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Use of priming principle in the induction dose requirement of propofol and its hemodynamic stability- A cross sectional study

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ABSTRACT

Background: In anesthesia propofol induction is administered at a dose of 2mg/kg as a single bolus and when given at this dose the commonest problem faced by the anesthetist is the sudden drop in the blood pressure, as the hypotensive effect of propofol is proportional to the dose and rate of administration.

Aim: To study the effect of auto co-induction (priming principle) in the requirement of induction dose of propofol and the resulting hemodynamic parameters.

Materials and Methods: A prospective randomized double blinded study was conducted for a period of one year in the department of anesthesia at a government medical college hospital in TamilNadu. A total of 60 patients were selected for our study and were randomly allocated into two groups of 30 each. Group A is the study group (priming) and group B is the control group (non-priming group). In the priming group, three minutes after premedication the co induction agent was administered (25% of the calculated dose of propofol) and two minutes later the patient received propofol at a rate of 30mg/10 sec until loss of vocalization was achieved. The hemodynamic parameters along with the total dose requirement of propofol and BIS values were monitored at regular intervals after induction.

Results: The mean total dose of propofol required among the priming group patients was 78.2 mg compared to the total dose requirement in the non-priming group which was 92.5 mg and the mean difference was found to be statistically significant. A statistically significant fall in the heart rate and blood pressure was observed at 1 min and 3 mins after induction in non priming group compared to priming group.

Conclusion: By applying priming principle the induction dose of propofol was reduced by 14.25% with a good hemodynamic stability.

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1. Introduction

One of the most crucial events in anesthesiology is induction of anesthesia as it is associated with changes in the hemodynamic system and in the physiology of the other body system. The preferred mode of inducing anesthesia is through intravenous injection. Various drugs have been used for induction having different pharmacokinetic and

dynamic properties.¹ Among most of the drugs propofol is being considered as the most preferred agent for induction because of its smooth induction, rapid awakening and orientation times, providing good intubating conditions like suppressing the upper airway reflexes, clear headed recovery and less incidence of post-operative nausea and vomiting.² In anesthesia propofol induction is administered at a dose of 2mg/kg as a single bolus and when given at this dose the commonest problem faced by the anesthetist is the sudden drop in the blood pressure, as the hypotensive

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effect of propofol is proportional to the dose and rate of administration.^{3,4} Various methods were proposed to alleviate this problem but each had one or the other side effect and finally a method called priming principle was introduced to overcome these problems. In this technique a precalculated dose of the induction agent is given prior to the full calculated dose of the same induction agent and so this technique is also called as auto-coinduction.⁵ This concept of priming principle was very well documented in the use of muscle relaxants in which 10% of the total dose is given 2- 4 minutes prior to the second large dose for tracheal intubation.⁶ The onset of blockade occurs in two steps firstly it binds to the receptors in which no effect is observed and secondly deepening of block occurs. Thus the first process of binding of the receptor occurs by a small priming dose and the priming shortens the onset of neuromuscular blockade and provides better intubating conditions. The same principle when applied to the induction agent, sedative, anxiolytic and amnestic properties can be obtained at sub-hypnotic dosage of the induction agent when given a few minutes prior to induction in the form of priming dose.^{7,8} As not much studies being conducted in using priming principle for induction agent in anesthesia the present study aimed to study the effect of auto co-induction (priming principle) in the requirement of induction dose of propofol and the resulting hemodynamic parameters.

2. Materials and Methods

A prospective randomized double blinded study was conducted for a period of one year in the department of anesthesia at a government medical college hospital in TamilNadu. The study was started after getting approval from the institutional ethical committee. All patients aged between 18 and 60 years with ASA grading I or II and were posted for elective surgeries under general anesthesia were included as our study subjects. Patients who were hemodynamically unstable, posted for emergency procedure, pregnant and lactating mothers and patients who were taking oral benzodiazepines, opioids for other complaints were excluded from the study. A total of 60 patients were selected for our study and were randomly allocated into two groups of 30 each. Group A is the study group (priming) and group B is the control group (non-priming group). Informed consent was obtained from all the study participants. A complete physical and airway examination supported by routine blood investigations along with chest X-ray and ECG was taken as a part of pre-anesthetic examination. All patients were kept on fasting for a period of 8 hours and the pre-anesthetic medications were given on the previous day night before surgery. On the day of surgery the patients were randomly allocated into one of the two groups with randomization being done using a sealed envelope technique. On the surgical table all patients

