

Comparative Analysis of Oral Clonidine against Oral Midazolam as Premedication in Adults

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Abstract

Introduction: The comparison was made between the clonidine 200 ug and midazolam 15 mg to check the clinical efficacy in respect to the sedative, attenuation of hemodynamics, anxiolytic and antisialogogue response in adult patient undergoing general anesthesia. *Material and Methods:* Total of 100 patients were included in the study, included patient belong ASA 1-2 physical status and the age group of 20 – 50 years. Males and females, both genders were included in the study. Of the total 100 patients; they were randomly divided into two groups with 50 patients in each group. Patients included in the group 1 were given Oral clonidine 200 ug, 90 mins prior to the surgery. Patients included in the group 2 were given oral midazolam 15 mg, 90 mins prior to the surgery. General anesthesia with thiopentone sodium, vecuronium, fentanyl, oxygen, nitrous oxide and sevoflurane were given to all the patients. Five point sedation score was used to assess the patient's level of sedation. We recorded the baseline values before medication and 90 mins after medication. After intubation period of 1, 5 and 10 mins the hemodynamic parameters were recorded. *Results:* The extent of sedation was seen in the patient given Midazolam as compared to the clonidine pretreated patients. In the clonidine group we see the antisialogogue effect. In the clonidine group all the haemodynamic parameters were well maintained throughout the period of study. *Conclusion:* There was significant attenuation of pressor response to laryngoscopy and intubation in the clonidine group as compared to midazolam therefore drug of choice for premedication.

Keywords: Clonidine; Laryngoscopy; Midazolam; Premedication.

Introduction

According to Rendell baker it is stated that no one, however phlegmatic, can contemplate the prospect of an operation without some apprehension or nervousness [1]. Before operation the premedication is an important step before giving the anesthesia to the patient. It is found that the premedication named midazolam which is benzodiazepine has short duration of action, there is report of muscular relaxation, sedation and hypnosis in higher dose, amnesia in lower dose, causes anxiolysis. Other medication names clonidine which is an alpha agonist causes reduction of analgesic and

anesthetic requirement; there is stability of hemodynamic parameters and antisialogogue effect [2].

The present study was conducted with the aim of comparison between the clonidine 200 ug and midazolam 15 mg to check the clinical efficacy in respect to the sedative, attenuation of hemodynamics, anxiolytic and antisialogogue response in adult patient undergoing general anesthesia.

Materials and Methods

Before conduction of the study, we obtained the approval from the ethical committee. We also

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obtained the informed consent from the patients who were included in the study. Total of 100 patients scheduled for the surgeries under the general anesthesia in different department likes orthopaedics, ENT, surgery and gynecology were included in the study. The duration of the surgery was one to three hours average in all the patients. All the patients included in the study were divided into two different groups with each group containing 50 participants. The patients included in the group 1 were planned to receive premedication oral clonidine 200 ug. The patient included in the group 2 were planned to receive premedication oral midazolam 15 mg. Both the oral predications were given 90 mins prior to the surgery.

Patient; male and female both with age group of 18-60 years, weight ranging between 50-70 kg with ASA physical status 1-2 were included in the study. Patients with renal dysfunction, obesity, baseline pulse rate < 50 beats/minute, pulmonary and psychiatric disorders, hypertension, anticipated difficult airway and known hypersensitivity to the drugs were excluded from the study.

Baseline resting parameters were recorded prior to premedication in the operation theater and 90 mins after the administration of oral premedication in both the groups. Detailed history, airway evaluation and physical examination were assessed for each and every patients included in the study. Visual Analog Scale was used for the assessment of anxiolytic effect. Five point sedation score was used to assess the sedative effect [3]: Grade 1- Patient is awake; Grade 2- Patient is drowsy but easily arousal to alert state by oral commands; Grade 3- Patient is asleep, there is no reaction to speech but there is immediate reaction to the tactile stimuli; Grade 4- Patient reacts only to the stronger tactile stimuli; Grade 5- There is difficulty in arousing patient and if awoken patients immediately asleep again. The IV access was secured with help of 18 gauge IV cannula and there was administration of lactate ringer solutions. Sufficient preoxygenation was administered with 100% oxygen for five minutes. IV thiopentone sodium 2.5% 4-5mg/kg was given for the induction.

The loss of consciousness was assessed by loss of reflex of eye lashes and 0.1 mg/kg dose of IV vecuronium was given. Nitrous oxide 60% and oxygen 40% were used for mask ventilation for three minutes. Laryngoscopy and tracheal intubation with appropriate sized cuffed tube were done. For analgesia, IV fentanyl 2µg/kg initial dose and top up of 1µg/kg was given as required. End tidal carbon dioxide was maintained around

35-40mmHg. One gram IV paracetamol infusion was given towards the end of surgery. At the end of surgery, neuromuscular blockade was reversed using IV neostigmine 0.05mg/kg and IV glycopyrrolate 0.01mg/kg.

