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Original Research Article

A comparative study of efficacy of propofol auto co induction versus midazolam propofol co induction using the priming principle

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Abstract

Background: Induction can be considered as one of the most crucial events in anaesthesiology and propofol is preferred induction agent nowadays due to its good properties. The aim of present study was to evaluate the clinical efficacy of propofol auto-co-induction compared to midazolam propofol co-induction in terms of: reduction in induction dose of propofol; and hemodynamic stability in peri-intubation period.
Method: A total of 90 patients were randomly allocated into 3 groups of 30 each. Group I received the priming agent IV propofol 0.5mg/kg, group II received 0.05 mg/kg IV midazolam and group III received 3 ml of normal saline. This was followed by IV induction with propofol 2 minutes later in all the three groups till the loss of eyelash reflex.
Results: Induction dose of propofol was significantly reduced in group II by 12.38% as compared to group I(5 %). After induction mean HR was significantly lower in group I as compared to group II and controls. Mean SBP and DBP was significantly higher in group II as compared to group I and controls in peri intubation period. While mean DBP of IV propofol group was lower than control group. Oxygen saturation was comparable among all three groups and maintained above 95% throughout the surgery. No complications were noted in any of the groups.
Conclusion: The results showed a significant decrease in induction dose requirement in both the groups but dose reduction was significantly more with midazolam. Haemodynamic stability during induction and intubation was more in propofol auto-co-induction group.
Keywords: Anaesthesiology, Propofol, Autocoinduction, Coinduction, Midazolam, Peri intubation

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1. Introduction

Induction can be considered as one of the most crucial events in anaesthesiology as it is associated with number of alternations in hemodynamic and physiology of various body systems [1]. This is an era of day care surgery and anaesthesia. Unusual and prolong hospital stay due to anaesthetic drugs definitely increases economic burden and risk of hospital acquired complications. Propofol is preferred induction agent nowadays due to its properties of smoother and more rapid induction, rapid awakening and orientation times, clear headed recovery, decreased incidence of post-operative nausea vomiting better intubating conditions and upper airway integrity [2, 3]. However, major disadvantage of rapid induction with propofol is the considerable dose dependent decrement in the systemic arterial pressure [4], primarily due to reduction in cardiac output and systemic vascular resistance.

Various methods to reduce the induction dose of propofol, like concurrent use of nitrous oxide, opioids, barbiturates like thiopentone, benzodiazepines like midazolam, clonidine, augmentation with local anaesthetics, magnesium sulphate and use of 'auto-co-induction' have been proposed [5, 6]. Priming technique is also known as auto co induction. It is the technique of giving a pre-calculated dose of induction agent prior to giving full intubating dose of the same agent [7].

Application of priming principle is well proved and explained in relation to the use of muscle relaxants. This technique involves giving a small sub-paralysing dose of the non-depolariser [8] (20% of the ED_{95} or about 10% of the intubating dose), 2–4 minutes prior to administering the second large dose for tracheal intubation. This technique, in relation to induction agents, aims at utilising the sedative and anxiolytic properties at sub-hypnotic dosage of induction agent when given a few minutes prior to induction [7].

Propofol and midazolam is a commonly used combination for induction and it shows synergistic interaction for hypnosis and reflex sympathetic suppression. Midazolam has shown to reduce the dose of propofol required to induce anaesthesia by up to 50% without affecting the recover profile when used as" co- induction" [9, 10]. The reduction in the induction dose by applying 'priming principle" could be attributed to the anxiolytic effect of propofol at subhypnotic doses [7].

However, there are fewer studies related to application of priming principle in induction agents. Therefore present study was undertaken to evaluate clinical efficacy of propofol auto-co-induction compared to midazolam propofol co-induction in terms of reduction in induction dose and hemodynamic stability in peri-intubation period.

2. Material and methods

After obtaining Institutional Ethical Committee approval, this prospective randomised active controlled study was conducted in 90 patients of either sex, belonging to ASA grade I and II, age between 18-60 years posted for surgery under general anesthesia during the period of one year. Patient with significant cardiac, endocrine, respiratory, renal, hematological and neurological disorders, known allergy to study drug and its constituents, patients allergic to egg and egg proteins, pregnant and lactating women, age of patients <18years or >60 years, patient with psychiatric illness and taking medications for psychiatric illness, patient with disorder of involuntary movements, patient refusal to participation in the study were excluded.

