



TO COMPARE THE HAEMODYNAMIC EFFECTS OF MIDAZOLAM AND PROPOFOL WHEN USED AS CO-INDUCTION AGENT TO PROPOFOL AND PROPOFOL ALONE

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Abstract

Background: Co-induction of anaesthesia, the rationale behind it being the combination therapy using two or more different drugs with the intention of reaching the same therapeutic goal was heavily criticized for a long time. However, it is accepted today, with the aim of achieving more specific 'target' responses, while minimizing side effects.

Aim: To compare the haemodynamic effects of midazolam and propofol when used as co-induction agent to propofol and thereby to find out which of these combinations, provides more haemodynamic stability as compared to propofol alone.

Methods: A profile 132 patients were divided into three groups Group A [n=41]: received only propofol for induction of anaesthesia. Group B [n=47]: received midazolam 0.03mg/kg prior to induction of anaesthesia with propofol and Group C [n=44]: received propofol 0.3mg/kg prior to induction of anaesthesia with propofol. The baseline hemodynamic parameters (mean arterial pressure, heart rate and spo₂) were recorded. After that parameters were recorded at 1, 2 and 5 minutes respectively. Graphically the data was presented by bar and line diagrams. A P-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

Results: The mean induction dose of propofol was 115.4±15.51 mg in Group A, 73.8±11.89mg in Group B and 81.4±15.34 mg in Group C. The difference was statistically significant with p value of < 0.001. There was statistically significant increase in heart rate from the baseline (P-value<0.01) at 1min, 2min and 5min after induction in Group C. whereas in other two groups (A and B) the difference was statistically insignificant. There was statistically significant increase in MAP in (Group C) from baseline at 2min and 5min after induction (p-value<0.05). Whereas in other two groups (A and B) the difference was statistically insignificant. The mean value of oxygen saturation were comparable at different time intervals among all the three groups. When compared all the values were statistically insignificant at all the times with p value of >0.05.

Conclusion: There was better hemodynamic stability in among the study population where coinduction agents were used, it was statistically insignificant. Also the difference among the study population where coinduction agents were used was statistically insignificant so far as hemodynamic stability is concerned.

Keywords: Coinduction, hemodynamic stability, midazolam, propofol, General anaesthesia.

Introduction:

In the world of anaesthesia, induction of anaesthesia is a very familiar word and one of those important events with which every anaesthesiologist and surgeon is well versed with. "Co-induction" (1,2,3) is defined as the concurrent administration of two or more drugs that facilitate induction of anaesthesia because of synergism(4,5). The term co-induction has been used to describe the practice of administering a small dose of sedative or another anesthetic agent(6) to reduce the dose of the induction agent required. The term co-induction was introduced in 1986 to describe the unplanned induction of anesthesia by non-anesthetically trained personnel practising sedation, unplanned anesthesia in unsuitable environment leading to several fatalities. Currently, planned co-induction of anesthesia is practised by anaesthesiologists exploiting drug interaction particularly synergism(7).

Over the years various intravenous drugs have been used for induction of anaesthesia. These include thiopentone, opioids, benzodiazepines, ketamine and propofol. Propofol is the most commonly used induction agent now a day.

The technique of co-induction with propofol would prove to be very useful to improve the ratio of desired versus adverse effects and to reduce the cost of induction (1). So far, the commonest co-induction agent to propofol has been midazolam (3). Midazolam is a benzodiazepine which increases the GABA mediated chloride ion conduction. It is used for premedication, anxiolysis, sedation, induction and co-induction of anaesthesia (8).

Methods:

The prospective observational study was conducted during November 2023 to February 2024 at Government Medical College Doda, on patients who were scheduled to undergo elective surgical procedures under general anaesthesia. Patients classified as American Society of Anaesthesiologist (ASA) I and II going for elective surgery between ages of 20-60 years were included.

Informed consent was taken from the patients who were included in this study. Final sample size in this study was 132. Patients observed, were those who had received either small dose of propofol(0.3mg/kg) or midazolam(0.03mg/kg) as co-inducing agent prior to induction of anaesthesia with propofol and those patients who had received only propofol as inducing agent. All the patients were induced with inj.propofol 40mg intravenous bolus then 10mg every 10seconds until the loss of verbal response. The baseline hemodynamic parameters(mean arterial pressure, heart rate and spo₂) were recorded. After that parameters were recorded at 1,2 and 5 minutes respectively.

STUDY DESIGN

All the patients who had matched the inclusion criteria were assessed by a pre-anesthetic examination. Baseline measurement of blood pressure(systolic blood pressure, diastolic blood pressure, mean arterial pressure), pulse rate, arterial oxygen saturation were recorded.

