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Research Article

Effect of priming principle on the induction dose requirements of propofol in patients undergoing elective surgeries under general anaesthesia

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ABSTRACT

Background: A major disadvantage of rapid induction with propofol is hypotension at a dose of 2 mg/kg. Priming principle is an effective technique to reduce the total induction dose of propofol. The hemodynamic changes are attenuated and the cost is reduced. The frequency and severity of dose related effects also falls.
Methods: This study of 100 patients was a prospective randomized controlled study. Patients were randomly divided into two groups of 50 each. The control group received 2mg/kg IV propofol till loss of eyelash reflex. The study or priming group received 30% of the calculated dose followed by the remaining dose after 30 seconds. The total induction dose and hemodynamic parameters were recorded. Incidence of apnoea and fasciculations as well as pain on injection were noted. Analysis of demographic data was done using chi-square test. Comparison between the groups for induction dose and hemodynamic parameters was done using the student 't' test. A p-value of <0.05 was considered statistically significant.
Results: The mean induction dose was significantly lower in the study or priming group. The difference in the heart rate was not significant except at 5 minutes after induction. Systolic, diastolic and mean blood pressure was significantly higher in the study group at all times. The incidence of apnoea was greater in the control group while fasciculations were more frequent in the priming group.
Conclusions: Priming principle can be effectively applied to propofol to reduce the total induction dose with concomitant attenuation of hypotension. The only disadvantage noted was that fasciculations due to scoline were more pronounced.

Keywords: Priming, Propofol, Hypotension

INTRODUCTION

Intravenous induction agents tend to be potent drugs with significant hemodynamic alterations. Propofol is the most popular at present as induction is rapid and smooth with quick recovery. It provides good intubating conditions and maintains upper airway integrity. However a major disadvantage of rapid induction with propofol is hypotension at a dose of 2 mg/kg. Various methods have been tried to reduce the induction dose like concurrent use of opioids, barbiturates, and benzodiapines. Priming principle is an effective technique. It refers to the administration of a subanaesthetic dose of an agent prior to its actual anaesthetic dose.

This technique has been widely used for non-depolarizing muscle relaxants so that the sum of the priming and intubation doses is smaller than the conventional dose. If total induction dose of propofol is reduced the hemodynamic changes are attenuated and the cost is reduced. The frequency and severity of dose related effects also falls. An initial small dose can also reveal idiopathic sensitivity to the agent preventing further injection. In our study, 30% of the calculated induction dose of 2 mg/kg was used as a priming dose and after 30 seconds the remaining dose of propofol was given till loss of eyelash reflex.

The objective of the study was to evaluate whether priming principle applied to the induction dose of propofol reduces the total dose requirements and to evaluate whether priming principle applied to the induction dose of propofol reduces the associated hemodynamic changes.

METHODS

Institutional ethics committee clearance was obtained. After taking written informed consent 100 patients of ASA I and 2 were enrolled. The patients were between 18 to 55 years of age.

They were scheduled for elective surgery under general anaesthesia. They were randomly allocated to two groups of 50 each. One group was the control while the other was the study group. Preoperative evaluation was done as per departmental protocol. All patients were premedicated with midazolam 0.03 mg/kg IV 15 minutes prior to induction. Baseline values of heart rate and blood pressure were noted. Patients in control goup were induced with 2 mg/kg of propofol. Patients in the study group were given 30% of the calculated dose of propofol and the remaining propofol after 30 seconds till loss of eyelash reflex. Subsequent intubation was achieved with scoline and anaesthesia was maintained with oxygen and nitrous oxide. Relaxation was maintained with vecuronium. No surgical stimulus was applied during the next 5 minutes after induction. Any complications during this period like apnoea, vomiting, involuntary movements laryngospasm and coughing were noted.

The following parameters were recorded just before induction, one minute after induction, immediately after intubation and five minutes after induction.

- Heart rate
- Systolic blood pressure
- Diastolic blood pressure
- Mean blood pressure
- Oxygen saturation.

All patients were observed for 24 hours after surgery.

Exclusion criteria

- Patients of ASA status 3 or 4.
- Patients with known allergy to propofol or egg or egg protein.
- Pregnant or lactating women.
- Patients with disorder of involuntary movements.

Statistical analysis

Sample size for our study was based on assuming a power of 80 % and a value of 0.05 as significant using the numerical testing. A sample size of 50 patients in each group was chosen.

Analysis of demographic data was done using chi-square test. Comparison between the groups for induction dose and hemodynamic parameters was done using the student 't' test. A p-value of <0.05 was considered statistically significant.