were premedicated with Inj. Glycopyrolate 0.04 mg/kg IV, Inj. Fentanyl 2mic/kg IV were given 3 minutes prior to induction. The co-induction agent (Propofol in priming group and saline in non-priming group) was prepared in a 5 ml syringe by a separate anaesthesiologist who was not a part of the study and the syringe covered by opaque paper wrap. In the priming group, three minutes after premedication the co induction agent was administered (25% of the calculated dose of propofol) and two minutes later the patient received propofol at a rate of 30mg/10 sec until loss of vocalization was achieved. In the non-priming group patients were given saline as priming and 2 minutes later they were induced with the calculated dose of inj. propofol 2 mg/kg at the rate of 30 mg/10 sec until the occurrence of loss of vocalization. Later intubation was done as per the procedure and the maintenance of anesthesia was achieved by O₂ & N₂O with sevoflurane 1% and Inj. Vecuronium Bromide- 0.1 mg/kg as loading dose & then 0.025mg/kg as per the requirement. The hemodynamic parameters along with the total dose requirement of propofol and BIS values at baseline, after premedication, just after priming, at 0 min, 1 min, 3 mins, 5min and 10 minutes after induction in both the groups as the study is taken as complete 10 mins after induction. All data were entered and analysed using SPSS version 24, mean and SD were calculated for all parametric variables and percentage was derived for frequency variables. Statistical inference was obtained using T test between the two groups.

3. Results

This randomized study was conducted on 60 patients with 30 subjects in each group with one group given the priming dose of propofol and the other group without giving the priming dose. Majority of the study subjects were in the age group between 30 and 40 years in both the groups with mean age of 36.8 in priming group and 40.2 years in non-priming group with no statistical significant difference in the age group between the two groups. Similarly gender wise distribution of the study sample shows that almost equal number of males and females among both the groups (Table 1). All the vital parameters such as heart rate, systolic blood pressure, diastolic blood pressure and the mean arterial pressure for the patients in both the groups were measured in the following intervals, at basal, after pre-medication, after priming dose, 1 minute, 3 minutes, 5 minutes and 10 minutes after the priming dose. The mean heart rate was found to be increased in the first and three minutes after giving the priming dose in group A compared to group B (non-priming group) and the difference was found to be statistically significant, whereas from fifth minute the heart rate between the two groups did not show statistically significant difference (Table 2). Similarly systolic and diastolic blood pressure along with the mean arterial pressure were also found to be statistically

significantly high in the first and three minutes after inducing the priming dose in group A patients compared to group B and from 5th minute there was no significant difference found between the two groups (Tables 3, 4 and 5). The bi-spectral index (BIS) was found to be slightly high in group A (priming group) compared to group B (non-priming group) and the significant difference was found at three minutes after the priming dose and from 5th minute onwards there was no statistically significant difference observed between the two groups (Table 6). The mean total dose of propofol required among the priming group patients was 78.2 mg compared to the total dose requirement in the non-priming group which was 92.5 mg and the mean difference was found to be statistically significant and so it was found to be lesser dose of propofol was required among the priming group compared to the non-priming group (Table 4).

4. Discussion

Induction of anaesthesia is one of the most important event in the conduct of general anesthesia as it is generally associated with a wide range of hemodynamic variations. Various induction agents have been used for the inducing anesthesia among which propofol had gained wider acceptance because to its pharmacokinetic profile, but the major disadvantage in it was its wide hemodynamic variations which is mostly dose dependant. So maintaining hemodynamic stability during induction is a challenging task for the anesthetist. To maintain the hemodynamic stability during the induction of propofol various methods were followed such as 1) concurrent use of N₂O, 2) giving Opioids, 3) use of Benzodiazepines like Midazolam, 4) augmentation with local anesthetics or Magnesium sulphate and 5) use of priming principle.^{9–13}

Among all the above mentioned methods we thought using priming principle for inducing propofol would be a better method with less adverse events. So we conducted a randomized double blinded study by applying the priming principle for the induction dose of propofol and monitored the total dosage requirement and the associated hemodynamic changes. We used 25% (0.5 mg/kg) of the calculated dose as the priming dose for propofol, taking a conventional dose of propofol as 2 mg/kg. Most of the previously done studies related to the usage of priming principle for inducing propofol were conducted with concomitant use of other synergistic agents, which would have masked the actual effect of the priming dose method and so in our study we haven't used any synergistic agents.^{14–16}

