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Original Research Article

The effect of propofol when injected at different speeds for induction of general anesthesia: an observational study

Zahid Mohd Rather*, Mohd Nazrull Islam, Barqul Afaq, Umar Farooq, Nighat Ara Majid

Department of Anesthesia and Surgery, Govt. Medical College Srinagar, Jammu and Kashmir, India

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***Correspondence:**
Dr. Zahid Mohd Rather,
E-mail: drzahidmrather@yahoo.com

ABSTRACT

Background: The hypotensive effect of propofol is attributable to a decrease in sympathetic activity, direct vasodilatation and myocardial depression. The aim of the study was to assess the effect of propofol when injected at different speeds for induction of general anesthesia on the following parameters: blood pressure, time of induction of anesthesia, dose of propofol used.
Methods: The present study was conducted in post Graduate Department of Anesthesia and Surgery, Govt. Medical College, Srinagar for a period of two years and included 90 patients from July 2014 to June 16, the study was prospective one.
Results: In our study patients divided into three groups with 30 patients in each group. The mean age in group P400, P600, P800 was statistically insignificant p>0.843.The mean weight in group P400, P600, P800 was statistically insignificant p>0.885.The mean height in group P400, P600, P800 was statistically insignificant p>0.748. The mean induction time in P400 and in P600 was statistically significant. The mean systolic blood pressure, pre and post induction in P400, in P600 and in group P800 was statistically significant. The mean diastolic blood pressure, in pre and post induction in P400, P600, P800 was statistically insignificant with a p>0.05. The mean arterial pressure in pre and post induction in P400, P600, P800 was statistically significant (p<0.05). The mean heart rate in pre and post induction was statistically insignificant. The mean oxygen saturation (%) pre and post induction was statistically insignificant.
Conclusions: We concluded that induction dose required for loss of consciousness increased with a faster rate of infusion while time for induction was shorter in P800 compared to P400 and P600, and the decrease in mean blood pressure was less after induction in P400. Propofol injection should be slow enough to prevent any hemodynamic deterioration in anesthesia induction.

Keywords: Propofol, Intravenous anesthetics, Hemodynamics, Induction time

INTRODUCTION

Many physiological changes occur during the administration an anesthetic agent intravenously. Amongst them, most important changes occur in the hemodynamics of the patients mainly blood pressure and heart rate. Although propofol is preferred over thiopentone sodium for induction of anesthesia but one of the disadvantages of propofol is significant hypotension. A typical induction dose of propofol 2 mg/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] Blood concentration of propofol depends on many factors such as age, gender, body weight, dose, cardiac output and infusion rate.[2-4] Dose requirements of propofol induction depend on patient characteristics and infusion rate.[4] Cardiac output (CO) is

thought to be an important factor affecting the induction of anesthesia.[5] Hypotensive effects of propofol are generally proportional to the dose and rate of administration.[6-8] When propofol is administered as a 2 mg/kg IV bolus (PG), SBP decreased by 20%. There was also a decrease in DBP and MAP by 16% and 19%. Studies have shown that a slower injection of propofol decreases cardiovascular effects.[9,10] However, slow injection may also result in longer induction times.[11] In a recent study using a target controlled infusion, 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.[12]

Aims and objectives

To study the effect of propofol when injected at different speeds for induction of general anesthesia on the following parameters: blood pressure, time of induction of anesthesia, dose of propofol used.

METHODS

The present study was conducted in Post Graduate Department of Anesthesia and Surgery, Govt. Medical college; Srinagar for a period of two years, from July 2014 to June 16, the study was prospective one. A written informed consent was obtained from the patients for participation in the study. A total of 90 American Society of Anesthesiologists (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 Anesthesia in supine position.

