Original Research Paper

Volume - 11 | Issue - 07 | July - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Anaesthesiology

UNDERSTANDING THE PRIMING PRINCIPLE: COMPARING THE EFFICACY OF AUTO-CO INDUCTION BY PROPOFOL AND MIDAZOLAM PROPOFOL CO-INDUCTION.

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ABSTRACT Co-induction is the administration of a small dose of a sedative or anaesthetic agent prior to induction of anaesthesia. The "priming technique" is a technique of giving a precalculated dose of induction agent before administrating the full dose of the same induction agent is known as "Auto- co-induction". Three groups of thirty subjects each undergoing elective surgery were included in the study. Patients who were categorized into three groups (Group I, Group II, Group III) were administered with priming agent 0.5 mg/kg IV propofol, 0.05 mg/kg IV midazolam and 3 ml of normal saline respectively. Two minutes after giving the priming agent, patients were administered with propofol by IV induction in all three groups until the BIs value became 40. Any complications were recorded. Propofol induction dose requirements were found to be highly significantly different in groups I and II as compared to control group. Mean induction dose requirement was found to be 42.27% lesser in midazolam co-induction group and 33.16% lesser in propofol auto-co-induction group as compared to the control group. The priming with propofol leads to haemodynamic stability both at post-induction interval and later on. There is total dose reduction in propofol by priming in relation to propofol, thus making it less costly.

KEYWORDS :

INTRODUCTION

Co-induction is the administration of a small dose of a sedative or anaesthetic agent prior to induction of anaesthesia, the aim being to reduce the dose of induction agent required.[1] The "priming technique" also known as the "Auto-co-induction" method. It is a technique of giving a precalculated dose of induction agent before administrating the full dose of the same induction agent is known as "Auto-co-induction".[2,3,4]

It includes administration of a small sub-paralysing dose of the non-depolariser.[5] (20% of the ED95 or about 10% of the intubating dose.) This dose should be administered approximately 2-4 minutes before the second large dose for tracheal intubation. Principles of priming techniques have been reported corresponding to the utilization of muscle relaxants. The simultaneous administration of two or more drugs that encourages induction of anaesthesia reporting synergism is defined as "co-induction".[6,7,8,9,10] However, there are very few such studies[2] archiving the utilization of priming principle in induction agents. When given a few minutes before the induction at sub-hypnotic dose, this technique shows sedative, anxiolytic and amnesic effects.

These wide range of properties make this technique more reliable. The whole study was conducted to assess the effect of this technique in reduction in effective dose of induction agent and influence on peri-intubation haemodynamic. The commonly used drugs for induction are propofol and midazolam and it shows synergistic interaction for hypnosis and reflex sympathetic suppression. Hence, priming technique can play an effective role in the field of anaesthetics.[11,12,13]

METHODS

After obtaining approval from the institutional ethical committee, the present study was conducted on ninety patients of age between 18 to 50 years, American society of anaesthesiologist (ASA) g I and II, from both the sexes. Written, informed consent was taken before the procedure. These patients have no past history of adverse anaesthetic reactions and were elective gastrointestinal surgeries. These ninety patients were randomly divided into three equal groups consisting 30 patients in each group :-

- Group I (Propofol)
- Group II (Midazolam)
- Group III (Normal Saline)

As these patients were admitted in the OR (operation room), routine monitoring was done i.e. non-invasive blood pressure (NIBP), continuous surface ECG, pulse oximetry, Bi-spectral index (BIs) monitor BIs xp model no. A-2000 (Aspect medical system Inc., USA). An intravenous line was secured in the upper limb for surgical procedure. After skin preparation, surface electrodes of fronto temporal (BIs quatro) part were placed on the patient's forehead. The smoothing rate was set at 15 sec and impedance of electrodes were evaluated. Before the induction of anaesthesia, pre-operative baseline values of blood pressure (an average of two consecutive readings) and heart rate (HR) were taken at a 5minutes difference and baseline Bis value were also recorded.

