ORIGINAL ARTICLE ANAESTHESIOLOGY

Journal of Contemporary Medicine and Dentistry
www.jcmad.com

ISSN [P-2347-4513]
ISSN [O-2349-0799]
Year: 2021, Volume: 9
Issue: 3, p:115 – 119

Oral Clonidine Versus Oral Diazepam as Premedication for General Anesthesia

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Abstract

Background: *In many high-risk patients, the sequence of anesthetic induction, laryngoscopy, and tracheal intubation are linked with significant hemodynamic changes and autonomic reflex activation, which may be cause for worry. The goal of this study is to assess the premedication effects of oral clonidine and oral diazepam in terms of anxiety relief, drowsiness, anesthetic needs, heart rate, blood pressure, attenuation of sympathetic reactions to laryngoscopy and intubation, respiration rate, and unwanted effects.* ***Methods:*** *A total of n=80 cases were studied in this study they were randomly allotted into two groups based on the computer-generated random numbers Group I (oral clonidine) with a dosage of 0.003 mg/Kg body weight 90 minutes before surgery. Group II included all the cases receiving oral diazepam 10 mg 90 minutes before the surgery. On the day of surgery, vital parameters such as SBP, DBP, HR, and RR were measured before premedications and 90 minutes following medication. The scoring was done for sedation, anxiolysis, and anti-sialogogue effects after premedication.* ***Results:*** *SBP and DBP are significantly different between groups I and II from 1 minute to 30 minutes (Table 5). ANOVA was also performed for effect p = 0.03 interaction groups effect p = 0.01 Analysis of heart rate revealed a significant time and interaction effect (Table 4) even after adjusting for sex. Overall, both groups saw a substantial shift in heart rate, however, the change in Diazepam (Group II) was much greater than the change in Clonidine (Group I). Significant variation was noted in Clonidine and Diazepam groups in systolic blood pressure before and 90 minutes after premedication.* ***Conclusion****: it was found that clonidine was superior in efficacy for mitigating the sympathetic responses to laryngoscopy and intubation because of its effects on reducing anxiety. It has the ability to reduce the overall anesthetic requirement and its property of potentiating postoperative analgesic requirements. Therefore, oral clonidine at the rate of 3 micrograms per kg body weight is better as compared to oral diazepam in our group population.*

Keywords*: Clonidine, Diazepam, Premedication, Attenuation, Pressor Anxiolysis, Sedation*

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Date of Acceptance: 01/11/2021

Introduction

Anxiety control is the normal process of general anesthesia achieved by pre-medications. Premedication is universally administered before any anesthesia. [1] An ideal premedicant should be effective and pleasant to be taken orally, should produce sedation, ease of separation, and facilitate smooth induction of anesthesia, should have an anti-sialagogue effect, have analgesia and non-emetic properties and should not impair cardiovascular stability or depress respiration, and should reduce the requirement of anesthetic drugs. The α-2 adrenoceptor agonists have been used as premedicant because of their beneficial properties in anesthesia. Clonidine is now commonly used for its antihypertensive and negative chronotropic effects but has many properties of an ideal premedicant and beneficial effects on hemodynamics during

stressful conditions like laryngoscopy and endotracheal intubation. During general anesthesia. [2] Clonidine reportedly enhances intraoperative circulatory stability by reducing catecholamine levels. This study was done to evaluate the effectiveness of oral Clonidine in attenuating the hemodynamic responses associated with laryngoscopy and endotracheal intubation and its effect was compared with commonly used premedicant diazepam.

Materials and Methods

This prospective study was conducted in the Department of Anesthesiology, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical committee permission was obtained for the study. Written consent was obtained from all the participants of the study. Elective surgery patients undergoing, ENT, Orthopedic, and General Surgical procedures were selected.

