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Effect of priming principle on the induction dose requirement of propofol-a randomized clinical trial

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Abstract

Background: Based on well-known properties of propofol over last few years this study was undertaken to evaluate whether priming principle applied for the induction dose of propofol would affect the total induction dose requirement and reduce the associated side effects.

Methods: The prospective randomized study was undertaken in 100 patients allocated randomly by envelop method, between 18-55 years of age of either gender belonging to ASA class I and II scheduled for elective surgeries under general anaesthesia. In group I Inj. fentanyl 2 µg/ kg administered over a period of 30 seconds intravenously and then induced with the calculated dose of Inj. Propofol 2mg/kg until the loss of eyelash reflex. In group II, 30 % of the total calculated dose of Inj. propofol 2mg/kg 30 seconds after the administration of Inj. Fentanyl 2µg/kg over 30 seconds, which will be followed by the administration remaining calculated dose till the loss of eyelash reflex. Statistical analysis of the demographic data was done using chi-square test. Comparison between the groups for the induction dose and haemodynamic parameters was done using student 't' test.

Results: The average induction dose required was 1.53mg/kg with a mean reduction of 23.89%in the induction dose requirement of propofol was observed in the study group. The haemodynamic parameters were better in study group II compared to the control group I.

Conclusion: Based on study result we recommend application of 'priming principle' for induction dose of propofol.

Keywords: Anaesthesia, induction dose, priming principle, propofol

Introduction

Discovery of intravenous anaesthetics has long been important milestone in the development of anaesthesia. Recently propofol has gained popularity as an alternative to other conventional induction agents as induction with propofol provides faster onset of action, antiemesis, rapid recovery, potent attenuation of pharyngeal reflex, laryngeal, tracheal reflexes and adequate depth of anaesthesia during intubation. However major disadvantage of rapid induction with this drug is considerable attenuation in systemic arterial blood pressure.

A decrease of 26-28% in systolic blood pressure and 18-20% in diastolic blood pressure has been observed when patients have been induced with 2 mg/kg of propofol [1,2]. Various methods to reduce the induction dose of propofol are concurrent use of nitrous oxide, opioids, barbiturates like thiopentone, benzodiazepines like midazolam[3-6]. Other agents like clonidine, magnesium sulphate, augmentation with local anaesthetic and use of 'priming principle' have been proposed[7-10].

Priming principle refers to the administration of a sub-anaesthetic dose of an agent prior to its actual anaesthetic dose.Its use is well documented in relation to the use of non-depolarizing muscle relaxants, wherein priming shortens the onset of neuromuscular blockade, provides better intubating conditions and reduces the total required dose of the drug [11]. If 'priming

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principle' achieves the purpose of reducing total dose requirements of propofol, two major benefits that occurs are, the haemodynamic alteration can be attenuated and secondly, the cost of the inducing agent is reduced, considering that propofol is quite expensive. In the present study we applied priming principle for the induction dose of propofol in the study group.

Materials and Methods

The study was carried out at Bidar Institute of Medical Sciences, Bidar Karnataka from July 2021 to Dec 2021. After obtaining institutional ethical committee clearance, the prospective randomized study was undertaken in 100 patients, between 18-55 years of age of both gender belonging to ASA class I and II scheduled for elective surgeries under general anaesthesia. After obtaining written informed consent for participation in the study, patients were allocated randomly by envelope method, using random number table into two groups (1 and 2) of 50 each.

Patient withASA I and ASA II, between the age of 18-55 years of either gender undergoing elective surgeries like laparoscopic cholecystectomy, mastoidectomy, hysterolaparoscopy, fibroadenoma excision, radius ulna fracture, neurosurgical cases etc. under general anaesthesia were included in study.Whilepatient who refuse to participate in study, ASA III and ASA IV patients, patient who are allergic to study medications, pregnant and lactating females, uncontrolled cardiovascular, respiratory, hepatic and renal disease were excluded.

All patients were pre-medicated with Inj. Glycopyrrolate 0.004mg/kg.Ringer lactate infusion was started. Inj. Midazolam 0.03 mg/kg I.V.15 minutes and Inj. Fentanyl 1 μg/kg I.V.30 seconds prior to induction was given.Pre-operative baseline values of blood pressure and heart rate were recorded as an average of two consecutive readings taken at least 10 minutes apart, 30 minutes before the surgical procedure.