Exclusion criteria

Emergency surgery, obesity (BMI >35), patients on anti-hypertensive drugs, diabetes mellitus and 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 anesthesia. Propofol was given in the form of infusion with the help of infusion pumps, at three different rates of 400 ml/hr, 600 ml/hr and 800 ml/hr to each group respectively. We choose these infusion rates based on previous studies.[13,14] 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 anesthesia. An intravenous line with 18 gauge canula 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 (1 g/kg) and atracurium (0.5 mg/kg) was administered and anesthesia 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 anesthesia, time required for induction of anesthesia (till entropy values reach 40), dose of propofol used for induction of anesthesia 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

The present study was conducted in post Graduate Department of Anesthesia, and Surgery Govt. Medical College, Srinagar for a period of two years and included 90 patients from July 2014 to Jun 16, the study was prospective one.

In our study 90 patients are included which were divided into three groups with 30 patients in each group. The mean age in group P400 was 38.9±9.21 years (range25-55), group P600 was 37.7±7.86 years (range 25-53) and in group P800 was 38.6±8.04 years (range 27-54). Which was statistically insignificant (p=0.843), as shown in Table 1.

Out 30 patients, in group P400 17 (56.7%) were males and 13 (43.3%) were female, in group P600 15 (50%) were males and 15 (50%) were females, in group P800 14 (46.7) were males and 16 (53.3) were females. P value =0.733 statistically insignificant. The mean weight in group P400 being 70.7±6.56 kg (range 55-83), group P600 being 71.4±5.64 kgs (range 62-81) and group P800 70.8±5.80kg (range 60-81) with a p>0.05, statistically insignificant (Table 1).

In our study the mean height in group P400 being 163.5±4.40 cm (range 156-172), group P600 being 164.3±3.98cms (range 158-175) and group P800 163.9±3.73 cms (range 158-171) with a p=0.748, statistically insignificant (Table 1).

In our study the distribution of patients as per ASA status with 23 (76.7%) patients of group P400 in ASA I and 7 (23.3%) in ASA II. In group P600 there were 26 (86.7%) and 4(13.3%) patients in ASA I and ASAII. There were 25 (83.3%) patients of group P800 in ASA I and 5 (16.7%) patients with ASA II, statistically insignificant (p=0.587) shown in Table 2.

Table 1: Patients characteristics data in groups.

	Group P400	Group P600	Group P800	P value
Age (years)	38.9±9.21 (25-55)	37.7±7.86 (25-53)	38.6±8.04 (27-54)	0.843
Gender M/F	17/13 (56.7/43.3%)	15/15 (50/50%)	14/16 (46.7/53.3%)	0.733
Weight (kg)	70.7± 6.56 (55-83)	71.4±5.64 (62-81)	70.8±5.80 (60-81)	0.885
Height (cm)	163.5±4.40 (156-172),	164.3±3.98 (158-175)	P800 163.9±3.73 (158-171)	0.748

Table 2: Distribution of patients as per ASA status.

Group	ASA I		ASA II		P value
	No.	%	No.	%	
P400	23	76.7	7	23.3	
P600	26	86.7	4	13.3	0.587
P800	25	83.3	5	16.7	

Table 3: Mean dose of propofol used for induction (mg/kg) among different groups.

Groups	Mean	SD	Range	Comparison	P value
P400	2.25	0.246	1.9-2.9	P400 vs. P600	<0.001
P600	2.71	0.285	2.3-3.4	P600 vs. P800	<0.001
P800	2.98	0.277	2.6-3.5	P800 vs. P400	0.005

Table 4: Comparison based on induction time (seconds) among different groups.

Groups	Mean	SD	Range	Comparison	P value
P400	180.9	8.78	161-199	P400 vs. P600	<0.001*
P600	166.7	5.53	154-175	P600 vs. P800	<0.001*
P800	129.3	4.13	121-139	P800 vs. P400	<0.001*

Table 5: Comparison of systolic blood pressure (mmHg) changes (pre and post induction) among different groups.

Groups	Pre induction		Post induction		Diff. in SBP	P value (ANOVA)
	Mean	SD	Mean	SD		
P400	123.3	6.19	110.8	4.92	12.5	
P600	122.6	4.39	105.7	4.35	16.9*	<0.001
P800	122.4	4.34	102.3	3.64	20.1**	

Table 6: Comparison of diastolic blood pressure (mmhg) changes (pre and post induction) among different groups.