Inclusion criteria

1. Patients aged 20 – 50 years
2. ASA grades I and II
3. Elective surgical procedures in General Anesthesia
4. Willing to participate in the study voluntarily

Exclusion criteria

1. Emergency surgical procedures
2. With neurological abnormalities
3. Significant cardiovascular morbidities
4. Renal or hepatitis diseases
5. Patients with a history of drug allergy
6. History of psychotropic substance abuse

A total of n=80 cases were studied in this study they were randomly allotted into two groups based on the computer-generated random numbers those numbers in set 1 of computer numbers allotted to Group I (oral clonidine) with the dosage of 0.003 mg/Kg body weight 90 minutes before surgery. Group II included all the cases with computer-generated set 2 numbers receiving oral diazepam 10 mg 90 minutes before the surgery. On the day of surgery, vital parameters such as SBP, DBP, HR, and RR were measured before premedications and 90 minutes following medication. The scoring was done for sedation, anxiolysis, and anti-sialogogue effects after premedication.

Table 1: Measurement of various parameters for scoring

Parameter	*Scores*
Degree of Sedation (4-point scale)	
Asleep	3
Moderately drowsy	2
Mild Drowsiness	1
Awake	0
Anxiety scoring (5-point scale)	
Quiet or comfortable	4
Uneasy	3
Anxious	2
Very upset or worried	1
Frightened or terrified	0
Anti-sialogogue effect scoring (3-point Scale)	
Dry Mouth	2
Moist	1
Wet	0

The degree of sedation, anxiety scoring was done and the anti-sialogogue effect was scored by checking drying of mouth with a blotting paper by blotting the tongue and inner aspect of the cheek for 30 seconds each, and scores were given as per table 1. Patients were connected to the cardiac monitor for recording the ECG in lead II. A pulse oximeter was connected to know the blood pressure non-invasively was used. Baseline recording of heart rate and arterial pressure was done and a breathing rate of 12–14 breaths per minute is a good pace. Inj. vecuronium bromide was supplied according to body weight to maintain relaxation. Systolic, diastolic blood pressures and heart rate were monitored during induction and at one, three, five, ten, fifteen, and thirty minutes after intubation of the trachea. A sedative was not given routinely and was given only if deemed necessary based on hemodynamic criteria. At the end of the surgery, reversal was done with Inj Neostigmine 0.05 mg/Kg and inj. Glycopyrrolate 0.01 mg/kg IV patients were extubated and shifted to the recovery room. All the available data was uploaded on an MS Excel spreadsheet and analyzed by SPSS version 19 in windows format. Continuous variables were expressed as mean and standard deviation and categorical variables were expressed by chi-square test and Fisher's exact test ($p<0.05$ was considered as significant).

Results

The age distribution in Clonidine and diazepam groups in this study found the age group was

around 20-50 years for both the groups. The mean values of age with standard deviations are 32.5 ± 6.5 and 34.1 ± 5.4 for Clonidine and diazepam groups respectively. There was no significant difference between the two groups (p>0.05). The sex-wise distribution of the cases in the study found in group I out of n=40 cases n=23(57.5%) were females and n=17(42.5%) were males and in group II out of n=40 cases n=24(60%) were males and n=16(40%) were females. The mean weight of the group I cases was 49.5 ± 6.5 Kgs and in group II the mean weight was 52.5 ± 6.6 Kgs. The minimum weight in patients was 45 Kgs and the maximum weight was 68 Kgs. Sedation was assessed on a 4-point sedation scale. Score 0 was fully awake and score 3 was an asleep patient's group. The details of the sedation scores are given in table 2. There was no significant difference in the sedation between the two groups (p>0.05)

Table 2: Sedation scores in two groups after premedication

Sedation Score	Group I		Group II	
	Frequency	*percentage*	*Frequency*	*percentage*
0	16	40.0	15	37.5
1	11	27.5	18	45.0
2	13	32.5	07	17.5
3	00	00.0	00	00.0
Total	40	100	40	100

Anxiolysis was assessed on a 5-point anxiolysis scale. Score 0 was a terrified or a frightened patient and score 4 was a quiet and comfortable patient. In group 1, the anxiolysis score of 3 was seen in 40% of patients and a score of 4 was seen in 50% of patients. There were no cases in the anxiolysis scores of 0, and 1 In group II the maximum number of cases were with score 3 with 55.0% cases depicted in table 3.

