

Comparative Efficacy of Oral Metoprolol Vs Oral Clonidine as Premedicants for Hypotensive Anesthesia for Patients Undergoing functional Endoscopic Sinus Surgery under General Anesthesia

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ABSTRACT

This prospective randomized study aimed to analyze the effect of metoprolol and clonidine premedication on the peri-operative characteristics of patients undergoing FESS procedure under GA and induced hypotensive anaesthetic technique. The Present study includes the Clonidine and metoprolol premedication produces predictable and superior hemodynamics during peri-operative period, with metoprolol being superior to clonidine and Clonidine and metoprolol premedication decreases the intra-operative requirement of vasodilators like NTG. This study focuses on Clonidine and metoprolol premedication decreases the requirement of inhalational anaesthetics like isoflurane to maintain hemodynamic control and Clonidine premedication produces increased incidences of undesirable alterations in BP, which extended into the early post-op period, but could be easily treated. It produces better sedation and anxiolysis pre-op and reduces the requirement of post-op analgesia as noted by delayed TAR times which also in turn reduces the incidence of post-anaesthetic shivering and leads to produce lesser perturbations in HR and BP in response to intubation in Metoprolol.

Keywords

hypotensive, FESS procedure, clonidine, metoprolol, endoscopic, surgical

INTRODUCTION

Anaesthesia for functional endoscopic sinus surgery is a challenging job. The surgeons' operating field itself is very small and surrounded with mucus membranes (1-5). It is imperative for the surgeons to look at a clear surgical field in order to identify the diseased tissue properly. A small amount of blood within the field is enough to occlude the view through the endoscope making the operation difficult for the surgeon. Incomplete removal of the diseased tissue will cause the disease to recur. Anaesthesiologists have devised various techniques to prevent this bleeding, of which induced hypotension has stood the test of time. This surgery per se is not a major one by its standards and surgeons recently have been trying to accomplish FESS as a daycare surgery (6-8). A good premedication with an antihypertensive agent can help to minimize the amount of volatile agents and vasodilators used to induce hypotension, thereby ensuring much hemodynamic stability and speedy recovery from anaesthesia (9-11). Thus I have chosen to study and compare the effects of clonidine and metoprolol as oral premedicants for the same. This study proposes to analyze the anaesthetic challenge of keeping the operating field free of blood through pharmacological therapy. It compares show premedicating with either metoprolol or clonidine affects the conduct of the fixed anaesthesia protocol evolved in our institute on patients

undergoing FESS procedure under GA, and requiring a hypotensive technique to improve operating conditions (12-15).

MATERIALS AND METHODS

After getting clearance from the ethics committee of SBMCH the study was formulated as follows. **Study Design**

Randomized experimental double blind study

Inclusion criteria:

1. Patients belonging to ASA I & II.
2. Patients between ages 18 to 60.
3. Patients undergoing FESS procedure.

Exclusion Criteria:

- Hypertensive patients.
- H/o Cerebro-vascular accident / Transient ischaemic attack.
- Moderate and severe IHD, EF < 40%
- Poor respiratory reserve.
- Significant hepatic or renal disease.
- Contraindication for the use of study drug like bronchospasm, COPD, conduction defects and hypersensitivity.
- Patients who are not willing to participate in the study.

Sampling Frame

Patients undergoing Functional endoscopic sinus surgery at the Department of Otorhinolaryngology, SreeBalaji Medical College and Hospital, Chennai, India. Probability Sampling Randomization using the lottery method. Sixty lots (twenty in each group) were placed to randomize the people who were willing to take part in the study. All the patients stand an equal chance of getting into any group with this method. All the patients were aware of the study and informed consent obtained. Sample Size Sixty patients, twenty in each of clonidine, metoprolol and placebo groups.

