International Journal of Research in Medical Sciences
Thakare DW et al. Int J Res Med Sci. 2016 Sep;4(9):3717-3723
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20162801

Research Article

Evaluation of efficacy of priming dose of propofol in reducing induction dose requirements in patients undergoing elective surgeries under general anaesthesia

Devendra W. Thakare[1]*, Urvi H. Desai[1], Kailash S. Sharma[2]

[1]Assistant professor Department of Anaesthesiology, LTMMC & LTMGH, Sion, Mumbai, India
[2]Director, Academics, TMC, Parel, Mumbai, India

Received: 04 July 2016
Accepted: 16 July 2016

***Correspondence:**
Dr. Devendra W. Thakare,
E-mail: devendra.thakare@gmail.com

ABSTRACT

Background: Priming principle refers to administration of a subanaestheic dose of an agent prior to its actual anaesthetic dose. Propofol is an effective substitute to thiopentone for intravenous induction. The objectives of the study were to evaluate whether priming with propofol would reduce induction of dose, reduce the peri-intubation haemodynamic changes, influence the severity of side effects and influence recall phenomenon.
Methods: Sixty patients of ASA Grade 1 and 2, between 18-55 years of age group, of both sexes, were selected on the basis of eligibility criteria and scheduled for elective surgery under general anaesthesia were divided into study and control groups of 30 patients each. The total dose of propofol including the priming (25% of total) dose of propofol, heart rate and blood pressure, baseline (before induction), immediately after intubation, 1 min, 3 min, 5 min after induction, SPO_2 (% of oxygen saturation), recall phenomenon and other side effects post operatively were studied.
Results: The demographic data were comparable for age, weight and sex in both the groups. Total patients were divided into two groups with 30 patients each. It was observed that total induction dose of propofol was significantly decreased in the study group 72.33±9.53mg compared to control group 115.83±9.00mg. Heart rate was better maintained in study group with minimal post-intubation response. The values of systolic, diastolic and mean blood pressure observed at 1 min after induction also showed significant decrease in control group compared to study group.
Conclusions: Propofol produces smooth, rapid, pleasant and safe induction. Priming with propofol can be practiced due to its cost effectiveness and better haemodynamic profile and safety.

Keywords: Propofol, Priming principle, Peri-intubation, General anaesthesia

INTRODUCTION

Recently, propofol has been accepted as an effective substitute to the time tested thiopentone for intravenous induction. Induction with propofol is smoother, more rapid, has rapid awakening and orientation times, better intubating conditions and upper airway integrity compared to thiopentone. However, major disadvantage of rapid induction with propofol is the considerable decrement in the systemic arterial blood pressure and its high cost.[1] Searching of various literatures reveals that several methods are available to decrease the induction dose requirements of propofol, viz, i) concurrent use of nitrous oxide, opioids, barbiturates like thiopentone, and benzodiazepines like midazolam, ii) augmentation with local anaesthetics, or magnesium sulfate and iii) use of Priming principle.[2]

Application of priming principle is well documented as regards to the use of non-depolarizing muscle relaxants,

whereas the studies using the priming principles for propofol induction are not many. Priming principle refers to administration of a subanaestheic dose of an agent prior to its actual anaesthetic dose.[3]

In this study priming has been done on induction agent propofol instead of neuromuscular blocking agent, 25% of the calculated induction was used as priming dose and after one minute remaining dose of propofol was given till loss of eyelash reflex. Propofol is the most recent intravenous anaesthetic agent. Propofol carries a list of merits to its name including fast induction, short duration of action, fast and clear headed recovery, inactive metabolites, no postoperative nausea, vomiting and patient rapidly becoming roadworthy.[4] The main disadvantage is hypotension, bradycardia associated with it; also the anaphylaxis reactions associated with its use. It reduces the mean arterial blood pressure, decreases cardiac output and systemic vascular resistance, which is mainly dose- related.

However this study was under taken to evaluate whether priming principle applied for the induction dose of propofol would affect the total induction dose requirements of propofol and thereby reduce the associated haemodynamic side effects.