The demographic data in this study were comparable for age and gender. In this current study we have limited the pre-op fasting period to 8 hours and after which the patient was started on IV fluids – RL @ 100 ml/hour to avoid dehydration due to excessive fasting as because dehydration

would lead to hypotension while inducing anaesthesia with propofol. In our study all patients were premedicated with Inj. Glycopyrrolate 4 mcg/kg 3 minutes prior to the induction for preventing reflex bradycardia caused when propofol is induced and it was similar to the study done by Claeys M A et al but in his study inj. Glycopyrrolate 0.4 mg was given one hour before induction.¹⁷

Total induction dose of propofol was calculated by considering total loss of vocalization as the end point of induction. In the present study we observed the total induction dose required in the non-priming group was 92.5 ± 9.6 and in the priming group it was 78.25 ± 14.98 in which 25% of the dose was used as a priming dose. Hence we observed 14.25% reduction in the mean total induction dose among priming group compared to non-priming group.

Similar to the results of our study a conducted by Karlo et al. in observed 10.23% reduction in the total dose requirement among priming group.¹⁸ Another study done by Kumar A et al in which they used 20% of the calculated dose as priming dose and loss of eyelash reflex was considered as end point for induction and they observed 27.48% reduction in the total induction dose.¹⁹ Similarly studies done by Srivastava U et al and Kataria R et al observed 40% and 31.8% reduction in the total induction dose which was found to be much higher compared to our study as because in those studies synergistic agents like midazolam were used as premedication.^{14,20}

Propofol is known to have biphasic effect on cardiovascular system. Immediately after injecting propofol there is a decrease in systemic vascular resistance and mean arterial pressure and this decrease in SVR causes reflex increase in sympathetic activity mediated by baroreceptors that are present in carotid sinus and aortic arch and thereby causing an increase in heart rate. Later from 2 minutes after injection, despite decreased systemic vascular resistance, the heart rate and stroke volume also tend to decrease which is attributed to “resetting” of baroreceptor reflex.

In our study we observed a statistically significant fall in the heart rate at 1 min and 3 mins after induction in non priming group compared to priming group and later from 5 mins onwards the difference in heart rate between the two groups was not found to be statistically significant and overall when comparing with the mean basal heart rate, more stability of the heart rate was seen in the priming group than in the non priming group and the previously done studies also had quoted a similar type of findings. A similar type of results was also observed for mean blood pressure and mean arterial pressure readings. Studies done by Pauline et al and Pensando et al had reported a similar finding and it was justified quoting it as hemodynamic changes are related to dose dependant.^{21,22}

In the present study we found a significant drop in the BIS (Bi-spectral index) value in post priming period, 77.1 ± 3.68 in priming group when compared to 88.45 ±

Table 1: Age and gender wise distribution of the study subjects

Age group	Group A (n=30)		Group B (n=30)		P value
	Male	Female	Male	Female	
<20	2 (14.2%)	0	2 (13.3%)	0	0.718
20 – 30	5 (35.7%)	4 (25%)	3 (20%)	4 (26.6%)	
31 – 40	4 (28.5%)	8 (50%)	5 (33.3%)	6 (40%)	
41 – 50	3 (21.4%)	1 (6.25%)	3 (20%)	4 (26.6%)	
51 – 60	0	3 (18.7%)	2 (13.3%)	1 (6.6%)	
Total	14 (100%)	16 (100%)	15 (100%)	15	

P value derived using chi-square test

Table 2: Heart rate

Heart Rate	Mean \pm SD		P value
	Priming Group (N=30)	Non Priming Group (N=30)	
Basal	84.75 \pm 15.34	84.75 \pm 9.51	1.000
After premedication	85.65 \pm 13.15	85.1 \pm 16.83	.909
Immediately after priming	83.65 \pm 15.14	81.4 \pm 12.02	.606
1 Minute	88.9 \pm 16.96	77 \pm 12.08	.015
3 Minutes	88.05 \pm 15.76	79.05 \pm 11.13	.044
5 Minutes	87 \pm 15.82	81.55 \pm 9.13	.190
10 Minutes	81.6 \pm 14.32	78.75 \pm 7.47	.435

