6):1373-177.

9. Apfelbaum JL, Caplan RA, Connis RT, Epstein BS, Nickinovich DG, et al. Practice Guidelines for Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration: Application to Healthy Patients Undergoing Elective Procedures: An Updated Report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology*. 2011;114(3):495-511.

10. Prys-Roberts C, Davies JR, Calverley RK, Goodman NW. Haemodynamic Effects oInfusions of Diisopropyl Phenol (Ici 35 868) During Nitrous Oxide Anaesthesia in Man. *Br J Anaesth*. 1983;55(2):105-111

11. Stephan H, Sonntag H, Schenk HD, Kettler D, Khambatta HJ. Effects of Propofol on Cardiovascular Dynamics, Myocardial Blood Flow and Myocardial Metabolism in Patients with Coronary Artery Disease. *Br J Anaesth.* 1986;58(9):969-975.

12. Morely AP, Papageorgiou, CH, Marinaki AM, Cooper DJ, Lewis CM. The Effect of Pre-Operative Anxiety on Induction of Anaesthesia with Propofol. *Anaesthesia*. 2008;63(5):467-473.