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Original Article

Hemodynamic changes following the administration of propofol to facilitate endotracheal intubation during sevoflurane anesthesia

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Abstract: Background: The common intravenous anesthetic agent, propofol, is frequently reported to have negative inotropic and chronotropic effects. In the pediatric population, propofol is commonly used after inhalation induction to facilitate endotracheal intubation without the need for a neuromuscular blocking drug agent. In this setting, we have noted that propofol administration is commonly followed by tachycardia. The current study prospective evaluates heart rate and blood pressure changes following the administration of propofol to pediatric patients anesthetized with nitrous oxide (N2O) and sevoflurane. Methods: ASA class 1 and 2 pediatric surgical patients were enrolled in the study. After premedication with midazolam and inhalation induction with N2O in oxygen and sevoflurane, a bolus dose of propofol was administered to facilitate endotracheal intubation. Heart rate (HR) was measured at baseline and at 30 second intervals following propofol administration. Blood pressure (MAP) was measured at baseline and 120 seconds post-administration. Results: The study cohort consisted of 40 patients who ranged in age from 1 to 15 years. After inhalation induction, propofol (average dose of 2.6 mg/kg) was administered. The end-tidal N2O and sevoflurane concentrations were 62.2 ± 10.3% and 5.7 ± 1.1% respectively. Nineteen of 40 patients had a HR increase >10 bpm. When comparing these patients to those who did not experience a HR increase >10 bpm, there were no differences in the demographic data. Those with a HR increase received a greater dose of propofol when compared to patients whose HR change was <10 bpm (3.0 ± 0.8 versus 2.2 ± 0.5 mg/kg; p=0.0007). There was a significantly greater decreased in the MAP at 120 seconds following propofol administration in the group that did not sustain a >10 bpm HR increase. Conclusion: Tachycardia following propofol administration occurs in approximately 50% of pediatric patients despite preceding inhalation induction and concurrent administration of N2O and sevoflurane. Future studies are needed to define the mechanism for this effect.

Keywords: Propofol, tachycardia, anesthetic induction, endotracheal intubation

Introduction

Propofol is a rapidly acting, intravenous agent used widely in both the adult and pediatric population for the induction of anesthesia [1]. Additionally, in the pediatric population, propofol is frequently administered as an adjunct following inhalational induction with sevoflurane to facilitate endotracheal intubation without the use of a neuromuscular blocking agent (NMBA) [2, 3]. Propofol's cardiovascular effects generally include peripheral vasodilation and negative inotropic properties thereby decreasing both preload and contractility. These effects can result in hypotension especially in patients with co-morbid cardiovascular diseases following its rapid administration or in the setting of hypovolemia [4]. Additional cardiovascular effects may be caused by augmentation of central vagal tone leading to bradycardia or conduction disturbances including heart block or asystole [5, 6]. The negative chronotropic effects have anecdotally been used to be a successful therapeutic maneuver to treat supraventricular arrhythmias [7].

In our clinical practice, we have noted the occurrence of tachycardia when propofol is administered to facilitate endotracheal intubation without a NMBA in pediatric patients anesthetized

Table 1. Demographics and baseline values of the entire study cohort

Age (years)	Weight (kg)	Gender	Baseline HR (beats per minute)	Baseline MAP (mmHg)	Propofol dose (mg/kg)	End-tidal sevoflurane concentration (%)	End-tidal nitrous oxide concentration (%)
5.9 ± 3.8	24.0 ± 12.5	24 M/16F	103 ± 26	75 ± 14	2.6 ± 0.7	5.7 ± 1.1	62.2 ± 10.3

with sevoflurane. The current study prospectively evaluates hemodynamic changes including heart rate and blood pressure in this scenario.

