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EFFECT OF ORAL CLONIDINE AS PREMEDICATION FOR CONTROLLED HYPOTENSION IN FUNCTIONAL ENDOSCOPIC SINUS SURGERY- PROSPECTIVE DOUBLE - BLINDED CLINICAL TRIAL

Anaesthesiology

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ABSTRACT

Objective: The present study was performed to evaluate the effectiveness of intravenous Clonidine as a part of premedication in controlled hypotensive anaesthesia during functional endoscopic sinus surgery (FESS). **Material & Methods:** This is a prospective double - blinded clinical trial performed on 52 patients at Department of Anaesthesia, Meenakshi Medical College and Research Institute, Kanchipuram a fulfilling the inclusion criteria were randomly allocated into 2 equal groups, Group P and Group C, by a closed envelop technique. GROUP C (Clonidine group, n=26) received tab clonidine 100 mcg, 3 hrs before surgery and GROUP P (Placebo group n=26) received placebo. The outcomes were measured by estimation of mean arterial pressure (MAP), extra requirement of isoflurane and nitrogycerine (NTG) to achieve target MAP, blood loss during the surgery, duration of surgery and post-operative complications. **Results:** Both the groups were matched in terms of age, sex and weight parameters. There was statistically significant difference between MAP in group I and group II before induction, average intra-operative and during immediate post-operative period. The average amount of blood loss in group II was significantly less (230±66 ml) than group I (356±75 ml). Similarly, the duration was 76±16 minutes in group I surgery and 59±12 minutes in Clonidine group. Quality of surgical field as per Boezart score was significantly better in Clonidine group. The incidence of postoperative complications like bradycardia, hypotension and prolonged sedation were not significant in both the groups. **Conclusion:** Clonidine is cheap and safe drug to use for controlled hypotensive anaesthesia without any significant side effect in FESS.

KEYWORDS

Clonidine, anaesthesia, Hypotension, Sinus surgery

INTRODUCTION

Clonidine is a drug with increasing popularity as an adjuvant in anesthesia because of its positive influence on hemodynamic profile in addition to sedative and analgesic effects.[1,2] Clonidine is an alpha-2 agonist drug causing constriction in the peripheral vessels[3] which has been proven in animal models to reduce nasal mucosal blood flow.[4] Numerous studies have been conducted about clonidine, there are only a few data regarding its effects on bleeding and surgical comfort in advanced nasal polyposis surgery which is among the most common applications of the Paranasal Sinuses.

The recent past has seen an enormous surge in Endoscopic Surgery of the Paranasal Sinuses. The nasal mucosa is rich in blood supply, hence impaired visibility ensues owing to excessive bleeding, leading to a prolonged surgical time. To avoid such complications, Endoscopic Sinus Surgery can be performed either with local anesthesia,with vasoconstrictors (e.g.Epinephrine, Phenylephrine) or under general anesthesia supplemented with controlled hypotension. Several reports have been recorded regarding various techniques for diminishing intraoperative bleeding. Many ENT surgeons prefer general anesthesia to local anesthesia. They are comfortable with hypotensive anaesthesia since the duration of surgery is reduced considerably with an excellent view of the surgical field.

Hypotension maybe induced with drugs and volatile anaesthetics each having its own advantages and drawbacks. For example, severe hypotension may occur due to potent and rapid effects of intravenous antihypertensive drugs. Clonidine is a centrally acting α2 agonist useful as a premedicant. It also decreases the need for analgesic consumption and the usage of multiple hypotensive agents intra-operatively. Post operative nausea, vomiting and shivering is also reduced. It has antihypertensive property with decreasing sympathetic outflow oral clonidine given as a premedication before surgery will enhance the hypotensive effect of an inhalation agent.thse avoiding the polypharmacy.

Aim and Objectives of the study was to analyze the effect of Oral clonidine given as a premedicant in patients undergoing FESS to reduce bleeding by inducing controlled hypotension.

METHODOLOGY

This is a prospective double - blinded clinical trial performed on 52 patients at Department of Anaesthesia, Meenakshi Medical College and Research Institute, Kanchipuram a fulfilling the inclusion criteria were randomly allocated into 2 equal groups, Group P and Group C, by a closed envelop technique. GROUP C (Clonidine group, n=26) received tab clonidine 100 mcg, 3 hrs before surgery and GROUP P (Placebo group n=26) received placebo. We aimed to induce hypotension(MAP at 60-65 mmHg) for producing a bloodless surgical field in both groups intraoperatively. The surgeons were asked to estimate the quality of the operative field by using an pre-defined category scale with scores 0-5.

