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Original Research Article

Effect of Pre-Treatment with Intravenous Midazolam on Propofol Infusion for Induction of General Anaesthesia: An Observational Study Conducted in Upper Assam, India

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Abstract

Background: Propofol has drawback of causing cardiovascular and respiratory depression. Midazolam has synergistic effect with propofol. Target controlled infusion of propofol for induction appears to be safer than bolus dose given at random rate.

Methods: One hundred and eight consecutive patients, aged 18-60 years of either sex belonging to ASA status I or II undergoing elective surgery under general anaesthesia and meeting the inclusion criteria were selected. These patients were divided into two groups - Group I and Group II alternatively, each having 54 patients. Group I received injection midazolam 0.03 mg/kg five minutes prior to induction with propofol infusion and group II did not receive midazolam. In both the groups, propofol (10mg/ml) was infused intravenously using syringe pump at the rate of 200 ml/hr for induction of anaesthesia. Hemodynamic parameters were recorded for statistical analysis at baseline, pre-induction, induction, laryngoscopy & intubation and at two minutes interval post laryngoscopy & intubation till 10 minutes.

Results: The mean duration in Group I to achieve the end point of induction was 2.63 ± 0.39 minutes and in Group II was 3.48 ± 0.49 minutes. Average dose of propofol infusion required before loss of verbal response in Group I was 1.35 ± 0.03 mg/kg & in Group II was 1.73 ± 0.02 mg/kg.

Conclusions: Using midazolam premedication, reduces the total dose of propofol infusion and induction time by 21.97 percent and 24.43 percent respectively compared to propofol infusion only. Dosage of propofol infusion, even without midazolam premedication, was seen to be lower by 13.5 percent than that of IV bolus dose of 2 mg/kg body weight. Myocardial depression and vasodilatation are dose dependant phenomena of propofol. Therefore, reduction in the total dose of propofol would be safe and ensure lesser chances of circulatory collapse during induction of general anaesthesia.

Keywords: Propofol infusion, midazolam premedication

Introduction

In this era, commonly used intravenous induction agents include propofol, sodium thiopental, etomidate, methohexital, and ketamine. Inhalational anaesthesia could also be chosen when intravenous access is difficult to get (e.g., children), when difficulty maintaining the airway is anticipated.

One of the most commonly used inducing agents, propofol has drawback of causing cardiovascular and respiratory depression in old age and dehydrated patients & in patients with cardiovascular compromise. Some researchers have used different drug combinations with propofol for induction which decreased side effects mainly by reducing dose of individual drugs by synergism. Midazolam has synergistic effect with propofol as a pre-medicant or coinductant [1]. It was proposed by some researchers that target controlled infusion of propofol for induction is safer than bolus dose given at random rate [2].

In this study we have compared the total dose of propofol infusion for induction of general anaesthesia employing two regimens – propofol infusion with midazolam as pre-medication versus propofol infusion alone in patients undergoing elective surgeries under general anaesthesia. Propofol was infused using a syringe pump and rate of infusion was identical in both the groups. We have also observed and compared the time to achieve the end point of induction in the two groups & the effects on haemodynamic parameters in the two groups starting from baseline till ten minutes post laryngoscopy (direct laryngoscopy) and intubation and analysed the data statistically.

Methodology

After approval from the institutional ethical committee, the study was conducted under the Department of Anaesthesiology and Critical Care at Jorhat Medical College and Hospital, Jorhat, Assam for a period of one year commencing from July 2020 to June 2021 in the General Surgery, Neurosurgery, ENT, Orthopaedic, & Gynaecology operation theatres of the teaching hospital. The present study was a hospital based observational study comparing propofol infusion with midazolam premedication versus propofol infusion only for induction of anaesthesia in patients undergoing elective surgery under general anaesthesia.

Convenience, purposive sampling method was used in our study. One hundred and eight consecutive patients aged 18-60 years of either sex belonging to ASA status I or II scheduled to undergo elective surgery under general anaesthesia and meeting the following inclusion and exclusion criteria were selected for the study.

