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A Randomised Controlled Comparative Study of Oral Clonidine with Oral Diazepam as Premedication in Patients for General Anaesthesia

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Abstract
Introduction: *Alpha-2 adrenoceptor agonists have been used as premedicants because of their beneficial properties in anaesthesia. Clonidine is now commonly used for its antihypertensive and negative chronotropic effects but has many properties of an ideal premedicant and also beneficial effects on haemodynamics during stressful conditions like laryngoscopy and endotracheal intubation. During general anaesthesia Clonidine reportedly enhances intraoperative circulatory stability by reducing catecholamine levels.*
Materials and Methods: *This randomized controlled trial study was conducted in tertiary care teaching Hospital, D.Y Patil Medical College and Hospital, Navi Mumbai After written informed consent from all the patients, 100 patients belonging to "American Society of Anesthesiologists" (ASA) GRADE I and II, Physical status aged between 18 to 56 years, scheduled for elective Orthopaedic, Otorhinolaryngology, Gynaecological and general surgeries were included in the study. Unwilling Patients, emergency Surgeries, patients with ASA Grade III or higher, patients with Neurological and endocrine abnormalities, renal impairment, hepatic disease, congestive heart failure, valvular heart disease, Hypotension, Ischemic heart disease, diabetes mellitus, patients on Psychotropic drugs or history of drug allergies were excluded from the study.*
Results: *There was no significant difference between the two groups with respect to age, weight and significant difference in the sex with male being higher in Group II (Table 1) was seen. Degree of sedation, anti-sialagogue effect and respiratory rate were comparable between the two groups studied (Table2-3). Table 3 shows that, in group I, the minimum dosage of Inj. Thiopentone that required for loss of eyelash reflex or induction was 150 mg and a maximum of 250 mg with a mean of 187.5 ± 28.2. In Group II, the minimum dosage of Inj. Thiopentone that required for loss of eyelash reflex or induction was 150 mg and a maximum of 300 mg with a mean of 236.0 ± 31.6. The requirement of Inj. Thiopentone for Induction between two groups was significantly higher in Group II as compared to Group I ($p<0.001$).*
Conclusion: *Premedication with oral Clonidine 3µgm/kg body weight, given 90 minutes prior to surgery provides better anxiolysis, reduces anaesthetic requirement and attenuates sympathetic responses to laryngoscopy and intubation, when compared to oral Diazepam 10 mg given as premedication 90 minutes prior to surgery.*
Key Words: *Otorhinolaryngology, laryngoscopy, American Society of Anesthesiologists*

I. Introduction

Alpha-2 adrenoceptor agonists have been used as premedicants because of their beneficial properties in anaesthesia. Clonidine is now commonly used for its antihypertensive and negative chronotropic effects but has many properties of an ideal premedicant and also beneficial effects on haemodynamics during stressful conditions like laryngoscopy and endotracheal intubation. During general anaesthesia Clonidine reportedly enhances intraoperative circulatory stability by reducing catecholamine levels.

This studywas 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. The aims and objectives of this study was to compare the premedication effects of oral Clonidine with oral diazepam with respect to anxiety, sedation, heart rate, blood pressure, dose of anaesthetic requirements, sympathetic responses to laryngoscopy and intubation, and respiratory rate.

II. Materials And Methods

This randomized controlled trial study was conducted in tertiary care teaching Hospital, D.Y Patil Medical College, Navi Mumbai After written informed consent from all the patients, 100 patients belonging to "American Society of Anesthesiologists" (ASA) GRADE I and II, Physical status aged between 18 to 56 years, scheduled for elective Orthopaedic, Otorhinolaryngology, Gynaecological and general surgeries were included

in the study. Unwilling Patients, emergency Surgeries, patients with ASA Grade III or higher, patients with Neurological and endocrine abnormalities, renal impairment, hepatic disease, congestive heart failure, valvular heart disease, Hypotension, Ischemic heart disease, diabetes mellitus, patients on Psychotropic drugs or history of drug allergies were excluded from the study.

Sample size was estimated based on the study done by Chattopadhyay S et.al.1In order to observe a minimum difference of 4 BPM on heart rate immediately after ET Tube Insertion with standard deviation of 4.08 and 7.01 in study groups 1 and group 2 with 1% level of significance (Adjusted for Multiple Comparison) and 80% power, the number of subjects required in each group was 47, we have considered recruiting 50 patients in each group, totally 100 patients.

A computer-generated randomization list was prepared using online software to randomize patients into group I and group II. 100 patients were randomly allocated into two groups with 50 patients in each group.

Group I: All patients in this groupreceived oral tablet Clonidine 3µgm/kg body weight 90 minutes before surgery.

Group II: All the patients in this group received oral tablet Diazepam 10mg, 90 minutes before surgery.