Patients were divided into two groups: Group I (Control)-Induced with the calculated dose of Inj. Propofol 2mg/kg until loss of eyelash reflex and Group II (Study)-Patients were to receive 30% of the total calculated dose of Inj. Propofol 2mg/kg. Inj. Propofol (from the remaining calculated dose) till loss of eyelash reflex. The speed of injecting propofol was at the rate of 30 mg/10 sec. Subsequent relaxation and intubation were achieved with Inj. Vecuronium 0.1mg/kg I.V. and anaesthesia was maintained on oxygen and nitrous oxide (50:50) and Inj. Vecuronium was used as a muscle relaxant intra-operatively. No stimulus was applied for initial 5 minutes. Any complications occurred during this period like apnoea, vomiting, involuntary movements, laryngospasm and coughing were noted down. The parameters recorded were total dose of propofol including priming dose (in group II), heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure, just before induction. One minute after induction, immediately after intubation, five minutes after induction.

Statistical analysis of the demographic data was done using chi-square test. Comparison between the groups using student 't' test. A p-value <0.05 was considered significant.

Results

In group I (control) mean age was 39.36 ±13.81, while in group II (study) mean age was 37.84 ± 11.26, which is statistically insignificant ($p > 0.05$).The mean induction dose of propofol was 53.40±11.58 mg in Group I (control) compared to 111.42 ± 24.75 mg in Group II (study) as shown in Table 1.The change in mean heart rate among group I and group II were comparable and the difference was not statistically significant (Fig 1). The mean systolic blood pressure (Fig 2), diastolic blood pressure (Fig 3), (Fig 4) was significantly higher in group II as compare to group I at one minute after induction, immediately after intubation and five minutes after induction. Overall, it observed that 8 (16%) patients in group I and no patients in group II had developed various complications (Table 2).

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Table 1: Mean induction dose

Variable	Group1		Group 2		Unpaired T test	P value
	Mean	Std.Dev.	Mean	Std.Dev.		
Propofol till loss of Eyelash reflex	111.42	24.75	53.40	11.58	15.015	0.000
Total Propofol requirement (mg/Kg)	2.01	0.15	1.53	0.11	18.383	0.000

*p-Significant.

