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Original Research Article

A Randomized Study to Determine the Effect of Priming Principle on the Induction Dose Requirement of Propofol and Associated Haemodynamic Changes

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Abstract

Background and Aims: Propofol as an induction agent has many advantages. But one major side effect of propofol as an induction agent is hypotension. The aim of this study was to determine the effect of 'Priming Principle' on the induction dose requirement of propofol and associated haemodynamic fluctuations.

Material & Methods: This study was carried out on 100 patients of either sex aged 20 to 60 years belonging to American Society of Anaesthesiologists physical status I/II scheduled for elective surgery under general anaesthesia. Patients were randomly allocated into two groups of 50 each. Group A (Priming) (n=50) patients were induced using priming principle. 20% of the calculated dose of propofol (2 mg/kg) was injected IV initially followed by remaining dose after 30 seconds till loss of eyelash reflex. Group B (Control) (n=50) patients were induced with total calculated dose (2mg/kg) of IV propofol till loss of eyelash reflex. Total dose of propofol required for induction and haemodynamic parameters were recorded in both the groups

Results: The demographic profile of the patients with respect to age and sex were comparable in both the groups with no statistical significant difference. The mean total dose of propofol required for induction was 79.21 mg in the group A (priming) and 93.7 mg in group B (control). This difference in the induction dose required was statistically significant. Statistically significant difference in the values of heart rate, systolic blood pressure and diastolic blood pressure was also noted between the two groups one minute after induction. Haemodynamic stability was better in group A (priming).

Conclusion: The results of this study shows that the induction dose of propofol can be significantly reduced by using priming principle. Using priming principle also results in haemodynamic stability in the immediate post induction and peri-intubation period.

Keywords: Priming principle, induction dose, propofol, haemodynamics

Introduction

Propofol is a routinely used induction agent. It provides a rapid and smooth induction with quick clear headed recovery, decreased incidence of postoperative nausea and vomiting, good intubating conditions and upper airway integrity. [1,2,3] However, an induction dose of propofol of 2 mg/kg can be hazardous because vasodilation and cardiovascular depressant action can cause profound hypotension. [3] Propofol causes profound haemodynamic instability due to direct myocardial depressant and decreased systemic vascular resistance. [3,4,5]

Various techniques like concurrent administration of opioids, barbiturates and benzodiazepines has been used to reduce the induction dose of propofol. [1,2,3] Priming principle also known as auto-co-induction is a technique of giving a fraction of the total calculated dose of an agent followed by the remaining amount of the calculated dose of the same agent after some time. [1,2,3,6] Priming principle

has been used for non-depolarising muscle relaxants, wherein 20% of the ED95 or about 10% of the intubating dose is given 2–4 minutes prior to administration of the remaining dose for tracheal intubation. [1,3,7,8]

Priming Principle has been successfully used to reduce the conventional dose of non-depolarizing muscle relaxants for early achievement of intubating condition. [3,7,9,10] The application of priming principle is well documented with regard to the use of non-depolarising muscle relaxants, where priming shortens the onset of neuromuscular blockade, provides better intubating conditions and reduces the total required dose of the drug.[7] The main disadvantages of propofol are pain on injection, hypotension, and high cost. A decrease of 26 to 28% of systolic blood pressure, 19% of diastolic blood pressure and 11% of mean arterial pressure, without any change in systemic vascular resistance and cardiac output were observed when patients are induced with 2mg/kg of propofol. [11,12] Most of these haemodynamic side effects of propofol are dose related.

Hence this study was conducted to determine the effect of priming principle on the induction dose requirement of propofol and haemodynamic alterations.

Material & Methods

This study was conducted at a tertiary care centre over a period of six months. 100 patients of either sex aged 20 to 60 years belonging to American Society of Anaesthesiologists physical status I/II scheduled for elective surgery under general anaesthesia were enrolled for this study after approval from the institutional ethical committee. Written informed consent was taken from all the patients.

Patients with allergy to propofol, eggs, on opioid analgesic, tranquilizer, sedatives, hypnotics or any other CNS depressants and anticipated difficult airway were excluded from the study.

Patients were randomly allocated into two groups of 50 each. Group A (Priming) (n=50) patients were induced using priming principle. 20% of the calculated dose of IV propofol (2 mg/kg) was injected initially followed by remaining dose after 30 seconds till loss of eyelash reflex. Group B (Control) (n=50) patients were induced with total calculated dose (2 mg/kg) of IV propofol till loss of eyelash reflex. All patients were kept nil per orally eight hours prior to surgery and were given anxiolytic in the form of tablet alprazolam 0.5 mg night prior to surgery. Multiparameter monitor was attached in the operation theatre and baseline heart rate (HR), non-invasive blood pressure (NIBP) and arterial oxygen saturation by pulse oximeter (Sp02) were recorded and electrocardiograph (ECG) monitoring done. IV fluid was started. After preoxygenation for three minutes, IV glycopyrrolate 0.2 mg and IV fentanyl citrate 2 µg/kg was given. Induction with propofol was done as per group allocation. Endotracheal intubation was facilitated by IV succinylcholine 1mg/kg body weight. Anaesthesia was maintained with O2 (40%) + N2O (60%) + isoflurane (1 MAC). IV vecuronium bromide 0.1mg/kg was given and repeated as and when required. Patients were mechanically ventilated using volume controlled mode. Multimodal IV analgesia was given as per the requirement. Patient's vitals were monitored throughout the surgery. IV ondansetron was given ten minutes before the completion of surgery. Neuromuscular block was reversed with appropriate dose of IV neostigmine methylsulphate and IV glycopyrrolate after the completion of the surgery and patients were extubated and shifted to the recovery room for monitoring.