Inclusion criteria:

1. Age between 18 to 60 years.
2. Patients undergoing elective surgical procedures under general anaesthesia.
3. ASA (American Society of Anaesthesiologists) physical status I or II.

Exclusion criteria:

1. Those undergoing emergency surgeries.
2. Patients unwilling to give consent.
3. Patients with sinus bradycardia, heart block, bronchospastic airway disease, uncontrolled hypertension and/or diabetes mellitus, impaired liver or kidney functions and any neurological disease.
4. History of drug or alcohol history.

5. Patients in whom duration of laryngoscopy and intubation took more than fifteen seconds.

The patients were divided into two groups (Group I and Group II) alternatively. Each group had an equal number of 54 patients each. Group I patients received injection midazolam 0.03 mg/kg five minutes prior to induction and Group II patients did not. It was pre-determined that only those patients would be considered for final statistical analysis in whom duration from direct laryngoscopy to intubation would take below fifteen seconds to prevent excessive sympathetic response which might lead to severe rise in HR and BP in some patients thus affecting the mean haemodynamic profile post laryngoscopy and intubation in each group. Ten (10) patients in Group I and eight (8) patients in Group II had to be excluded from the study as duration of laryngoscopy and intubation exceeded 15 seconds in these patients. Therefore, finally, ninety (90) patients i.e. – forty-four (44) patients in Group I and forty-six (46) patients in Group II, included in the study, underwent the final statistical analysis.

In both the groups, propofol was infused intravenously using syringe pump at the rate of 200 ml/hr i.e. 33.3 mg/min for induction of anaesthesia. Group I - received injection midazolam 0.03 mg/kg five minutes prior to induction with propofol infusion. Group II – did not receive midazolam.

Thorough pre-anaesthetic checkups of the selected patients were performed prior to operation. Every patient selected for the study were explained about the procedure and written informed consent taken. Patients thus selected who satisfied the inclusion criteria were divided alternatively into two groups till sample size was reached.

On the day of surgery, patients selected for the study, were shifted to the pre-operative holding room 45 minutes prior to induction of general anaesthesia. Patients were asked to lie down on trolleys inside the pre-operative holding area and take rest for 15 mins. Patients were then connected to standard monitors {NIBP, SpO_2, HR & ECG (lead II)} and the baseline parameters recorded in each patient.

Intravenous access was secured in each patient with 18 G I. V. cannula and a Bi-Valve three way stop cock was used to facilitate the access for both IV drip set (for IV fluids) and PM-O line of syringe pump (for propofol infusion). 0.9% Normal Saline infusion started as per perioperative fluid guidelines for adults.

All patients were pre-medicated with injection metoclopramide 10 mg slow IV, injection glycopyrrolate 0.004 mg/kg IV & injection tramadol 2 mg/kg IV. All patients were supplemented with oxygen at the rate of 5 litre per minute via Hudson mask (simple face mask) after the pre-medication.

After 15 mins following premedication with injection metoclopramide, injection glycopyrrolate & injection tramadol, second recordings of NIBP, HR, SpO2, ECG (Lead II) were taken. Patients were then shifted to operation theatre table in trolleys.

Group I patients received injection midazolam 0.03 mg/kg five minutes prior to induction with propofol infusion. (i.e. 25 minutes post premedication with metoclopramide, glycopyrrolate & tramadol). Group II patients didn't receive midazolam. NIBP, HR, SpO_2, ECG were recorded again in patients of both the groups at 25 minutes & 30 minutes (pre-induction) following first premedication with metoclopramide, glycopyrrolate & tramadol.

Inside operation theatre all patients in both the groups were preoxygenated with 100% oxygen for 03 minutes. After pausing normal saline drip momentarily, patients in both groups were induced with propofol infusion using syringe pump at the rate of 200ml/hr (each ml containing 10 mg of Propofol) i.e. 33.3 mg/min. Loss of verbal response was taken as the end point of induction and propofol infusion was terminated. The total dose of propofol infused and the time to achieve the end point of induction were recorded. HR, SBP, DBP and MAP readings were taken at this moment (Induction). ECG, SpO2 were also monitored at all times. Preoxygenation was continued. Intravenous saline drip was resumed again as per intra- operative IV fluid management protocol. Intra-operative intravenous fluid management was done using Ringer's lactate and 0.9% Normal saline. Colloids were kept in hand for any emergency. Availability of cross matched PRBC/Whole blood in Blood Bank was ensured for any unpredictable emergency need intra-operatively due to the undergoing surgical procedure.