P value derived using student T test

Table 3: Systolic blood pressure

Systolic blood pressure	Mean \pm SD		P value
	Priming Group (N=30)	Non Priming Group (N=30)	
Basal	121.3 \pm 14.08	127.6 \pm 14.77	.175
After premedication	114.45 \pm 11.34	122.05 \pm 14.68	.075
Immediately after priming	109.4 \pm 12.97	116.5 \pm 11.23	.072
1 Minute	105.05 \pm 13.86	92.8 \pm 9.12	.002
3 Minutes	105.9 \pm 12.39	97.65 \pm 8.93	.021
5 Minutes	102.75 \pm 15.36	103.15 \pm 10.95	.925
10 Minutes	109.1 \pm 14.54	102.95 \pm 9.56	.122

P value derived using student T test

Table 4: Diastolic blood pressure

Diastolic blood pressure	Mean \pm SD		P value
	Priming Group (N=30)	Non Priming Group (N=30)	
Basal	73.65 \pm 8.57	75.65 \pm 10.16	.505
After premedication	83.65 \pm 9.4	76.25 \pm 6.57	.006
Immediately after priming	68.25 \pm 9.37	71.9 \pm 10.22	.246
1 Minute	65.9 \pm 11.12	58.65 \pm 7.79	.022
3 Minutes	66.5 \pm 12.68	59.7 \pm 8.07	.050
5 Minutes	67.3 \pm 10.36	67.75 \pm 6.62	.871
10 Minutes	72.3 \pm 10.68	65.85 \pm 11.22	.070

Diastolic blood pressure

Table 5: Mean arterial pressure

Mean arterial pressure	Mean \pm SD		P value
	Priming Group (N=30)	Non Priming Group (N=30)	
Basal	89.6 \pm 9.67	92.9 \pm 8.75	.265
After premedication	93.8 \pm 9.78	91.6 \pm 8.28	.447
Immediately after priming	81.95 \pm 9.75	86.75 \pm 9.45	.122
1 Minute	78.95 \pm 11.71	70.05 \pm 7.54	.007
3 Minutes	79.6 \pm 12.35	72.4 \pm 7.89	.034
5 Minutes	78.95 \pm 11.31	79.6 \pm 7.36	.831
10 Minutes	84.6 \pm 11.04	78.3 \pm 9.84	.064

P value derived using student T test

Table 6: Comparison of bispectral index (BIS) value between the two study groups

BIS	Mean \pm SD		P value
	Priming Group (N=30)	Non Priming Group (N=30)	
Basal	88.2 \pm 2.86	89.15 \pm 3.15	.324
After premedication	87.1 \pm 3.68	88.45 \pm 2.09	0.219
Immediately after priming	97 \pm 0.86	97.15 \pm 1.18	.649
1 Minute	48.95 \pm 2.76	47.4 \pm 2.76	.084
3 Minutes	49.6 \pm 2.26	47.75 \pm 3.61	.059
5 Minutes	49.9 \pm 2.38	48.95 \pm 1.67	.152
10 Minutes	51.05 \pm 2.42	49.8 \pm 1.77	.069

P value derived using student T test

Table 7: Comparison of total dose of propofol required between the two groups

Study group	Total dose Mean \pm SD	Mean difference	95% CI		P value
			Lower	Upper	
Priming Group	78.25 \pm 14.98	-14.25	-22.32	-6.18	<0.001
Non Priming Group	92.5 \pm 9.67				

P value derived using student T test

2.09 in the non priming group. This evidence supports the proposed mechanism behind the use of priming principle with propofol that the amnestic and sedative property of propofol at sub hypnotic doses facilitates induction of anaesthesia at lower induction dose of propofol, as proven by previous studies.^{18,19,23}

The only adverse event reported in both the group was pain on injection and the incidence was almost similar in both the groups (15%) and a similar type of result was shown in the study done by Rilin Karlo et al. but the cause for the pain remains unknown.²⁴

5. Conclusion

Based on the results from this study it is concluded that application of priming principle to the induction dose of propofol will reduce the total induction dose of propofol by 14.25% and it also provides better stable hemodynamics in the immediate post induction and peri intubation period which is found to be statistically significant.

6. Source of Funding

None.

7. Conflict of Interest

None.

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