- Intravenous cannula was placed.
- During pre-oxygenation all the patients had received intravenous fentanyl (1µg/kg)

One minute later, patient received co-induction agent which was either midazolam(0.03mg/kg) or propofol(0.3mg/kg). After the injection of co-induction agent, each patient received i.v. lignocaine 20mg followed by propofol 40mg i.v. then 10mg i.v. propofol after every 10s. Patients were encouraged to keep talking. If there was no response to verbal command, propofol injection was stopped. Propofol for induction was given immediately after administration of co-induction agents. After propofol induction, succinylcholine 2mg/kg i.v. was given and the endotracheal intubation were done.

Patients were divided into three groups A, B and C as follows:-

Group A [n=41]: received only propofol for induction of anaesthesia.

Group B [n=47]: received midazolam 0.03mg/kg prior to induction of anaesthesia with propofol.

Group C [n=44]: received propofol 0.3mg/kg prior to induction of anaesthesia with propofol.

Statistical Methods

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Statistical software SPSS (version 20.0) and Microsoft Excel were used to carry out the statistical analysis of data. Continuous variables were expressed as Mean±SD and categorical variables were summarized as percentages. Analysis of variance (ANOVA) was employed for inter group analysis of data and for multiple comparisons, least significant difference (LSD) test was applied. For intra-group analysis, a repeated measure ANOVA was used. Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables. Graphically the data was presented by bar and line diagrams. A P-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

Results:

One hundred and thirty two patients were included in this observational study. In Group A (n=41) patients, Group B (n=47) patients and Group C (n=44) patients. All patients were comparable with regard to demographic profile among the study population [Table 1].

Table 1: Demographic characteristics among the study population

Variables	Group A	Group B	Group C	P Value
Age (years)	40.3±11.89	39.7±11.36	38.7±9.97	0.347
Sex M/F	22/19	26/21	25/19	0.874
ASA I/II	37/4	41/6	40/4	0.951
Weight (kg)	58.7±8.11	62.3±9.21	59.3±7.27	0.231

The average mean induction dose of propofol was 115.4 mg in group A, the mean induction dose of propofol was 73.8 mg in group B, and in Group C, the average mean induction dose of propofol was 81.4 mg. The difference was statistically significant with p value of < 0.001.

Table 2: Average induction dose of propofol (mg) among various groups

Groups	Mean ±SD	P Value
Group A	115.4±15.51	<0.005
Group B	73.8±11.89	
Group C	81.4±15.34	

Baseline mean heart rate (beats/min) in study groups were 83.22 (Group A), 86.36 (Group B) and 84.32 (Group C). Before induction mean heart rate (beats/min) were 84.20 (Group A), 87.30 (Group B), and 85.48 (Group C). At 1 minutes after induction mean heart rate (beats/min) in were 82.20 (Group A), 84.19 (Group B) and 83.07 (Group C). At 2 minutes after induction mean heart rate (beats/min) in study groups were 83.88 (Group A), 87.70 (Group B) and 87.61 (Group C). At 5 minutes after induction mean heart rate (beats/min) were 87.24 (Group A), 85.02 (Group B) and 88.91 (Group C) [Fig 1].

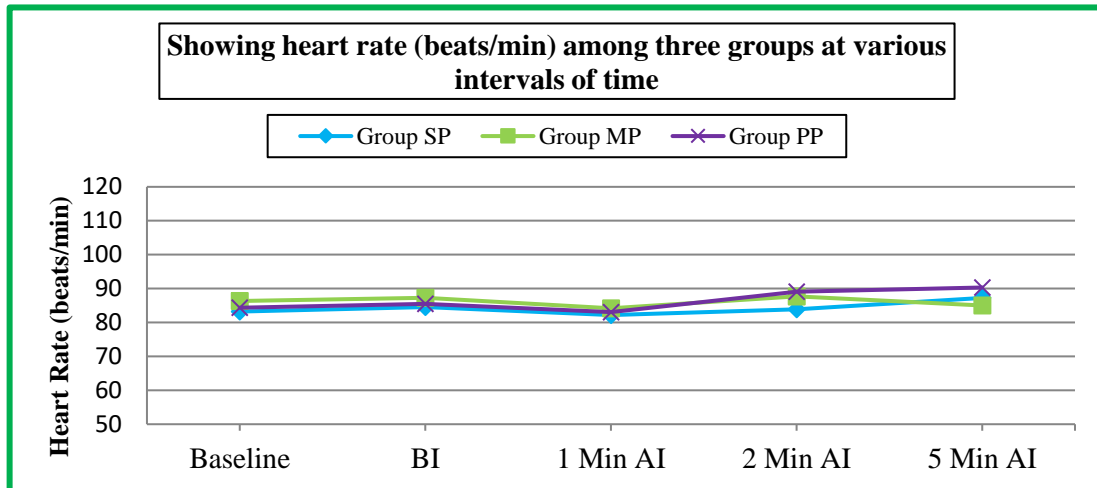


Fig 1.

Mean arterial pressure (MAP) (mmHg) in all three study groups were statistically significant (p-value<0.05) [Fig 2].