RESULTS

Demographic data was comparable for age, weight and gender in both the groups. The mean induction dose was significantly lower in the study group (58.44 mg) as compared to the control group (96.20 mg). The difference in the heart rate was significantly lower in the control group only at 5 minutes after induction. Systolic, diastolic and mean blood pressure was significantly higher in the study group at one minute, immediately after intubation and five minutes after induction. This indicates that the lower dose in the study group led to lesser hypotension. Incidence of clinically significant apnoea (>30 seconds) was observed in 8 % of patients in the control group but only in 2% of patients in the study group.

Table 1: Mean induction dose of propofol.

Group	Mean induction dose	P-value
Control	96.20±14.05	
Study	58.44±11.98	0.0000

The mean induction dose in priming group was significantly lower.

Table 2: Comparison of changes in heart rate.

Heart rate	Group1	Group 2	P-value
	Mean±sd	Mean ± sd	
Preinduction	84.66±10.41	87.08±11.48	0.272
1 min after induction	91.78±10.90	93.42±11.64	0.496
After intubation	98.02±11.64	100.24±11.37	0.311
5 min after induction	83.58±10.12	88.00±11.71	*0.046

p <0.05 significant. The difference in heart rate was significant only 5 minutes after induction.

Table 3: Comparison of changes in SBP.

SBP	Group 1	Group 2	P-value
	Mean±sd	Mean±sd	
Preinduction	113.44±8.16	116.88±7.50	0.031
1 min after induction	101.84±6.60	112.76±0.51	*0.000
After intubation	116.40±9.80	123.72±0.07	*0.000
5 min after induction	103.04±6.36	116.48±7.93	*0.000

The incidence of apnoea seems to be related to a higher dose of propofol. Fasciculations were observed in 10% of patients in the study group but only in 2% of patients in the control group. The incidence of fasciculations seems to be related to a lower dose of propofol.

Table 4: Comparison of changes in DBP.

DBP	Group 1	Group 2	P-value
	Mean±sd	Mean±sd	
Preinduction	75.64±6.15	78.20±7.19	0.059
1 min after induction	67.60±5.03	76.48±.10	*0.000
After intubation	78.60±7.25	83.96±.29	*0.002
5 min after induction	68.64±4.30	78.52±7.11	*0.000

P < 0.05 significant. The DBP was significantly higher in group 2 at 1 minute after induction, immediately after intubation and 5 minutes after induction.

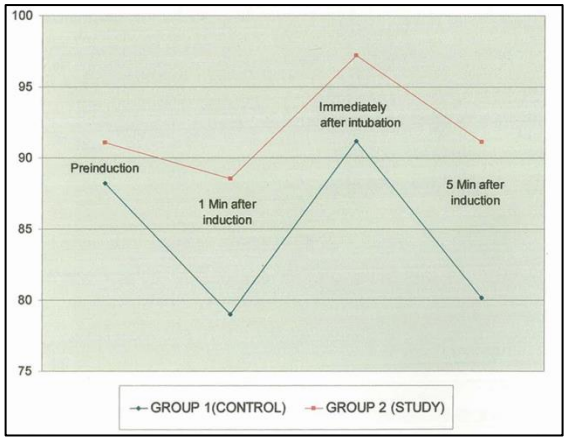

Figure 1: Comparison of changes in mean arterial pressure (mmHg).

Table 5: Comparison of changes in MAP.

MAP	Group 1	Group2	P-value
	Mean±sd	Mean±sd	
Preinduction	88.24±6.28	91.09±6.64	*0.030
1 min after induction	79.01±4.98	88.57±7.33	*0.000
After intubation	91.20±7.66	97.21±8.54	*0.000
5 min after induction	80.19±4.38	91.17±6.71	*0.000

P <0.05 significant. The map was significantly higher in group 2 at i minute after induction, immediately after intubation and 5 minutes after induction.

Table 6: Complications.

Group	N	Complications	%	Apnoea	Hypotension	Pain	Fasciculations
Group 1 (Control)	50	11	22	4 (8%)	3 (6%)	3 (6%)	1 (2%)
Group 2 (Priming)	50	9	18	1 (2%)	1 (2%)	2 (4%)	5 (10%)

DISCUSSION

The principle of priming in relation to neuromuscular blockade has been extensively studied and reported.[1] A large proportion of acetylcholine receptors must be occupied by a non-depolarizing muscle relaxant before blockade can be detected. Thus, the onset of neuromuscular blockade consists of two steps:

- Binding of the 'spare' receptors during which no effect is observed and
- Deepening of the block

Thus the onset time is reduced if the first of these processes is completed before induction by a small 'priming' dose.

