ORIGINAL ARTICLE

A COMPARATIVE STUDY BETWEEN INTRAMUSCULAR MIDAZOLAM AND ORAL CLONIDINE AS A PREMEDICATION FOR GENERAL ANESTHESIA

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ABSTRACT

Background: Most anesthesiologists agree on the need for efficient pre-medication. The pattern of desired effects of a pre-medication is however, complex and includes relief of anxiety, sedation and relaxation of the patient. The present study was undertaken to compare the effects of Midazolam and clonidine as premedication.

Methodology: A comparative study between midazolam and clonidine as a premedication for general anesthesia was conducted. Patients were divided in two groups: Group I: Inj. Midazolam 0.07 mg/kg i.m. before surgery; Group II Tab.Clonidine 4μg/kg oral, 2 hours before surgery. Pulse rate, blood pressure, state of excitement, apprehension and sedation were noted at the time of giving premedication.

Results: Majority of cases in both the groups were in the age group of 16-30 years (56%). Gender wise distribution shows 40% cases were males and 60% were females. The sedation score, apprehension score and excitement score in both the groups before and after induction was statistically significant. There is no significant difference in dose requirement of pentothal for induction between midazolam and clonidine group. The amnesia score shows that midazolam produces more potent and perfect amnesia as compared to clonidine. Amnesia score in both the groups was statistically significant

Conclusion: It was concluded from the present study that midazolam was superior to clonidine in its sedative and anxiolytic effects, had a potent amnesia and does not attenuate hemodynamic response to laryngoscopy and intubation and does not prolong recovery time.

Keywords: Premedication, Midazolam, Clonidine, Sedative

INTRODUCTION

The use of pre-operative medication to facilitate induction, maintenance and recovery after anesthesia has been debated over years. Most anesthesiologists agree on the need for efficient premedication. The pattern of desired effects of a premedication is however, complex and includes relief of anxiety, sedation and relaxation of the patient.

Midazolam is a benzodiazepine with a rapid and near complete absorption pattern after intramuscular (i.m.) injection, and a short elimination half-life.[1] Although one study reported anxiolysis without side effects after midazolam premedication,[2] other studies indicated that an effective dose of oral midazolam prolonged recovery times. [3] Midazolam has property to produce amnesia. Benzodiazepine is used frequently as premedication before general anesthesia, because of their anxiolytic, sedative and hypnotic properties.

Clonidine attenuates sympathoadrenal responses to painful (tracheal intubation or surgery [4]) and other stimuli *(e.g.,* sodium-nitroprusside induced hypotension4). $\dot{\alpha}_2$- Adrenoceptor agonists activate presynaptic $\dot{\alpha}_2$-adrenoceptors, thus inhibiting release of norepinephrine from sympathetic nerve endings. [5] The exact mechanism of the reduction of the anesthetic requirements is unknown but it is presumed that the decrease is caused by actions on both pre- and postsynaptic $\dot{\alpha}_2$-adrenoceptors in the central nervous system. [6]

The present study was undertaken to compare the effects of Midazolam and clonidine as premedication.

MATERIALS AND METHODS

A comparative study between midazolam and clonidine as a premedication for general anesthesia was conducted on 50 patients of either cases at New Civil Hospital, Surat. All the patients belong sto ASA I or II. The age of patients ranged from 15-65 years. On the day before the operation preoperative assessment was carried out. A complete systemic examination was done, to rule out any major systemic dysfunction. Routine investigations like hemoglobin estimation, urine analysis for albumin and sugar and X-ray chest were done in all cases. No sedation was given the night before operation. Informed consent was taken up for anesthesia and surgery. Patients were divided in two groups: Group I: Inj. Midazolam 0.07 mg/kg i.m. before surgery; Group II Tab.Clonidine 4μg/kg oral, 2 hours before surgery. Pulse rate, blood pressure, state of excitement, apprehension and sedation were noted at the time of giving premedication.

Technique: After 15 minutes of premedication intravenous line was taken. Pulse rate, blood pressure, state of excitement, apprehension and sedation were noted before induction of anesthesia. Patients were given Inj. Glycopyrrolate 0.004 mg/kg intravenously before induction. All patients were given general anesthesia with Inj. Thiopentone sodium (2.5%) intravenous and inj. Suxamethonium 2 mg/kg intravenous. Inj. Thiopentone sodium was given upto the loss of eyelid reflex and given dose was noted. Anesthesia was maintained on O_2 + N_2O+isoflurane+ non-depolarizing muscle relaxant (Pancuronium bromide). At the end of surgery, anesthesia was reversed with inj. Neostigmine 0.05 mg/kg intravenous and inj. Glycopyrrolate 0.008mg/kg intravenous.

Pulse rate and blood pressure were measured during laryngoscopy and intubation and 5 min., 10 min. and 15 min. after intubation. Post-operatively, recovery score was noted just after reversal and upto 2 hours according to recovery score mentioned in proforma. Post operative sedation and amnesia were also noted.

RESULTS

Majority of cases in both the groups were in the age group of 16-30 years (56%). Gender wise distribution shows 40% cases were males and 60% were females. Majority of cases in both groups were between 41-50 kg (56%) (Table 1).