Informed consent was taken on the day of surgery before taking patient inside operating room. Patients starvation was confirmed and monitors were attached like pulse oximeter, ECG, non-invasive blood pressure monitor and capnography, preoperative readings was noted. Patients were pre-medicated with glycopyrrolate 4mcg/kg IV 15 min before induction. Pre-operative baseline values of heart rate (HR) and blood pressure (BP) were noted. An intravenous line appropriate for the surgical procedure was secured. All the patients were randomly allocated into three groups of 30 each using computer generated sequence method. Group I received the priming agent IV propofol 0.5mg/kg, group II received IV midazolam 0.05mg/kg and group III received IV normal saline 3 cc. This was followed by IV induction with propofol 2 minutes later in all the three groups till the loss of eyelash reflex. The speed of injecting IV induction dose of propofol in all cases was at the rate of 30 mg/10 seconds. Subsequent relaxation and intubation was accomplished with Inj. Rocuronium 1 mg/kg IV and anaesthesia was maintained on O2/N2O (35%, 65%); inj. Fentanyl 2 mcg/kg; inhalational agent, i.e., Isoflurane and injection Vecuronium (0.02 mg/kg). Groups I and III had not received midazolam.

Total dose of propofol required in achieving loss of eyelash reflex, hemodynamic parameters (HR, BP, and Spo2) was measured just before induction (baseline), immediately after induction, immediately after intubation, and 5 minutes after intubation. Any complications during the duration of surgery were also noted.

2.1 Statistical Analysis

Statistical analysis was performed using unpaired "t" test, Man Whitney U test and Chi square test. A 'p' value of <0.05 was considered as statically significant. All statistical calculations were done using computer programs Microsoft Excel version 7 (Microsoft Corporation, NY, USA) and SPSS software version 21.0.

3. Observations and results

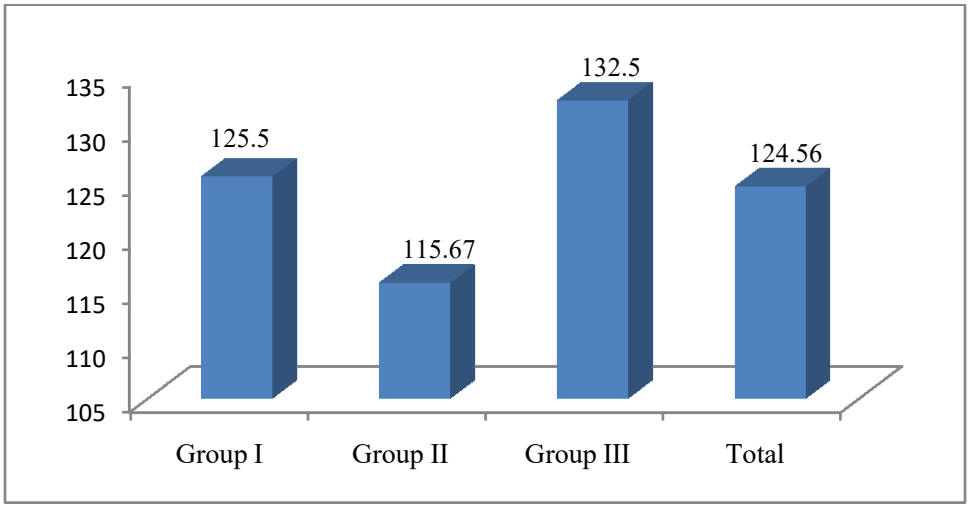
The demographic profiles of the patients were comparable in all the three groups and difference was statistically not significant, (p>0.05), (Table 1).

Table 1: Demographic Data of the patients

Parameters	Group I	Group II	Group III	Total	P value
Age (years)	44.60±10.57	44.00±11.74	41.63±10.74	43.41±10.98	0.547
Weight (kg)	57.63±5.58	56.70±6.11	57.77±6.65	57.37±6.08	0.746
Male/Female	16 / 14	16 / 14	14 / 16	46 / 44	0.837