Group	Pre induction		Post induction		Diff. in DBP	P value (ANOVA)
	Mean	SD	Mean	SD		
P400	81.4	4.04	75.4	2.56	6.0	
P600	81.5	3.25	75.2	1.90	6.3	0.785#
P800	80.9	3.14	74.0	2.54	6.9	

Table 7: Comparison of mean arterial pressure (mmHg) changes (pre and post induction) among different groups.

Groups	Pre induction		Post induction		Diff. in MAP	P value (ANOVA)
	Mean	SD	Mean	SD		
P400	95.4	4.67	87.2	3.23	8.2	
P600	95.2	3.58	85.4	2.53	9.8*	<0.001
P800	94.8	3.45	83.4	2.77	11.4**	

Table 8: Comparison of changes in heart rate (beats/min) (pre and post induction) among different groups.

Groups	Pre induction		Post induction		Diff. in HR	P-value (ANOVA)
	Mean	SD	Mean	SD		
P400	87.8	4.12	83.6	4.25	4.2	
P600	88.2	3.48	83.8	3.65	4.4	0.878#
P800	88.9	4.27	84.6	4.3	4.3	

Table 9: Comparison of changes in SpO2 (pre and post induction) among different groups.

Groups	Pre induction		Post induction		Diff. in HR	P-value (ANOVA)
	Mean	SD	Mean	SD		
P400	99.3	0.94	98.3	1.18	1.0	
P600	98.8	1.13	98	1.65	0.8	0.785#
P800	99.1	0.94	98.2	1.04	0.9	

In our study the mean dose of propofol used (mg) for induction among the studied groups was 2.25±0.246 in P400 (range 1.9-2.9) p<0.001, 2.71±2.285 in P600 with (range 2.3-3.4) p<0.001, and in group P800 the mean dosage was 2.98±0.277 with a range of 2.6-3.5, p=0.005, which was statistically significant, as shown in Table 3. In our study the mean induction time (seconds) among the studied groups was 180.9+8.78in P400 (range 161-199) p<0.001, 166.7±5.53 in P600 with (range 154-175), p<0.001 and in group P800 the mean time was 129.3±4.13 with a range of 121-139 P<0.1. The difference was statistically significant as shown in Table 4.In our study the mean systolic blood pressure (mmHg) pre and post induction was 123±6.19 and 110.8±4.92 in 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 difference was statistically significant with a p<0.05, as shown in Table 5. 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 i 80.9±3.14 and 74.0±2.54 in group P800 respectively. The difference was statistically insignificant with a p>0.05 as shown in Table 6.

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 i 94.8±3.45 and 83.4±2.77 in group P800 respectively. The difference was statistically significant with a p<0.05 as shown in Table 7. 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 as shown in Table 8. 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 as shown in Table 9.

DISCUSSION

The best and ideal method for induction of anesthesia is by injecting an anesthetic agent intravenously. Many drugs have been used for this purpose. In the recent past propofol has been largely been used because of certain advantages over the other drug. Amongst them is rapid recovery from anesthesia and lesser incidence of nausea and vomiting in the postoperative period, but one of the disadvantages of propofol is significant hypotension. A typical induction dose of propofol 2 mg/kg results in approximately 30% reduction in systolic blood pressure.[1] The mechanism of hypotension is attributed to a decrease in sympathetic activity, myocardial depression and direct vasodilation.[1,2,6,16] Hypotensive effects of propofol are generally proportional to the dose and rate of administration.[6-8] Induction with propofol is known to cause decrease in blood pressure. Studies have demonstrated up to a 28% decrease in SBP, an 11% decrease in MAP, and a 19% decrease in DBP.[6,17] When propofol is administered as a 2 mg/kg IV bolus (PG), SBP decreased by 20%. There was also a decrease in DBP and MAP by 16% and 19%. Due to the inhibitory effect of propofol on baroreflexes and sympathetic activity, the effect of propofol on heart rate is variable with many studies showing decrease in heart rate.[18,19] The objective in the present study was to investigate the effect of injection speed of propofol for induction of anesthesia primarily on blood pressure and secondarily on time and dose of anesthesia. Age wise distribution of patients in our study was not statistically significant P=0.843. Similarly male and female ratio in our study was not significant p=0.733, as shown in Table 1. Sennur et al in their study of 72 patients have similar results.[20] In our study group, the mean weight of the patients was comparable among all the three groups as the difference was statistically insignificant (p=0,885). Mean weight in group P400 being 70.7±6.56kg (range 55-83), group P600 being 71.4±5.64kgs (range 62-81) and group P800 70.8±5.80kg (range 60-81). Sennur et al in their study of

