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PROPOFOL INFUSION WITH MIDAZOLAM PREMEDICATION VERSUS PROPOFOL INFUSION ONLY FOR INDUCTION OF ANAESTHESIA: A COMPARATIVE STUDY

Anaesthesiology

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ABSTRACT

Background: Propofol is a popular anaesthetic agent used for induction. However, it causes cardiorespiratory depression in vulnerable patients.
Methods: In this study, fifty patients were randomly allocated into two groups receiving Inj. midazolam 0.03 mg/kg five minutes before induction with propofol infusion (Gp I) and only propofol infusion (Gp II).Total dose of propofol required for induction was noted. Haemodynamic parameters were noted from baseline till 10 minutes post laryngoscopy & intubation.
Results: In comparison with bolus dose of propofol for induction, the reduction in the dose of propofol in group-I and group-II was 0.71mg/kg and 0.30 mg/kg respectively. The reduction in the dose of propofol in group I as compared to group II was 0.41 mg i.e.24.06% which is statistically highly significant (P<0.001). No statistically significant changes in haemodynamic parameters were observed (p>0.05)
Conclusion: Propofol infusion with midazolam premedication for induction of anaesthesia is more advantageous technique.

KEYWORDS

Propofol, midazolam, induction, infusion

INTRODUCTION

Induction of anaesthesia by intravenous route is the most commonly practiced technique of induction of general anaesthesia due to introduction of newer and safer anaesthetic agents. However, quest for ideal intravenous anaesthetic agent for induction is still ongoing. An ideal anaesthetic agent used for induction must have rapid onset and offset of action. It should confer haemodynamic stability. It shouldn't get accumulated and have active metabolites. It should have analgesic and amnesic properties. It should be compatible with all solutions and have longer shelf life. It should be painless on injection

Modern intravenous anaesthetic agents like propofol and midazolam possess most of the characteristics mentioned above. But they have certain undesirable effects offsetting the smooth course of anaesthesia. Propofol has drawback of causing cardiovascular and respiratory depression in geriatric and dehydrated patients & in patients with cardiovascular compromise.[1] Some investigators used different drug combinations with propofol for induction which decreased side effects mainly by reducing dose of individual drugs by synergism[1,2]. Midazolam is demonstrated to be hypnotically synergistic with propofol as a premedicant or coinductant.[8] It was proposed by many workers that target controlled infusion of propofol for induction is safer than bolus dose given at random rate.[10] In this study we have compared induction with propofol infusion with midazolam premedication versus propofol infusion only and the effects on hemodynamic parameters.

METHODOLOGY

This prospective randomised controlled study was carried out in a tertiary care hospital spanning over 12 months. A sample size of 50 patients of either sex was studied and randomly allocated into two groups of 25 patients each – Group I and Group II receiving Inj. midazolam 0.03 mg/kg five minutes prior to induction with propofol infusion and only propofol infusion respectively for induction of general anaesthesia. Ethical clearance was obtained from hospital ethical committee.

INCLUSION CRITERIA

- Age between 12 to 65 years
- Patients undergoing elective neurosurgical procedures under general anaesthesia
- ASA (American Society of Anaesthesiologist) physical status I & II

EXCLUSION CRITERIA

- Emergency cases
- Patients with sinus bradycardia, heart block, bronchospastic airway disease and diabetes mellitus.

Baseline heart rate (HR), systolic blood pressure (SBP), Diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded.

Premedication:

Patients in both the groups were premedicated with Inj. glycopyrrolate 0.004 mg/kg and Inj butarphanol 20 microgram/kg intravenously half an hour before induction of general anaesthesia. Patients in group I received Inj. midazolam 0.03 mg/kg intravenously 05 minutes prior to induction of anaesthesia.HR, SBP, DBP & MAP were recorded at the time of premedication (preoperative baseline), at 15 th & 25 th minute after premedication with glycopyrrolate and butarphanol in both the groups and at 30 th minute (preinduction) in 'group I' to observe the effect of midazolam premedication.

