Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

A Unit of Scholars Academic and Scientific Society, India
www.saspublishers.com

Anesthesiology

To Study the Effect of Different Injection Speeds of Propofol on Blood Pressure, Dose and Time of Induction

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Original Research Article

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Article History
Received: 04.02.2018
Accepted: 15.02.2018
Published: 28.02.2018

DOI:
10.36347/sjams.2018.v06i02.029

Abstract: Dose requirements of Propofol induction depend on patient characteristics and infusion rate. To avoid cardiovascular depression of propofol, slow infusion is recommended during induction. The aim of this study is to determine the best propofol dose with different infusion rates of propofol administered by infusion pumps. A total of 90 American Society of Anaesthesiologists (ASA) I & II patients of both sexes aged 25-55 years were included in this observational study. Patients included in this study were scheduled for elective surgery under general anaesthesia in supine position. Patients were randomly allocated to one of three groups each including 30 patients according to different Propofol infusion speeds used before induction of general anaesthesia. Groups P400, P600 and P800 were infused propofol in rates of 400ml/hr, 600ml/hr and 800ml/hr to each group respectively, until loss of eyelash reflex. The duration of induction was recorded with the amount of propofol infused. The induction dose in mg kg -1 body weight was calculated. Arterial blood pressure and heart rate were recorded before and five consecutive minutes following induction. The doses required to abolish eyelash reflex was 2.25±0.246, 2.71±0.285, and 2.98±0.277 mg kg-1 body weight for Groups P400, P600 and P800 respectively and found significantly different between groups ($p<0.05$). The decrease in mean arterial pressure was more profound in groups P600 and P800 (30%), in the second minute following induction. Group P400 showed a slight decrease (14%) in the 3rd minute of induction. At faster rates of injection of Propofol the dose required for induction of anaesthesia increased while time for induction was shorter and the decrease in mean blood pressure was more pronounced.

Keywords: Anaesthetic techniques: hemodynamic changes: infusion rates, venous propofol.

INTRODUCTION

Induction of general anaesthesia means rendering the patient asleep to enable laryngoscopy and endotracheal intubation with ease. This is one of the most critical stages in the administration of general anaesthesia. The best and ideal method for induction of anaesthesia is by injecting an anaesthetic agent intravenously. Many drugs have been used for this purpose. Among them Thiopentone sodium, Ketamine, Etomidate and Propofol have been used extensively. Many physiological changes occur during the administration of these drugs. Amongst them, most important changes occur in the hemodynamics of the patients mainly blood pressure and heart rate. Until recent past Thiopentone sodium was the commonly used drug for induction of general anaesthesia. In the recent past it has been largely replaced by Propofol because of certain advantages of the latter drug. Amongst them is rapid recovery from anaesthesia and lesser incidence of nausea and vomiting in the postoperative period. Although Propofol is preferred over Thiopentone sodium for induction of anaesthesia but one of the disadvantages of Propofol is significant hypotension. A typical induction dose of Propofol 2mg/kg body weight results in approximately 30% reduction in systolic blood pressure [1].

The hypotensive effect of Propofol is attributable to a decrease in sympathetic activity, direct vasodilatation and myocardial depression [2]. This fall in blood pressure is of little significance in normal healthy patients but can be of great significance in patients who have coronary artery disease etc. because it can lead to myocardial ischemia. Blood concentration of Propofol depends on many factors such as age, gender, body weight, dose, cardiac output and infusion rate [3,4].

Dose requirements of Propofol induction depend on patient characteristics and infusion

rate. Cardiac output (CO) is thought to be an important factor affecting the induction of anesthesia [5]. Particularly high concentrations could be expected if a normal dose of Propofol was injected into a patient with low CO. Consistent with the experience of most anesthesiologists, critically ill patients with low CO usually require very small doses of Propofol [6]. Both CO and its peripheral distribution are important determinants of the relation between early drug concentration and time in intravenously administered drugs, especially with a slow administration rate [7]. However, CO, which varies with age, does not account for age-related differences in Thiopental dose requirements [8].

The mechanism of hypotension is attributed to a decrease in sympathetic activity [9], myocardial depression, and direct vasodilation. Hypotensive effects of Propofol are generally proportional to the dose and rate of administration [10].

Several studies with varied methods of delivery have demonstrated reduced hemodynamic effects and a decrease in dose requirements of Propofol. Studies have also shown that a slower injection of Propofol decreases cardiovascular effects [11,12]. However, slow injection may also result in longer induction times [13]. In a recent study using a target controlled infusion (TCI), Liu *et al.* demonstrated that the decrease in SBP was significantly less when Propofol was given in a step wise technique with an initial plasma concentration of 2.0 mg/ml and then raised to a target plasma concentration of 4.0 mg/ml [14].