Total dose of propofol required for induction was noted in both the groups.

Heart rate (HR), Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MAP), oxygen saturation (SpO2) were recorded at baseline, 1 minute after induction, immediately after intubation, 5 minutes after induction.

Statistical Analysis

Unpaired Student's t-test and Chi-square test was used to analyze the compiled data. Statistical Package for Social Science (SPSS) Version 20.0 (IBM SPSS Statistics) was used to compare the continuous variables between the two groups. Data are expressed as mean ± standard deviation. P value < 0.05 was considered to be statistically significant.

Results

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

Age group	Group A (N=50)		Group B (N=50)		P value
	Male	Female	Male	Female	
20 – 30	11	8	4	6	
31 – 40	6	14	10	12	0.644
41 – 50	4	2	6	5	
51 – 60	1	4	5	2	
Total	22	28	25	25	

Majority of the study subjects were in the age group between 30 and 40 years in both the groups with mean age of 38.6 in priming group and 42.4 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 2: Comparison of total dose of propofol required between the two groups

Study group	Total dose Mean±SD	Mean difference	95% CI		P Value
			Lower	Upper	
Group A	79.21 ± 15.95	-15.25	-23.87	-5.25	<0.001
Group B	93.7 ± 8.52				

The mean total dose of propofol required for induction in the priming group patients was 79.21 mg and in the non-priming group was 93.7 mg The mean difference was found to be statistically significant. So patients could be induced with a significantly lesser dose of propofol using the priming principle.

Table 3: Heart rate

Heart Rate	Mean ±SD		P value
	Group A	Group B	
Baseline	83.77 ± 14.36	85.65 ± 9.54	1.000
1 Minute after induction	88.6 ± 15.95	78 ± 12.08	0.018
Immediately after intubation	88 ± 16.84	82.58 ± 8.12	0.196
5 minutes after induction	82.8 ± 13.37	79.71 ± 7.43	0.432

Difference in heart rate variation one minute after induction in both the groups was statistically significant.

Table 4: Systolic and diastolic blood pressure

Systolic blood pressure	Mean ±SD		P value
	Group A	Group B	
Baseline	122.4 ± 15.07	125.5 ± 12.78	0.172
1 Minute after induction	106.04 ± 12.88	93.7 ± 9.21	0.003
Immediately after intubation	108.2 ± 15.55	102.92 ± 8.52	0.128
5 minutes after induction	103.77 ± 14.36	102.14 ± 10.94	0.931
Diastolic blood pressure			
Baseline	74.66 ± 8.52	75.55 ± 10.15	0.510
1 Minute after induction	64.6 ± 10.12	57.63 ± 7.73	0.025
Immediately after intubation	73.36 ± 10.64	65.85 ± 12.24	0.072
5 Minutes after induction	68.2 ± 10.38	68.72 ± 6.64	0.872

Post induction fall (recorded one minute after induction) in systolic and diastolic blood pressure was also lesser in the priming principle group (Group A) when compared to group B. This difference was statistically significant.

Discussion

Intravenous induction agents tend to be potent drugs with significant haemodynamic 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 in a dose of 2 mg/kg is hypotension. Various methods have been tried to reduce the induction dose like concurrent use of opioids, barbiturates and benzodiazepines. Priming principle is an effective technique. It refers to the administration of a sub-anaesthetic dose of an agent prior to its actual anaesthetic dose. We are living in the era of day care surgery and anaesthesia. Unusual and prolonged hospital stay due to anaesthetic drugs definitely increases economic burden and risk of hospital acquired complications. Propofol is the most commonly used intravenous anaesthetic induction agent used due to its property of smooth and more rapid induction, rapid awakening, clear headed recovery, decreased incidence of post-operative nausea and vomiting, better intubating conditions and upper airway integrity compared to thiopentone. [4,13]

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. [8,9,14] Majority of the study subjects were in the age group between 30 and 40 years in both the groups with mean age of 38.6 in priming group and 42.4 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 almost equal number of males and females among both the groups. Similar to the results of our study, the study conducted by Karlo et al[10] observed 10.23% reduction in the total induction dose requirement of propofol in priming group. Another study done by Kumar A et al [3] 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. Similarly studies done by Srivastava U et al [15] and Kataria R et al [8] 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 for priming. Difference in heart rate variation one minute after induction in both the groups was statistically significant. Post induction fall (recorded one minute after induction) in systolic and diastolic blood pressure was also lesser in the priming principle group (Group A) when compared to group B. This difference was statistically significant. Studies done by Cullen PM et al [16] and Pensado A et al [12] had reported a similar finding and it was justified quoting it as hemodynamic changes are dose dependent.

The mean total dose of propofol required among the priming group patients was 79.21 mg compared to the total dose requirement in the non-priming group which was 93.7 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.

Conclusion

Based on the results of this study it is concluded that using priming principle significantly reduces the total induction dose of protocol and it also provides stable haemodynamics in the immediate post induction and peri-intubation period.

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