Table 3: Anxiolysis scores in two groups after premedication

Anxiolysis scores	Group I		Group II	
	Frequency	*percentage*	*Frequency*	*percentage*
0	00	00.0	00	00.0
1	00	00.0	07	17.5
2	04	10.0	00	00.0
3	16	40.0	22	55.0
4	20	50.0	11	27.5
Total	40	100.0	40	100.0

The anti-sialagogue effect was assessed on a 3-point anti- sialagogue scale. Score 0 was a wet mouth and score 2 was a dry mouth. In group 1 (clonidine), the anti-sialagogue score 0 was seen in 4 (40.0%) patients, anti- sialagogue score 1 in 24 (27.5%) patients and in group 2 diazepam, the anti-sialagogue score 0 was seen in 37.5% cases the score 1 in 45% and scoring of 2 in 17.5% depicted in table 4.

Table 4: Anti Sialagogue Score in two groups after premedication

Anti-Sialagogue Score	Group I		Group II	
	Frequency	*percentage*	*Frequency*	*percentage*
0	16	40.0	15	37.5
1	11	27.5	18	45.0
2	13	32.5	07	17.5
3	00	00.0	00	00.0
Total	40	100	40	100

The mean respiratory rates in group I before medication was 16.52 ± 0.53 and in group II at the same time it was 6.85 ± 0.81 After medication the rate of respiration in group I was 15.55 ± 0.45 and in group II it was 15.90 ± 0.65. The differences were not found to be significant. The mean dose of Inj Thiopentone required in group I was 190.23 ± 9.85 mg and in group II it was 225.3 ± 10.2 mg the p values were (<0.05) hence considered significant.

Table 5: Comparison of Heart rate, SBP, and DBP between the Two Groups of Patients Studied

	Heart Rate (BPM)		SBP mm Hg		DBP mmHg	
	Group I	Group II	Group I	Group II	Group I	Group II
Pre-operative	81.7 ± 5.5	78.3 ± 2.4	115.3 ± 6.8	117.2 ± 4.5	78.2 ± 4.3	80.2 ± 4.5
Induction	83.4 ± **3.2**	75.6 ± 2.8	118.6 ± 8.8	121.2 ± 3.5	79.3 ± 3.5	79.8 ± 2.5
1-minute	90.2 ± 4.3	105.3 ± 3.0	122.2 ± 9.0	139.7 ± 4.2	86.1 ± 6.7	92.0 ± 6.4
5-minutes	91.6 ± 3.9	102.2 ± 2.7	121.3 ± 7.5	135.6 ± 6.5	84.6 ± 5.5	88.3 ± 3.4
15 minutes	84.6 ± 4.3	94.3 ± 3.5	118.3 ± 6.5	127.5 ± 5.2	80.6 ± 4.2	84.3 ± 2.6
30-minutes	78.9 ± 3.5	90.4 ± 3.7	116.3 ± 5.6	124.3 ± 3.4	79.2 ± 3.2	93.3 ± 4.0

Except for pre-op and induction, SBP and DBP are significantly different between groups I and II from 1 minute to 30 minutes (Table 5). ANOVA was also performed for effect p = 0.03 interaction groups effect p = 0.01 Analysis of heart rate revealed a significant time and interaction effect (Table 4) even after adjusting for sex. Overall, both groups saw a substantial shift in heart rate, however, the change in Diazepam (Group II) was much greater than the change in Clonidine (Group I). Significant variation was noted in Clonidine and Diazepam groups in systolic blood pressure before and 90 minutes after premedication. A rise of systolic blood in group I was lesser as compared to group II similarly, for the diastolic blood pressure maximum rise in BP was noted in group II following laryngoscopy, and

attenuation of DBP was lesser in group II as compared to group I at 30 minutes.

