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CLONIDINE 100MCG VERSUS 200 MCG AS THE MAIN STAY FOR CIRCULATORY MANIPULATION IN FUNCTIONAL ENDOSCOPIC SINUS SURGERY: A RANDOMISED COMPARATIVE STUDY

Anaesthesiology

Dr. Vikrant. M. Goswami* — 3rd year resident, Department Of Anaesthesia, Critical Care And Pain Medicine MGH Jaipur. *Corresponding Author

Dr. Avnish Bhardwaj — Professor in anaesthesia, Department Of Anaesthesia, Critical Care And Pain Medicine MGH Jaipur.

Dr. Shubhina Gupta — 3rd year resident, Department Of Anaesthesia, Critical Care And Pain Medicine MGH Jaipur.

ABSTRACT

Background: Functional endoscopic sinus surgery (FESS) is most widely recognized surgery done for management of chronic sinusitis. The aim of this study was to compare the optimization of operating conditions produced by either 100 µg or 200 µg oral tablet clonidine as the mainstay for circulatory manipulation during Functional Endoscopic Sinus Surgery.

Method: A double-blind randomized comparative study was done in 60 cases divided into two groups. Group 1(n=30) patients were given 100 µg tablet clonidine; group 2(n=30), patients were given 200 µg of tablet clonidine orally 1 hour 30 minutes before surgery with 75ml water. Hemodynamic monitoring (HR, NIBP, SBP, DBP, MAP, SPO_2, $ETCO_2$). Quality of bloodless surgical field created intraoperatively was assessed by Fromme-Boezzart scale, Likert's scale at the end of procedure. Postoperatively, patients were assessed using Brussel's sedation score, and adverse effects like Bradycardia, Somnolence, Delayed recovery were recorded.

Result: No statistically significant difference seen in age, weight, gender, and ASA grading in both groups. Comparison of quality of surgical field created, assessment through Fromme-Boezzart grading system and Surgeon's satisfaction using Likert scale between both the groups was not statistically significant between the groups (P-value >0.05). We infer that both doses of clonidine tablets were equally effective in creating bloodless surgical field.

Conclusion: Non inferiority of 100microgram oral clonidine compared with 200 microgram oral clonidine for induction of hypotension during FESS surgery with less side effects and creating an intraoperative blood less surgical field.

KEYWORDS

Functional Endoscopic sinus surgery, tab. Clonidine, Bloodless surgical field, Hemodynamic monitoring.

INTRODUCTION:

Functional endoscopic sinus surgery (FESS) requires blood less field. Several drugs, including Clonidine had been used in different doses to achieve optimum operating condition in FESS, however no standard technique /regime has emerged as yet. Clonidine is an alpha2 blocker that reduces BP both centrally and peripherally thus improving surgical field visualization by reducing bleeding. Clonidine in the doses used clinically causes substantial adverse effect viz. Postural hypotension, Bradycardia, somnolence and prolongation of recovery from anaesthesia. Clonidine had been used by intravenous as well as oral route, however there is paucity of literature regarding oral use of relatively high doses (200µ and 300 µ). The aim of study was to compare the optimization of operating conditions produced by either 100 µg or 200 µg oral tablet clonidine as the mainstay in circulatory manipulation during Functional Endoscopic Sinus Surgery.

MATERIAL AND METHOD:

it is a prospective, randomized, double blind study undertaken to evaluate the effectiveness of 100microgram oral clonidine for induction of hypotension during FESS surgery and compare with 200 microgram oral clonidine. Institutional ethical committee and institutional research review board approval was obtained. Subsequently, the study was registered with the Clinical Trials Registry – India (www.ctri.nic.in) (reference /registration identity :CTRI /2021 /08/035811).

Following institutional ethics board approval and informed written consent, 60 American Society of Anaesthesiologists (ASA) grade I and II patients of 18-55 years of either sex scheduled for Functional Endoscopic Sinus Surgery under general anaesthesia were included in this study. Patients belonging to ASA III/IV/V or on cardiovascular medications viz. anti hypertensive, anti platelet or drugs affecting coagulation or those having any contraindication for induced hypotension were excluded from the study.