Participants with Age <60 yrs, Weighing 40-60 kgs, ASA1 and ASA 2 and Patient undergoing FESS procedure were included in the study. While participants with Asthmatics and patients already on clonidine, Hypertension/ Ischaemic Heart Disease (IHD)/ Rheumatic heart disease., Sinus bradycardia / heart blocks / conduction defects, H/O CerebroVascular Disease (CVA), Chronic renal disease with increased renal parameters, Preoperative Hypotension, Anticipated difficult airway and those who refused to participate in the study were excluded from the study.

Pre-Operative Assessment

All the patients were examined prior to surgery. Routine Clinical Examination, Biochemical Tests, Electrocardiogram and Chest X-Ray were done before the conduct of anaesthesia. Nil per oral guideline was explained.

Pre-Medication

Patients were randomly allocated into two groups by closed envelope method, Group C (Clonidine) and Group P (Placebo). Baseline Heart Rate and Blood Pressure both Systolic and Diastolic and MAP were recorded prior to pre-medication in both the study groups. Group C patients received oral Clonidine 100 µg with sips of water 3 hrs before surgery. This period ensures maximum plasma concentration after oral ingestion of the drug. Group P patients received placebo drug. All the patients received a nasal packing of 2% xylocaine mixed with 1:200000 dilution of adrenaline. Inj.Glycopyrolate 0.2 mg i.m was given as an anti-sialogogue 45 minutes prior to Induction.

Conduct of Anaesthesia

Pre-induction Heart Rate and Blood Pressure both Systolic, Diastolic and MAP were recorded. After Pre-oxygenation with 100% oxygen for 3 minutes, anaesthesia was induced with Inj.Propofol 2mg/kg,Inj. Fentanyl 2µg/kg and Inj.Atracurium 0.5mg/kg. Then laryngoscopy was performed and the trachea was intubated after 3 minutes of mask ventilation with 100% oxygen. In all patients ventilation was controlled manually. Anaesthesia was maintained with Nitrous oxide and oxygen (2:1 ratio) and Sevoflurane MAC of 1%.

Atracurium top-up doses were given as and when required. Thereafter the Heart Rate and Blood Pressure were measured at 1 and 5 minutes after induction of anaesthesia and every 5 minutes for the first 30 minutes and then every 15 minutes thereafter throughout the procedure.

To maintain hypotension for producing a bloodless surgical field, mean arterial pressure was proposed to be 60 - 65 mm Hg.? Sevoflurane was administered with a minimum MAC of 1% in both the Groups and later escalated to a maximum 1.5% if necessary.

When sevoflurane has failed to attain the desired target,Inj. Fentanyl bolus of 1µg/kg was given follwed by Inj.Nitroglycerin diluted to a concentration of 100µg/ml and given as a continuous infusion (0.2-1 µg/kg/min). Intraoperative bleeding was assessed by the surgeon according to the Bleeding severity score (Jabalmeli Et AL).

Bleeding severity score (Jabalmeli Et AL).

0 – No bleeding.
1 – Slight bleeding, no suction of blood required.
2 – Slight bleeding, occasional suctioning required, surgical field not threatened.
3 – Slight bleeding, frequent suctioning required, bleeding threatened surgical field a few seconds after suction was removed.
4 – Moderate bleeding, frequent suctioning required. Bleeding threatened surgical field directly after suctioning was removed.
5 – Severe bleeding, constant suction required. Bleeding appeared faster than could be removed by suction surgical field severely threatened and surgery was not possible.

Patients with a MAP below 60mmHg were treated with IV fluids and Inj. Ephedrine 6mg boluses. Inj.Atropine 0.6mg was given intravenously if symptomatic bradycardia occurs. Once procedure got over Inj.Neostigmine 0.05mg/kg body weight and Inj.Atropine 0.02mg/kg was given. Extubation was done after the patient was completely awake & responding to oral commands & takes adequate tidal volume as evidenced by the chest movements and reservoir bag.

Statistical Analysis

Sample size of 15 per group was taken for this study. Data was expressed as mean ± standard deviation (SD) or absolute values. Qualitative data were compared with the Chi square test and fisher's exact test. Quantitative variables were compared with the student 't' test. The above interpretations were confirmed by repeated measures of ANOVA. Statistical software SPSS version 23.0 was used for the analysis of the data and Microsoft word and excel have been used to generate graphs and tables. The p value of ≤0.05 was considered statistically significant.