Data collection

A structured assessment schedule was constructed using experts opinion for measuring the haemodynamic stability and to monitor the use of intraoperative drugs. Patient data, vital signs, baseline investigations like haemogram, Hb%, Urea, Creatinine, 12 lead EKG and chest X-ray were collected preoperatively. Hemodynamic and ventilation parameters like Heart rate, NIBP, Oxygen saturation, Lead II ECG were monitored. FiO₂, and ventilatory parameters were monitored using the inbuilt ventilator in the ETCO₂ monitored intraoperatively. Continuous lead II EKG monitoring, SpO₂, NIBP and heart rate monitoring continued for a minimum of six hours postoperatively in the post anesthesia care unit.

Anaesthesia protocol

Two 18G IV lines started for the patient on table, standard monitoring (ECG, NIBP, SpO₂, Temp, ETCO₂) were carried out intra-operatively. All the patients are preloaded with 500 ml normal saline before induction. Nasal packing done with 4% lignocaine with 1:200000 epinephrine. Patient preoxygenated for 5 minutes, Anesthesia carried out with Glycopyrrolate 0.2 mg + fentanyl 2.0 mcg/kg + Xylocard 1.0 –2.0 mg/kg + Propofol 2.5 mg/kg + Vecuronium 0.1 mg/kg. Endotracheal intubation done orally with appropriate size ET tube. Throat packing done within 1 –3 minutes post-intubation. Anesthesia maintained with 66% nitrous, 33% oxygen, 0.75% isoflurane, with IPPV and vecuronium.

Plan:

We need to maintain the MAP at 70 mm Hg. If MAP is more than the set value the following plan of action was taken.

Step 1: Increase isoflurane up to 1%. If no response in 10 minutes go to step 2.

Step 2: To start a titrated NTG infusion. (Each increase in NTG dose done with an interval of 5 minutes to allow equilibration of serum therapeutic levels.). Intra-operative hypotension was managed by

- IV fluids LR/NS 200 ml
- Taper down NTG/volatiles
- Ephedrine 3mg i.v. boluses

Intra-op Arrhythmias:

If the patient was haemodynamically stable, we continued with the study but with close and increased monitoring. If unstable, we abandon hypotension, volume resuscitate and manage accordingly. At the end of procedure standard reversal (Neostigmine 50mcg/kg + Glycopyrrolate 8mcg/kg) and extubation carried out.

Data Management and Analysis

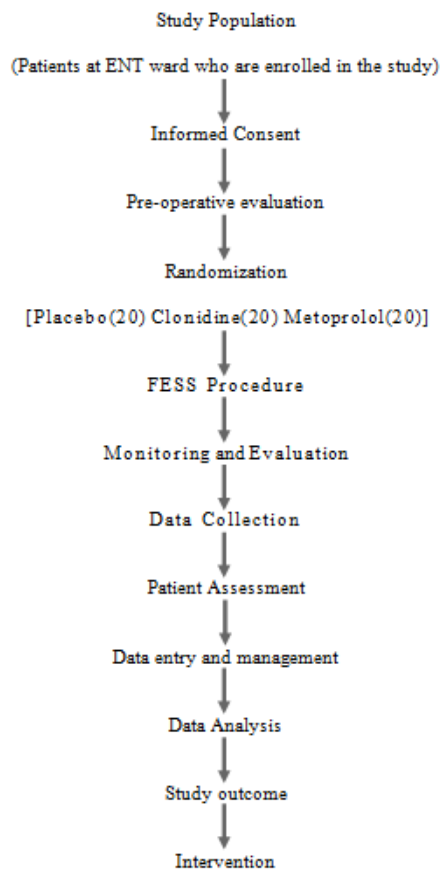
The variables were entered into SPSS, version 11, statistical software for analysis. The descriptive statistics of the variables studied are represented as two-way tables. The categorical factors are represented by the number and frequency (%) of cases. The continuous variables are represented by measures of central frequency (like mean, median & mode) and deviation (say, standard deviation and range). The differences in the proportions of are tested for statistical significance using non-parametric Chi-square test for variables measured on nominal scale. For variables measured on a continuous scale, one-way analysis of variance (ANOVA) is employed to elicit the statistical significance of three variables taken together.

