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Comparison of Two Different Doses of Oral Midazolam Premedication on Induction Dose and Characteristics of Propofol: A Double Blind Study

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ABSTRACT

Background-The objective of our study was to study the effect of two different doses of oral midazolam premedication on propofol induction dose andcharacteristics.

Methods- Randomized, prospective, double blind study conducted on 60 ASA I and II patients, falling between the age group of 18-50yrs were randomly divided in to two groups, group A and group B, who received 7.5mg and 15mg midazolam orally 45 mins before the surgery respectively.

Results- Mean time taken for induction in group-A was significantly higher in group-A as compare to group-B. No significant difference was noted with respect to degree of sedation, changes in the heart rate and means arterial pressure, oxygen saturation between the two groups ($p>0.05$).

Conclusion-Our study concluded that 15mg midazolam premedication offers more benefits than 7.5mg midazolam by reducing induction dose of propofol without any undesirable effects like excess sedation, bradycardia and hypotension.

Key words- Induction, Propofol, midazolam, premedication

INTRODUCTION

Premedication is one of the most valuable elements in the production of good anesthesia and is of great psychological importance. Every an3esthetist knows how difficult it is at times to get good relaxation, without deepening the anesthesia to a dangerous degree; with a suitable narcotic administered one hour before operation, these difficulties should be greatly lessened.[1]

Anxiety in response to impending surgery is a common emotional phenomenon, but it also leads to perioperative physiological and psychological changes.The major goal of pre-medication is to allay anxiety. An ideal pre-medicant should have a non-invasive route of administration, rapid and reliable onset, rapid elimination, consistent and predictable results and good patient acceptance. At the same time, it should also be free of side effects like haemodynamic instability, respiratory obstruction and delayed recovery.[2]

Propofol is used for induction and maintenance of anaesthesia, as well as for sedation in and outside the operating room.Though propofol has replaced thiopental as inducing agent because of its smooth induction, rapid and more complete awakening after induction, it produces significant cardio respiratory depression at doses used for induction.[3]

Studies have shown that the induction dose of propofol can be reduced without compromising its beneficial effects by midazolam premedication. Also it has been shown that midazolam acts in synergy with propofol[4-5].

MATERIALS AND METHODS

Design of the Study: The type of study was randomized, prospective, double blind study.

Inclusion Criteria:

- Adult patients of either sex, of ASA grade I or II,
- Age group between 20-50 yrs
- Weights ranging from 40-70kg,
- Presenting for elective surgery under general anaesthesia were included in the study

Exclusion criteria:

- Patients with the history ofasthma
- Patients with history of cardiac or hepaticdisorders
- Patients who were taking centrally acting drugs likebenzodiazepines, antidepressants.
- Patients who were on betablockers.
- Patients with history of allergy to propofol ormidazolam.
- Pregnantwomen.

The patients (subjects) were randomly divided in to 2 groups.

Anaesthesiologist 1 blinded to the induction sequence administered the oral midazolam premedication to both the groups.

1. Group A - received 1 oral midazolam tablet (7.5mg) 45 min beforesurgery.
2. Group B - received 2 oral midazolam tablets (15mg) 45mins beforesurgery.

Data analysis

Collected data was analyzed by paired and unpaired 't' test. Data was summarized and presented in the form of mean, S.D. percentages and by diagrams. A confidence interval was calculated for the doses at which the end points were achieved. For the analysis of significance Chi-square test was used to obtain other possible association.

1. p value >0.05 = notsignificant.
2. p value <0.05 =significant.
3. p value <0.01 = highlysignificant.
4. p value <0.001 = very highlysignificant.

RESULTS

60 patients with ASA physical status 1 and 2 were selected for the study. They were randomly allocated in to two groups of 30 each –Group A (Midazolam 7.5mg) and group B (Midazolam 15mg).

Table 1: Socio-demographic variable

Variable	Group-A	Group-B	p-value
Age in yrs	32.14±6.21	32.14±6.21	0.321
Sex (F:M)	20:10	18:12	0.235
ASA I:II	22:8	23:7	0.69

The both group were comparable.

Table 2: Ramsay sedation score

Ramsay sedation score	Group-A		Group-B		p-value
	No	%	No	%	
1	3	10.00	1	3.33	0.061
2	21	70.00	13	43.33	
3	4	13.33	13	43.33	
4	2	6.67	3	10.00	
Total	30	100.00	30	100.00	

There was no statistically significant difference between the two groups with respect to Ramsay sedation score.

Table 3: Clinical end point

Clinical endpoint	Group-A	Group-B	p-value
Endpoint -1	106.23±18.32	79.23±20.12	0.01
Endpoint -2	182.36±16.35	92.36±19.63	0.01
Endpoint -3	193.21±18.23	145.36±16.32	0.01
Total time	142.36±19.36	101.23±19.31	0.01

Mean time taken for induction in group-A was significantly higher in group-A as compare to group-B.

No significant difference was noted with respect to degree of sedation, changes in the heart rate and means arterial pressure, oxygen saturation between the two groups ($p>0.05$).

DISCUSSION

Combination of drugs has long been used by anaesthesiologists because no single agent provides all components of general anaesthesia. Also the synergistic actionbetween drugs helps to decrease the dose of a single agent leading to fewer sideeffects.

Both midazolam and propofol act partially through the same inhibitory transmitter Gamma Amino Butyric Acid located in post synaptic membrane. Their synergy in pharmacologic profiles makes it an excellent combination for co-induction. Propofol is the most frequently used intravenous anaesthetic today. Though it causes smooth induction, rapid and more complete awakening, it is associated with significant decreases in arterial blood pressure. This decrease in blood pressure is a dose dependent phenomenon[6] and can be avoided by reducing the dose of propofol.

lthough in our study we did not observe any significant difference in the degree of sedation between the two groups, group B patients had higher sedation scores compared to group A.

Eren and colleagues[7] compared dexmedetomidine and three different doses of midazolam in preoperative sedation. Dexmedetomidine 1µg/kg and midazolam 0.02mg/kg, 0.04mg/kg, 0.06mg/kg were compared. They observed marked sedation in dexmedetomidine group and midazolam 0.06mg/kg group but of shorter duration in midazolam group because of shorter half-life of midazolam. This study shows midazolam can cause marked but short duration of sedation.

Trivedi and co-workers[8] compared the sedation characteristics of intranasal and sublingual midazolam 0.3mg/kg in 60 paediatric patients reffered for body MRI. They observed that the patients of both the groups were adequately sedated without any adverse effects.

Wilder-Smith and colleagues[9] investigated the propofol requirements for multiple anaesthetic end points in midazolampremedicated patients. They observed that midazolam 0.05mg/kg prior to induction reduced the propofol requirements for multiple end points.

Adachi and others[10] showed that the administration of small doses of midazolam (10µg/kg) decreases the time to achieve hypnosis when compared to placebo. In their study the time required to achieve hypnosis was 180 seconds in midazolam group compared to 262 seconds in placebo group (reduction by 31%).

CONCLUSION

We conclude from our study that oral premedication with midazolam 15mg offers more benefits than midazolam 7.5mg in reducing the propofol dose requirements without any undesirable effects like excess sedation, bradycardia or hypotension.

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