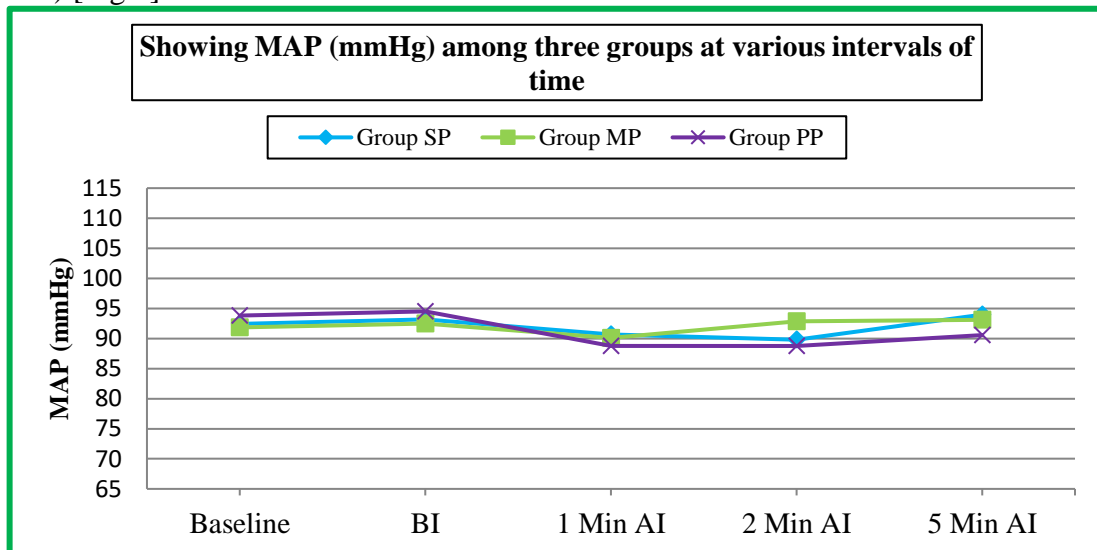


Fig 2.

Discussion:

The co-induction of anesthesia has been used to describe the practice of administering a small dose of a sedative or other anesthetic agent to reduce the required dose of the induction agent (9). Midazolam, when used as co-induction agent for general anesthesia (GA), has been shown to reduce the dose of propofol required for induction by up to 50% without affecting the recovery profile (10).

The development of hemodynamic changes is one of the most significant adverse effects associated with GA. Evidence suggests that the occurrence of hypotension/hypertension during GA is an independent factor that influences the treatment outcomes of surgical patients (11). Hemodynamic changes (mostly hypotension) can often occur after induction of GA and before surgical incision (11). Even short periods of hypotension can lead to tissue hypoperfusion and the development of complications that can increase postoperative morbidity and mortality (12).

In our study, average induction dose of propofol (in mg) among three groups was 115.4±15.51, 73.8±11.89 and 81.4±15.34 in group A, B and C respectively. The difference between the study groups was statistically significant with a p value of <0.001. There is 36.04% reduction in dose of propofol when midazolam is used as co-induction agent as compared to propofol group. The results of our study were comparable to study done by **JyothiMallikarjuna,Purneema K in 2015**

(13). Similarly in study done by **Anderson et al in 1998(4)**: A comparison between midazolam co-induction and propofol pre-dosing for the induction of anaesthesia in the elderly, they observed that the dose of propofol required to induce anaesthesia was significantly smaller in patients given propofol (1.87mg/kg) or midazolam (1.71mg/kg) when compared to control group (2.38mg/kg). More reduction of propofol dose in midazolam co-induction with propofol.

In our study, Hemodynamic parameters at 1min, 2min and 5min post induction. Comparing the mean values of heart rate at 1min, 2min and 5min post induction among the three groups. Our results regarding hemodynamic parameters were similar to **Jyothi Mallikarjuna, Purneema K in 2015 (13)**. **Cressy DM et al.**, (14) in 2001 compared the effects of pretreatment with midazolam at two different doses (0.025 and 0.05mg/kg) with placebo, on the induction dose requirements of propofol in two different age groups: 60 younger patients (aged 18-35 years) and 60 older patients (aged 60 years). There were no demonstrable benefits in terms of hemodynamic stability with midazolam co-induction or propofol pre-dosing. Our findings regarding the hemodynamic stability thus confirm with this study as in our study, midazolam and propofol combination did not show demonstrable benefits in terms of haemodynamic stability. **Salah Mostafa Asida (15)** in the year 2004 did a study to compare the effect of midazolam co-induction and propofol pre-dosing on the induction dose requirements of propofol.

Conclusion:

The average dose of propofol for induction of anaesthesia was found to be significantly less in those patients where coinduction agents were used as compared to the group where no coinduction agent was used.

There was better hemodynamic stability in all three study groups where coinduction agents were used, it was statistically insignificant. Also the difference among these study groups where coinduction agents were used was statistically insignificant so far as hemodynamic stability is concerned.

Conflict of interest: nil

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