Aims and objectives

The study was aimed to prove the priming with 25% dose of propofol reduces the induction dose of propofol compared to total calculated dose in mg per kg body weight and priming decreases the adverse effects associated with propofol. The objectives of the study were to evaluate whether priming with propofol would reduce induction of dose, reduce the peri-intubation haemodynamic changes, influence the severity of side effects and influence recall phenomenon.

METHODS

The study was conducted from August 2007 to September 2007 in 500 bedded tertiary cancer research hospital after approval from institutional scientific and ethics committee. Sixty patients of American Society of Anesthesiologist (ASA) physical status of I or II were enrolled who underwent elective surgeries under general anaesthesia. The patients were selected on the basis of following inclusion and exclusion criteria.

Inclusion criteria

Healthy ASA class I and II patients between 18-55 years of age of both sexes scheduled for elective surgery under general anaesthesia.

Exclusion criteria

- Cardiac, endocrine, respiratory, hepatic, renal, haematological and neurological disorders
- Known allergy to study drug and its constituents. Patients allergic to egg and egg proteins.
- Pregnant and lactating women.
- Age <18 years or >55 years.
- Patients with psychiatric illness and taking medications for psychiatric illness.

A day prior to surgery thorough pre-operative assessment which included detailed history, general and systemic examination, body weight and vital parameters was done for cardiovascular, respiratory system and general health of the patient.

Patients were explained about the type of anaesthesia and a written informed consent was taken from patient after confirming adequate starvation. All patients were monitored with electrocardiogram, pulse oximetry, non-invasive blood pressure and capnography. All patients were pre-medicated with inj. midazolam 0.05 mg/kg intramuscularly 30 minutes prior to induction. Inj. glycopyrrolate 0.004 mg/kg, inj ondansetron 0.1 mg/kg and inj ranitidine 1 mg/kg were given 15 min prior to induction. Inj fentanyl 1 mcg/kg was given over 30 seconds. Pre-operative baseline values of heart rate and blood pressure, an average of two consecutive readings were taken at least 10 minutes apart, 15 minutes before the surgery.

Sixty patients scheduled for elective surgery under general anaesthesia were divided into study group 1 and control group 2 of 30 patients each. All patients were preoxygenated with 100% O_2 for 5 minutes.

Patients in group 1 received 25% of the total calculated dose of inj. propofol (2 mg/kg) 30 seconds after the administration of inj. fentanyl 1 mcg/kg (over 30 seconds) at 4ºC to decrease the pain on injection. One minute after the priming dose, the remaining drug was given till the loss of eyelash reflex. Speed of injecting propofol was at the rate of 30 mg per 10 seconds.

Patients in Group 2 were induced with the calculated dose of inj. propofol 2 mg/kg until the loss of eyelash reflex. The speed of injection was 30 mg/10sec.

Heart rate, B.P. and O_2 saturation were recorded and monitored. After confirming that patients could be ventilated, inj scoline 2 mg/kg i.v. was given. After patient was relaxed, direct laryngoscopy was done and intubation with appropriate size endotracheal tube was achieved. Bilateral air entry was confirmed and ETT was firmly secured using adhesive tapes.

The endotracheal tube was connected to anaesthesia breathing circuit. Anaesthesia was maintained with nitrous oxide 60%, oxygen 40% and isoflurane 1-2% on IPPV with circle absorber. No stimulus was applied for the first 5 minutes. Muscle relaxation was maintained using top ups of inj. vecuronium till the end of surgery. The total dose of propofol including the priming (25% of

total) dose of propofol, heart rate and blood pressure, baseline (before induction), immediately after intubation, 1 min, 3 min, 5 min after induction, SPO_2, recall phenomenon and other side effects post operatively were studied. After completion of surgery patients were reversed with neostigmine and glycopyrrolate in both groups.

All data were reported as mean values ±2SD. Statistical analysis of the demographic data was done using chi-square test. Comparison between the groups for induction dose and haemodynamic parameters was done using student 't' test. A p-value < 0.05 was considered statistically significant. The tests of significance were calculated using the computer based programme SPSS version 15.0.

RESULTS

The demographic study results are presented in Table 1. Both the groups were comparable demographically with no statistically significant difference.