72 patients, the mean weight were 70.7±14.4 in p200, 77.5±14.2 in p300 and 75.3±17.6 in p400. In our study group, the mean height of the patients was comparable among all the three groups as the difference was statistically insignificant (p=0.748). Mean height in group P400 being 163.5±4.40cm (range 156-172), group P600 being 164.3±3.98cms (range 158-175) and group P800 163.9±3.73cms (range 158-171). Sennur et al in their study of 72 patients, the mean height was 165±9 in p200, 169±11 in p300 and168±10 in p400.[20] In our study group, the patients were distributed as per ASA status with 23 (76.7%) patients of group P400 in ASA I and 7 (23.3%) in ASA II. In group P600, 26 (86.7%) were in ASAI and 4 (13.3%) were in ASA II and in group P800 25 (83.3%) patients were in ASA I and 5 (16.7%) patients were in ASA II. No statistical significant difference was found between three groups p=0.587. This shows close resemblance with Kazama.[2] In our study, patients were divided into 3 groups with 30 patients in each group according to different propofol infusion speeds used before induction of general anesthesia. Propofol was given in the form of infusion with the help of infusion pumps, at three different rates of 400 ml/hr, 600 ml/hr and 800 ml/hr to each group respectively. Monitoring of unconsciousness was done using entropy. In our study 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 1.9-2.9 mg/kg) p<0.001, 2.71±2.285 mg/kg in P600 with (range 2.3-3.4 mg/kg) p<0.001, and in group P800 the mean dosage was 2.98±0.277 mg/kg with a range of 2.6-3.5 mg/kg p=0.005. The difference was statistically significant, p<0.05. Our study shows close resemblance with the study conduct by Peacock, by Stokes and Sennur et al.[20-22] In our study 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. Similar results found by the study conducted by, Rolly, et al 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.[11] Anesthesia 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 in their study, propofol was administered at 300, 600 or 1200 ml h-1 until loss of consciousness.[21] 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 et al in their study of 72 patients, the induction time was 177±38s in p200, 182±58s in p300 and134±38 in p400. 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.[20] The group difference was statistically significant with a p<0.05. Thus mean systolic pressure was reduced as rate of infusion increases from 400 ml/hr to 600 ml/hr to 800 ml/hr. Rolly 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.[11] 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 et al in their study, propofol was administered at 300, 600 or 1200 ml h-1 until loss of consciousness.[21] 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).[22] Stokes 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 et al in their study of 72 patients observed a decrease in systolic and mean blood pressure with infusion rate of 200 ml/h, 300 ml/hand 400 ml/h.[20] 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 et al 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, 2 and 3 respectively.[11] Peacock et al in their study, propofol was administered at 300, 600 or 1200 ml h-1 until loss of consciousness.[21] 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 et al 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.[22] 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 et al in their study, mean arterial pressure decreased to the same extent in all three groups.[11] 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 et al 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.[11] The difference was statistically insignificant p>0.05. Thus infusion rate has less effect on oxygen saturation. Rolly et al 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.[11] Peacock in their study, the incidence of apnoea was also significantly less in the slower infusion group.[21]

CONCLUSION

We concluded that induction dose required for loss of consciousness increased with a faster rate of infusion while time for induction was shorter in P800 compared to P400 and P600, and the decrease in mean blood pressure was less after induction in P400. Propofol injection should be slow enough to prevent any hemodynamic deterioration in anesthesia induction

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