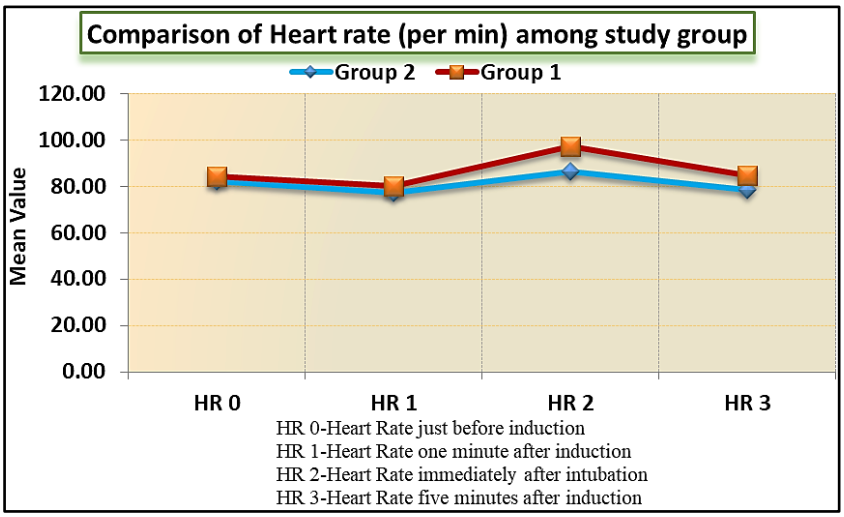

Fig 1: Mean heart rate comparison

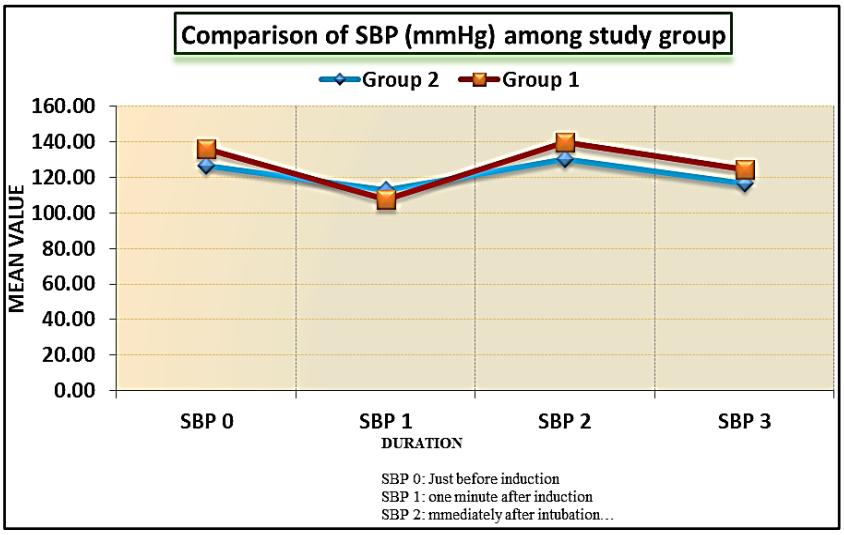

Fig 2: Mean systolic blood pressure (SBP)

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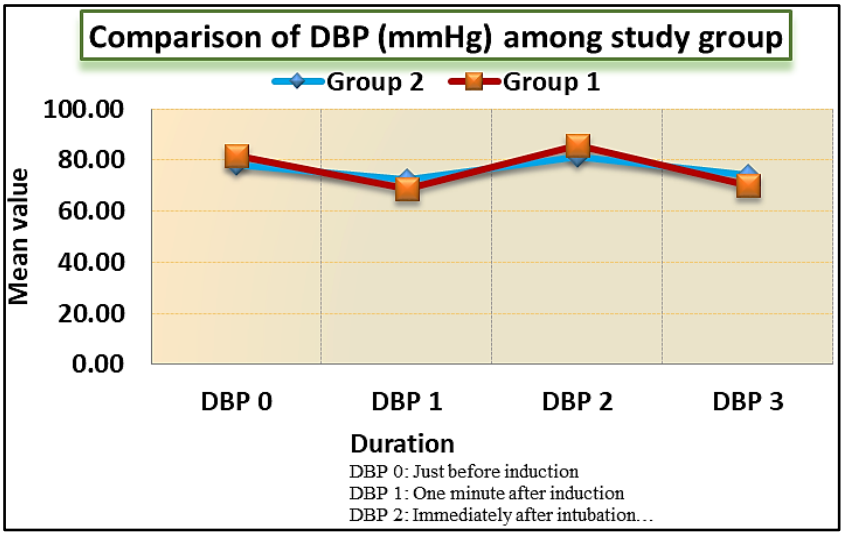

Fig 3: Mean diastolic blood pressure (DBP)

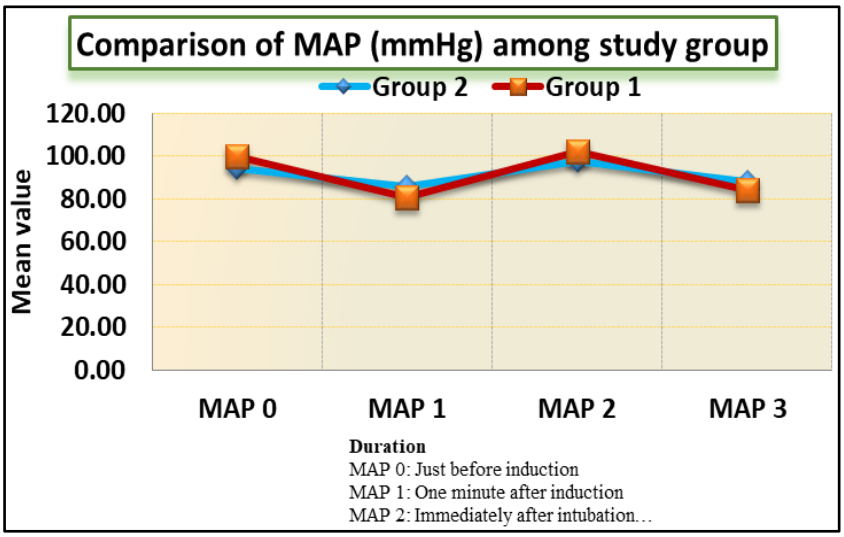

Fig 4: Mean arterial pressure (MAP)

Table 2: Complications

Group		Complications				Total
		Apnea	Hypotension	Pain	None	
Group 1	Count (Percent)	4 (8.0%)	3 (6.0%)	1 (2.0%)	42 (84.0%)	50 (100.0%)
Group 2	Count (Percent)	0 (0.0%)	0 (0.0%)	0 (0.0%)	50 (100.0%)	50 (100.0%)
Total	Count (Percent)	4 (4.0%)	3 (3.0%)	1 (1.0%)	92 (92.0%)	100 (100.0%)
Chi Square Test		**Value**	**df**	**P value**	**Association is**	
Pearson Chi-Square		8.696	3	0.034	Significant	