Table 1: Demographic data of the study groups.

		Group 1 (N=30)	Group 2 (N=30)	P Value
Age (mean±SD)		37.86±8.328	38.06±7.165	0.923
Sex, N (%)	F	24 (80)	22 (73.33)	0.542
	M	6 (20)	8 (26.67)	
Weight (kg)		55.2±10.15	58.66±1.03	0.108
Types of surgery	Head and neck	6 (20)	11 (36.67)	
	Breast	20 (66.67)	14 (46.67)	
	Bone and soft tissue	2 (6.67)	3 (10)	
	Genitourinary-Gynec	2 (6.67)	2 (6.67)	

Table 2: Comparison of total dose of propofol between two groups.

	Group 1 (N=30)	Group 2 (N=30)	P Value	
Total dose of propofol (mg)	72.33±9.53	115.83±9	0.000	Significant

Table 3: Comparison of total dose of Propofol between priming group and precalculated study group.

	Priming group	Precalculated study group	P Value	
Total dose of propofol (mg)	72.33 ± 20.56	109.26 ± 9.53	0.000	Significant

The results of comparison of total dose propofol between group 1, 2 and between priming group and precalculated study group were tabulated in Table 2 and 3 respectively. In both the comparisons, the values were very significant (p=0.000). The values of heart rate at various intervals and their comparisons were documented in Table 4.

Table 4: Comparison of heart rate (beats/min) at various intervals.

Time	HR	Group 1 (n=30)		Group 2 (n=30)		Unpaired 't' Test	
		Mean	SD	Mean	SD	P Value	Difference
Preinduction	HR0	80.56	5.28	82.20	5.31	0.237	Not significant
1 min after induction	HR1	78.70	5.51	78.96	5.89	0.857	Not Significant
Immediately after intubation	HRint	88.96	4.89	92.50	5.15	0.009	Significant
3 min after induction	HR3	80.56	2.37	81.16	8.20	0.702	Not Significant
5 min after induction	HR5	79.83	3.09	78.66	6.19	0.360	Not Significant

The values were given in terms of mean and SD of both the tested groups. Among all the intervals heart rate immediately after intubation showed significant difference (p=0.009) between the two groups. P values were calculated by unpaired t test. If the values of heart rate at various intervals were compared with preinduction

then all the data are significantly different. Systolic and diastolic blood pressure of the patients in both the groups at various intervals with their comparisons were tabulated in terms of mean and SD in Table 5 and 6 respectively.

Table 5: Comparison of systolic BP (mm oh Hg) at various intervals.

Time	SBP	Group				Unpaired 't' Test	
		Group 1 (n=30)		Group 2 (n=30)			
		Mean	SD	Mean	SD	P Value	Difference
Preinduction	SBP0	121.06	6.51	122.20	6.37	0.499	Not significant
1 min after induction	SBP1	111.16	3.96	101.00	6.34	0.000	Significant
Immediately after intubation	SBPint	117.73	6.57	118.86	6.40	0.502	Not Significant
3 min after induction	SBP 3	106.33	2,46	104.20	6.69	0.107	Not Significant
5 min after induction	SBP 5	109.86	4.51	109.50	5.72	0.784	Not Significant

Table 6: Comparison of diastolic BP (mm oh Hg) at various intervals.

Time	DBP	Group				Unpaired 't' Test	
		Group 1		Group 2			
		Mean	SD	Mean	SD	P Value	Difference
Preinduction	DBP0	77.33	4.52	78.13	3.85	0.464	Not significant
1 min after induction	DBP1	73.66	3.64	64.53	4.48	0.000	Significant
Immediately after intubation	DBPint	74.33	5.56	75.86	4.66	0.252	Not Significant
3 min after induction	DBP 3	72.93	3.70	72.00	4.23	0.367	Not Significant
5 min after induction	DBP 5	74.43	4.16	75.00	4.29	0.606	Not Significant

Among the intervals blood pressure at 1 minute after induction showed a very significant result (p=0.000) between both the groups. P values were calculated by unpaired t test. If the values at various intervals were compared with preinduction then all the data shows significant results.