Induction:

All patients were preoxygenated with 100% oxygen for 05 minutes. Patients in both groups were induced with Inj.propofol infusion using syringe infusion pump at the rate of 200ml/hr i.e.33.3 mg/min. Loss of verbal response was taken as the end point of induction and propofol infusion was stopped. The dose of propofol infused was noted.

Endotracheal intubation was facilitated with Inj rocuronium, 1mg/kg. Direct laryngoscopy was performed 60 seconds after injection of rocuronium and trachea intubated within 15 seconds with proper size flexometallic endotracheal tube. Hemodynamic parameters (HR, SBP, and DBP & MAP) were recorded for statistical analysis at induction, laryngoscopy & intubation and at 02 minutes interval post laryngoscopy and intubation till 10 minutes.

RESULTS

The values obtained were statistically analysed using unpaired student 't' test on account of small sample size (<30) and unknown population variance assumed unequal. In this study mean age of patients was 34.88 years in group I and 37.64 years in group II. The difference was not statistically significant. Mean weight of the patients was comparable in both the groups and 68.72% of total cases were male in both the groups as depicted in table 1.

Table 1: Demography of data

Parameters	Group I	Group II
No. of patients	25	25
Age (years)		37.64±15.28
Mean	34.88±1462	12-65
Range	12-65	
Weight (kg)		
Mean	46.60±12.72	52.00±12.83
Range	20-70	27-70
Sex%		
Male	17(68.0)	18(72.0)
Female	08(32.0)	07(28.0)

The dose of propofol for induction observed in group I and group II was compared with the bolus dose of propofol as used by other workers mentioned in this study. The dose of propofol required for induction in group I and group II was 1.29 mg/kg and 1.70 mg/kg respectively. The percentage of reduction in the dose of propofol was 35.5% and 15% respectively as compared to standard bolus dose of propofol i.e. 2mg/kg used in current practice.(Table 2) The profile of propofol doses is as shown in figure 1.

Table 2: Comparison of propofol dose in group I and Group II

Method of administration	Propofol dose (mg/kg)	Reduction in dose of propofol (mg/kg)	Reduction in dose of propofol (%)
Standard practice – Propofol bolus	2	-	-
Group I, Propofol infusion + Midazolam premedication, 0.03 mg/kg	1.29	0.71	35.5%
Group II, Propofol infusion	1.70	0.30	15%

Profile of propofol doses in mg/kg body weight

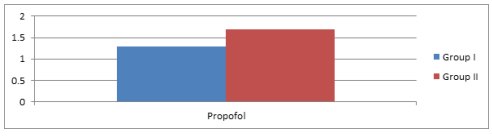

Figure 1

The reduction in mg/kg dose of propofol in group I as compared to group II was 0.41 mg which is 24.06%. The reduction was statistically highly significant. (Table 3)

Table 3: Comparison of propofol dose in group I & group II

Group	Midazolam (mg/kg)	Propofol dose		
		Required dose of propofol (mg/kg)	Reduction (mg/kg)	Reduction %
Group I	0.03±0.00	1.29±0.09	0.41	24.06
Group II	-	1.70±0.04	-	-

P< 0.001 (significant)

On comparison of haemodynamic parameters in group I and group II, the changes in heart rate, SBP, DBP and MAP were comparable and statistically insignificant (tables 4-7 & figures 2-5).

Table 4: Changes in mean heart rate (beats/min)

Period	Mean±SD	
	Group I	Group II
Preoperative baseline	86.36±13.54	83.16±10.25
Premedication (15 minutes)	86.08±11.41	81.68±10.03
Premedication (25 minutes)	85.32±9.59	81.48±9.33
Preinduction (30 minutes)	85.08±9.71	81.36±9.04
At Induction	83.00±9.59	80.24±9.09
Laryngoscopy & Intubation	86.60±9.66	87.84±6.39
02 Minutes	85.44±9.08	87.12±6.58
04 Minutes	84.40±8.98	86.96±6.26
06 Minutes	83.48±8.31	85.44±6.04
08 minutes	82.36±8.37	85.00±6.93
10 minutes	81.44±8.63	83.32±7.68

By student 't' test p>0.05 (not significant)

