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Original research article

Effect of using priming principle on the induction dose requirements of propofol: A randomized controlled trial

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Abstract

Propofol is a costly drug and one of the most prominent effect of Propofol is a decrease in arterial blood pressure during induction of anesthesia. So a reduction in dose requirements may reduce the haemodynamic perturbations and can improve the cost effectiveness of the drug. All the patients included in the study underwent a detailed pre-anaesthetic checkup. Patients and nearest relatives were given a consent form and written informed consent was taken. Age and weight were noted. Pulse rate, blood pressure, respiratory rate, relevant clinical signs if any were recorded. Pre-operative baseline values of heart rate and blood pressure were an average of two consecutive readings taken at least 10 minutes apart 30 minutes before the surgery. Patients were allocated randomly. In our study the demographic data were comparable for age, weight and sex in both groups. Mean induction dose of Propofol was compared in group I (control) compared to group II (test) patients. We observed a reduction in induction dose requirement of Propofol by applying the priming principle.

Keywords: Priming principle, Induction dose, propofol

Introduction

Induction with Propofol is smoother, more rapid, has rapid awakening and orientation times [1]. Propofol is a costly drug and one of the most prominent effect of Propofol is a decrease in arterial blood pressure during induction of anesthesia. So a reduction in dose requirements may reduce the haemodynamic perturbations and can improve the cost effectiveness of the drug [2].

The decrease in systemic pressure after an induction dose of Propofol is primarily due to vasodilation. Clinically, the myocardial depressant effect and the vasodilation seem to be dose dependent and plasma concentration dependent. Independent of the presence of cardiovascular disease, an induction dose of 2 to 2.5 mg/kg produces a 25% to 40% reduction in systolic blood pressure, a 15% decrease in cardiac output and a 15% to 25% reduction in systemic vascular resistance [3, 4].

Methodology

Design

Randomized Controlled Trial

Setting

Study was conducted in Department of Anaesthesiology

Study Subjects

ASA I and II patients, of either sex, between 18-55 years, scheduled for elective surgeries under general anaesthesia

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Sample Size

60 patients belonging to the American Society of Anesthesiology (ASA)physical status classification class I & II, of either sex, between 18-55 years, scheduled for elective surgeries under general anesthesia in Sree Gokulam Medical College were divided into two groups each consisting of 30 patients. Patients were allocated randomly using envelope randomization. With available data [5, 6], sample size was calculated using the formula

$n = 2 \times \sigma^2 (Z\alpha - Z\beta)^2 / \delta^2$

α was taken as 0.01

β was taken as 0.05

σ = pooled standard deviation

δ = effect size

n is found out to be 20. To increase the accuracy of study n is taken as 30. So the final sample size (n) of each group is 30.

Inclusion criteria

ASA-I or ASA-II patients in the age group 18-55 years of age posted for elective surgeries under general anaesthesia.

Exclusion criteria

- Patient refusal.
- Pregnant and lactating women.
- Patients allergic to study medications.
- Patients with uncorrected hypotension.
- Patients with valvular heart disease.

Methodology

All the patients included in the study underwent a detailed pre-anaesthetic checkup. Patients and nearest relatives were given a consent form and written informed consent was taken. Age and weight were noted. Pulse rate, blood pressure, respiratory rate, relevant clinical signs if any were recorded. Pre-operative baseline values of heart rate and blood pressure were an average of two consecutive readings taken at least 10 minutes apart 30 minutes before the surgery. Patients were allocated randomly.

Group I: Patients who were not given priming dose.

Group II: Patients who were given priming dose.

Premedication

The patients were asked to keep nil orally for 8 hours prior to the procedure. All were given Tab. Alprazolam 0.25 mg PO and Tab. Ranitidine 150 mg on the preoperative day at night and on the morning of surgery.

On the morning of surgery after securing intravenous access Inj. Glycopyrrolate 0.004 mg. per kg., Inj. Midazolam 0.02 mg. per kg and Inj. Ondansetron 4mg, were given 15 minutes prior to induction.

Monitors

ECG, Pulse Oximeter, Non-invasive blood pressure monitor, End-tidal CO_2 monitor.