Table 7: Comparison of mean BP (mm oh Hg) at various intervals.

Time	MBP	Group				Unpaired 't' Test	
		Group 1		Group 2			
		Mean	SD	Mean	SD	P Value	Difference
Preinduction	MBP0	91.56	3.96	92.46	3.89	0.379	Not significant
1 min after induction	MBP1	85.83	2.76	76.40	4.22	0.000	Significant
Immediately after intubation	MBPint	88.46	5.02	89.63	4.85	0.364	Not Significant
3 min after induction	MBP 3	83.80	2.91	82.50	4.58	0.195	Not Significant
5 min after induction	MBP 5	85.8	3.69	86.03	3.82	0.811	Not Significant

Mean blood pressure of the patients of the two groups at different intervals with their comparisons were presented in terms of mean and SD in Table 7. Among all the intervals mean blood pressure of the two tested groups at 1 minute after induction exhibited a very significant result (p=0.000). P values were calculated by unpaired t test. If the values of both groups at different intervals were compared with preinduction then all the values shows significant results.

DISCUSSION

Induction of anaesthesia is one of the vital events in general anaesthesia. Prior to the introduction of intravenous anaesthetic agents, induction of general anaesthesia necessarily required inhalation of gases or vapors which was an unpleasant experience to most of the patients.

Application of priming principle is a well-established fact with use of non-depolarizing muscle relaxants wherein 'priming' shortens the onset of neuromuscular blockade and provides better intubating conditions.[5,6] In the present study the authors evaluated, 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.

In our trial sixty patients were studied as regards to induction character, associated haemodynamic response and recall phenomenon. In this study, premedication given to the patients was inj. glycopyrrolate 4 mcg/kg i.v. immediately before the induction. Glycopyrrolate acts as an antisialogogue and an anticholinergic thereby preventing reflex bradycardia if any. Besides propofol used in this study itself causes bradycardia and it is advised in the literature to premedicate the patients with an anticholinergic drug before propofol injection.

Claeys M.A. et al used inj. Glycopyrrolate 0.4 mg i.m. one hour before the study. They concluded that the arterial hypotension associated with induction and infusion of propofol is mainly a result of the decrease in afterload without compensatory increase in the heart rate or cardiac output.[7] Bassil A et al studied comparision of propofol and thiopentone for induction in patients undergoing outpatient surgery. They used inj. pethidine and inj. atropine as premedicant drugs. In propofol group, both systolic blood pressure and heart rate decreased after induction and increased after intubation. In thiopentone group, systolic blood pressure decreased after induction but after intubation both systolic blood pressure and heart rate increased.[8]

In the study by Scheepstra et al no premedication was used.[9] Inj. midazolam was used in dose of 0.05 mg/kg in our study. Midazolam has been used to facilitate induction of general anaesthesia (co-induction).[10] The rationale for such approach is the moderation of dose requirements, as well as side effects and costs of the primary induction agents. Drug combinations which have demonstrated synergistic properties include thiopentone and midazolam and propofol and midazolam. Tigh and his co-worker confirmed from their study that co-induction with a subanaesthetic dose of midazolam reduced the induction dose of propofol upto 50%. Inj. pentazocine was used in dose of 0.6 mg/kg intravenously along with inj. Midazolam before induction of anaesthesia. [11]

Peacock et al used inj. fentanyl 0.75 mcg/kg intravenously 5 min before induction of anaesthesia in his study of effect of different rates of infusion of propofol for induction of anaesthesia in elderly patients.[12] In present study, priming with inj. propofol was done in the patients in the study group. At the speed of 30 mg/ 10sec 25% of the precalculated dose of 2 mg/kg was administered to the patients, then after 1 minute the remaining dose was titrated and given till the loss of consciousness, the endpoint of which was taken as the loss of eyelash reflex. The induction dose was reduced from the mean value of 109.26±9.53 in study group to 72.33±9.53 in which priming with 25% of the precalculated dose, 2 mg/kg was done (p=0.000) which was <0.05) which is highly significant. The mean induction dose of propofol in the control group was much higher than the study group and was stastically significant.