METHODS

The observational study was conducted at the SMHS Hospital which is one of the associated hospitals of Government Medical College Srinagar. After obtaining approval from hospital ethical committee, a written informed consent was obtained from the patients for participation in the study.

A total of 90 American Society of Anaesthesiologists (ASA) I & II patients of both sexes aged 25-55 years were included in this observational study. Patients included in this study were scheduled for elective surgery under general anaesthesia.

Exclusion criteria

- Emergency surgery
- Obesity (BMI >35)
- Patients on anti-hypertensive drugs
- Diabetes mellitus
- Known allergy to Propofol

Patients were divided into 3 groups with 30 patients in each group according to different Propofol infusion speeds used before induction of general anaesthesia.

Propofol was given in the form of infusion with the help of infusion pumps, at three different rates of 400ml/hr, 600ml/hr and 800ml/hr to each group respectively. Monitoring of unconsciousness was done using entropy.

Hypotension, time of induction and dose of Propofol used was compared among the three groups. Heart rate, ECG, pulse oximeter and non-invasive blood pressure were monitored in UN premedicated patients who were fasting for at least 8 hours before the induction of anaesthesia.

An intravenous line with 18 gauge cannula was secured and IV fluids started. Then 1% Propofol was administered to the patients with the help of infusion pump to deliver appropriate rate until the entropy values reach 40. After that Fentanyl (1g/kg) and Atracurium (0.5mg/kg) was administered and anaesthesia was maintained with Isoflurane in 50% O_2-N_2O.

All patients were intubated and ventilated in volume controlled ventilation mode.

Following parameters were noted:

- Demographic profile of the patient
- Blood pressure before and after induction of anaesthesia.
- Time required for induction of anaesthesia (till entropy values reach 40).
- Dose of Propofol used for induction of anaesthesia till entropy values reach 40.

STATISTICAL ANALYSIS

The results of the observations at the end of the study were entered in Microsoft Excel and descriptive analysis of the data was done. Categorical variables were summarized as frequency and percentage. Two ways cross tabulation was used to summarize relationship between categorical variables. Mean and standard deviation was used to summarize continuous variables. A ‘P’ value of less than 0.05 was taken as significant.

RESULTS

There was no significant difference with respect to age, sex, weight, height, and ASA physical status among the study groups [Table 1].

Table-1: Demographic characteristic of patients in study groups (Mean±SD)

VARIABLES	GROUP P400 (N=30)	GROUP P600 (N=30)	GROUP P800 (N=30)	P
Age (years)	38.9±9.21	37.7±7.86	38.6±8.04	0.843*
SEX MALE/FEMALES	17/13	15/15	14/16	0.73*
WEIGHT (KG)	70.7±6.56	71.4±5.64	70.8±5.80	0.885*
HEIGHT	163.5±4.40	164.3±3.98	163.9±3.73	0.748*
ASA I/II	27/07	26/04	25/05	0.587*

ASA American society of Anaesthesilogy, SD standard deviation, * Level of significance

Larger Propofol dose were required as rate of infusion increased. Mean dose of Propofol was 2.25±0.246 mg/kg, 2.71±2.285mg/kg and 2.98±0.277mg/kg in group P400, P600, P800 respectively. The mean induction time was shorter in P800 as compared to P400 and P600. Mean induction time was 180.9±8.78, 166.7±5.53 and 129.3±4.13 seconds in group P400, P600 and P800 respectively table.2

Table-2: Dose of propofol for induction and induction time in study groups (Mean±SD)

variables	GROUP P400 (N=30)	GROUP P600 (N=30)	GROUP P800 (N=30)	P
Induction time (seconds)	180.9±8.78	166.7±5.53	129.3±4.13	0.001*
Propofol (1%) amount during induction (mg)	157.3 ± 7.65	204.9 ± 6.84	210.5 ± 6.78	0.003*
Calculated propofol dose during induction (mg kg-1)	2.25±0.246	2.71±2.285	2.98±0.277	0.005*

SD standard deviation, * Level of significance

Table-3: Hemodynamic changes among the study groups (Mean±SD)

Variables	GROUP P400 (N=30)	GROUP P600 (N=30)	GROUP P800 (N=30)	P
systolic blood pressure (mmHg) pre and post induction	123±6.19 110.8±4.92	122.6±4.39 105.7±4.35	122.4±4.34 102.3±3.64	0.001*
diastolic blood pressure (mmHg) pre and post induction	81.4±4.04 75.4±2.56	81.5±3.25 75.2±1.90	80.9±3.14 74.0±2.54	0.785
arterial pressure (mmHg) pre and post induction	95.4±4.67 87.2±3.23	95.2±3.58 85.4±2.53	94.8±3.45 83.4±2.77	0.002*
heart rate change pre and post induction	87.8±4.12 83.6±4.25	88.2±3.48 83.8±3.65	88.9±4.27 84.6±4.3	0.878