On the day of surgery, 60 consenting patients fulfilling inclusion criteria were randomly assigned for group allocation in the pre operative holding area. Randomisation was done by CHIT in BOX METHOD. In group 1(n=30) patients received 100 µg clonidine per orally one hour 30 minutes before surgery with 75ml water. While in group 2(n=30), patients received 200 µg of clonidine per orally one hour 30 minutes before surgery with 75mlwater. Randomization and drug administration was done by a person not connected with the study. On arrival in OT, standard monitoring including ECG, NIBP, SpO2 and EtCO2 was attached. Patients were preoxygenated for 3 minutes using 100% oxygen. Intravenous line was established in one of the forearm. Premedication was done with intravenous injection glycopyrrolate 0.04mg/kg, injection midazolam 0.1mg/kg, injection fentanyl 2mcg/kg, injection Lignocaine; Anaesthesia induction was done by injection propofol 2mg/kg. Injection succinylcoline 1.5mg/kg was used to facilitate tracheal intubation. Tracheal tube was connected to anaesthesia machine through breathing circuit. Proper tracheal tube placement was confirmed using auscultation of lung fields and appearance of regular squire wave pattern on capnogram. Further maintenance of anaesthesia was done with Vecuronium, isoflurane in nitrous oxide and oxygen on intermittent positive pressure ventilation. Catheterization of urinary bladder was done for urine output monitoring after induction of anaesthesia. At the end of the surgery, extubation was done after recovery of consciousness and reversal of residual neuromuscular blockade. Hemodynamic monitoring (HR, NIBP, SBP, DBP, MBP, SpO2, EtCO2) was done throughout the intraoperative procedure at 5 minute interval. Mean blood pressure was maintained between 60-65 mm Hg, ensuring urine output=> 1.0 ml/hour. Nitro-glycerine infusion 25 mg in 50 ml saline used for further reduction of blood pressure. Nor epinephrine 2 mg in 50 ml saline used to raise and maintain the MBP within the desired limits. Quality of surgical field was graded by surgeon using Fromme-Boezzart scale at the end of procedure. Intraoperative bleeding was assessed according to the following gradingsystem[1].

- Grade 0- No bleeding seen in the sinus cavity.
- Grade 1- Slight bleeding seen and no suctioning of blood required.
- Grade 2- Slight bleeding seen with occasional suction required in which surgical field is not threatened.
- Grade 3- Slight bleeding with frequent suction required in which bleeding from surgical site threatens surgical field a few seconds after suction is removed.
- Grade 4- Moderate bleeding occurring with frequent suctioning required in which bleeding from surgical site threatens surgical field as soon as suction is removed.
- Grade 5- Severe bleeding with constant suctioning required in which bleeding from surgical site appears faster that can be removed by suction, surgical field severely compromised and performing surgery is impossible.

Further, the intraoperative condition regarding the surgical field was assessed with the help of surgeon. After completion of operation surgeon was asked regarding his satisfaction with the bloodless surgical field created intraoperatively and to grade his experience based on Likert's scale as one of the following: [2]

- VERY GOOD
- GOOD
- MODERATE
- BAD
- VERY BAD

Post operatively, patients were monitored for any complaints and adverse effects. The degree of sedation of the patients was assessed using Brussel's sedation score according to the patient' awfulness status and the maneuvers used to awake the patient postoperatively at the time of extubation[1], as follows

- Unarousable patient.
- Responding to painful stimulation (i.e. trapezius muscle pinching) not responding to the auditory stimulation.
- Patient is responsive to the auditory stimulation (i.e. responding to the speech).
- Patient became awake as soon as intraoperative procedure is completed and very calm.
- Agitated.

STASTICALANALYSIS:

Data were collected and recorded in a specified Performa in excel sheet. Statistical analysis was done under guidance of statistician. Mean and standard deviation of the measurements were recorded. Parameters were analysed with chi-square test. Results were considered significant for at $p<0.05$.

RESULTS:

Comparison of quality of surgical field created for FESS, assessment through Fromme-Boezzart grading system and Surgeon's satisfaction using Likert scale between both the groups was not statistically significant between the groups (P-value >0.05). This shows that both doses of clonidine tablets were equally effective in creating bloodless surgical field. Intraoperative Bradycardia was recorded in six patients in group 2 (n=30, chi- square value of 6.72 and significant P value of 0.035). No instance of bradycardia was recorded in group 1 patients receiving 100 microgram clonidine, suggesting higher risk of Bradycardia with 200 mcg clonidine.

Table 1:Demographic variables.