Methods

Following approval by the Institutional Review Board of Nationwide Children's Hospital (Columbus, Ohio), patients undergoing surgical procedures requiring endotracheal intubation without the use of a NMBA were considered eligible for inclusion. Exclusion criteria included age less than 1 year, American Society of Anesthesiologists (ASA) classification 3 or above, underlying genetic or metabolic disorder, acquired or congenital cardiac disease and a history of prematurity less than 30 weeks of gestation. After premedication with oral midazolam (0.5 mg/kg) and placement of standard ASA monitors, general anesthesia was induced with sevoflurane in nitrous oxide (50-70%) and oxygen. Following loss of consciousness, a peripheral gauge (20 or 22) intravenous cannula was placed and the bolus dose of propofol was administered over 10-15 seconds to assist endotracheal intubation without the need for a NMBA. The dose of propofol was at the discretion of the attending anesthesiologist. Heart rate (HR) was measured at baseline just prior to the propofol injection and at 30, 60, 90, and 120 seconds following the administration of propofol. Blood pressure (BP) was measured at baseline and 120 seconds after the administration of propofol Mask ventilation was maintained during these measurements and endotracheal intubation was performed 120 seconds after the administration of propofol following the completion of data collection. Additional data recorded included the propofol dose as well as the end-tidal nitrous oxide and sevoflurane at the time of propofol administration. Signs of pain or discomfort with the injection of propofol such as limb withdrawal, grimacing or movement were recorded.

Statistical analysis included an analysis of variance to compare HR and BP pressure changes following the administration of propofol. A non-paired t-test was used to compare the propofol dose, end-tidal nitrous oxide concentration, and end-tidal sevoflurane concentration between patients who had an increase in HR ≥ 10 bpm. A Fisher's exact test with a contingency table was used to compare the size of the peripheral intravenous cannula and its location between the two groups.

Results

The study cohort consisted of 40 ASA 1 or 2 patients ranging in age from 1 to 15 years (5.9 ± 3.8 years) and in weight from 11 to 50 kilograms (24 ± 12.5) (**Table 1**). There were 16 girls and 24 male boys. The average dose of propofol administered was 2.6 ± 0.7 mg/kg. At the time of propofol administration the end-tidal nitrous oxide and sevoflurane concentrations were 62.2 ± 10.3% and 5.7 ± 1.1% respectively. No signs of pain or discomfort on injection of propofol, such as limb withdrawal, grimacing or movement were noted in any of the study patients.

The baseline HR was 103 ± 26 beats per minute (bpm) at the time of propofol administration. Following propofol administration, 19 of the 40 patients (47.5%) had an increase in HR ≥ 10 bpm. This increase in HR was sustained at 120 seconds by 14 of these 20 patients. The magnitude of the HR increase of these 19 patients was greatest at 30 seconds following propofol administration and became progressively less at each time interval (**Table 2**). When comparing the group of patients that had a HR increase ≥ 10 bpm with those who either had no change, an increase less than 10 bpm or a decrease of HR, there was a significant difference in the propofol dose (3.0 ± 0.8 mg/kg versus 2.2 ± 0.5; p=0.0007) (**Table 3**). Additionally, the BP decrease was significantly greater in those patients without a HR increase ≥ 10 bpm following propofol administration (**Table 3**). There was no significant difference in the end-tidal sevoflurane or nitrous oxide concentration at the time

Table 2. HR and BP changes following propofol administration.

	Baseline HR (bpm)	30 seconds	60 seconds	90 seconds	120 seconds
HR increase ≥ 10 bpm	91 ± 24†	125 ± 18*†	118 ± 20*†	113 ± 21*†	108 ± 23*
No HR increase	114 ± 23	98 ± 23*	101 ± 22	98 ± 23*	98 ± 24*
	Baseline MAP (mmHg)			120 seconds	
HR increase ≥ 10 bpm	74 ± 15			62 ± 11*	
No HR increase	78 ± 12			57 ± 9*	

HR = heart rate; BP = blood pressure, bpm = beats per minute. Data expressed as mean ± SD. *p<0.05 compared to baseline values. †p<0.05 when compared to group without HR increase.