SD standard deviation, * Level of significance

The mean systolic blood pressure (mmHg) pre and post induction was significantly reduced as the rate of infusion increases. The mean systolic blood pressure was 123+6.19 and 110.8+4.92, 122.6+4.39 and 105.7+4.35, 122.4+4.34 and 102.3+3.64 in P400, P600 and P800 respectively. The mean diastolic blood pressure (mmHg) pre and post induction was reduced as the rate of infusion increases. The mean diastolic pressure pre and post induction was 81.4+4.04 and 75.4+2.56 in P400, 81.5+3.25 and 75.2+1.90 in P600 and 80.9+3.14 and 74.0+2.54 in group P800 respectively. The mean arterial pressure (mmHg) pre and post induction was reduced as the rate of infusion increases. The mean arterial pressure was 95.4+4.67 and 87.2+3.23 in P400, 95.2+3.58 and 85.4+2.53 in P600 and 94.8+3.45 and 83.4+2.77 in P800 respectively. The heart rate change (bpm) were insignificant pre and post induction The heart rate change pre and post induction were 87.8+4.12 and 83.6+4.25 in P400, 88.2+3.48 and 83.8+3.65 in P600 and 88.9+4.27 and 84.6+4.3 in P800 respectively.tabe.3

DISCUSSION

Although Propofol is preferred over Thiopentone sodium for induction of anaesthesia but one of the disadvantages of Propofol is significant hypotension. A typical induction dose of Propofol 2mg/kg results in approximately 30% reduction in systolic blood pressure [1].

The hypotensive effect of Propofol is attributable to a decrease in sympathetic activity, direct vasodilatation and myocardial depression [2].

Dose requirements of Propofol induction depend on patient characteristics and infusion rate [15]. Cardiac output (CO) is thought to be an important factor affecting the induction of anesthesia [5]. Particularly high concentrations could be expected if a normal dose of Propofol was injected into a patient with low CO. Consistent with the experience of most anesthesiologists, critically ill patients with low CO usually require very small doses of Propofol[6].

It was observed that larger Propofol doses were required as the rate of infusion increased. The mean dose of Propofol used (mg) for induction was 2.25+0.246 mg/kg in P400 (range 1.9-2.9mg/kg) p <0.001, 2.71+2.285mg/kg in P600 with (range 2.3-3.4mg/kg) p<0.001, and in group P800 the mean dosage was 2.98+0.277mg/kg with a range of 2.6-3.5mg/kg. p =0.005. The difference was statistically significant, p < 0.05. Our study shows close resemblance with the study conduct by Peacock JE *et al***.** [16] in their study the total dose used was(1.2, 1.6 and 2.5 mg kg-1, respectively), which was significantly less (P< 0.001). Another study conduct by Stokes DN *et al*. [17] shows similar results, with mean doses of Propofol (1.40, 1.96, 2.61, and 2.15 mg/kg in groups 1, 2, 3, and 4, respectively). Sennur UZUN *et al*. [18] in their study of 72 patients, the mean dose of Propofol used for induction of anaesthesia was 2.32±0.61in p200,2.64±0.43 in p300 and 2.85±0.52 in p400.

The mean induction time was shorter in P800 when compared to P400 and P600.the mean induction time among the studied groups was 180.9+8.78 seconds in P400 (range 161-199 s) p<0.001, 166.7+5.53 secopnds in P600 with (range 154-175 s), p<0.001 and in group P800 the mean induction time was 129.3+4.13 seconds with a range 121-139 s, p <00.1 The difference between three groups was statistically significant, <0.05. Rolly G *et al*. [19] in their study of sixty patients received an induction dose of Propofol 2 mg kg-1 over 5, 20 or 60 s to a forearm vein. Anaesthesia was induced satisfactorily in all 20 of the patients in the 5-s group, in 19 of the patients in the 20-s group and in 18 of the patients in the 60-s group. The rate of injection had a significant influence on induction time. Mean induction time increased from 21.5 to 34.7 and 50.5 s, when injection time was increased from 5 to 20 to 60 s, respectively. Peacock JE *et al.* [16] in their study, Propofol was administered at 300, 600 or 1200 ml h-1 until loss of consciousness. The duration of induction was significantly longer (P< 0.001) with the slower infusion rates (104, 68 and 51 s), but the total dose used was significantly less (P< 0.001) in these patients (1.2, 1.6 and 2.5 mg kg-1, respectively). Sennur UZUN *et al*.[18] in their study of 72 patients, the induction time was 177±38s in P 200, 182±58s in P 300 and 134±38 in P 400.