Endotracheal intubation was facilitated with injection succinylcholine 1.5 mg/kg. Direct laryngoscopy was performed 60 seconds after injection of succinylcholine (1.5 mg/kg) and trachea was intubated within 15 seconds from laryngoscopy with proper size endotracheal tube. HR, SBP, DBP and MAP readings were taken just after intubation. SpO2, ECG were also monitored continuously. Duration from direct laryngoscopy to intubation was completed within 15 seconds for each patient in both the groups.

Hemodynamic parameters (HR, SBP, and DBP & MAP) were recorded for statistical analysis at pre-induction, induction, laryngoscopy & intubation and at two minutes interval post laryngoscopy & intubation till 10 minutes. The baseline haemodynamic parameters (i.e. when the patients arrived the pre-operative holding areas) were also noted down for statistical analysis.

IPPV with nitrous oxide, oxygen (2:1 ratio) was started following intubation (after checking bilateral air entry in lungs) & inhalational anaesthetic sevoflurane was used as and when required during the surgical procedure.

Non-depolarising muscle relaxant injection atracuium besylate was used as per body weight for muscle relaxation during the surgical procedure. During the surgery, Paracetamol infusion (15mg/kg body weight) was given for peri-operative analgesia.

At the end of the surgery residual neuromuscular blockade was antagonized by injection Neostigmine (0.05 mg/kg body weight) and injection Glycopyrrolate (0.01 mg/kg body weight). Pharyngeal suctioning was done and when adequate spontaneous ventilation was established, patients were extubated. Patients were then shifted to recovery room for observation. Subsequently, after stabilisation of patients, they were sent back to their respective wards.

Statistical analysis

Data were presented as frequency, percentage and mean ± standard deviation. The statistical analysis was done using the computer program Statistical Package for the Social Sciences (SPSS for Windows, version 20.0 Chicago, SPSS Inc.)and Microsoft Excel 2010.

1. **Student's t-test** determines whether two populations express a significant or non- significant difference between population means. Results on continuous measurements were

presented as mean ± standard deviation. They were compared using unpaired t test (for intergroup differences) and paired t test (for intragroup differences).

2. **Fischer exact test** examines the significance of the association (contingency) between the two kinds of classification. Sex distribution, ASA physical status of the two groups were analysed employing Fischer exact test.

For all statistical analysis, the statistical significance was fixed at 5% (p value <0.05).

Results & Observations

The demographic characteristics of the patients in the two study groups were comparable as shown in Table 1. The average age in years in Group I & Group II were 36.82 ± 12.56 and 37.69 ± 13.68 respectively. The average weight in kilograms in Group I was 64.68 ± 9.52 and Group II was 66.97 ± 9.64. The ASA status and sex distribution of the patients in the two groups were also comparable as shown in Table 1.

Table 1: Demographic Characteristics

S.N.	Demographic Variable	Group I (Mean ± SD)		Group II (Mean ± SD)		p value
1	Age (years)	36.82 ± 12.56		37.69 ± 13.68		0.754
2	Weight (kg)	64.68 ± 9.52		66.97 ± 9.64		0.260
	Demographic Variable	**Group I**		**Group II**		
3	ASA status	ASA I	34	ASA I	34	0.808
		ASA II	10	ASA II	12	
4	Sex	Male	28	Male	36	0.164
		Female	16	Female	10	

Student's t test was used to calculate p value for Sl. Nos. 1 and 2. **Fischer exact test** was used to calculate p value for Sl. Nos. 3 and 4

It was observed that the total dose of propofol needed (via infusion) - with injection midazolam 0.03 mg/kg five minutes prior to induction decreased by 32.5% (compared to usual IV bolus dose of 2 mg/kg for adults) and without injection midazolam decreased by 13.5% (compared to usual IV bolus dose 2 mg/kg).

