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Original Research Article

Clinical analysis of oral clonidine and intramuscular pethidine with glycopyrrolate as premedication in patient under general anaesthesia

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Abstract

Objective: Various drugs have been endorsed but no standardized premedication protocol exists for patients. Various opioids combination is in practice for long time with some ill effects. Alfa 2 agonist group are newer drugs in anaesthesia practice. This study was designed to evaluate the efficacy oral clonidine and intramuscular pethidine with glycopyrrolate as premedication in patient under general anaesthesia.

Methodology: Prospective, randomised study in patients, 18–50 years of age, undergoing surgeries. Patients to receive premedication either pethidine (1mg/kg) + Glycopyrrolate 8 mcg/kg I.M (group A, n=50) or clonidine 5µg/kg (group B; n = 50) preoperatively. The sedation level, salivation scale, haemodynamic response and ill effects were recorded perioperatively.

Results: The baseline haemodynamic (HR, MAP, RR, and SpO_2) parameters were normal and comparable in both the groups. By the time of induction only 20 percent of patients were moderately, and 2 percent deeply sedated in group B, whereas in the group A 80 percent of the patients were deeply sedated ($p<0.05$). 74% in the control B patients had dry mouths time of induction, where as all patients in the group A were found to have dry mouth ($p<0.05$). There was not much variation in heart rate (HR) from basal value till time before intubation in Group A whereas there was a definite fall in Group B. The rise in HR due to intubation in Group B was less in comparison to rise which occurred in group B.

Conclusion: We can conclude that oral clonidine is a better premedication in comparison to inj pethidine and inj glycopyrrolate which is commonly used in hospitals.

Keywords: Clonidine, premedication, pethidine.

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1. Introduction

Since the establishment of premedication agent for general anesthesia (GA), no flawless premedication drug has yet been uncovering in term of providing complete anxiolysis and sturdy hemodynamics during endotracheal intubation. Preoperative anxiety, salivation, and haemodynamic changes in perioperative period especially during laryngoscopy and intubation are an integral part of anaesthesia and surgery [1-3]. The use of various premedication to provide a state of acquiescence to induction and intubation however resulted in prolonged recovery time, drug toxicity and cardio respiratory complications. Hence, there has been a hunt for an ideal premedication drug which should be effective with minimum ill effects.

For many years clonidine, has been used as an antihypertensive. It is a centrally acting alpha-adrenergic agonist, having an inhibitory action on the central dopaminergic system [4]. The present study has been carried out to evaluate the effectiveness of clonidine as an

oral premedicant and to compare its effects with the commonly used premedicant like pethidine and glycopyrrolate.

2. Material and methods

This study was conducted in a 600 bedded tertiary care super specialty hospital in India. After Approval from the Institutional Ethics Committee, written informed consent was obtained from the patients. Out of a total of 245 patients admitted for GA in operation theatre during the study period, 12 patients did not meet inclusion criteria and 33 were excluded due to unavailability of investigator. A total of 100 patients of ASA physical status I and II in the age group of 18 years to 50 years, of either sex, posted for elective surgery under GA were enrolled for this prospective, randomized double blind study. Patient with cardiovascular, respiratory, renal, hepatic diseases and obesity and with known allergy / hypersensitivity to study drug were excluded from the study.

According to a computer-generated randomization chart, the patients were assigned to one of the treatment groups. To ensure blinding, premedication was given by an anaesthesiologist who didn't involve in the study. Patients in group "A" received Inj Pethidine1 mg /kg + Glycopyrrolate 8 mcg/kg I.M. 01 hrs before surgery and patients in group "B" received oral clonidine 5mcg/kg 90 minutes before surgery. The test drug was prepared and administered by a nurse who was blinded to drug assignment. All patients received inj fentanyl 2 mcg/kg body weight during intubation for intra op analgesia. Vitals were recorded by blinded treating clinician. All standard ASA monitoring were attached and all basal parameters were recorded. Tracheal intubation was facilitated by using Inj Vecuronium 0.1 mg kg^{-1} IV and GA was maintained with O_2, N_2O and Sevoflurane. For assessment of sedation patient was subjectively assessed on a 4-point grading scale at 0 min, 15 min and 30 min before induction. (0= Alert, 1= Mildly drowsy, 2= Moderately drowsy, 3= Asleep). Antisialogogue effect of the drugs was observed pre operatively at 0 min,15 min and 30 min before induction subjectively assessed on a 2 point scale (0=Moist tongue and 1=Dry tongue). Monitoring of heart rate (HR), Systolic Blood pressure(SBP), Diastolic Blood Pressure(DBP), Mean blood Pressure (MBP) and Oxygen saturation (SpO_2) would be done baseline and at 0,15 and 30 min before induction and 5 min and 10 min after intubation. Each patient was monitored intra-operatively for any significant changes of vital parameters, blood loss, urine output, analgesic and anaesthetic requirements. Patients were followed up postoperatively for any instability in vital parameters or any untoward occurrence.

The data was analyzed using Statistical Package for Social Science (SPSS version 16.0). Sample size was calculated keeping in view at most 5% risk, with minimum 80% power and 5% significance level (significant at 95% confidence level). After considering which the past data, which gives idea of variation in variable, play important role in calculating the sample size .Sample size should be 50 in each group for safer side and normality of the data. Physical characteristics, SBP, DBP, MBP, HR values, all time intervals are compared using one way ANOVA, was followed by suitable post hoc test for multiple comparison (Tukey HSD). All differences were considered significant at $p<0.05$.