Table 3. Comparison of results between patients with and without an increase in HR ≥ 10 bpm with propofol administration

	Patients with HR increase ≥ 10 bpm	Patients with no HR increase or HR increase <10 bpm
Number	19	21
Age (years)	6.5 ± 4.5	5.4 ± 3.1*
Weight (kg)	24.7 ± 14.1	23.3 ± 11.3*
Size of PIV (gauge)	22 (n=13), 20 (n=4)	22 (n=15), 20 (n=6)*
Site of PIV	11 in hand, 3 in foot, 4 in arm, 1 NR	18 in hand; 2 in forearm; 1 NR*
Propofol dose (mg/kg)	3.0 ± 0.8	2.2 ± 0.5**
End-tidal sevoflurane @ propofol administration (%)	5.5 ± 0.9	5.9 ± 1.2*
End-tidal N2O @ propofol administration (%)	63.2 ± 9.7	61.3 ± 10.9*
MAP decrease 120 seconds post propofol administration (mmHg)	12 ± 12	21 ± 14+
HR change 30 seconds post propofol administration (bpm)	34 ± 18 (increase)	16 ± 13 (decrease)++

The data are expressed as mean ± SD or as number of patients. *p= NS; **p=0.0007; +p=0.037; ++p=0.0001 when compared to patients with no HR increase. NR = not recorded; Et = end-tidal; N2O = nitrous oxide; sevo = sevoflurane.

of propofol administration, the size of the peripheral intravenous cannula, and its location between the two groups.

Discussion

The current study examines the hemodynamic changes following the administration of propofol to facilitate endotracheal intubation without a NMBA during sevoflurane intubation. This remains a common practice as illustrated by the literature on the subject as well as the clinical experience of practicing pediatric anesthesiologists [2, 3]. In this scenario, approximately half of the patients were noted to have an increase in HR ≥ 10 bpm following the administration of propofol. This is in contrast to the generally accepted notion that propofol results in a decrease in HR and even bradycardia especially in the adult population [4-6]. For patients that had an increase in HR, the peak effect was noted at 30 seconds following the injection of propofol with a decrease over the ensuing 2 minutes. However, the effect persisted even at 2 minutes in many of the patients.

The tachycardia may have been a response to the well documented pain which may occur with propofol injection [8, 9]. However, no other objective signs of discomfort were noted such as hand withdrawal in our study population. Additionally, there was a decrease in BP rather than an increase which might be expected if the problem were related to pain perception. Additionally, given the combination of sevoflurane and nitrous oxide, we believe that pain is an unlikely explanation. Nitrous oxide in oxygen has been shown to lower the incidence of pain on propofol injection to a comparable degree to a lidocaine-propofol mixture [10-12]. Additionally,

the patients were also receiving sevoflurane at an end-tidal concentration greater than 2 MAC. Further investigation as to whether pain is the factor responsible could include the pre-administration of lidocaine or other agents shown to decrease the incidence of propofol-injection pain or even the use of fos-propofol [13]. Although not FDA-approved for use in children, fos-propofol (Lusedra, Eisai Inc, Woodcliff Lake, NJ), a pro-drug of propofol introduced into the market in 2009, is purported to cause less pain than propofol on intravenous injection [14].

Secondly, tachycardia could be a response to the hypotension induced by propofol administration. However, this is not supported by our study as there was no statistically significant difference in the blood pressure decrease following propofol administration between the group with an increase in HR and the group with no change or a decrease in HR. In fact, the decrease in MAP was less in those patients who manifested a HR increase suggesting that the tachycardia may mitigate some of the negative effects of propofol on hemodynamic function.

In summary, we demonstrate that tachycardia can be seen following propofol administration to pediatric patients during the administration of N2O and sevoflurane. In our cohort of patients, this was a common phenomenon, occurring in approximately 50% of patients. Future studies are necessary to clearly delineate the etiology of this response.

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