Table 2: Different methods of Propofol administration

Method of Administration of Propofol	Propofol dose (mg/kg)	Reduction in dose of Propofol (mg/kg)	Percentage reduction in dose of Propofol
Usual practice of IV bolus dose	2	-	-
Group I (Infusion with injection midazolam premedication, 0.03mg/kg)	1.35 ± 0.03	0.65	**32.5**
Group II (Infusion without injection midazolam premedication)	1.73 ± 0.02	0.27	**13.5**

Moreover, in group I patients, using injection midazolam 0.03 mg/kg body weight five minutes prior to induction, there was a reduction of total dose of propofol infusion by 21.97 % (p < 0.0001) to achieve the end point of induction compared to group II patients, who did not receive injection midazolam. The average durations of infusion in Group I and Group II to achieve the end point of induction (loss of verbal response)

were 2.63 ± 0.39 minutes and 3.48 ± 0.49 minutes respectively.

Table 3: Duration of Propofol infusion to achieve loss of verbal response

Variable measured	Group I	Group II	p value
Durations in minutes (Mean ± SD)	2.63 ± 0.39	3.48 ± 0.49	< 0.0001

The groups were tested for homogeneity with respect to HR, SBP, DBP, MAP. Student's t-test was applied to calculate the p value for the differences in mean haemodynamic parameters between the two groups. The differences in baseline vital parameters in the two groups were not significant statistically (p > 0.05).

While observing the intra-group mean vital parameters at pre-induction period (5 mins after injection midazolam in group I) compared to the baseline parameters as shown in Table 4, drop was seen in all the vital parameters - HR, SBP, DBP, MAP in group I. We could see there was a slight increase in mean HR and SBP in group II. Notably the decrease in DBP and MAP in group I was statistically significant.

Table 4: Intergroup & intragroup haemodynamic alteration at pre-induction period (5 minutes after injection midazolam in group I) compared to baseline mean

Vital Parameters		Baseline	Pre-Induction period	% Change	Intragroup p value
Heart Rate (BPM)	Group I	79.95 ± 6.52	77.81 ± 4.13	2.68 (decreased)	0.04
	Group II	78.65 ± 7.15	79.52 ± 4.82	1.11 **(increased)**	0.36
	Intergroup	**p value=0.37**	**p value=0.07**		
SBP	Group I	123.81 ± 7.21	122.39 ± 5.69	1.15 (decreased)	0.08
	Group II	122.43 ± 6.48	124.19 + 6.26	1.44 **(increased)**	0.02
	Intergroup	**p value=0.33**	**p value=0.16**		
DBP	Group I	73.32 ± 5.31	70.09 ± 4.57	4.41 (decreased)	<0.001
	Group II	71.35 ± 4.67	69.76 ± 3.88	2.23 (decreased)	0.008
	Intergroup	**p value=0.06**	**p value=0.71**		
MAP	Group I	90.27 ± 5.69	87.5 ± 4.56	3.07 (decreased)	<0.001
	Group II	88.39 ± 4.89	87.87 ± 4.36	0.59 (decreased)	0.36
	Intergroup	**p value=0.09**	**p value=0.69**		

(unpaired t test was used to calculate the p value for intergroup differences and paired t test was used to calculate the p value for intragroup differences)

The haemodynamic parameters in the two groups at the time of induction (pre-intubation) was compared to the baseline mean vital parameters. we could see a greater fall in all the vital parameters - HR, SBP, DBP, MAP in group I than in group II. Paired t-test was used to statistically compare the mean vital parameters at induction with that of baseline within each group(intragroup). Table 6 shows that Group I, which received injection midazolam 5 mins prior to induction, showed a slightly lesser rise in HR, SBP, DBP and MAP at laryngoscopy and intubation than Group II.