3. Observation and Results

Evaluation of effectiveness of clonidine as an oral premedicant with the commonly used premedicant like pethidine and glycopyrrolate was studied during GA in 100 adult patients. Each group had 50 patients each. Demographic parameters and clinical characteristics were comparable between the groups. Of them 51% were males and 49% were females and most of them belonged to ASA physical status I (Table 1). All patients were reported to OT and received premedication and GA.

In the present study, it was found that, by the time of induction only 20 percent of patients were moderately, and 2 percent deeply sedated in the control group, whereas in the group A 80 percent of the patients were deeply sedated, most of them had to be woken up before taking to the theatre for induction ($p<0.05$). At the time of induction, 74% in the control group had dry mouths, where as all patients in the group A were found to have dry mouth ($p<0.05$). There was not much variation in HR from basal value till time before intubation in Gp A whereas there was a definite fall in Gp B (Table 2) The rise in HR due to intubation in Gp B was less in comparison to rise which occurred in group B. Mean HR settled down more steadily towards pre intubation value and even less than that.

No complications were observed for two hours postoperatively in either group. SpO_2 was between 98 to 100 percent in all the patients. There were no significant ECG abnormalities observed perioperatively in either group of patients.

Table 1: Baseline demographic parameters and clinical characteristics of patients in both groups

Patient data	Group A (n=50)	Group B (n=50)	P value
Age (yr)	34.98±17.6	33.94 ±18.6	0.44
Weight (kg)	56.69±13.1	60.02 ±13.8	0.46
Gender M/F	27/23	23/27	0.67
ASA (I/II)	22/3	21/4	

All values expressed as mean ± SD or as expressed otherwise

Table 2: Sedation, salivation and mean heart rate of group A and group B

		Groups (A/B)		
		T1	**T2**	**T3**
Sedation scores	0	46/3	16/0	7/0
	1	4/25	32/7	32/1
	2	0/21	2/37	10/9
	3	0/1	0/6	1/40
Salivation scores	0	41/17	14/6	13/0
	1	9/33	36/44	37/50
		Group A	Group B	P Value
Heart Rate	T0	88.12±8.4	85.11± 6.15	0.04
	T1	88.88± 10.51	82.38±14.61	0.01
	T2	88.81±10	78.88±13.65	0.0001
	T3	88.78± 10.3	74.82±11.41	0.0001
	T4	80.7± 13	86±16.49	0.0001
	T5	101.3± 11	78.34± 1.65	0.0001
	T6	99.88± 12.64	76.28±14.56	0.0001
	T0	88.12± 8.4	85.11±6.15	0.01

(Values expressed as mean± SD or number) at various time points in the groups. A= clonidine group, B= pethidine + glycopyorrate, T0 = Baseline values, T1= 30 min before induction, T2= 15 min before induction, T3- at induction, T4- Just after intubation, T5- 5 min after intubation, T6=10 min after intubaion.

4. Discussion

Oral clonidine is commonly used premedication as having sedative, antisiaglouges and anxiolytic properties and also helps in smooth induction of anaesthesia. The alpha-2 agonist property of dexmedetomidine and clonidine also blunt rise in HR, MAP and intracranial pressure in response to tracheal suctioning in ICU [5]. In this study inj pethidine and glycopyrrolate were chosen for control group, as it is the commonly used premedicant in our hospitals.

Studies have been done to quantify the suitable dose of clonidine. Our results were quite similar to the previous study done by Carabine *et al* who used clonidine at a dose of 0.3 mg and showed that clonidine is an effective sedative, anxiolytic agent with significant benefits [6]. Previous studies done by Wright *et al* taken thirty patients and pretreated them with clonidine 1.25mcg/kg or 0.625 mcg/kg IV 15 min before induction and showed clonidine completely abolished increase in HR in response to intubation[7]. Chadha *et al* in their study had shown that hypertensive response to laryngoscopy and intubation was significantly less with clonidine as premedication [8].

The major limitation of this study was the waiting period not mentioned before taken patients to operation theatre after premedication. It is practicable that we may have noted eminent sedative condition in the clonidine with combination group if we had waited longer. The other limitation being we have not measured plasma level of drugs without which we cannot rule out their systemic effects at different time intervals. We used grades for sedation and salivation which is not validated. When using these scales, we confront some difficulties in the appraisal of patient.

Other limitations of this study were non inclusion of intraoperative haemodynamics monitoring, effect on recovery, and effect on emergence.

5. Conclusion

Thus, clonidine provided an acceptable level of sedation and dryness of mouth by the time of induction in comparison to control group and its efficacy to blunt the stress response to laryngoscopy and intubation is better in comparison to injection pethidine and glycopyrrolate taking into account of blood pressure. Furthermore with this study we can conclude that oral clonidine at a dose of 5 mcg /kg 90 min before induction is a better premedication in comparison to inj pethidine and inj glycopyrrolate which is commonly used in our hospitals

Conflict of Interest:

No conflict of interest was declared by the authors.

Financial Disclosure:

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Ethics Committee Approval:

Ethics committee approval was received for this study from the ethics committee of Armed Forces Medical College Pune and Command Hospital PUNE.

Informed Consent:

Written informed consent was obtained from patients who participated in this study.

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