Parameters for hemodynamics were assessed with the help of pulse rate, diastolic and systolic blood pressure and mean arterial pressure at different time intervals. P0 - Prior to premedication; baseline parameters, P1-90 mins after premedication; preinduction, P2 - post induction, P3 - one minute after intubation, P4 - five minutes after intubation, P5 - ten minutes after intubation. Rate pressure product (RPP) was calculated using the following formula: systolic blood pressure in mm of Hg x pulse rate (beats/minute). Patients were monitored for adverse effects such as bradycardia [4], hypotension [5], dysrhythmias [6], respiratory depression [7] and grade 5 sedation.

Statistical Analysis

Qualitative data will be expressed as percentages and proportions. Quantitative data will be expressed as mean and standard deviation. The differences between two groups with respect to continuous variables will be analysed using t-test while categorical variables will be analysed using chi-square test. All the statistical tests will be performed in SPSS version 15 software. p value <0.05 will be considered as statistically significant while p value < 0.01 will be considered as statistically highly significant. The between group comparison of compressive strength of samples in Group A and B was done using One-way ANOVA test. Within group comparison was done using Bonferroni correction test. In the tests, p value of ≤ 0.05 was considered as statistically significant.

Results

When comparisons were done in respect to the sex, weight and age no significant difference was found between the two groups. Antianxiety effect with respect to VAS score was similar in both the groups.

Sedation score: the patient who were included in group 2; who were given midazolam premedication were found to be significantly more sedated as compared to the patients included in the group 1; who were given clonidine premedication, with P value is less than 0.05. Of the total 50 patient included in the group 1, 36 did experienced

antisialogogue effect, however none of the patients in group 2; who were given midazolam had any antisialogogue effect.

Pulse Rate

When the comparison was between the two groups in respect to the baseline mean pulse rate, it was found to be 82.44 beats per minute in group 1 and was found to be 82.92 beats per minute in group 2. Following the induction of anesthesia, the pulse rate was found to be significantly lower in group 1 when compared to the base line, 1 minute (p3), following intubation i.e. p2 of 74.60 beats per minutes ($p < 0.05$) and p3 of 77.88 beats per minutes ($p < 0.05$). however in group 2, there was significant rise in the p2 that is 80.04 beats/mins and p3 that is 88.48 beats/mins when compared to base line ($p < 0.05$). Figure 1 shows the pulse rate inter group comparison.

Blood Pressure

There was no significant difference in respect to the diastolic, systolic and mean arterial blood pressure between the both groups. The values of mean DBP, MAP and SBP one minute after intubation were found to be low as compared to base line values in group 1. However there was significant increase in the values in group 2 as compared to base line values. Thus increase in blood

pressure in group 2 was statistically significant ($p < 0.05$) in the intergroup comparison (Figure 1).

Rate Pressure Product

In group 1 the baseline mean rate pressure product is 9869.68 units and in group 2 it was found to be 9859.76 units. The difference was not found to be significant between the two groups with p value = 0.969. One minute after the administration of the intubation the RPP remained significantly lower in clonidine group with 9017.76 units as compared to base line with $p < 0.05$ whereas in group 2, it was found to be significantly increased to 12,462.40 units when compared to baseline with $p < 0.05$. Two patients developed transient dysrhythmias during intubation which got subsided without any pharmacological intervention in the midazolam groups.

Discussion

The purpose of using premedication is to remove preoperative anxiety and fear, to produce analgesia and amnesia, to depress the vagal activities, to reduce the salivary gland secretions, to produce sedation, to reduce the risk associated with aspiration an regurgitation and mainly to reduce the stress and reduce the amount of general anesthesia required. The mean weight of the

