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A Prospective Comparative Study of Oral Clonidine and Oral Midazolam As Premedicants For General Anaesthesia

Dr. Somnath Dey[1*]
[1*]*Associate Professor, Department of Anaesthesia, Calcutta Medical College, Kolkata, West Bengal.*
Corresponding Author: Dr.Somnath Dey

Abstract
Introduction: *Premedication is an important step before giving anaesthesia to patient. Midazolam, a benzodiazepine, has short duration of action, causes anxiolysis, muscular relaxation, amnesia in lower doses and sedation, hypnosis in higher ones. Clonidine, an alpha-2 agonist, causes reduction of anaesthetic and analgesic requirements, haemodynamic stability, sedation, antisialogogue effect.*
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 Department of Anaesthesia, Calcutta Medical College, Kolkata, and West Bengal. All the patients belongs to ASA I or II. The age of patients ranged from 15-65 years. On the day before the operation pre-operative assessment was carried out.*
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.*
Key Words: *Premedication, midazolam, Clonidine, benzodiazepine*

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I. Introduction

Premedication is an important step before giving anaesthesia to patient. Midazolam, a benzodiazepine, has short duration of action, causes anxiolysis, muscular relaxation, amnesia in lower doses and sedation, hypnosis in higher ones. Clonidine, an alpha-2 agonist, causes reduction of anaesthetic and analgesic requirements, haemodynamic stability, sedation, antisialogogue effect.[1]

Midazolam is a benzodiazepine with a rapid and near complete absorption pattern after intramuscular (i.m.) injection, and a short elimination half-life.[2] Although one study reported anxiolysis with-out side effects after midazolam premedication, 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 hypo-tension4).[4] ά2- Adrenoceptor agonists activate pre-synaptic ά2-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 ά2-adrenoceptors in the central nervous system.[5]
The present study was undertaken to compare the effects of Midazolam and Clonidine as premedication.

II. 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 Department of Anaesthesia, Calcutta Medical College, Kolkata, and West Bengal. All the patients belongs to ASA I or II. The age of patients ranged from 15-65 years. On the day before the operation pre-operative 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: 0ral. Midazolam 0.25mg/kg. 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 pres-sure, 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 up to the loss of eyelid reflex and given dose was noted. Anesthesia was maintained on O2+N2O+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 up to 2 hours according to recovery score mentioned in proforma. Post operative sedation and amnesia were also noted.

III. 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 in 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 Before Induction	0 1.80 ± 0.80	0 1.12 ± 0.711	p<0.001
Apprehension score	Before premedication Before Induction	-0.52 ± 0.299 -0.12 ± 0.256	-0.52 ± 0.223 -0.3 ± 0.288	p<0.005
Excitement score	Before premedication Before Induction	-0.5 ± 0.283 -0.12 ± 0.256	-0.52 ± 0.223 -0.52 ± 0.223	p<0.001

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.

Blood pressure: Baseline systolic, diastolic and mean arterial blood pressure difference in both the groups were not statistically significant. In group 1, mean SBP, DBP, MAP one minute post intubation remained low compared to baseline values. But in group 2 there was a statistically significant increase in SBP, DBP, and

MAP from baseline. Thus increase in blood pressure in group 2 was statistically significant (P<0.05) in the intergroup comparison.