When testing for two groups, Student “t” test is used to test for statistical significance in the differences of the two means. Line graphs were used to illustrate the hemodynamic monitoring

at different time points. Box plot graphs were employed to depict the distribution of other factors in the three groups.

METHOD DESIGN

Study Population



RESULTS

TABLE I : DEMOGRAPHIC DATA

Age	PLACE BO	CLONIDI NE	METOPROL OL	P-VAL UE
No of Cases	20	20	20	
Mean	27.0	25.9	23.5	
S.D	7.36	7.66	4.72	
Median	25	24	22	
Mode	22	19	10	
Range	19-50	16-45	18-36	
<u>Stat.significa</u> <u>n</u> <u>ce</u>		<u>p-value</u>		
C vs.P		0.66		
M vs.P		0.08		
C vs.M		0.23		

not statistically significant*

The mean age between the comparison groups are almost similar. The minimum age taken for the study is 16 and the maximum is 48.

Table II : Sex distribution

	Placebo (P)		Clonidine (C)		Metoprolol (M)		p- value
	No.	%	No.	%	No.	%	
Male	14	70.0	13	65.0	11	55.0	0.61
Female	6	30.0	7	35.0	9	45.0	
Stat	p-value 0.52						
<u>significance</u> C vs.P	0.33						
M vs.P	0.74						
C vs.M							