Sr. no.	Variables	Group 1	Group 2	Chi-square	P-value
1	Age (years) (Mean ±SD)	34.27±13.40	30.20±11.46	1.264	0.211
2	Weight (Mean ±SD)	68.10±9.60	65.47±10.26	1.027	0.309
3	Haemoglobin (Mean ±SD)	13.41±1.62	13.55±1.69	0.312	0.756
4	Male: Female	11:19	10:12	0.073	0.787
5	ASA Grade ½	26/4	27/3	0.162	0.688

Table 2: Comparison of Hemodynamic Parameters for group 1(100 mcg tab. Clonidine) and Group 2(200 mcg tab. Clonidine).

Parameters	Group 1	Group 2	P Value	Group 1	Group 2	P Value
	(Baseline)	(Baseline)		5 min.	5 min.	
Heart rate	91.56 ±18.38	87.83 ±16.29	0.408	87.07 ±13.70	78.07 ±14.64	0.026
SBP	121.67 ±21.87	122.87 ±24.96	0.844	112.53 ±11.58	103.47 ±21.28	0.045
DBP	77.97 ±14.63	80.60 ±15.08	0.495	79.90 ±11.54	68.17 ±16.55	0.021
MAP	92.53 ±15.76	94.69 ±17.66	0.62	88.78 ±10.72	79.93 ±17.31	0.021

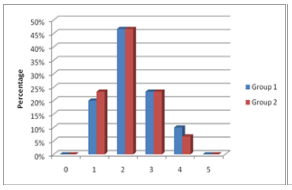
Table 3: Endoscopic Surgical field grading assessment using Fromme-Boezaart Scoring 1.

Endoscopic Surgical Field Grading System	Group 1 (n=30)		Group 2 (n=30)		Total	Chi-square value	p-value
	No. of cases	% age	No. of cases	% age			
0	0	0%	0	0%	0		
1	6	20%	7	23%	13	0.098	0.754
2	14	43%	14	47%	28	0.067	0.795
3	7	23%	7	23%	14	0.000	1.000
4	3	10%	2	7%	5	0.218	0.640
5	0	0%	0	0%	0		

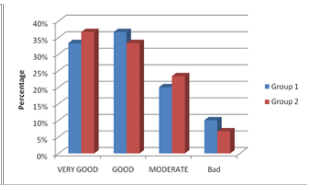
Table 4: Surgeons satisfaction score on Likert scale in the groups among the study population[2].

Surgeons Satisfaction on Likert Scale	Group 1		Group2		Total	Chi-squarevalue	p-value
	No. of cases	% age	No. of cases	% age			
VERY GOOD	10	33%	11	37%	21	0.073	0.787
GOOD	11	37%	10	33%	21	0.073	0.787
MODERATE	6	20%	7	23%	13	0.098	0.754
Bad	3	10%	2	7%	5	0.218	0.640
Very Bad	0	0%	0	0%	0		

Graph 1



Graph 2



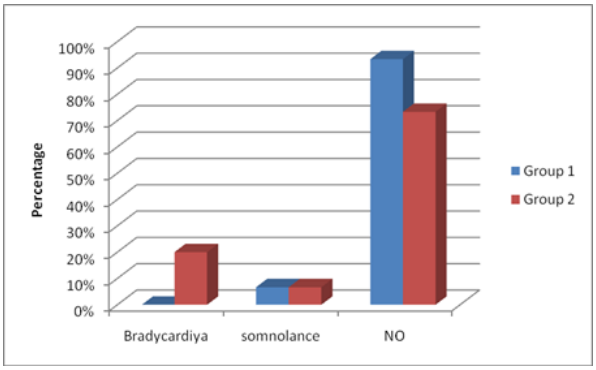
Graph1: Comparison between the groups based on Fromme-Boezaart reference: Endoscopic Surgical field grading system/ grade assessment among the study groups.

Graph 2: Surgeons satisfaction score on Likert scale in the groups among study population.

Table 5: Distribution of adverse events recorded during the study.

Side effects	Group 1		Group 2		Total	Chi-square value	p-value
	No. of cases	% age	No. of cases	% age			
Bradycardia	0	0%	6	20%	6	6.72	0.035
somnolence	2	7%	2	7%	4		
Total	30	100%	30	100%	60		

Graph 3



Graph3: Comparison of adverse events encountered among the study population.