Discussion

Induction of anaesthesia is one of the important events in the conduct of general anaesthesia. Propofol has got established as an excellent I.V. anaesthetic agent because of its faster onset of action, antiemesis, rapid recovery, potent attenuation of pharyngeal, laryngeal, tracheal reflex, better intubating conditions, adequate depth of anaesthesia during intubation and

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minimal postoperative complications [12]. However, rapid induction with propofol is associated with fall in the blood pressure, which is dose dependent [13]. Hence, a reduction in the induction dose would thereby reduce the associated side effects.

Application of 'Priming Principle' is a well-known fact with use of non-depolarizing muscle relaxants wherein 'priming' shortens the onset of neuromuscular blockade and provides better intubating conditions [11].

The present study was conducted to evaluate whether 'Priming Principle' applied for induction dose of propofol would affect the total induction dose requirements of propofol and thereby reduce the associated haemodynamic changes. The average induction dose required was 1.53mg/kg with a mean reduction of 23.89% in the induction dose requirement of propofol was observed in the study group. The haemodynamic parameters were better in study group II compared to the control group I. Similar results were observed by Djaiani*et al*. who had administered 0.4mg/kg (20%) of induction dose prior to induction with propofol.It has been observed that pre-administration of sub-hypnotic doses of drug propofol produces anxiolysis which reduces the associated sympathetic drive and the induction dose required to produce hypnosis[14].Naphade*et al*. (35%) observed higher reduction in induction dose whereas Maroof*et al*. (21.4%), observed lower reduction in induction dose as compared to our study results [9,10]. The heart rate was better maintained in the study group as compared to the control group as Propofol is known to have a biphasic effect on cardiovascular system. First effect is observed immediately after injection as there is decrease in the systemic vascular resistance and mean arterial pressure predominate in this phase. This decrease in the systemic vascular resistance causes reflex increase in the sympathetic activity, which is mediated by the baroreceptor present in the carotid sinus and aortic arch, thereby causing an increase in the heart rate. Secondly, from 2 minutes after injection, despite less than volume is decreased to less than baseline. This is attributed to 'resetting' of the baroreceptor reflex to a smaller pressure value than normal by propofol[15].The findings did not agree with those observed by Pensado*et al*. and Caleys*et al*. wherein there was no associated change in the heart rate following induction with 2 mg/kg of propofol[1, 2].They attributed it to the concurrent use of nitrous oxide during induction with propofol, which appears to induce marked 'resetting' of the heart rate baroreflex set point to allow lower arterial pressures without inducing tachycardia and myocardial depression pronounced by other medications used in their study. In this study no nitrous oxide was used during induction, which possibly could explain tachycardia. The mean systolic, diastolic blood pressure and arterial pressure were significantly higher in the study group, at one minute after induction, immediately after intubation and five minutes after induction (Fig 2 and 3) confirming that haemodynamic side effects were dose dependent as stated by Pauline *et al*.[13]There was a lesser deviation from the mean value of heart rate, systolic, diastolic and mean blood pressure in the study group as compared to the control group. These deviations in haemodynamic values are statistically significant which suggest the haemodynamic in the study group were better maintained as compared to the control group. The greater haemodynamic variation in the control group might be attributed to the larger total dose of propofol required in this group. Caleys*et al*. in their study of haemodynamic changes due to induction and maintenance with propofol concluded that hypotension was due to a decrease in afterload reduction without compensatory increase in heart rate and cardiac output[2].The incidence of various complications upon induction with propofol was 6% (8 out of 50 patients) in group I and 0% in group II (Table 2). Higher incidence of clinically observed apnea (>30 sec) and hypotension (systolic blood pressure <90 mm of Hg) in group I could be attributed to the cardiorespiratory depressant effects of propofol, which are dose dependent. The lower incidence of pain (2%) on injection of propofol in this study compared to the higher incidence of pain (28%-90%) on injection in other studies, could be attributed to injecting propofol in the large vein in the antecubital fossa and prior administration of 2µg/kg of fentanyl[13].

Conclusion

Based on the study results, we recommend that application of 'priming principle' for induction dose of propofol reduces the induction dose requirements by 23.89%associated with minimal peri intubation haemodynamic alterations.

Conflict of interest: Nil.

Acknowledgment: Nil.

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