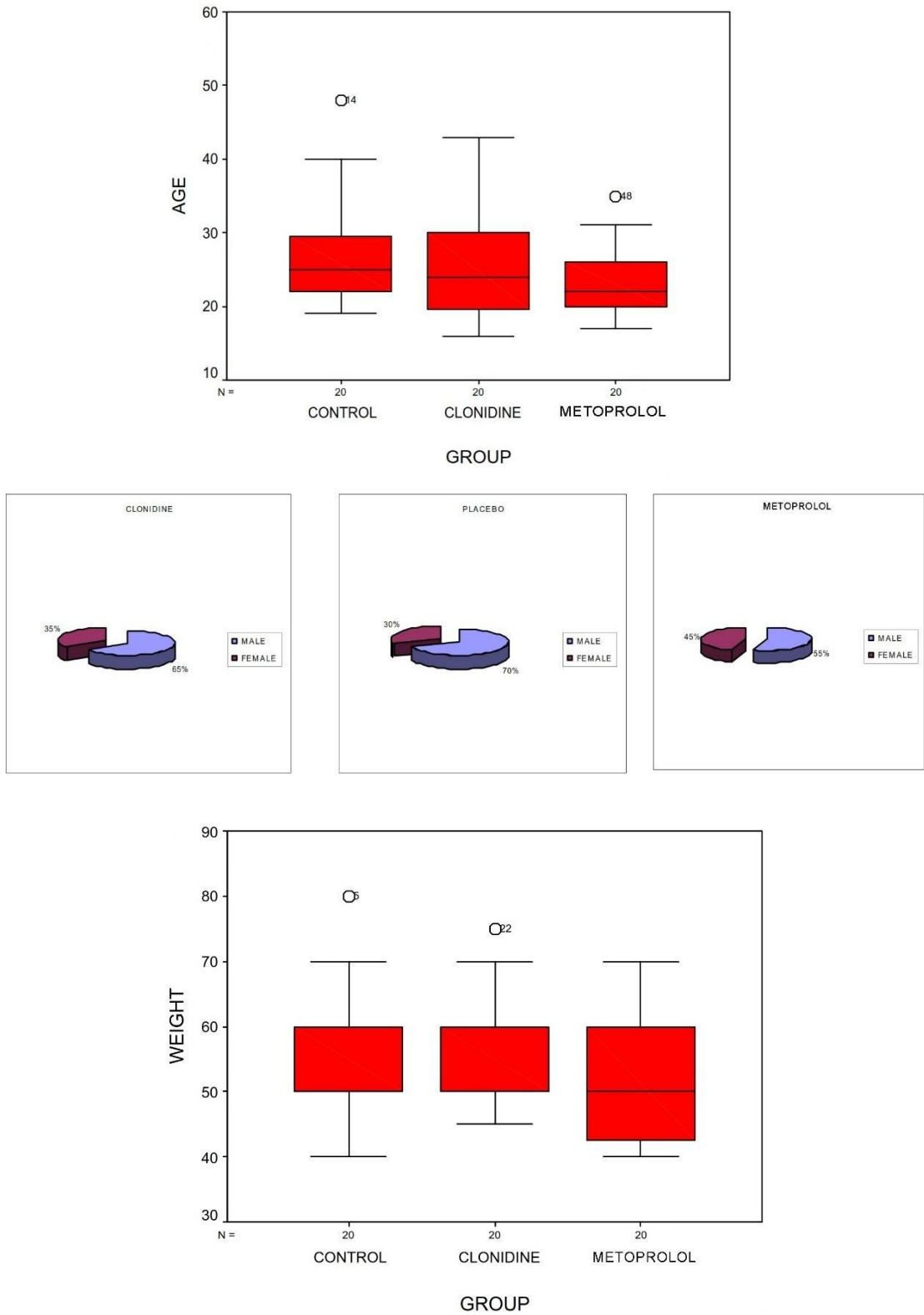
Not statistically significant*

A male preponderance is forth coming in all the study groups.however,the distribution of sex among the group is not statistically significant

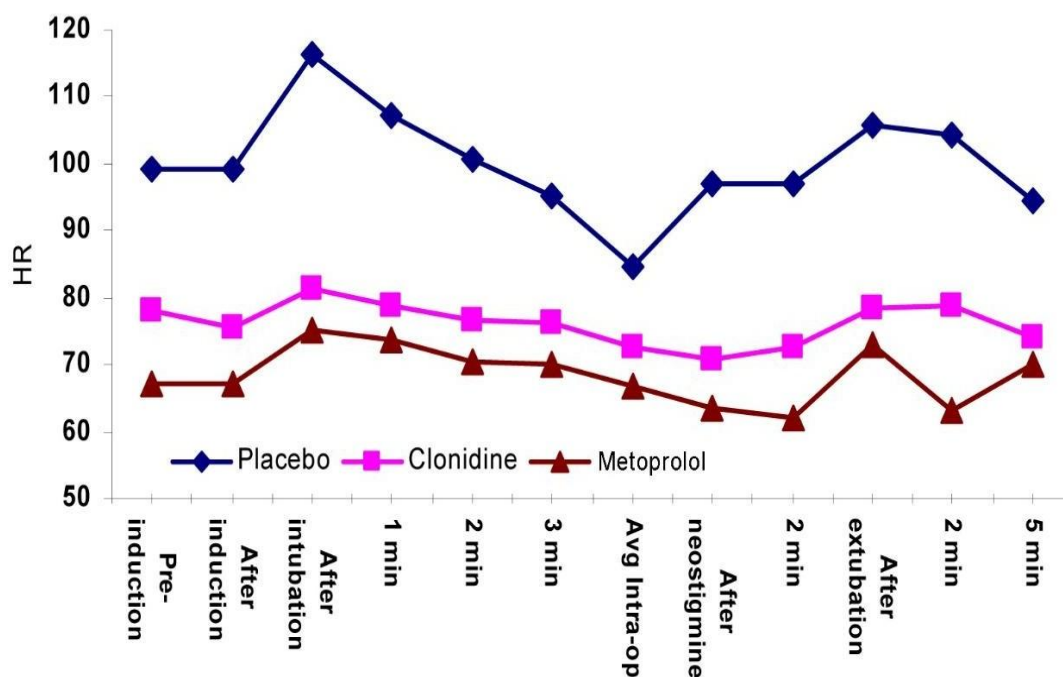
TABLE III: WEIGHT DISTRIBUTION

Weight	PLACEBO (P)	CLONIDINE (C)	METOPROLOL(M)	p- value
No.of	20	20	20	0.36
cases	53.9	55.4	51.3	
Mean	9.47	8.65	9.44	
S.D.	50	50	50	
Median	50	50	40	
Mode	40-80	45-75	40-70	
Range				
Stat	p-value			
Significance	0.59			
C vs.P	0.39			
M vs.P	0.16			
C vs.M				