RESULTS

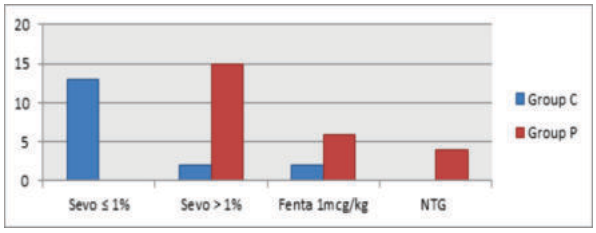
Table 1 – Demographics and coagulation profile.

Variable	Group C (n = 26)	Group P(n = 26)	Statistic p
Age (years)	43.2 ± 8.3	41.9 ± 6.7	p = .395
Sex (Male/Female)	15/11	13/13	p = .419
Weight (kg)	69.7 ± 11.5	72.4 ± 10.9	p = .267
ASA PS (1/2)	21/5	20/6	p = .634
Hemoglobin	12.5 ± 1.3	12.4 ± 1.2	p = .871
(mg/dl)	36,7 ± 4.8	36.9 ± 4.9	p = .904
Hematocrit (%)	248 ± 35	226 ± 29	p = .401
Platelet Count	12.5 ± 1.5	12.3 ± 1.3	p = .938
(100/mm3) PT (s)			
PTT (s)	32.7 ± 3.5	32.1 ± 2.7	p = .637
NOSE score	85.6 ± 9.2	86.3 ± 10.7	p = .294

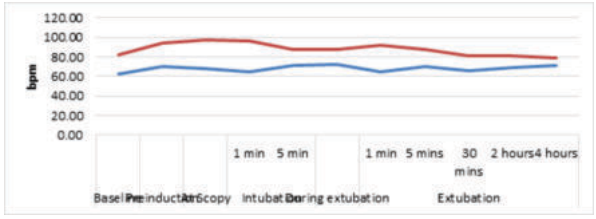
TIVA: total intravenous anesthesia, PT: prothrombin time, PTT: partial thromboplastin time, ASA: American Society of Anaesthesiologist Grades 1 & 2. NOSE: Nasal Obstruction Symptom Evaluation Scale. Mann–Whitney U test was used for comparison with the data measured changing. ($p < 0.05$ was considered significant). Fisher exact test was used for comparison with the data number changing. ($p < 0.05$ was considered significant).

There was no statistically significance difference in the demographic parameters between two groups.

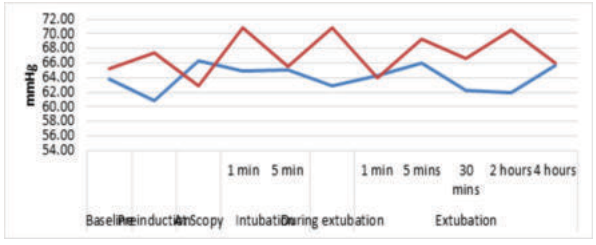
There is a statistically significant difference in intra-op drug requirements between two groups (p=0.003). In group P, 12 patients got intra-op drugs, and in group C 4 patients got intra-op drugs. There is a statistically significant difference in HR,SBP,DBP,MAP between group C and group P at preinduction, at scopy, 1 min,5 min after intubation and 1 min,5 mins, 30 mins after extubation.



Intraop Drug Recquirement



Heart Rate

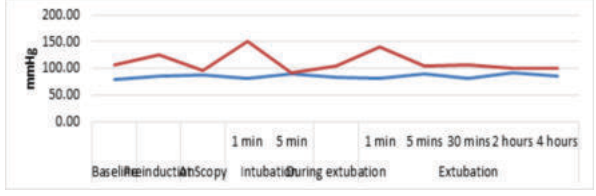


Map

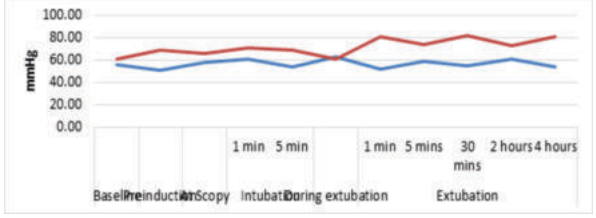
Table 2 – Outcomes of blood pressure during the surgery.