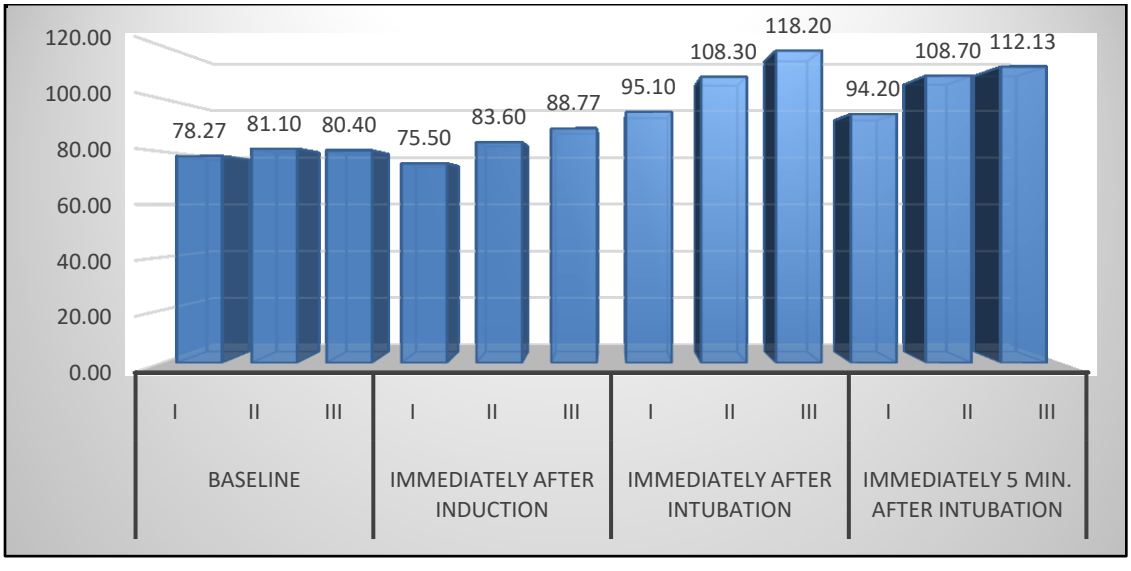
The mean induction dose of propofol in group I was 125.50 ± 10.03 mg compared to 115.67 ± 11.50 mg in group II and 132.50 ± 10.57 mg in group III. The p value was 0.01 which was statistically significant. In group II there was decrease in the induction dose requirement of propofol. Induction dose of propofol was significantly reduced in patients who received induction by IV midazolam as compared to those who received IV propofol co-induction. However the induction dose was significantly less for both groups than controls.

Figure 1: Mean Induction Dose of Propofol (mg)



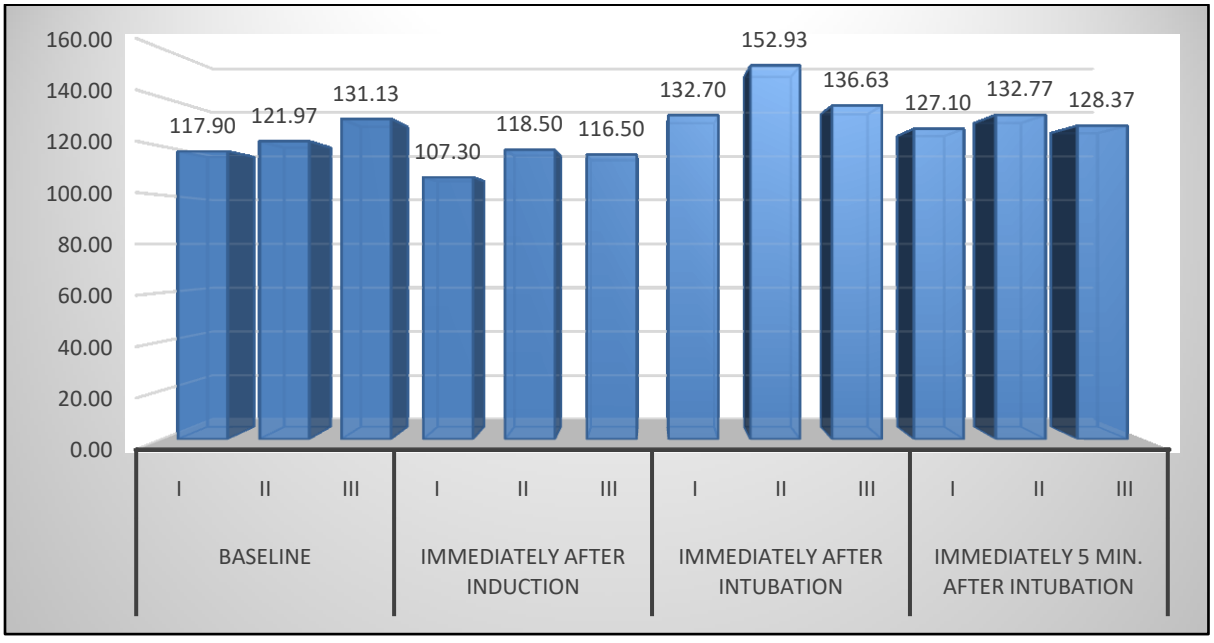
The heart rate just before induction was statistically not significant in all three groups. Immediately after induction there was significant reduction in heart rate in group I to 75.50 ±7.54 compared to 83.60 ± 6.09 in group II which was increased slightly after induction. Immediately after intubation there was rise in heart rate in all three groups compared to baseline, but the increase was statistically significant in group III compared to other groups. The heart rate immediately after intubation was 118.20 ±5.63 compared to 95.10 ± 7.28 in group I and 108.30 ± 6.00 in group II. Similar results were obtained five minutes after intubation. After induction mean heart rate was significantly lower in IV propofol group as compared to IV midazolam group and controls. Mean heart rate of IV midazolam group was also significantly lower than control group, (Figure 2).