Maroof et al studied priming principle with propofol. Thirty patients of ASA I and II were selected and 2 groups of 15 each were taken. In both groups patients were premedicated with in. meperidine 1 mg/kg and inj. Promethazine 0.25 mg/kg intramuscular 45-60 min prior to surgery. Group I patients were induced with inj. fenatnyl 1 mcg/kg and inj. propofol at the speed of 30 mg/ 10sec till loss of eyelash reflex.

Group II Patients received 20% of the precalculated dose of propofol 2 mg/kg at the speed of 30 mg/ 10sec. 30 sec later, fentanyl 1 mcg/kg and propofol at the speed of 30 mg/ 10sec was administered till loss of eyelash reflex. Anaesthesia was maintained with isoflurane and O_2: N_2O. Vecuronium was the muscle relaxant used. He concluded that priming reduced the induction dose significantly. Peri-intubation haemodynamic stability remained in both the groups and recall phenomenon was absent in both the groups.[13]

Singleton studied to determine the clinical effectiveness of administering pre-induction doses of propofol versus lignocaine for decreasing pain during induction with propofol. Thirty unpremedicated patients of ASA I and II were randomly assigned to receive 20 mg propofol or 40 mg lignocaine intravenously. A minimum of 30 seconds but not more than 40 seconds following the administration of randomized drug along with open flow intravenous fluid, the induction dose of propofol (2.5 mg/kg) was begun through the same intravenous site.

When one half of the dose was given, patient was asked for pain in hand. If yes, the severity of pain as mild, moderate or severe was asked. Then the anaesthetic process continued normally. In the lignocaine group, 53% of patients were pain free and in propofol group. 47% were pain free. No difference existed in the ability of propofol or lignocaine to decrease the incidence of pain during induction dose of propfol.[14]

In the present study it was found that significant changes in relation to heart rate in control group compared to study group. After giving propofol there was a decrease in heart rate in both the groups. But this was more in control group as compared to study group because of more dose of propofol being used in control group. In addition, there was increase in heart rate in both the groups immediately after intubation in response to laryngoscopy and intubation. Overall the heart rate was better maintained in study group as compared to control

group. The probability value at the time of immediate post intubation is significant while the pre-induction, 1 min after induction, 3 min after induction and 5 min after induction P values are insignificant. The highest mean heart rate values for study and control group are 88.96 and 92.50 respectively while the lowest mean heart rate values for both the groups are 78.80 and 78.66 respectively, which clearly shows greater heart rate variations in control group than study group.

Here the authors observed the values of systolic, diastolic and mean blood pressure and found that changes were significant 1 min after induction and they were insignificant at pre induction, immediately after intubation, after 3 min and 5 min after induction. There is a fall in value of the systolic blood pressure in both the groups but there is more fall in the control group than the study group because of the less dose of propofol being used in study group. The highest values of mean systolic blood pressure for the control and the study groups are 122.20 & 121.06 respectively while the lowest mean systolic blood pressure values for both groups are 101 and 106.33, which shows greater variations of systolic blood pressure in the control group than the study group.

Same is the case with diastolic blood pressure so overall blood pressure is better controlled in study group as compared to control group. The highest values of mean diastolic blood pressure for control and study groups are 78.13 and 77.33 and lowest mean diastolic blood pressure values for both groups are 64.53 and 72.93 respectively. This shows greater variations of diastolic blood pressure in the control group than the study group.

Similar was the case with mean blood pressure so overall blood pressure is better controlled in study group as compared to control group. The highest mean values of mean blood pressure for control and study groups are 92.46 and 91.56 and lowest mean blood pressure values for both groups are 76.40 and 83.80 respectively. This shows greater variations of mean blood pressure in the control group than the study group.

There is less deviation from the mean values of heart rate, systolic. diastolic and mean blood pressure in the study group as compared to control group as shown by the tables in results. Though the deviation in haemodynamic values is statistically significant, it is clinically not significant in study group as compared to control group. So the study group haemodynamics are better maintained as compared to control group.