In our study the mean systolic blood pressure (mmHg) pre and post induction was 123+6.19 and 110.8+4.92 in group P400, 122.6+4.39 and 105.7+4.35 in P600 and in group P800 was 122.4+4.34 and 102.3+3.64 respectively. The group difference was statistically significant with a p <0.05. Thus mean systolic pressure was reduced as rate of infusion increases from 400ml/hr to 600ml/hr to 800ml/hr. Rolly G *et al*. [19] in their study, mean induction time increased from 21.5 to 34.7 and 50.5 s, when injection time was increased from 5 to 20 to 60 s, respectively. Mean arterial pressure decreased to the same extent in all three groups. Two minutes after induction, mean systolic arterial pressure was reduced by 15.1, 13.5 and 19.3 mm Hg in the 5-, 20- and 60-s groups, respectively. Peacock JE *et al.* [16] in their study, Propofol was administered at 300, 600 or 1200 ml h-1 until loss of consciousness. The decrease in systolic and diastolic arterial pressure was significantly less in the 300-ml h-1 group at the end of induction and immediately after induction (P< 0.01). Stokes DN *et al*. [17] in their study, Propofol was delivered at 50, 100, or 200 mg/min by the Ohmeda 9000 infusion pump (groups 1, 2, and 3, respectively) or by bolus of 2 mg/kg (group 4) until loss of verbal contact. Slow infusion (groups 1 and 2) caused less depression of systolic and diastolic blood pressure than rapid infusion (groups 3 and 4), but the differences were not statistically significant. Sennur UZUN *et al*. [18] in their study of 72 patients observed a decrease in systolic and mean blood pressure with infusion rate of 200ml/h,300ml/hand 400ml/h.

In our study, the mean diastolic blood pressure (mmHg) pre and post induction was 81.4+4.04 and 75.4+2.56 in P400, 81.5+3.25 and 75.2+1.90 in P600 and 80.9+3.14 and 74.0+2.54 in group P800 respectively. The difference was statistically significant with a p<0.05. Thus mean diastolic pressure reduced as the infusion rate increased. Rolly G *et al*. [19] in their study, they received an induction dose of Propofol 2 mg kg-1 over 5, 20 or 60 s to a forearm vein and mean diastolic arterial pressure was reduced by 10.3, 13.2 and 13.7 mm Hg in group 1,2and 3 respectively. Peacock JE *et al.* [16] in their study, Propofol was administered at 300, 600 or 1200 ml h-1 until loss of consciousness The decrease in systolic and diastolic arterial pressure was significantly less in the 300-ml h-1 group at the end of induction and immediately after induction (P <0.01). Stokes DN *et al*. [17] in their study Propofol was delivered at 50, 100, or 200 mg/min by the Ohmeda 9000 infusion pump (groups 1, 2, and 3, respectively) or by bolus of 2 mg/kg (group 4) until loss of verbal contact. Slow infusion (groups 1 and 2) caused less depression of systolic and diastolic blood pressure than rapid infusion (groups 3 and 4).

In our study the mean arterial pressure (mmHg) pre and post induction was 95.4+4.67 and 87.2+3.23 in P400, 95.2+3.58 and 85.4+2.53 in P600 and 94.8+3.45 and 83.4+2.77 in group P800 respectively. The difference was statistically significant with a p <0.05. Thus mean arterial pressure decreases as infusion rate increases. Rolly G *et al.* [19] in their study, Mean arterial pressure decreased to the same extent in all three groups. In our study, the mean heart rate (bpm) pre and post induction was 87.8+4.12 and 83.6+4.25 in P400, 88.2+3.48 and 83.8+3.65 in P600 and 88.9+4.27 and 84.6+4.3 in group P800 respectively. The difference was statistically insignificant with a p >0.05. Similar results were found in the study conduct

by Rolly G *et al.* [19] in their study, heart rate change were also insignificant.

In our study, the mean oxygen saturation (%) pre and post induction was 99.3+-0.94 and 98.3+1.18 in P400, 98.8+1.13 and 98.0+1.65 in P600 and was 99.1+0.94 and 98.2+1.04 in group P800 respectively. The difference was statistically insignificant P>0.05. Thus infusion rate has less effect on oxygen saturation. Rolly G *et al.* [19] in their study, Apnoea of more than 10 s duration was seen frequently in all three groups, but the results suggest that the incidence was not influenced by the rate of injection. Peacock JE [16] in their study, the incidence of apnoea was also significantly less in the slower infusion group.