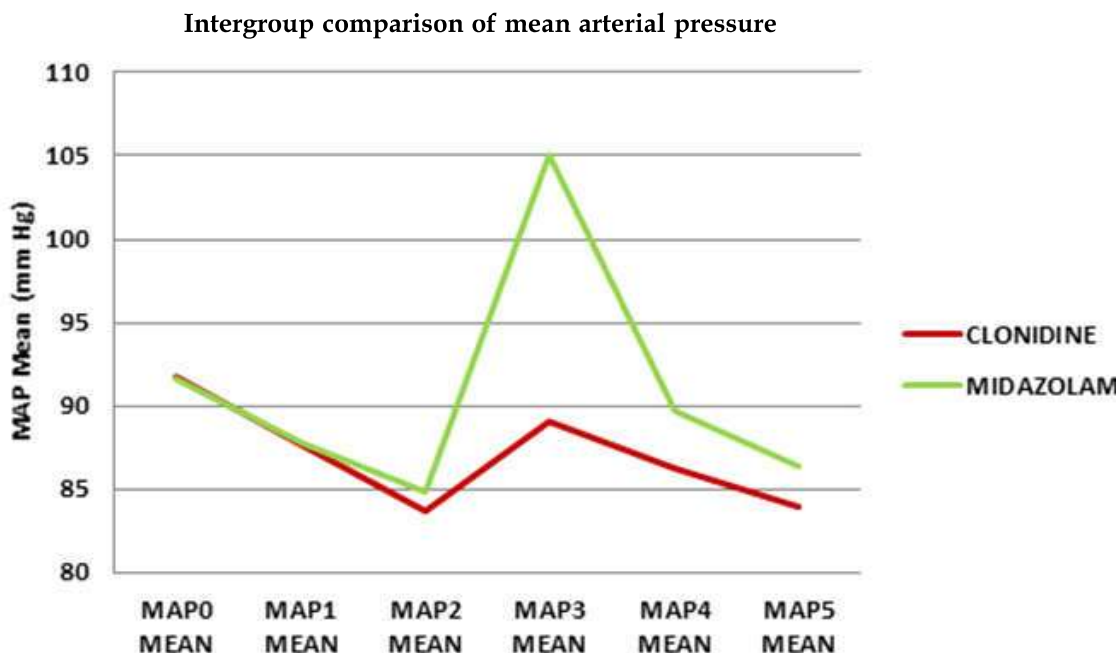


Fig. 1: Intergroup Comparison of Mean Arterial Pressure

participants included in the study was approximately 60 kg. Taking the weight into consideration, the mean dose of oral midazolam used in the study was 0.25 mg/kg and that of oral clonidine was approximately 3.3 µg/kg. In the present study, the anxiolytic effect was calculated with VAS. Of the two oral medication used both of them showed positive anxiolytic effect. Similar results were also obtained by Frank T et al. [8] and Paris A et al. [16].

A five point sedation score was used to assess the sedation, 90 min after the sedation was administered. It was seen from the present study that midazolam was found to cause more sedation than oral clonidine. All the patients included in the midazolam group were sedated whereas in clonidine group 26% of the patient did not experience any sedation. There were cases of dryness of mouth in few patients included in the clonidine group. Total of 72% patients did experience mouth drying. Oral clonidine is found to cause decrease in salivary flow and so dryness of mouth was experienced with patients taking oral clonidine. None of the individuals in the midazolam group experienced any type of dryness of mouth. Chaurasia SK et al. [9] reported similar results.

Hypertension, dysrhythmic elevation in arterial pressure and tachycardia starts within five seconds of laryngoscopy, they reach to highest level in one or two minutes and return to normal level in five seconds [10]. Patients with limited coronary or myocardial reserves, Patients with glaucoma and having open eye surgery have less tolerance power to haemodynamic response [11-13].

There is slowing of heart rate with the use of Clonidine as it stimulates the parasympathetic outflow and decreases the central sympathetic outflow [14]. Similar results were obtained by Paris et al [16]. found that with the use of oral clonidine the increase in heart rate is prevented however the same was not obtained with use of midazolam.

The decrease in diastolic, systolic and mean arterial pressure was obtained in both the study group after the premedication. Because of the sedative and anxiolytic property there is decrease in systolic blood pressure. The decrease in diastolic, systolic and mean blood pressure was seen in both the groups after the induction of anesthesia with thiopentone. In the oral midazolam premedicated group; one minute after the intubation there was increase in diastolic, systolic and blood pressure. However in the oral clonidine premedicated group there was no rise of parameters above the baseline.

The above results were in accordance with the result obtained by Paris A et al.[16], he found that clonidine augmented hemodynamic stability and blunted stress responses as determined by adrenocorticotrophic plasma levels. Attenuation of haemodynamic response to intubation and intraoperative haemodynamic stability with clonidine was also demonstrated in studies conducted by Talebi H et al. [17], Laurite CE et al [18], Traill R, Gillies R [19], Wawrzyniak K et al [20]. and Singhal SK et al [21].

Rate pressure product is defined as the product of pulse rate and peak systolic blood pressure. There is a correlation between rate pressure product and myocardial blood flow, myocardial oxygen consumption as a result of which it correlates with signs of ischaemia. This study shows that Clonidine effectively attenuates increase in rate pressure product following laryngoscopy and intubation; in accordance with studies conducted by Thomas MG et al [22]. and Montazeri K et al [6].

Conclusion

Clonidine, when used as premedication showed a comparable anxiolytic effect, with no sedation, better antisialogogue effect and well maintained haemodynamic parameters following laryngoscopy and intubation as compared with midazolam therefore constitutes optimal choice of two drugs.

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