Table 1: Age and gender wise distribution of cases

Age group (years)	Midazolam			Clonidine		
	Male (%)	Female (%)	Total (%)	Male (%)	Female (%)	Total (%)
16-30	8 (32)	6 (24)	14 (56)	7 (28)	7 (28)	14 (56)
31-45	2 (8)	5 (20)	7 (28)	1 (4)	7 (28)	8 (32)
46-60	2 (8)	2 (8)	4 (16)	2 (8)	1 (4)	3 (12)

Table 2: Sedation, apprehension and excitement score in both groups

Variables		Midazolam	Clonidine	p value
Sedation score	Before Premedication	0	0	p<0.001
	Before Induction	1.80 ± 0.80	1.12 ± 0.711	
Apprehension score	Before Premedication	-0.52 ± 0.299	-0.52 ± 0.223	p<0.005
	Before Induction	-0.12 ± 0.256	-0.3 ± 0.288	
Excitement score	Before Premedication	-0.5 ± 0.283	-0.52 ± 0.223	p<0.001
	Before Induction	-0.12 ± 0.256	-0.34 ± 0.278	

Table 3: Pentothal dose reduction in both groups

Group	Required dose of Pentothal	Given dose of Pentothal	% reduction	P value
Midazolam	336.88 ± 46.89	280.0 ± 40.62	17.76 ± 3.09	<0.001
Clonidine	345.48 ± 38.36	278.8 ± 35.16	19.76 ± 4.33	<0.001

The sedation score, apprehension score and excitement score in both the groups before and after induction was statistically significant ($p<0.001$) (Table 2).

Midazolam and clonidine both caused significant reduction in thiopentone dose required to induce anesthesia. There is no significant difference in dose requirement of pentothal for induction between midazolam and clonidine group (Table 3). There is statistically significant difference in systolic blood pressure and heart rate between before pre-medication and induction but no statistically significant difference between before induction and during laryngoscopy in clonidine group while in Midazolam group there is no statistically significant difference between before pre-medication and induction, but significant difference in blood pressure and heart rate between before induction and during laryngoscopy.

Table 4: Amnesia score in Midazolam and Clonidine group

Group	Venous puncture	Application of mask
Midazolam	1.76 ± 0.709	-1.2 ± 0.489
Clonidine	-2.52 ± 0.499	-2.24 ± 0.427
p value	<0.001	<0.001

It was observed that there is a complete recovery from anesthesia in both groups. But there is significant difference in post operative sedation between two groups. The amnesia score shows that midazolam produces more potent and perfect amnesia as compared to clonidine. Amnesia score in both the groups was statistically significant (Table 4).

DISCUSSION

In the present study we observed that midazolam produced rapid and better sedation as compared to clonidine and it was maintained in post-operative period. In the study conducted by H.Ronald et al[7], midazolam produced significantly better sedation than placebo and hydroxyzine given intramuscularly 60-90 min. before anesthesia. McAtteer et al[8] also observed the similar results in their study that midazolam compared to papaverretum produced similar degree of sedation. T.G. Short[9] and his colleagues and J.Hargreaves at al[10] in 1989 observed that midazolam and temazepam, both the drugs of benzodiazepam group provided similar degree of sedation.

We studied the anxiolytic effect of midazolam and clonidine and we observed that midazolam had better anxiolytic effect as compared to clonidine. McAteer and Dixon J. et al [8] observed that midazolam was satisfactory agent foe pre-medication producing adequate anxiolysis. J. Hangreaves[10] and T.G.Short[9] and his co-workers also observed that midazolam as well as tamezepam were potent anxiolytic agents, but midazolam was superior to temazepam and produced significant degree of anxiolysis. P.M.Wright et al[11] observed that in clonidine group, there was significantly more anxiolysis compared to inert group.

In the present study, we observed that there was 17.76% reduction in induction dose of thiopentone in Midazolam group and 19.76% reduction in clonidine group. P.M. Wright[11] and his co-workers noted that clonidine reduced dose of induction agent (methohexitone) by 14.3%. The study conducted by Riku Antaa et al[12] observed that Dexmedetomidine caused 37% reduction in thiopentone requirement. J Hargreaves[10] supports our study with his result that midazolam received patients required significantly smaller doses of thiopentone than placebo or temazepam.

In the present study, we observed the post-operative recovery score as well as post-operative sedation in both the groups. Our observations correlated with F. Bonnet et al[13] who observed that clonidine does not delay recovery from anesthesia. R. Aantaa et al[12] observed that Dexmedetomidine caused dose dependent decrease in recovery time after anesthesia. In contrast to our study R. Aantaa et al[12] concluded that time needed to regain consciousness was increased significantly after midazolam 0.08mg/kg and not after Dexmedetomidine.

CONCLUSION

It was concluded from the present study that midazolam was superior to clonidine in its sedative and anxiolytic effects, had a potent amnesia and does not attenuate hemodynamic response to laryngoscopy and intubation and does not prolong recovery time.

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