Comparison of changes in mean heart rate (per minute) in group I & II

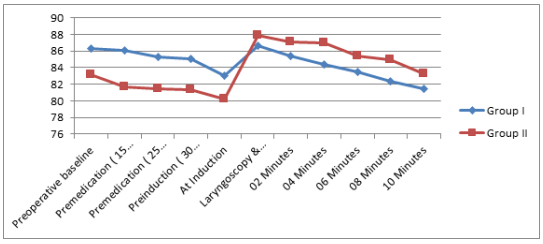

Figure 2

Table 5: Changes in systolic blood pressure (mm Hg)

Period	Mean±SD	
	Group I	Group II
Preoperative baseline	123.88±9.51	127.48±12.00
Premedication (15 minutes)	123.32±8.39	126.24±8.49
Premedication (25 minutes)	122.52±9.61	125.40±8.61
Preinduction (30 minutes)	121.36±9.11	124.68±8.67
At Induction	120.04±8.55	123.64±8.64
Laryngoscopy & Intubation	125.92±11.20	129.72±8.61
02 Minutes	123.80±8.50	128.00±8.70
04 Minutes	123.24±8.28	127.52±7.89
06 Minutes	122.24±8.23	126.44±8.20
08 minutes	121.80±8.19	124.44±8.31
10 minutes	121.12±8.11	122.60±8.64

By student 't' test p>0.05 (not significant)

Comparison of changes in mean systolic blood pressure in group I & II

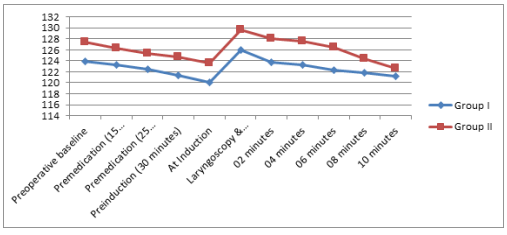

Figure 3

Table 6: Changes in *mean diastolic* pressure (mm Hg)

Period	Mean±SD	
	Group I	Group II
Preoperative baseline	78.36±5.92	78.44±6.94
Premedication (15 minutes)	76.60±6.80	76.60±5.76
Premedication (25 minutes)	76.36±5.45	76.40±6.01
Preinduction (30 minutes)	75.84±5.53	76.12±5.76
At Induction	74.48±5.49	75.16±5.28
Laryngoscopy & Intubation	79.68±5.50	80.72±4.89
02 Minutes	77.44±6.22	79.32±5.00
04 Minutes	76.16±7.32	78.56±4.94
06 Minutes	75.64±6.35	77.52±4.71
08 minutes	75.48±6.80	76.64±4.89
10 minutes	75.16±6.71	75.16±4.74

By student 't' test p>0.05 (not significant)

Comparison of changes in mean diastolic blood pressure in group I & II

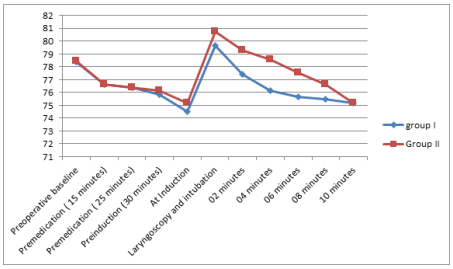

Figure 4

Table 7: Changes in mean arterial pressure (mm Hg)

Period	Mean±SD	
	Group I	Group II
Preoperative baseline	92.53±5.82	94.79±7.92
Premedication (15 minutes)	92.17±6.43	93.15±5.89
Premedication (25 minutes)	91.75±5.54	92.73±6.12
Preinduction (30 minutes)	91.01±5.65	92.31±6.00
At Induction	89.67±5.42	91.32±5.53
Laryngoscopy & Intubation	95.09±6.25	97.05±4.83
02 Minutes	92.89±5.65	95.55±5.29
04 Minutes	91.85±6.50	94.88±5.04
06 Minutes	91.17±5.89	93.83±5.21
08 minutes	90.92±6.17	92.57±5.30
10 minutes	90.48±6.03	90.97±5.18