The greater haemodynamic variation among control group might be attributed to large total dose of propofol in this group and because of giving small and divided total dose of propofol in the study group. The pharmacodynamic properties of propofol are dependent upon the therapeutic blood propofol concentrations. Undesirable side effects such as cardiorespiratory depression are likely to occur at higher blood concentrations, which may result from bolus dosing. Edelist in 1987 reported that propofol causes decrease in heart rate, systolic, diastolic and mean blood pressures that were significantly greater than thiopentone.[6]

Claeys et al in their study of haemodynamic changes with propofol concluded that hypotension was due to decrease in after load reduction without compensatory increase in heart rate and cardiac output.[7] In present study all, the patients in both groups were monitered for peri-intubation ECG changes. None of the patients showed any ECG changes. Maroof et al in his study found ECG changes of premature ventricular contractions in two patients and sinus bradycardia in patient in whom priming was done and premature ventricular contraction in one patient and junctional rhythm in one patient in that total dose was given.[13] Recall phenomenon was observed in none of the patients in both the control and the study group.

CONCLUSION

Based on the results obtained from this study it can be conclude that, priming with propofol significantly reduces the induction dose and attenuates the extent of hypotension and bradycardia following induction with propofol. Propofol produces smooth, rapid, pleasant and safe induction. Priming with propofol can be practiced due to its cost effectiveness and better haemodynamic profile and safety.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Rajkumar G, Thokchom R, Pradhan PC, Singh MKH, Singh HT, Singh RN. Co-induction effects of midazolam, thiopentone and ketamine with propofol in general anesthesia. J Med Soc. 2013;27(2):110-3.
2. Karlo R, Singh NR, Singh KM, Singh TH, Devi NA, Devi MB. Priming effects of propofol during induction of anesthesia. J Med Soc. 2015;29(2):92-5.
3. Shashank DS, Singh NR, Singh LK. Effects of pretreatment with different neuromuscular blocking agents on facilitation of intubation with rocuronium: A prospective randomized comparative study. IJA. 2014;58(3):303-8.
4. Khan KS, Hayes I, Buggy DJ. Pharmacology of anaesthetic agents I: intravenous anaesthetic agents. Contin Educ Anaesth Crit Care Pain. 2013. doi: 10.1093/bjaceaccp/mkt039.
5. Doze VA, Shafer A et al. Propofol- Nitrous Oxide versus thiopentone-isoflurane- nitrous Oxide foe general anaesthesia. Anaesthesiology. 1988;69:63-71.

6. Edelist G. A Comparision of thiopentone and propofol as induction agents in outpatients surgery. Can J Anaesth.1987;34(2):110-6.
7. Claeys M. A. Gepts E, Camu F. Haemodynamic changes during Anaesthesia induced and maintained with propofol . Br.J.Anaesth 1998;60(1):3-9.
8. Bassil A et al. Propofol versus Thiopentone for induction of Anaesthesia in patients undergoing out patient surgery. Middle East J. Anaesthesia 1989;10:307-14.
9. Scheepstra GL, Booij LH, et al. Propofol for induction and maintenance of anesthesia: comparision between younger and older patients. Br J Anaesth. 1989;62:54-60.
10. Briggs L.P. White M. The effects of premedication of anaesthesia with propofol. Post grad. Med J 1985;61 (Suppl 3) 35-47.
11. Tighe KE, Warner JA. The effect of co-induction with midazolam upon recovery from propofol infusion of anaesthesia. Anaesthesia. 1997;52:998-1014.
12. Peacock JE, Lewis RP, et al. Effect of different rates of infusion of propofol for induction of anaesthesia in elderly patients. Br J Anaesth. 1990;65:346-352.
13. Maroof M, Khan RM, Bhatti TH. Priming Principle and induction dose of propofol. Anaesth Analg. 1996;82:S1 – S15.
14. Singletone JD. Induction pain perception after Premedication with propofol vs lignocaine: a pilot study. AANA J. 2000;68(2):149-51.

Cite this article as: Thakare DW, Desai UH, Sharma KS. Evaluation of efficacy of priming dose of propofol in reducing induction dose requirements in patients undergoing elective surgeries under general anaesthesia. Int J Res Med Sci 2016;4:3717-23.