Procedure

Patients in group I were given Fentanyl 1 micro gm per kg intravenously, administered over a period of 30 seconds. Then they were induced with calculated dose of Propofol 2mg/kg, 30 seconds after the administration of Fentanyl. The end point of induction is the loss of verbal response.

Patients in group II were given 1 microgram /kg of Fentanyl intravenously over 30 seconds and then administered 30% of the total calculated dose of Propofol, 2 mg per kg. This was done 30 seconds after the administration of Fentanyl. This was followed by the administration of the remaining calculated dose after 30 seconds till the loss of verbal response. Speed of injection of Propofol was at the rate of 30 mg per 10 seconds.

Subsequent muscle relaxation and intubation was accomplished with Suxamethonium 2 mg per kg IV and anesthesia was maintained with N_2O and O_2 and Sevoflurane and injection Vecuronium was used as the muscle relaxant intra operatively. No surgical stimulus was applied for the first 5 minutes.

The following parameters were recorded.

1. Total dose of Propofol including the priming dose.
2. Pulse rate and arterial blood pressure by auscultatory method just before induction, after induction, immediately after intubation and 5 minutes after induction.

Results

The mean induction dose of Propofol is 135.3 mg in group I (control) compared to 92.7 mg in group II (test) as shown in table (p-value < 0.01). Hence there is significant reduction in dose requirement in

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Group II, compared to Group I.

Table 1: Comparison of dose based on group

Group	Mean	SD	N	T	p
Control	135.3	20.5	30	8.31**	0.000
Study	92.7	19.3	30		

**: - Significant at 0.01 level, *: - Significant at 0.05 level

Comparison of haemodynamic parameters

The haemodynamic parameters are compared at the time of just before induction, after induction, immediately after intubation and five minutes after induction.

Comparison of effect on heart rate

Table 2: Comparison of Heart Rate based on Groups

		Mean	SD	N	t	p
Baseline	Control	74.7	10.2	30	0.59	0.559
	Study	73.0	11.7	30		
Before induction	Control	75.3	9.1	30	0.24	0.811
	Study	74.6	11.1	30		
After induction	Control	69.1	10.3	30	0.63	0.533
	Study	70.6	8.6	30		
After intubation	Control	87.7	7.2	30	0.10	0.918
	Study	87.9	7.8	30		
5 Min After induction	Control	69.1	8.4	30	0.66	0.514
	Study	70.6	8.9	30		

Significant at 0.01 levels

There is no significant difference in the base line heart rate values in both groups. The changes in heart rate are not statistically significant in both groups during the time of before induction, after induction, after intubation and 5 minutes after induction.

Comparison of effect on systolic blood pressure

There is no statistical difference in the baseline systolic blood pressure and systolic blood pressure before induction in both groups (P>0.05). Statistically significant reduction in systolic blood pressure occurred in group I patients during the time of after induction, after intubation, and 5 minutes after induction, p-value <0.05.

Table 3: Comparison of Systolic Blood Pressure based on Groups

		Mean	SD	N	t	p
Baseline	Control	118.8	10.4	30	0.46	0.647
	Study	117.6	9.8	30		
Before induction	Control	118.9	7.5	30	0.31	0.756
	Study	118.3	8.2	30		
After induction	Control	90.6	7.5	30	8.54**	0.000
	Study	106.2	6.5	30		
After intubation	Control	125.6	8.4	30	2.99**	0.004
	Study	133.7	12.3	30		
5 Min After induction	Control	109.7	6.4	30	2.45*	0.017
	Study	114.0	7.1	30		

**: - Significant at 0.01 level, *: - Significant at 0.05 level

Table 4: Comparison of diastolic blood pressure based on groups

		Mean	SD	N	t	p
Baseline	Control	75.1	7.2	30	0.64	0.522
	Study	76.3	7.3	30		
Before induction	Control	75.9	7.1	30	0.07	0.941
	Study	75.7	6.7	30		
After induction	Control	60.8	5.4	30	4.79**	0.000
	Study	66.9	4.5	30		
After intubation	Control	81.7	7.9	30	2.77**	0.008
	Study	87.3	7.7	30		
5 Min After induction	Control	69.4	5.2	30	1.58	0.120
	Study	71.7	5.9	30		

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**: - Significant at 0.01 level

The diastolic BP is low in Group I compared to Group II after induction and after intubation and is statistically significant.