Table: 5 Intergroup & intragroup haemodynamic alteration at the time of induction (pre- intubation) compared to baseline mean

Vital Parameters		Baseline	Induction (pre-intubation)	% Change	Intragroup p value
Heart Rate (BPM)	Group I	79.95 ± 6.52	75.34 ± 4.15	5.77 (decreased)	<0.0001
	Group II	78.65 ± 7.15	75.28 ± 5.01	4.28 (decreased)	0.002

	Intergroup	**p value=0.37**	**p value=0.95**		
SBP	Group I	123.81 ± 7.21	119.06 ± 5.30	3.84 (decreased)	0.0007
	Group II	122.43 ± 6.48	121.67 ± 6.01	0.62 (decreased)	0.34
	Intergroup	**p value=0.33**	**p value=0.03**		
DBP	Group I	73.32 ± 5.31	68.68 ± 4.51	6.33 (decreased)	0.012
	Group II	71.35 ± 4.67	68.17 ± 3.41	4.46 (decreased)	<0.001
	Intergroup	**p value=0.06**	**p value=0.55**		
MAP	Group I	90.27 ± 5.69	85.52 ± 4.57	5.26 (decreased)	<0.001
	Group II	88.39 ± 4.89	86.04 ± 3.82	2.66 (decreased)	<0.001
	Intergroup	**p value=0.09**	**p value=0.56**		

(unpaired t test was used to calculate the p value for intergroup differences and paired t test was used to calculate the p value for intragroup differences)

Table 6: Intergroup & intragroup haemodynamic alteration at laryngoscopy and intubation compared to baseline

Vital Parameters		Baseline(mean)	At laryngoscopy & Intubation (mean)	% change	Intragroup p value
Heart Rate (BPM)	Group I	79.95 ± 6.52	92.54 ± 5.28	15.74	<0.0001
	Group II	78.65 ± 7.15	93.32 ± 5.79	18.65	<0.0001
	Intergroup	**p value=0.37**	**p value=0.51**		
SBP	Group I	123.81 ± 7.21	141.40 ± 4.44	14.20	<0.0001
	Group II	122.43 ± 6.48	143.04 ± 5.09	16.83	<0.0001
	Intergroup	**p value=0.33**	**p value=0.11**		
DBP	Group I	73.32 ± 5.31	92.02 ± 3.13	25.50	<0.0001
	Group II	71.35 ± 4.67	93.02 ± 3.58	30.37	<0.0001
	Intergroup	**p value=0.06**	**p value=0.16**		
MAP	Group I	90.27 ± 5.69	108.43 ± 3.37	20.12	<0.0001
	Group II	88.39 ± 4.89	109.69 ± 3.93	24.10	<0.0001
	Intergroup	**p value=0.09**	**p value=0.11**		

(Unpaired t test was used to calculate the p value for intergroup differences and paired t test was used to calculate the p value for intragroup differences)

Group I, which received injection midazolam 5 mins prior to induction, showed faster stabilisation of HR, SBP, DBP & MAP within 10 mins post laryngoscopy and intubation than group II.

It is to be noted from Table 7, the intragroup haemodynamic changes in group II were 'highly significant' at 10 minutes following laryngoscopy and intubation when compared with the baseline mean vitals (p value < 0.001). Group I, too showed certain increase in haemodynamics from baseline at the same time interval which was statistically 'significant' (p value < 0.05 but > 0.001).

The intergroup differences of mean DBP and MAP at 10 mins post laryngoscopy and intubation were statistically significant as p values respectively were 0.01 and 0.02.

Throughout the entire study period, no patient showed any unexpected or serious change in haemodynamics peri-operatively or any untoward complication whatsoever. Recovery after the surgical procedure in both the groups were rapid, smooth and uneventful. The mean recovery time in both the groups were below five minutes.