Pre-anaesthetic checkup was done prior to the surgery. Patients were evaluated for systemic diseases and routine laboratory investigations recorded. On the day of surgery, systolic and diastolic blood pressures, heart rate and respiratory rate were measured before premedication and scoring was done for sedation, anxiolysis and anti-sialagogue effects 90 minutes after premedication.

All the patients were pre-oxygenated with 100% oxygen for 3 minutes before induction with a tight-fittingface mask. Patients were induced with Inj. Thiopentone sodium 2.5% and administered slowly till the loss of eyelash reflex. Injection Glycopyrrolate 0.2mg IV was given prior to thiopentone. Intermediate acting neuromuscular blocking agent Inj. Vecuroniumwas given as muscle relaxant. Laryngoscopy was done using rigid laryngoscope with standard Macintosh blade. Intubation was done with appropriatelysized disposable, high volume low pressure cuffed endotracheal tube. The patients were then ventilated with 60% nitrous oxide and 40% oxygen with a tidal volume of 10-12 ml/kg and a rate of 12-14 breaths per minute. 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. At the end of the surgery, patient was extubated after reversal of non-depolarizing muscle relaxant with Inj. Neostigmine 0.05mg/kg IV and Inj. Glycopyrrolate 0.01mg/kg IV.An observation was made related to adverse effects of drugs and anaesthesiarelated problems and were attended to appropriately.

Statistical Methods: Descriptive statistical analysis has been carried using mean with SD for the continuous measurements and number and % for the categorical measurements. Independent t test was used to test the significance of study parameters on continuous scale between two groups. Chi-square test was used to test the association between study parameters with study groups. Repeated measures ANOVA was carried out to assess the time and interaction effect (time x group) between study groups on vital parameters adjusted for sex. Probability value less than 5% was considered statistically significant. All the analyses were carried using SPSS version 23.0.

III. Results

There was no significant difference between the two groups with respect to age, weight and significant difference in the sex with male being higher in Group II (Table 1) was seen. Degree of sedation, anti-sialagogue effect and respiratory rate were comparable between the two groups studied (Table2-3). Table 3 shows that, in group I, the minimum dosage of Inj. Thiopentone that required for loss of eyelash reflex or induction was 150 mg and a maximum of 250 mg with a mean of 187.5 ± 28.2. In Group II, the minimum dosage of Inj. Thiopentone that required for loss of eyelash reflex or induction was 150 mg and a maximum of 300 mg with a mean of 236.0 ± 31.6. The requirement of Inj. Thiopentone for Induction between two groups was significantly higher in Group II as compared to Group I ($p<0.001$).

	Group I	Group II	P Value
Age in years	36.45±10.20	36.17±9.24	0.657
Sex			
Male	21(42.6)	33(65.0)	0.016
Female	28(57.3)	17(34.0)	
Weight	48.64±6.15	50.54±5.35	0.515

Table 1: Comparison of Baseline Characteristics between Group I and II

	Group I	Group II	P Value
Degree of sedation			
0	**15(30)**	**16(32.0)**	
1	**11(21)**	**14(28.0)**	**0.685**
2	**23(48)**	**20(40)**	
3	**0**	**0**	
Anxiolysis Score			
0	-	**4(8.0)**	
1	-	**10(20.0)**	
2	-	**26(52.0)**	**0.0001**
3	**16(31.0)**	**10(26.0)**	
4	**33(67.0)**	**0**	
Anti Sialagogue Score			
0			
1	**4(8.0)**	**0**	**0.123**
2	**24(48)**	**27(53)**	
	22(44)	**23(46.0)**	

Table 2: Comparison of Clinical Characteristics between Group I and II

	Group I	Group II	P Value
Respiratory Rate (Breaths/min)			
Before medication	14.34±0.87	14.34±0.88	0.538
After medication	13.54±0.65	14.47±0.64	0.473
Dosage of Inj.Thiopentone (mg)	189.5±26.6	232.5±30.5	0.001

Table 3: Comparison of Respiratory Rate and Dosage of Inj. Thiopentone between the Two Groups Studied

	Heart rate (Beats /min)		SBP (mm Hg)		DBP (mm Hg)	
	Group I	Group II	Group I	Group II	Group I	Group II
Pre OP	72.6±6.2	74.3±5.6	115.2±8.3	118.2±12.8	79.2±4.5	76.5±5.4
Induction	74.3±6.6	76.2±6.5	107.2±8.6	120.2±13.5	78.13±6.5	80.5±3.6
1 M*	85.3±7.2	75.4±6.9	126.2±9.4	153.2±10.2	75.12±6.5	97.3±2.4
3 M*	82.5±6.3	76.5±5.8	120.3±10.2	147.2±8.3	85.12±4.2	80.5±3.7
5 M*	80.9±5.6	98.3±7.5	118.0±10.3	135.2±7.5	140.2±7.6	90.2±3.3
10 M*	78.1±6.5	97.3±6.5	115.20±8.4	128.2±5.3	132.3±6.3	87.9±5.8
15 M*	75.5±5.6	92.2±7.3	113.5±8.2	122.5±4.2	126.2±5.64	85±6.3
30 M*	76.4±6.2	89.0±7.3	114.5±8.0	124.3±3.2	124.2±3.12	83±8.3