The application of this priming principle to the use of propofol either as an induction agent or as an infusion for ICU sedation has a few distinct advantages. First, the total dose of propofol required for induction is significantly lesser and the cost therefore lower. Secondly the pain on injection appears to diminish considerably, allowing it to be used as an infusion in the postoperative or ICU setting. The hemodynamic changes are also less pronounced. However, if scoline is used for intubation the fasciculations due to scoline tend to be more pronounced with the lower dose of propofol.

Total induction dose

In the present study we have tried to evaluate if the priming principle applied to the induction dose of propofol reduces the total dose requirement and

attenuates the peri-intubation hemodynamic changes. 50 patients in control group received a calculated 2 mg/kg of propofol while 50 patients in the study (priming) group received 30 % of the calculated dose as a priming dose followed by the remaining dose 30 seconds later till loss of eyelash reflex. The demographic parameters were comparable in both the groups.

The mean induction dose required in the priming group was significantly lower (58.44 mg) than in the control group (96.20 mg). This was a difference of more than 30%.

Maroof et al studied the priming principle as applied to propofol.[2] They used 20% of the calculated 2 mg/kg dose for priming. They concluded that priming facilitated a reduction of the total induction dose required. However they did not find any significant difference in the periintubation hemodynamic changes. Also, recall phenomenon was absent in both the groups.

Kumar A et al studied the effect of priming as applied to propofol. They concluded that a priming dose of 20% of calculated dose reduced the total dose by 27%.[3] The reduction in the total induction dose in our study was greater as we used a 30% of the calculated dose for priming.

Hemodynamic parameters

In our study there was an increase in heart rate in both the groups after administration of propofol. This was related to the higher dose of propofol in the control group. There was an increase in the heart rate in both the groups after induction and immediately after intubation.

But five minutes after induction there was a fall in heart rate in both the groups with a greater fall in the control group due to the higher dose of propofol. Overall the heart rate was better maintained in the priming group as compared to the control group and the difference was statistically significant at five minutes after induction.

Propofol is known to have a biphasic effect on the cardiovascular system. Firstly, immediately after injection, a decrease in the systemic vascular resistance and mean arterial pressure predominate. This decrease in the SVR causes a reflex increase in the sympathetic activity which is mediated by the baroreceptors in the carotid sinus and aortic arch, thereby leading to tachycardia.[4]

In our study at one minute after induction we observed a greater fall in the systolic blood pressure in the control group due to the higher dose of propofol. The SBP rose in both the groups after intubation and five minutes after induction. The mean SBP was significantly higher in the priming group due to a lower dose of propofol. Pauline et al studied the effect of propofol anaesthesia on baroreceptor reflex activity in humans and concluded that the hemodynamic side effects are dose dependent.[5]

A similar variation was observed with diastolic blood pressure. The mean DBP was significantly higher in the priming group at one minute after induction and immediately after intubation and five minutes after induction. Mean blood pressure showed a greater variation in the control group due to the higher dose.

There was a lesser deviation from the mean values of heart rate and blood pressure in the priming group leading to greater hemodynamic stability. Pensado A et al in their study of hemodynamic effects of propofol during coronary artery bypass surgery concluded that propofol reduces systemic arterial pressure by a decrease in SVR but not in cardiac output or ventricular filling pressures.[6] The mechanism by which priming lowers the total dose offers interesting possibilities. At a molecular level interaction between the ligand and the receptor causes a change in the conformation of the receptor to an active state. The ligand energetically favours the activated state. The probability of being in an active state increases in the presence of an agonist, in this case, the priming dose of propofol potentiates GABA mediated effects of inhibition at spinal and supraspinal level. Prior administration of sub hypnotic doses of propofol produces anxiolysis, thereby reducing the associated sympathetic drive and the induction dose to produce hypnosis.[7] Apnoea was noted in 4 patients in the control group as opposed to one in the priming group.

These patients were given IPPV to maintain oxygen saturation. The incidence of pain on injection was similar in both groups, 3 in the control and 2 in the priming group. The incidence of fasciculations due to scoline was greater in the priming group due to the lower dose. Patients who had fasciculations were treated with an analgesic to prevent myalgia.

CONCLUSION

Priming principle can be effectively applied to propofol to reduce the total induction dose. Also, the hypotension is less marked. The heart rate five minutes after induction is significantly higher. The only disadvantage noted was that fasciculations due to scoline were more pronounced.

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