Patients who were categorized into three groups (I,II,III) were administered with priming agent 0.5 mg/kg IV propofol, 0.05 mg/kg IV midazolam and 3 ml of normal saline respectively. Two minutes after giving the priming agent, patients were administered with propofol by IV induction in all three groups until the BIs value became 40. The rate of administration of same dose propofol in all the cases was 30 mg/10 seconds. Any complications during this induction process were noted such as apnoea, vomiting, laryngospasm, coughing, involuntary movements etc. Inj. Rocuronium 1mg/kg I.V. was administered to achieve relaxation and intubation. For maintenance of anaesthesia, O2/N2O (35%, 65%) , inhalational agent , i.e. isoflurane and injection vecuronium (0.02 mg/kg) was used. No stimuli were applied during the 5 minutes post - intubation period.

The following parameters were recorded: -

- SpO2, BIs value, NIBP and HR [(systolic blood pressure (SBP) and diastolic blood pressure (DBP)] were measured just before and after the induction immediately. Just after intubation and 5 minutes after intubation.
- Total dose of propofol required for getting targeted BIs value.
- Post-operative recall phenomenon was also recorded.

RESULTS

The groups had no statistically significant differences among them in demographic details such as age, sex(gender), weight and ASA grade. [Table 1] All data have been reported as mean value ±2 SD. The data were analysed statistically using the SPSS statistical package version 16.0 software.

Comparison between the groups for the induction dose and haemodynamic parameters was done using analysis of variance (ANOVA) with Tukey's *post-hoc* test. A P value of <0.05 was considered to be significant and $P<0.001$ was considered to be highly significant.

Propofol induction dose requirements were found to be highly significantly different in groups I and II as compared to control group. ($p<0.001$) Mean induction dose requirement was found to be 42.27% lesser in midazolam co-induction group and 33.16% lesser in propofol auto-co-inductiongroup as compared to the control group [Table 2]. In the post-priming BIS values a highly significant difference was

observed among all three groups. The propofol group had the highest fall at post- induction interval. No significant differences were seen in BIS numbers at post-induction and postintubation and 5 minutes post-intubation for both propofol auto-co-induction and midazolam co-induction groups. [Table 3]

Among the other parameters under observation in the study, SpO2 (oxygen saturation) level showed no significant changes in any of the groups under study. At the post-priming level in propofol auto- co-induction group a statistically significant fall in heart rate was observed. ($p<0.001$) [Table 4] Post- intubation rise in heart rate was seen in all groups the smallest in the group I (propofol group). Mean SBP was observed to be maintained at induction in the control group and a slight fall was observed in other two groups. Maximum rise in SBP after intubation (20.19%) from pre-induction value was observed in the midazolam co-induction group. [Table 5].

Table 1: Demographic Values

Groups	Age (years)	Gender distribution (M:F)	ASA grade (I:II)	Weight
Propofol (I)	35.8 (14.1)	17:13	22:8	57.75 (15.0)
Midazolam (II)	37.1 (10.23)	14:16	20:10	62.10 (13.20)
Normal saline (III)	32.6 (11.45)	22:12	19:11	62.90 (9.12)
P value	0.510	0.423	0.485	0.601

All values in mean (2SD), Statistically not significant, ASA: American Society of Anaesthesiologist.

Table 2: Propofol Induction Dose Of The Three Study Groups

Groups	Propofol (Group I)	Midazolam (Group II)	Normal Saline (III)	Post -hoc (P value)
Propofol induction dose (mg)	73.4 (16.68)	63.4 (15.12)	109.83* (30.10)	<0.001

All values in mean (2SD), *Statistically significant from other two groups

Table 3: BIS Values Among The Three Groups

BIS Values				
	I	II	III	P value
Baseline	95.90	96.84	95.45	0.123
Post-priming	76.90*	84.50*	96.10*	<0.001
Post-induction	42.30	42.07	41.85	0.055

*Statistically significant between these two groups, BIS: Bi spectral Index

Table 4: Heart Rate Changes At Different Points

	Heart rate		
	Group I	Group II	Group III
Baseline	82.83	82.80	84.30
Post-priming	80.16*	84.06	90.40*
Post-induction	80.23	83.70	91.73**
Post-intubation	99.43*	105.80	110.13*
5 minutes post- intubation	98.73	106.16	104.93