Table 7: Intergroup & intragroup haemodynamic alteration at 10 minutes post laryngoscopy and intubation compared to baseline

Vital Parameters		Baseline(mean)	10 mins post laryngoscopy & Intubation (mean)	% change	Intragroup p value
Heart Rate (BPM)	Group I	79.95 ± 6.52	82.95 ± 2.60	3.75%	0.006
	Group II	78.65 ± 7.15	82.39 ± 1.57	4.76%	0.0008
	Intergroup	**p value=0.37**	**p value=0.22**		
SBP	Group I	123.81 ± 7.21	127.20 ± 4.29	2.73%	0.0008
	Group II	122.43 ± 6.48	129.16 ± 4.91	5.49%	<0.001
	Intergroup	**p value=0.33**	**p value=0.05**		
DBP	Group I	73.32 ± 5.31	75.79 ± 3.83	3.37%	0.005
	Group II	71.35 ± 4.67	77.85 ± 3.76	9.11%	<0.001
	Intergroup	**p value=0.06**	**p value=0.01**		
MAP	Group I	90.27 ± 5.69	92.93 ± 3.71	2.94%	0.002
	Group II	88.39 ± 4.89	94.89 ± 3.99	7.35%	<0.001
	Intergroup	**p value=0.09**	**p value=0.02**		

(Unpaired t test was used to calculate the p value for intergroup differences and paired t test was used to calculate the p value for intragroup differences)

Discussion

In daily practice, bolus IV dose of propofol for inducing general anaesthesia ranges from 2 to 2.5 mg/kg in young healthy adult. Several studies previously have been carried out to study the effect of propofol infusion on the dose requirement and time taken for induction.

According to the study by P S Gill *et al* (2001)[3], patients who were given midazolam required significantly less propofol to achieve satisfactory laryngeal mask insertion. They concluded that midazolam reduces the dose of propofol required for induction of anaesthesia and successful insertion of the laryngeal mask airway. In our study too, we have observed a 21.97% decrease (p value <0.0001) in the total dose of propofol infusion – with injection midazolam 5 minutes prior to induction compared to propofol infusion without midazolam, to achieve the end point of induction which is concurrent with the study by PS Gill *et* al [3]. Oliver H. G. Wilder-Smith et al (2011) [4] in their study investigated the interactions between midazolam premedication and propofol infusion induction of anaesthesia for multiple anaesthetic endpoints including loss of verbal contact, dropping an infusion flex, loss of reaction to painful stimulation and attainment of EEG burst suppression. They found at the hypnotic, motor and EEG endpoints, midazolam premedication significantly and similarly reduced propofol ED50 (reduction: 18%, 13% and 20% respectively; P <0.05 vs unpremedicated patients) and ED95 (reduction: 20%, 11% and 20% respectively; P <0.05 vs unpremedicated patients). For antinociception (LRP), dose reduction by premedication was greater for propofol ED95 (reduction: 41%; P <0.05 vs unpremedicated patients) than ED50 (reduction: 18%; P <0.05 vs unpremedicated patients). Hemodynamic values were similar in both groups at the various endpoints. From their study, they concluded that midazolam premedication 20 min prior to induction of anaesthesia reduced the propofol doses necessary to attain the

multiple anaesthetic endpoints studied without affecting the haemodynamics in the otherwise healthy population. They also concluded that the interaction differed for different anaesthetic endpoints (e.g., antinociception vs hypnosis) and propofol doses (e.g., ED 50 vs ED 95). In our study we administered injection midazolam (0.03mg/kg) in Group I five minutes prior to induction of anaesthesia. Propofol was infused at a constant rate of 33.3 mg/min till attaining the end point of induction (loss of verbal response). Whereas Oliver H. G. Wilder-Smith *et al*4 (2011) administered a larger dose of injection midazolam 0.05mg/kg twenty minutes prior to induction with propofol infusion. Moreover, their rate of propofol infusion varied with the weight of the patient i.e. 30mg/kg/hr unlike in our study. We infused propofol using an infusion pump at the same rate i.e. 33.3 mg/min to all patients and we calculated the total dose infused till achieving the end point of induction. In both the studies, we can see midazolam pre- medication reduced the total dose of propofol requirement for attaining the anaesthetic endpoints in our respective studies. In the study by Irene G Chainaki *et al* (2011) [5] on deep sedation for ERCP, the authors had got similar findings that combination of propofol and midazolam significantly reduced the total propofol amount required for sedation and consequently reduced the risk of apnoea during conscious sedation. This finding was specifically useful for conscious sedation for octogenarians where large doses of propofol can lead to cardiovascular collapse.