Table 4: Comparison of Heart rate, SBP and DBP between the Two Groups of Patients Studied

IV. Discussion

In our study, there was no significant change in the heart rates during the premedication and 90 minutes after premedication between the two groups, however heart rate increased by a maximum of 15.1% in Clonidine group when compared to 42.3% in the Diazepam group at 1 minute following laryngoscopy and intubation. Clonidine group attenuated the heart rate significantly ($p<0.001$). It reaches a value which is clinically less significant by the end of 30 minutes in Clonidine while remaining on a higher range in the Diazepam group even after 30 minutes. Attenuation of maximum rise in the heart rate by Clonidine is evident and statistically highly significant when compared with Diazepam group ($p < 0.001$). A similar finding was found in a study done by Roy S et al8 and R Brindha et al9that Clonidine was highly significant in the attenuation of maximum rise in the heart rate whencompared to Diazepam. Chattopadhyay S et al study showed that clonidine attenuated heart rate effectively. Even study done by Chaurasia SK et al5 showed similar findings that Clonidine was a better drug to attenuate rise in heart rate comparing it to a combination of Diazepam and atropine.

In our study, the Clonidine group systolic blood pressure reduced by 6.7%, 90 minutes after premedication but there was no change in the Diazepam group. It increased maximally after 1 minute from onset of laryngoscopy and intubation. It gradually decreased to preinduction value over 10-15 minutes. With Diazepam group, the maximum rise in systolic blood pressure was 28.6% above the preoperative values (During premedication) at 1 minute did not come to baseline even after 30 minutes following laryngoscopy and intubation. Similar attenuation of sympathoadrenal response to laryngoscopy and intubation was observed by Pouttu et al.4Clonidine showed a better drug to attenuate rise in systolic blood pressure comparing it to Diazepam ($p<0.001$).

In our study maximal rise in diastolic blood pressure was 11.1% in Clonidine group and in Diazepam group it was 20.3% ($p<0.001$). In Clonidine group, the diastolic blood pressure almost reached the baseline by the end of 10-15 minutes following laryngoscopy and intubation while it remained high even after 30 minutes

following laryngoscopy and intubation ($p<0.001$) in the Diazepam group. Similar attenuation of sympathoadrenal response to laryngoscopy and intubation was observed by Pouttu et al4and Chaurasia SK et al.5

V. Conclusion

Premedication with oral Clonidine 3µgm/kg body weight, given 90 minutes prior to surgery provides better anxiolysis, reduces anaesthetic requirement and attenuates sympathetic responses to laryngoscopy and intubation, when compared to oral Diazepam 10 mg given as premedication 90 minutes prior to surgery.

References

[1]. Leslie K, Mooney PH. Effect of intravenous clonidine on the dose of thiopental required to induce anesthesia. Anesth Analg. 1992; 75: 530-5.
[2]. Stoelting RK, Hillier SC. Antihypertensive drugs. In: Pharmacology and Physiology in Anesthetic Practice. 4th edn. Philadelphia, Lippincott Williams & Wilkins. 2006; 340-43.
[3]. Moss J, Glick D. the Autonomic nervous System. In: Miller's Anesthesia, Miller RD Editor. 6th edn. Philadelphia. Churchill Livingstone. 2005; 650-51.
[4]. Morgan GE, Michael MS, Murray MJ. Adrenergic agonists and antagonists. In: Clinical Anesthesiology, 3rd edn. New York. Mc Graw Hill. 2002; 216-17.
[5]. Collins VJ. Principles of pre anesthetic medication. In: Principles of Anesthesiology. 3rd edn. Malvern. Lea & Febiger. 1993; 292.
[6]. NishikawaT, Taguchi M. Effects of clonidine premedication upon haemodynamic changes associated with laryngoscopy and tracheal intubation. Masui, 1991; 40(7): 1083-88.
[7]. Nishina K, Mikawa K, Maekawa N, Takao Y, Obara H. Clonidine decreases the dose of thiamylal required to induce anesthesia in children. Anesth Analg. 1994; 79: 766-8.
[8]. Baskaran N, Rath PC. Oral clonidine premedication: Its effect on the induction dose of thiopentone sodium. Ind J Anaesth. 1996; 44: 173-76.
[9]. Goyagi T, Tanaka M, Nishikawa T. Oral clonidine reduces induction dose and prolongs awakening time from propofol-nitrous oxide anesthesia. Can J Anaesth. 1999; 46(9): 894-96.
[10]. Carabine UA, Wright PMC. Cardiovascular effects of intravenous clonidine. Anaesthesia 1991; 46: 634-7.