Table 5: Systolic Blood Pressure At Different Points

	Systolic Blood Pressure		
	Group I	Group II	Group III
Baseline	131.4	122.85	128.5
Post-priming	121.0	114.86	129.0**
Post-induction	115.0	112.16	117.2
Post-intubation	135.0	142.5**	138.80
5 minutes post- intubation	138.0	131.5	125.65

DISCUSSION

This study was undertaken to compare the propofol co-induction and midazolam co-induction with respect to reduction in induction dose propofol and improved haemodynamic stability in peri- intubation period. The clinical efficacy of both the groups were compared. In group I, when priming with propofol, mean induction dose requirement of propofol [Table 2] was 73.40 mg as compared to the mean induction dose of 109.83 mg in the control group. We observed a 33.16% reduction in induction dose of propofol by applying auto-co-induction.

Our result is similar to many previous studies which show a reduced pre-dosing of propofol.[2,4] The sedative and amnesic effects of propofol at sub-hypnotic doses are supposed to facilitate the induction of anaesthesia at a lower induction dose.[13] Kumar et al found a 27.485 reduction in induction dose of propofol.2 In group II, when primed with midazolam, mean induction dose of propofol [Table 2] was 63.40 mg as compared to the mean induction dose of 109.83 mg in the control group. There was 42.27% reduction in the induction dose of propofol with midazolam co- induction. Similar changes are seen in earlier studies that there is reduction in induction dose of propofol with midazolam pre-induction.[14,15]

In the present study a predetermined BIS value (i.e., BIS 40) was taken as an endpoint of induction.[16,17] The maximum reduction in BIS [Table 3] at post-priming interval was found in propofol auto-co-induction group; but contrary to that, reduction in the induction dose requirement of propofol was maximal in midazolam group.

It is suggested that Propofol caused decrease in vascular smooth muscle tone, reducing sympathetic actions and total peripheral resistance. This leads to reduced blood pressure. There is stability in cardiovascular stability due to either propofol or midazolam pre-dosing.[18] The reduction in blood pressure on induction of anaesthesia is maximum in the midazolam group, there is a significant decrease in blood pressure, but less than midazolam, in the induction dose of propofol used in this group. It is observed that reduced induction dose of propofol causes less adverse effects.[1,7] Short and Chui et al[12] studied the synergistic actions of midazolam and propofol and found that 'synergism extended to the hypotension that occurred at induction of anaesthesia'. Adams et al. [19] investigated the sympatho-adrenergic, haemodynamic and stress response to co-induction in the elderly and found that in spite of a halving in the dose of propofol required for induction, that the prior administration of midazolam conferred no cardiovascular benefit. Djaiani et al. also reported, similarto this study, that there was less post-induction hypotension when there is significantly less dose in propofol auto-co-induction.[4] The rise in HR secondary to intubation [Table 4] was observed in all the study groups but it was significantly lesser in propofol auto-co-induction group. The rise in SBP and DBP [Table 4] immediately after intubation and 5 minutes post-intubation was significantly higher in midazolam co-induction group. The rise in SBP and DBP in propofol auto-co-induction group was comparable to the control group where much higher induction dose of propofol was used. Although propofol pre-treatment does not completely attenuate reflex sympathetic stimulation secondary to intubation, it is definitely more advantageous than the other two groups. These observations point that although midazolam co-induction significantly reduces the induction dose of propofol, it does not provide haemodynamic stability in peri-intubation period. Similar results were also obtained by Cressy *et al*.[14] where significant dose reduction in propofol was found in midazolam pre-treatment group but there were no demonstrable benefits in terms of cardiovascular stability.

CONCLUSIONS

The present study compared the efficacy of propofol auto-co-induction versus midazolam propofol co-induction. The following conclusions and inferences can be drawn from this study, in both the groups under study there is a significant reduction in induction dose requirement of propofol. The priming with propofol leads to haemodynamic stability both at post-induction interval and later on. There is total dose reduction in propofol by priming in relation to propofol, thus making it less costly.

Sample size of this study is a limitation and more studies are needed.

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