REFERENCES

1. Sebel PS, Lowdon JD. Propofol, a new intravenous anaesthetic. Anesthesiology 1989; 71: 260-77.
2. Kazama T, Ikeda K, Morita K, Ikeda T, Kikura M, Sato S. Relation between initial blood distribution volume and Propofol induction dose requirement. Anesthesiology 2001; 94: 205-10.
3. Adachi YU, Watanabe K, Higuchi H, Satoh S. The determinants of Propofol induction of anaesthesia dose. Anesth Analg 2001; 92: 656-61.
4. Kazama T, Ikeda K, Morita K, Kikura M, Ikeda T, Kurita T, Sato S. Investigation of effective anesthesia induction doses using a wide range of infusion rates with undiluted and diluted propofol. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2000 Apr 1;92(4):1017-28.
5. Kazama, T Ikeda, K Morita, K Kikura, M Ikeda, T Kurita, T Sato, S Ludbrook GL, Upton RN: A physiological model of induction of anaesthesia with Propofol in sheep. 2. Model analysis and implications for dose requirement. Br J Anaesth 1997; 79: 505–13.
6. Ludbrook GL, Upton RN, Upton RN, Ludbrook GL, Grant C, Martinez AM. Cardiac output is a determinant of the initial concentrations of Propofol after short-infusion administration. Anesth Analg 1999; 89: 545–52.
7. Upton, RN Ludbrook, GL Grant, C Martinez, AM Upton RN, Ludbrook GL: A physiological model of induction of anaesthesia with Propofol in sheep. 1. Structure and estimation of variables. Br J Anaesth 1997; 79: 497–504.
8. Upton, RN Ludbrook, GL Avram MJ, Sanghvi Reema, Henthorn TK, Krejcie TC, Shanks CA, Fragen RJ, Howard KA, and Kaczynski DA. Determinants of thipental induction dose requirements. Anesth Analg 1993; 76: 10–7.
9. Robinson BJ, Ebert TJ, O'brien TJ, Colinco MD, Muzi M. Mechanisms whereby Propofol Mediates Peripheral Vasolidation in HumansSympathoinhibition or Direct Vascular Relaxation?. Anesthesiology: The Journal of the American Society of Anesthesiologists. 1997 Jan 1;86(1):64-72.
10. Propofol. Med Lett Drugs Ther; 1990, 32:22.
11. Kanto J, Gepts E. Pharmacokinetic implications for the clinical use of Propofol. Clin Pharmacokinet 1989; 17: 308-26.
12. Wagner BK, Berman SL, Devitt PA, O'Hara DA. Retrospective analysis of postoperative nausea and vomiting to determine antiemetic activity of droperidol added to propofol: a possible drug interaction. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 1994 Sep 10;14(5):586-91.
13. Rolly G, Versichelen L, Huyghe L, Mungroop H. Effect of speed of injection on induction of anaesthesia using propofol. BJA: British Journal of Anaesthesia. 1985 Aug 1;57(8):743-6.
14. Liu SH, Wei W, Ding GN, Ke JD, Hong FX, Tian M. Relationship between depth of anesthesia and effect-site concentration of propofol during induction with the target-controlled infusion technique in elderly patients. Chinese medical journal. 2009 Apr;122(8):935-40.
15. Kazama T, Ikeda K, Morita K, Kikura M, Ikeda T, Kurita T, Sato S. Investigation of effective anesthesia induction doses using a wide range of infusion rates with undiluted and diluted propofol. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2000 Apr 1;92(4):1017-28.
16. Machata AM, Willschke H, Kabon B, Kettner SC, Marhofer P. Propofol-based sedation regimen for infants and children undergoing ambulatory magnetic resonance imaging. British journal of anaesthesia. 2008 Aug 1;101(2):239-43.
17. Stokes DN, Hutton P. Rate-dependent induction phenomena with propofol: implications for the relative potency of intravenous anesthetics. Anesthesia and analgesia. 1991 May;72(5):578-83.
18. Uzun Ş, Özkaya Ba, Yilbaş Ös, Ayhan B, Şahin A, Aypar Ü. Effects of different propofol injection speeds on blood pressure, dose, and time of induction. Turkish Journal of Medical Sciences. 2011 Jun 1;41(3):397-401.
19. Rolly G, Versichelen L, Huyghe L, Mungroop H. Effect of speed of injection on induction of anaesthesia using propofol. BJA: British Journal of Anaesthesia. 1985 Aug 1;57(8):743-6.