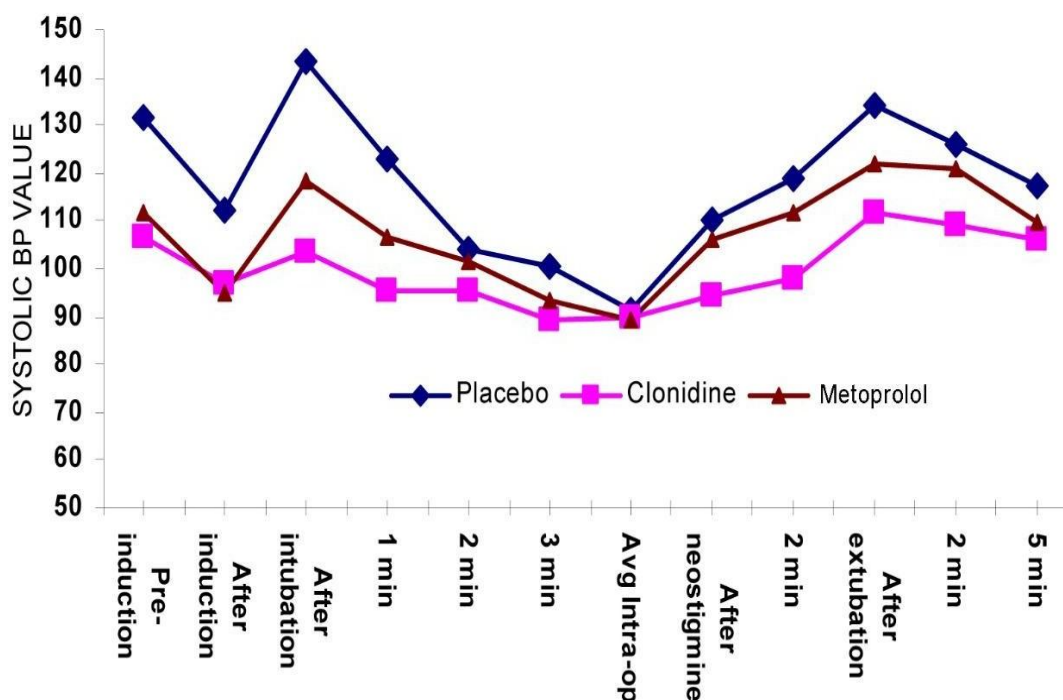
The mean distribution of cases by weight was observed to be not statistically significant between Group 1 and Group 2 as well as between the groups and control.