Table 5: Comparison of Mean Blood Pressure based on Groups

		Mean	SD	N	t	p
Baseline	Control	89.6	7.8	30	0.21	0.833
	Study	90.1	7.8	30		
Before induction	Control	90.4	6.4	30	0.27	0.791
	Study	90.0	6.8	30		
After induction	Control	70.9	5.6	30	6.69**	0.000
	Study	80.0	4.9	30		
After intubation	Control	96.4	7.6	30	2.98**	0.004
	Study	102.8	9.0	30		
5 Min After induction	Control	82.9	5.1	30	2.10*	0.040
	Study	85.8	5.7	30		

**: - Significant at 0.01 level, *: - Significant at 0.05 level

The mean arterial pressure is low in group I compared to group II after induction, after intubation and 5 minutes after induction and is statistically significant.

Discussion

Induction of anaesthesia is one of the important events in the conduct of general anaesthesia. Propofol is now the commonest induction agent used in anesthesia. Methods which can decrease the dose requirements of the drug may be helpful in reducing the side effects and also the cost. Application of priming is a well-established technique with the use of non-depolarizing muscle relaxants where in priming shortens the onset of neuromuscular blockade and provides better intubating conditions. A similar priming technique was applied to the induction dose of Propofol earlier by Maroof, *et al.* but in a smaller group of patients.

In our study we evaluated whether priming technique applied for induction dose of Propofol would affect the total induction dose requirement of Propofol and thereby reduce the associated haemodynamic changes.

In our study the demographic data were comparable for age, weight and sex in both groups.

Mean induction dose of Propofol was compared in group I (control) compared to group II (test) patients. We observed a reduction in induction dose requirement of Propofol by applying the priming principle.

The reduction in the induction dose requirement was more than that observed by Maroof *et al.* (21.4%) [5], Anil Kumar, Kotur *et al.* (27.48%) [6] but less than Naphade *et al.* (35%) [7]. The reduction in the induction dose observed by the use of priming dose of Propofol could be attributed to the anxiolysis, sedation and amnesia produced by Propofol at sub hypnotic doses. Prior administration of sub-hypnotic doses of Propofol produces anxiolysis, thereby reducing the associated sympathetic drive and thus reducing the induction dose required to produce hypnosis.

We also evaluated, whether applying priming technique would affect the associated haemodynamic parameters. In this study, there were no significant changes in the heart rate at various time intervals in both groups. The effect of Propofol on heart rate is influenced by various factors including the extent of hypotension, the ability of the patient to compensate and the use of any other concomitant drugs. An increase in heart rate is seen in certain studies while in others the heart rate remained unchanged or decreased. As already mentioned, the myocardial depressant effect and the vasodilation noted with use of Propofol seem to be dose dependent. So an increase in the induction dose may decrease the systemic pressure to a greater extent and this may influence the heart rate also. Another reason for the tachycardia can be an initial, transient vagolysis.

Pensado *et al.* [8] and Caleys *et al.* [9] have observed that there was no associated changes in heart-rate following induction with 2 mg per kg of Propofol. They attributed it to the concurrent use of N_2O during induction. In our study no N_2O was used and this factor also may explain tachycardia. In our study the change in heart rates between the groups were not statistically significant.

Mean systolic blood pressure and mean arterial pressure was higher in group II during after induction, after intubation and 5 minutes after induction and is statistically significant confirming the haemodynamic side effects were dose dependent as stated by Pauline *et al.* and Major *et al*. With an increase in the induction dose of Propofol from 1.5 mgkg-1 to 2.5 mgkg-1 the mean arterial pressure was lowest when 2.5 mgkg-1 of Propofol was used in the study by Major *et al.* [10].

Thus we observed a significant reduction in dose requirement and minimal peri-intubation blood pressure alterations with the use of priming technique.

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Conclusion

Based on the results obtained in this study, it can be concluded that the administration of a priming dose of Propofol for induction reduces the induction dose requirement and hence the associated blood pressure variations. Hence priming with Propofol is an effective method to reduce the dose requirement, when used in induction of general anaesthesia.

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