Variable	Group 1 (n = 26) (SAP + Clonidine)	Group 2 (n = 26) (SAP)	Statistic p
Systolic blood pressure (mmHg)	80.6 ± 11.3	112.4 ± 15.9	p = .018
Diastolic blood pressure (mmHg)	52.5 ± 8.3	68.2 ± 13.5	p = .043
Mean blood pressure (mmHg)	58.7 ± 9.4	79.5 ± 14.1	p = .024

Mann–Whitney U test was used for comparison with the data measured changing. ($p < 0.05$ was considered significant).



Systolic Blood Pressure



Diastolic Blood Pressure

DISCUSSION

Functional Endoscopic Sinus Surgery is the preferred surgical method to treat chronic sinusitis which are refractory t medical treatment. Bloodless field is often required in FESS for better visibility of surgical field and to avoid complications and failure. Many pre-operative and intra-operative strategies have been explored till now to minimize the risk of bleeding in patients undergoing FESS. The success of these

strategies is determined based on their impact on amount of blood loss during surgery, duration of surgery, quality of surgical field explained by surgeon and postoperative complications. Various methods are preoperative antibiotics and steroids, position of the patient (reverse Trendelenburg position), intra-operative use of local decongestant, local vasoconstrictor injections, warm saline irrigation, controlled hypotensive anaesthesia and use of tranexemic acid.[5] The present study is a placebocontrolled study performed to assess the hypotensive effect of intravenous Clonidine in FESS surgery. In present study, we successfully achieved the target MAP between 50-70 mmHg in all the patients. The average MAP during intra-operative period in group I and group B were 73±6 mmHg and 68±4 mmHg respectively. Thus, it was observed that average MAP was significantly lower in Clonidine group than placebo group. Further, to achieve the target MAP, there was high to moderate requirement of extra isoflurane or NTG in placebo group while very less requirement was there in Clonidine group. (Table 3)Similar results were observed in a study done by V. A. Praveen and R. Krishna Prabu in 2016. They studied the effect of Clonidine as a part of hypotensive anaesthesia for FESS and found that 60% patients of placebo group required high amount of extra isoflurane and NTG while in clonidine group, there was very less requirement of extra isoflurane and NTG to achieve target MAP.[6]

Similar results were obtained in other studies by Jabalameli et al, Hackmann et al, Howie et al. and Engelman E et al. [7, 8, 9, 10] The average amount of blood loss in Clonidine group (230±66 ml) was significantly less than placebo group (356±75 ml) in present study. The results were similar to another study done by Okuyama et al[13] in 2005. They studied the effects of clonidine and prostaglandin E1 on blood loss during FESS and concluded that Clonidine constricts peripheral blood vessels and reduces nasal mucous blood flow which accounts for the reduction of blood flow. [11] Jabalameli et al also had the similar results with their studies on effect of Clonidine on reducing bleeding in FESS.[7] The average duration of surgery was also very less in Clonidine group (59±12 min) as compared to placebo group (76±16 min). The results were similar to studies done by Nair S et al and Wawrzyniak et al. [11,12] In present study, the surgical field grading showed that Clonidine group had better grading than the placebo group. The results were highly correlated with results of past studies done by Jabalameli M et al and Anvari et al [7,14] 28% cases from clonidine group developed complications like hypotension (in 12% cases), bradycardia (in 8% cases) and prolonged sedation (in 8% cases) but the complications were not severe and relieved without any treatment. 20% cases from placebo group developed similar complications. The incidence of complications was similar in both the groups. Similar results were obtained by Meghna Jiwanmall et al[15] in their study to assess the effect of intravenous Clonidine in FESS. They also used 3µg/kg Clonidine in premedication and compared the results with placebo group. The incidence of complication between two groups was statistically insignificant. Out of 52 patients in Clonidine group, 3 patients had prolonged sedation, 10 patients had hypotension and 1 patient had bradycardia. The results were hoghly correlated with the results of present study. Similar results were obtained by Sahajananda and Rao et al and Samantaray et al.[16,17] They also used 3µg/kg Clonidine as a part of premedication and observed no significant incidence of complications like hypotension, bradycardia which required treatment and thus correlates better with the results of present study.[16,17]

CONCLUSION

A single intravenous dose of Clonidine (3µ/kg) as a part of premedication is effective to achieve controlled hypotensive anaesthesia in FESS. It maintains the mean arterial pressure within limits without additional requirement of isoflurane or NTG. It significantly reduces the amount of blood loss and provides a better field of visibility for surgery and thus shortens the duration of surgery. Clonidine is cheap and safe drug to use for controlled hypotensive anaesthesia without any significant side effect.

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