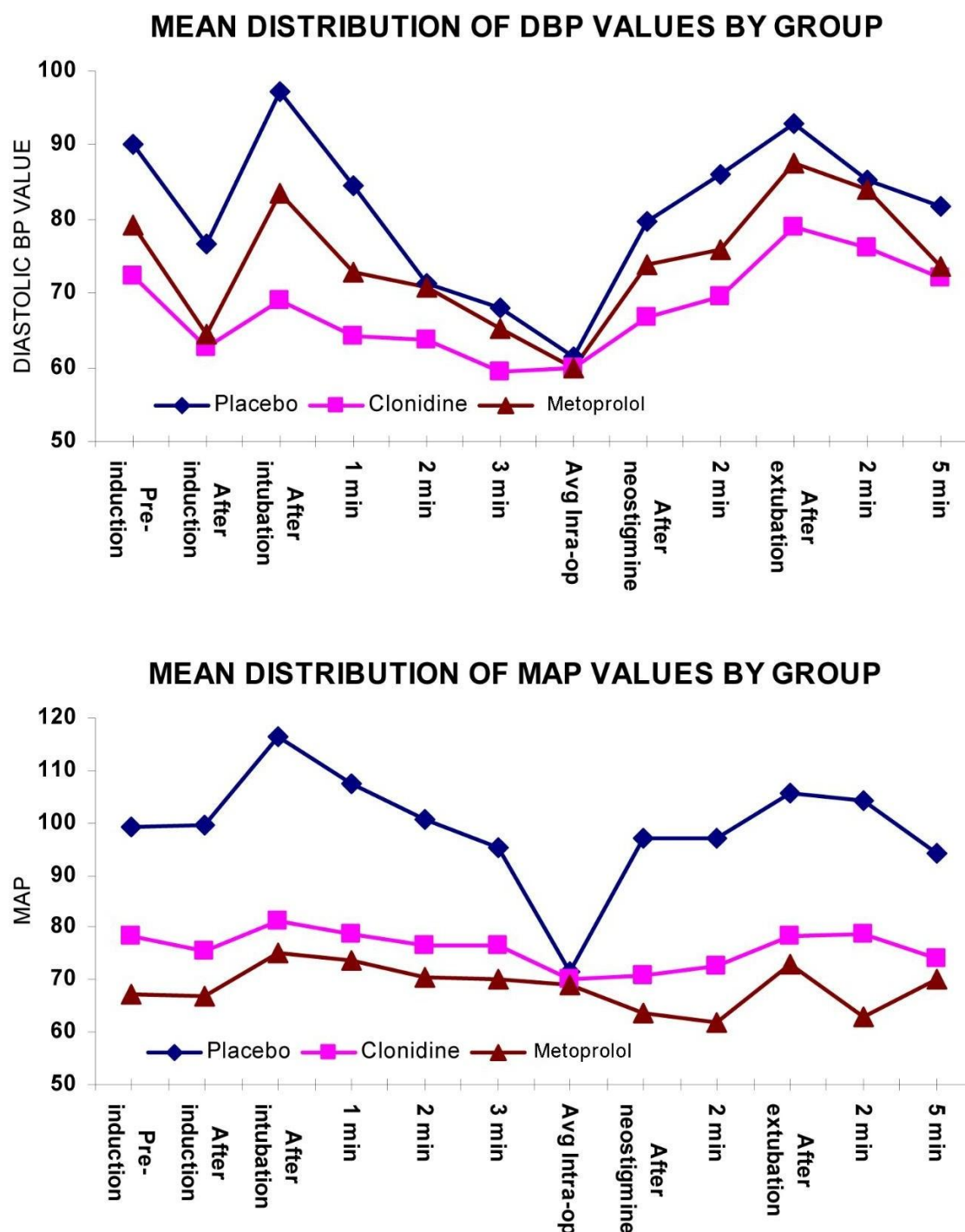


MEAN DISTRIBUTION OF HR VALUES BY GROUP



MEAN DISTRIBUTION OF SBP VALUES BY GROUP





There is a statistically significant difference in the mean heart rate measured during the five intraoperative events (presented in the tables 4, 5 and 6) among the placebo and the treatment groups. There is a significant reduction in heart rate in the metoprolol group when compared to the clonidine group. There is a statistically significant difference in systolic BP between the placebo group and the treatment groups during the five events. However there is no statistically significant difference between the clonidine and the metoprolol group.

Diastolic BP, when measured before and after induction had a statistically significant difference among the placebo and the treatment groups. Between the clonidine and metoprolol groups there is a significant difference only before induction. All other events were not statistically significant. The mean arterial pressure before induction is statistically significant between the placebo group and the treatment group. Here again between the clonidine and the metoprolol group no statistical significance is demonstrated.

Majority cases in the treatment group have a low requirement of isoflurane intraoperatively which is in contrast to the majority of cases in the placebo group which has a high requirement of isoflurane intraoperatively. None of the cases in either of the treatment groups had a high requirement of isoflurane intraoperatively. Majority of cases in the control group required nitroglycerin intraoperatively. None of the cases in either of the treatment groups required nitroglycerin intraoperatively.