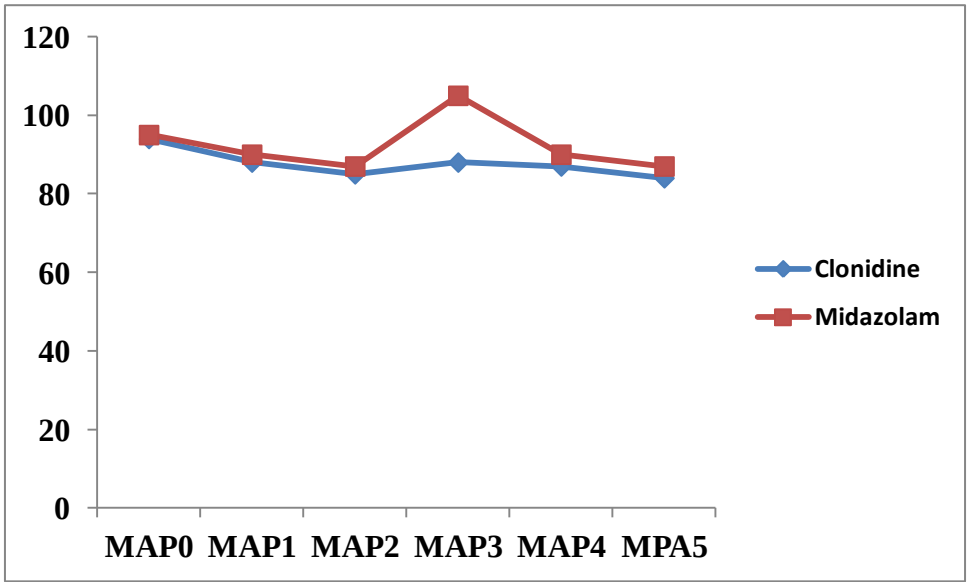

Figure 1: Intergroup Comparison of Mean Arterial Pressure

Table 4: The haemodynamic changes before induction, during laryngoscopy and intubation and at 5 minutes after extubation

Midazolam Group							
	Baseline	Before induction	P value	During laryngoscopy and intubation	P value	5 min after extubation	P value
Mean Pulse rate (per min)	86.93±9.49	96.8±9.31	<0.001	130.66±11.35	<0.001	123.66±10.57	<0.001
Mean BP(mmHg)	98.66±6.91/ 65.86±4.32	91.8±6.08/ 59.33± 3.94	<0.001	132.06±4.37 / 82.40±2.48	<0.001	125.13±4.56 / 77.33±3.29	<0.001
Clonidine Group							
	Baseline	Before induction	P value	During laryngoscopy and intubation	P value	5 min after extubation	P value
Mean Pulse rate (per min)	85.93±7.69	76.0±7.93	<0.001	97.86±7.71	<0.001	87.33±7.13	<0.05
Mean BP(mmHg)	100.46±7.34/ 65.13±4.71	89.66±6.54 / 56.26±3.95	<0.001	114.93±7.69/ 76.06±4.74	<0.001	104.66±6.58 / 68.46±4.65	<0.001

We also observed the effects of both the drugs on the haemodynamics before induction, during laryngoscopy and intubation and at 5 minutes after extubation. In Group M, there was a significant increase in the pulse rate and a decrease in the blood pressure before induction as compared to the baseline values and in Group C, there was a significant decrease in both the pulse rate and the blood pressure. During laryngoscopy and endotracheal intubation and also at 5 minutes after extubation, there was a significant increase in the pulse rate and blood pressure above the baseline level, however, this increase was much higher in Group M as compared to Group C. Overall, in intergroup comparison Clonidine resulted in a better haemodynamic profile in the perioperative period. As far as untoward effects are concerned, only 3 (10%) children in Group M had postoperative nausea and vomiting and 1 (3.33%) children had postoperative shivering. But this was statistically not significant.

IV. 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, midazolam produced significantly better sedation than placebo and hydroxyzine given intramuscularly 60-90 min.[6] before anesthesia. McAtteer et al also observed the similar results in their study that midazolam compared to papaverretum produced similar degree of sedation. T.G. Short and his colleagues and J.Hargreaves at al 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.[7] McAteer and Dixon J. et al 8 observed that midazolam was satisfactory agent foe pre-medication producing adequate anxiolysis. J. Hangreaves and T.G.Short and his coworkers also observed that midazolam as well as tamezepam were potent anxiolytic agents, but midazolam was superior to temazepam and produced significant degree of anxiolysis.[8] P.M.Wright et al 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.[9] P.M. Wright and his coworkers noted that clonidine reduced dose of induction agent (methohexitone) by 14.3%. The study conducted by Riku Antaa et al observed that Dexmedetomidine caused 37% reduction in thiopentone requirement. J Hargreaves 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 who observed that clonidine does not delay recovery from anesthesia. R. Aantaa et al observed that Dexmedetomidine caused dose dependent decrease in recovery time after anesthesia. In contrast to our study R. Aantaa et al concluded that time needed to regain consciousness was increased significantly after midazolam 0.08mg/kg and not after Dexmedetomidine.[10]

V. 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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