Discussion

Benzodiazepines (particularly diazepam) have been utilized as premedicant for a long time among the various agents employed because of their specialized activities. [3] In many high-risk patients, the sequence of anesthesia induction, laryngoscopy, and tracheal intubation are linked with significant hemodynamic alterations and autonomic reflex activation, which may be cause for worry. [4] Intubation and laryngoscopy are linked to an increase in heart rate, blood pressure, and the occurrence of cardiac arrhythmias. Within 5 minutes of laryngoscopy, these potentially harmful abnormalities tend to disappear. [5, 6] Even though the responses are short-lived they are harmful in some high-risk cases especially in persons with existing cardiovascular abnormalities and increased intracranial pressures or anomalies of cerebral blood vessels. [7] In this study, we found SBP and DBP are significantly different between groups I and II from 1 minute to 30 minutes. Analysis of heart rate revealed a significant time and interaction effect (Table 4) even after adjusting for sex. Overall, both groups saw a substantial shift in heart rate, however, the change in Diazepam (Group II) was much greater than the change in Clonidine (Group I). Significant variation was noted in Clonidine and Diazepam groups in systolic blood pressure before and 90 minutes after premedication. Studies have shown that the average rise of mean arterial pressure of 25 mmHg to 47 mmHg is documented. [8] The increase of mean arterial pressure of 26.5 mmHg and 20 - 40 mmHg has been shown when compared with awake control levels and 35 – 60 mmHg with pre-intubation values after the placement of the endotracheal tube. [9, 10] Variations of heart rate have shown that young patients show more extreme changes. [11] and geriatric patients have a greater degree of hemodynamic responses. [12, 13] In the current study we have selected the optimal age group of 20 – 50 years. Clonidine though primary an antihypertensive has been increasingly used as premedication. [14, 15] Since it reduces anesthetic requirements, improves hemodynamic stability. [16] Especially during laryngoscopy and intubations and potentiates post-operative analgesic regimens. Thiopentone was selected for induction since it continues to be the most popular agent for induction. In normovolemic patients, thiopentone 5 mg/kg i.v can transiently decrease 10-20 mm Hg of blood pressure and increase the heart rate by 15- 20 beats/min. [17] There is an increase in catecholamine levels, both noradrenaline, and adrenaline. [17] The most significant laryngoscopic factor influencing cardiovascular responses is found to be the duration of laryngoscopy. [11] A linear increase in heart rate and mean arterial pressure during the first seconds have been observed. [11] Further prolongation has little effect. As the duration of laryngoscopy is normally less than 30 seconds, the results of studies in which it takes longer than this have less clinical relevance. The force applied during laryngoscopy has only minor effects. [12] In our study the duration of laryngoscopy and intubation was limited to 20 seconds. Adequate care was taken to achieve the required depth of anesthesia avoiding hypoxia and hypercarbia which can influence the hemodynamic variations. Excluding hypoxia and hypercarbia, other contributory causes of hypertension and tachycardia could be continued manifestation of anxiety concerning anesthesia and surgery, glycopyrrolate premedication, reflex baroreceptor effect after thiopentone, and the possible effect of suxamethonium. [13]

Conclusion

Within the limitations of the current study, it was found that clonidine was superior in efficacy for mitigating the sympathetic responses to laryngoscopy and intubation because of its effects on reducing anxiety. It has the ability to reduce the overall anesthetic requirement and its property of potentiating postoperative analgesic requirements. Therefore, oral clonidine at the rate of 3 micrograms per kg body weight is better as compared to oral diazepam in our group population.

***Conflict of Interest*: None**
***Source of support*: Nil**
***Ethical Permission*: Obtained**

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