By student 't' test p>0.05 (not significant)

Comparison of changes in mean arterial pressure in group I & II

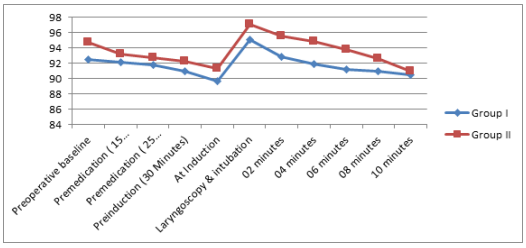

Figure 5

DISCUSSION

Although propofol is a popular anaesthetic agent used for rapid and smooth induction with minimal hemodynamic changes, it can cause remarkable hypotension in geriatric and dehydrated patients. It is also known to cause hypotension with concomitant use of opioids & benzodiazepines and in patients with cardiovascular compromise[1]

Drug combinations are often tried in the practice of anaesthesia to reduce side effects mainly by reducing doses of individual drugs by synergism. [1, 2, 3] The dose of propofol for induction of anaesthesia depends on several variables. Some of the important variables widely studied by many workers are rate of injection, age of the patient,use of premedication and anaesthetic end points viz. Loss of verbal contact, dropping of infusion flex (motor), loss of reaction to painful stimuli (antinociception) and attainment of EEG burst suppression.[(4)]

In conventional induction, the dose of propofol ranges from 2 to 2.5 mg/kg in unpremedicated young healthy adults [5, 6] In elderly patients who are premedicated with midazolam, the dose of propofol required for induction is shown to be 1.2 mg/kg. This is an effective and reliable method of reducing propofol dose as shown by Cressy DM et.al[1,6,7,8,9]

Several studies are carried out to study the effect of propofol infusion on the dose requirement and time taken for induction. The dose of propofol for induction is reduced when given by infusion.[10] In this study, induction was carried out with propofol infusion at the rate of 200 ml/hr i.e.33.3 mg/minute. Loss of verbal contact as the end point of induction was adopted in both the groups.

Group I which is considered as study group received injection midazolam 05 minutes before induction with propofol infusion at the rate of 33.3 mg/min.Onset of action of midazolam ranges from 54 seconds to 05 minutes hence maximum time limit was chosen in this study. Group II also received propofol infusion at the rate of 33.3 mg/min for induction but premedication with midazolam was not carried out.

All the patients in both groups were premedicated with Inj.glycopyrrolate 0.004 mg/kg and Inj butarphanol 20 microgram/kg intravenously 30 minutes prior to induction. The analysis of observations and results is as follows:-

The baseline values of age, sex and weight in both the groups are comparable as depicted in table 1.

The average dose of propofol in group I which received midazolam premedication was 1.29±0.09 mg/kg as shown in table 2. This is concurrent with study of Cressy DM et.al.[6] showing the dose of propofol for induction as 1.2 mg/kg when premedicated with midazolam prior to induction with propofol infusion. The average dose of propofol for induction in group II was 1.70±0.04 mg/kg.

Bolus dose of propofol for induction in standard practice is considered to be 2mg/kg. The percentage of reduction in propofol dose as compared to bolus dose observed in both the groups of this study is as follows (Table 2):-

a) 2mg/kg bolus Vs 1.29 mg/kg in group I – 35.5%
b) 2mg/kg bolus Vs 1.70 mg/kg in group II – 15%

Further on comparison of reduction in dose of propofol required for induction in group I versus group II, the reduction in dose of propofol in group I was 0.41 mg/kg i.e. 24.12 %.(Table 3)

In this study, hemodynamic changes from premedication till 10 minutes post laryngoscopy and intubation were statistically insignificant (Tables 4-7 & Figures 2-5). The findings correlate well with the studies already carried out on the subject. [4,8,10]

CONCLUSION

There is remarkable reduction in the dose of propofol for induction of anaesthesia without significant hemodynamic changes when administered as intravenous infusion with midazolam premedication. Propofol infusion with midazolam premedication is an advantageous technique of induction of general anaesthesia.

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Nil

Conflict of interest
Nil

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