DISCUSSION

Premedication is not only for sedation and anxiolysis, but also to enhance the quality of induction, maintenance and recovery from anaesthesia (16-18). The primary goal of an anaesthetist in FESS procedure is to provide better surgical access, a bloodless operating field, conduct of balanced anaesthesia and prompt recovery. To provide a bloodless operating field, induced hypotension is a clear answer in addition to proper positioning (15 O reverse trendelenberg position) to promote venous drainage. In order to achieve a better operating field, the surgeon on his part packs the nasal cavity with vasoconstrictor and infiltrates the field with adrenaline before incision (19-21). Most surgeons use concentrations of more than 1:200000 for this purpose. This infiltration of adrenaline poses a challenge to the anaesthetist in performing induced hypotension along with the problem of managing intubation responses. The patient's anxiety compounds the problem.

In order to manage all these problems, adequate and appropriate premedication plays an important role in this regard (22-25). This study has compared the efficacy of oral clonidine and oral metoprolol to achieve these desired conditions. As per this study the three groups did not demonstrate any statistical significance in demographic distribution. The resting heart rate and blood pressure were significantly reduced in the treatment groups compared to the placebo group, with metoprolol faring better than clonidine. The pre-op sedation score did not vary between the three groups, but the clinical significance was demonstrated with two patients in the placebo group presenting with restlessness before surgery. Intubation responses were blunted among the treatment groups when compared with the placebo groups, once again metoprolol doing better. The results of the study of Mikawa et al (18), that premedication with oral clonidine attenuates intubation response concurs with the findings of the study. Patients in the treatment group mostly had a low requirement for isoflurane, with 5 -10% of the patients requiring isoflurane of 0.75% or more for more than 15 minutes. In the placebo group, 40% of the patients required more than 0.75% isoflurane for more than 15 minutes, while 60% of the cases required 1% isoflurane for more than 15 minutes. In the clonidine group 10% of the patients had a moderate requirement of isoflurane in comparison with only 5% in the metoprolol group. The metoprolol group fared better than clonidine group in the intra-op requirements for isoflurane. There was no significant difference in the hemodynamic parameters intra-operatively among the three groups.

Hypertension was encountered in three patients in the placebo group, two patients in clonidine group and none in metoprolol group. The hypertension that occurred in the clonidine group was

possibly in response to adrenaline infiltration. Failure to standardize the concentration of adrenaline used for infiltration has been a limitation in this study to merit any further comment. One patient in each group experienced bradycardia which was promptly treated with intravenous atropine. The metoprolol group encountered the least number of intra - operative problems. Excellent to good operating field conditions were provided with all the three groups. No significant difference in the duration of surgery was produced between the treatment and placebo groups. Failure to standardize the operating surgeon limits further comment. There was a statistically significant difference with extubation responses between the placebo group and the clonidine group with no statistically significant difference between the metoprolol and the placebo group. None of the patients experienced post operative shivering in the clonidine group, whereas 30 – 35% patients suffered post-op shivering in the other two groups (26).

Patients in the clonidine group did not require post-op analgesic supplement for a mean duration of 6.4 hours after surgery in comparison with 0.2 and 0.4 hours in placebo and metoprolol groups respectively. Thus clonidine has offered better post-op analgesia in comparison with other groups. Only 10% of the patients in placebo group met the discharge criteria at 6.00 pm on the day of surgery, none meeting the criteria in the treatment groups. While 90 – 95% of the patients in the three groups met the discharge criteria at 6.00 am on the next day of surgery. Patients in clonidine group scored lower in PADSS when compared to the other two groups. The findings in this study seem to suggest that FESS procedure is not ideal for being performed as a daycare surgery. The fact that the patients in clonidine group landed up with poor PADSS score precludes the use of oral clonidine as premedicant when daycare anaesthesia is contemplated.

CONCLUSION

Clonidine and Metoprolol premedication provides superior and predictable perioperative hemodynamic control, reduces the requirement of hypotensive agents and produces acceptable recovery characteristics. The lesser incidence of complications recorded with Metoprolol gives it a more favorable profile when compared to Clonidine. Clonidine or Metoprolol premedication can form an important and desirable part of hypotensive anaesthesia for surgical procedures like FESS.

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Ethical approval: The study was approved by the Institutional Ethics Committee

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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