T. J. Ebert *et al* (1990) [6] in their study on 'Midazolam & fentanyl effects on muscle sympathetic nerve activity and baroreflex function in humans', found that administration of sedative doses of midazolam produced a transient decrease in BP, which they said, was attributed to reductions in sympathetic outflow to blood vessels supplying skeletal muscle. T. J. Ebert *et al* (1990) [6] also concluded that midazolam induced decrease in HR and the demonstration of unchanged R-R interval baroreflex slopes indicated that midazolam reset the heart rate limb of the baroreflex to a lower operating point. Midazolam also appeared to lower the operating point without altering the gain of the baroreflex control of MSNA. Though in our study, we did not find any statistically significant difference in mean HR at any point in between the two groups studied. Tomoki Nishiyama (2018) [7] studied on eighty patients aged 40-60 years, (ASA grade I and II) who all underwent general anaesthesia for neck and body surface surgery. They were randomized & in one group midazolam was given as premedication (0.06 mg/kg) IM 15 mins before anaesthesia induction. He concluded that midazolam inhibited sympathetic activation at induction of anaesthesia. [8]

In our study, with respect to DBP in group I, we saw that at pre-induction period there was a fall in mean DBP by 4.41% from baseline (p value < 0.001) whereas at the same time interval, group II showed a 2.23 % fall in DBP (p value $= 0.008$) but the intergroup differences of mean DBP at pre-induction period was not significant ($p > 0.05$). At induction (pre-intubation), the DBP in group I fell further by 6.33% from baseline ($p = 0.012$) which may be attributed to reductions in sympathetic outflow to blood vessels supplying skeletal muscle. Even in group II, at induction (pre-intubation), we saw a decline in DBP by 4.46% from baseline ($p < 0.001$) which was also statistically significant which may be the result of

comparatively increased dose of propofol infused in group II compared to group I. The intergroup comparison of DBP at induction remained statistically nonsignificant ($p > 0.05$). But to be noted that, though the intergroup comparison of mean DBP at 10 mins post intubation is significant, p value 0.02; group I showed lesser alteration of DBP from baseline than group II at 10 minutes (p 0.002 vs <0.001). With respect to MAP, during pre-induction (5 mins following injection midazolam in group I), the MAP in group I fell by 3.07% ($p < 0.001$ i.e. statistically highly significant) which can be attributed to reductions in sympathetic outflow to blood vessels supplying skeletal muscle.[7] Group II, showed a slight alteration of MAP by 0.59% ($p = 0.39$) which was not significant statistically. At the time of induction (pre-intubation), in group I and II there were a dip in mean MAP by 5.26% (p value <0.001) and 2.66% (p value 0.01) respectively from baseline. But, notably the intergroup differences in mean MAP at both pre-induction and induction (pre-intubation) were not significant (p value > 0.05). The intergroup differences in mean MAP at 10 minutes post laryngoscopy and intubation were statistically significant (p value < 0.05).

Conclusion

Total dosage of propofol infusion was seen to be lower by 13.5 percent with respect to the usual practice of administration of IV bolus dose of 2 mg/kg body weight in otherwise healthy adult patients for induction of anaesthesia. Using midazolam premedication, 5 minutes prior to induction, reduces the total dose of propofol infusion by 32.5 percent and 21.97 percent (p value < 0.0001) compared to propofol administered as IV bolus - 2 mg/kg (traditionally) and propofol infusion only - 1.73 ± 0.02 mg/kg respectively. Myocardial depression and vasodilatation are dose dependant phenomena of propofol. Therefore, reduction in the total dose of propofol would be safe and ensure lesser chances of circulatory collapse during induction of general anaesthesia. The effect of propofol infusion with midazolam premedication versus propofol infusion only on hemodynamic parameters during laryngoscopy and intubation were comparable ($p > 0.05$), both regimen showing similar rise in haemodynamic parameters (during laryngoscopy and intubation) but haemodynamics in the midazolam premedication plus propofol infusion group stabilised faster than propofol only (without midazolam) infusion group post intubation.

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