Figure 2: Mean Heart rate changes in peri intubation period (beats per minute)



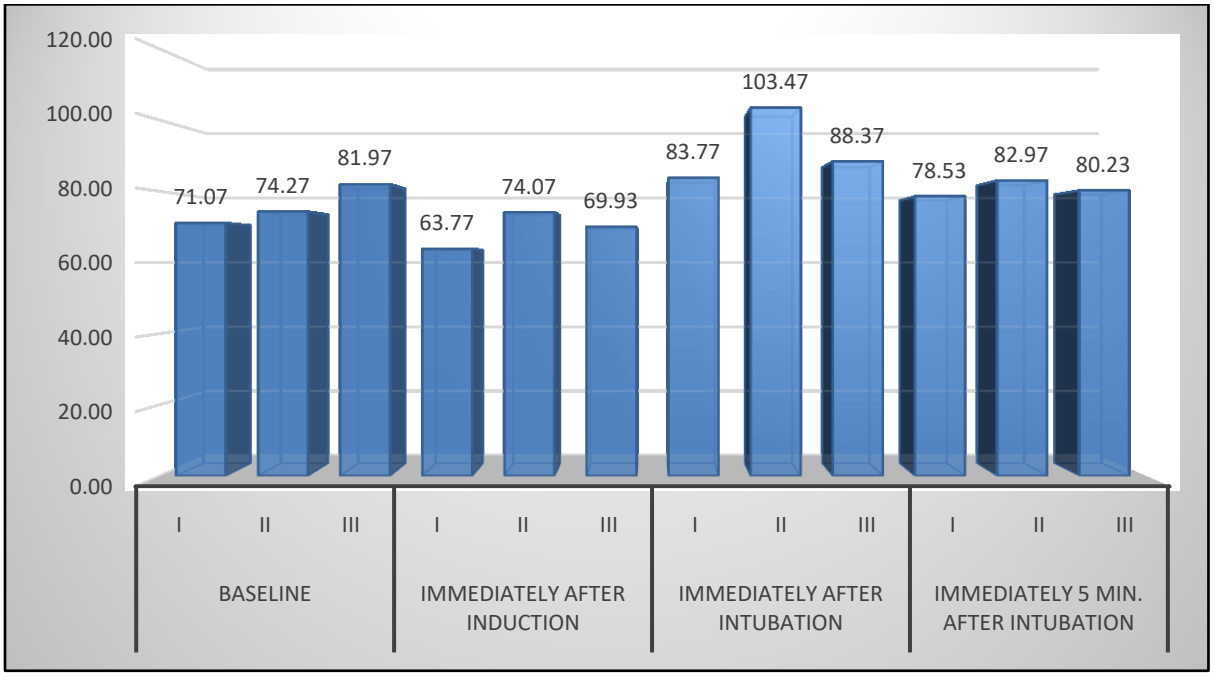
There was significant less fall in systolic blood pressure in propofol primed group compared to other groups, (Figure 3). Propofol decreases muscle tone of vascular smooth muscles and decreasing total peripheral resistance. The mean systolic blood pressure in propofol primed group that is group I was 117.90 ± 2.63 which decreased to 107.30 ± 2.77 immediately after induction. Immediately after intubation there was rise in systolic blood pressure in all the groups but it was statistically significant in group II which was primed by midazolam. Immediately after induction the mean systolic blood pressure was 118.50 ± 1.91 which increased to 152.93 ± 1.98. Five minutes after intubation again the mean systolic blood pressure decreased. After induction mean systolic blood pressure was significantly higher in IV midazolam group as compared to IV propofol group and controls. While mean SBP of IV propofol group was lower than control group.

Figure 3: Mean SBP changes in peri intubation period



The mean diastolic blood pressure in group I (propofol primed group) was 71 ± 1.36 which was decreased to 63.77 ± 1.52 immediately after induction. The mean diastolic blood pressure of group II (midazolam primed group) was 74.27 ± 1.96 which increased to 103.47 ± 2.36 immediately after intubation which was significant. After induction mean diastolic blood pressure was significantly higher in IV midazolam group as compared to IV propofol group and controls, (Figure 4). While mean DBP of IV propofol group was lower than control group.

Figure 4: Mean DBP changes in peri intubation period



The mean SpO2 in group I was 97.80 ± 0.81, in group II was 97.87 ± 0.86 and in group III was 98.00 ± 0.83. The p value was 0.64 which was statistically significant. Thus, oxygen saturation was comparable among all three groups and maintained above 95% throughout the surgery. No complications like hypotension, bradycardia or nausea, etc. were noted in any of the groups.

4. Discussion

In the present study all the groups were comparable with respect to age and gender distribution and the difference among three groups was not statistically significant. The induction dose of propofol was significantly reduced in patients who received induction by IV midazolam as compared to those who received IV

propofol co-induction. However, the induction dose was significantly less for both groups than controls. This result is correlated with the previous studies [11-15] that priming with propofol ormidazolam significantly reduces the induction dose of propofol.

After induction lesser variations in heart rate and blood pressure were seen in midazolam group as compared to propofol group and controls. Immediately after induction there was significant reduction in heart rate in group I. In group II from baseline heart rate was 81.2 ± 6.21, which was not decreased after induction (83.60 ± 6.09). In post intubation there was increase in heart rate in all three groups but the increase was significant in control group compared to midazolam and propofol primed groups. Mean heart rate was increased from baseline value of 80.40 ± 6.3 to 118.2 ± 5.63. So midazolam primed group has lesser variations in heart rate as compared to control group and propofol primed group. Similar results were obtained by Kataria *et al* [13].

Propofol is known to have a biphasic effect on the cardiovascular system. Firstly, immediately after injection, a decrease in systemic vascular resistance and mean arterial pressure predominate. This decrease in the systemic vascular resistance causes a reflex increase in sympathetic activity, which is mediated by baroreceptors present in the carotid sinus and aortic arch, there by leading to increase in the heart rate. The mean systolic blood pressure in propofol primed group was 117.90 ± 2.63 which decreased to 107.30 ± 2.77 immediately after induction while immediately after intubation there was rise in systolic blood pressure in all the groups but it was statistically significant in group II which was primed by midazolam. Immediately after induction the mean systolic blood pressure was 118.50 ± 1.91 which increased to 152.93 ± 1.98 in group II. Similar results were obtained by Cressy *et al* [16]. The mean baseline diastolic blood pressure in group I was 71 ± 1.36 which was decreased to 63.77 ± 1.52 immediately after induction. The mean diastolic blood pressure of group II was baseline 74.27 ± 1.96 which increased to 103.47 ± 2.36 immediately after intubation which was significant. Thus the propofol primed group showed no major variations in systolic and diastolic blood pressure compared to midazolam primed group. These findings were comparable with the study done by Kataria *et al* [13]. Amatya *et al* [14] observed greater hemodynamic stability in midazolam primed group compared to other groups.

We observed a greater reduction in blood pressure during induction in the control group as compared to other groups, which could be because of higher doses of Propofol needed in control group, as the control group did not receive any priming agent at the start of the study unlike the other two groups. Use of priming agent helps in reduction of dose of induction agent according to principle of synergism [17, 18]. Decreased dose will result in less fall in blood pressure. Oxygen saturation was comparable among all three groups and maintained above 95% throughout the surgery. No complications were noted in any of the groups.

However in considering the results of current study and others of its type it is notable that end-points are controversial and difficult to assess. We used loss of eyelash reflex as end point as BIS monitoring was not available in our institute. Other end-points are loss of verbal contact and response to placement of a face mask and BIS monitoring [19, 20].The results could vary because specific advanced monitoring. More studies with larger sample size with advanced monitoring may be required.

5. Conclusion

The present study supports that priming with both, midazolam and propofol is effective in reducing the dose of propofol induced anaesthesia. Dose reduction was significantly more with midazolam. Propofol auto co induction provides haemodynamic stability in peri intubation period.

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