DISCUSSION:

Hypotensive strategies are utilized broadly in techniques where significant blood loss is expected or to create a 'bloodless surgical field' during endoscopic surgery and microsurgery. Limiting blood loss has likely advantages as far as length of procedure, less complexities and transfusion prerequisites.

Inhalational Anesthetic procedure dependent on agents like isoflurane, total intravenous anesthetic method utilizing propofol, drugs with essential cardiovascular impact, for example, beta-blockers and vasodilators, for example, glyceryl trinitrate and sodium nitroprusside are being utilized in surgical procedures like FESS.

It has been proposed that decrease of MAP during general sedation (GA) can decrease intraoperative bleeding. But in regards to hemodynamic factors, MAP, yet in addition venous pressure and capillary blood flow represent the degree of bleeding in surgery. Of

these factors, just arterial pressure is effectively and promptly recorded[3].Circulatory manipulation with drugs has turned into an exceptionally supportive method in FESS where a bloodless field is required. FESS is the treatment modality that is liked for the inflammatory disease of the paranasal sinuses. Any operation which includes the nasal mucosa can cause severe sympathetic response causing tachycardia as well as hypertension, and being exceptionally vascular, the nasal and paranasal areas tend to bleed easily[1].

The goal of our study was to evaluate the effectiveness of 100microgram oral clonidine for induction of hypotension during FESS surgery and compare with 200 microgram oral clonidine. Hemodynamic monitoring (HR, NIBP, SBP, DBP, MBP) and SpO2, EtCO2 recording was done throughout the intraoperative procedure at 0, 5, 10, 15, 20, 30, 45, 60, 75, 90, post extubation interval.

Comparison of surgical field through Fromme-Boezzart grading system[1] between both the group was done throughout the procedure and there was no significant difference was found with p value >0.05.This suggest that both the doses (i.e. 100 mcg and 200 mcg) of tablet clonidine are equally affective in creating blood less surgical field intraoperatively. Puthenveeti[3] also conducted a study on 40 patients undergoing FESS and divided it into 2 groups .group A receiving 300mcg oral clonidine and group B with metoprolol 50mg orally 2 hrs before surgery. Comparison of category scale between the groups at pre- induction time point revealed no difference between groups with a *P* value of 0.95. While comparing the category scale at 15 min time interval there was a significant difference between groups ($P = 0.032$) with the majority of Group A patients manifesting a lower category scale. Similar observation was made at 30, 45 and 60 min. However, there was a no significant difference between the groups thereafter, i.e. at 75, 90, 105 and 120 minutes.

Comparison of surgical field was done with the help of surgeons satisfaction through Likert scale assessment[2] between both the group throughout the procedure and there was no significant difference was found with the p value>0.05. Ghorbani J et.al[2] conducted a double-blind, randomized, clinical trial on 52 patients with ASA class 1-2 with age group of 13-75 years suffering from rhinosinusitis with or without polyposis who underwent FESS. The first group received intravenous TXA 15mg/kg diluted in 100ml normal saline, administered during 10-min. infusion after induction. In second group,0.2 mg oral clonidine was given 1 to 1.5 hours before surgery, at the end of the surgery surgeon satisfaction based on likert's scale were recorded in the groups and their observation with surgical field with P value 0.757 which is insignificant which is similar to our observation. These investigators also used Likert scale[2] for assessment of surgeon's satisfaction, however they compared 200 microgram clonidine and intravenous Tranexamic acid in contrast to us.

We have studied in total 60 patients in total with 30 patients in each group with 100 mcg tablet clonidine and 200 mcg tablet clonidine respectively each. Not a single patient in group one had an episode of Bradycardia intraoperatively were as six patients out of 30 patients in group two had an episode of Bradycardia with chi-square value of 6.72 and significant P value of 0.035 which suggest higher risk of Bradycardia in 200 mcg clonidine group.

Intraoperative Bradycardia was recorded in six patients in group 2 (n=30, chi- square value of 6.72 and significant P value of0.035). No instance of Bradycardia was recorded in group 1 patients receiving 100 microgram clonidine, suggesting higher risk of Bradycardia with 200 mcg clonidine.

Findings in the present study will pave the way for further work on the issue. More studies on standard technique /regime for the doses of tablet Clonidine are recommended.

Limitations of our study were use of non invasive monitoring for blood pressure, all the patients belonged to ASA class I or II and did not have any significant cardiovascular disease and these were reasons we could not draw further conclusions.

CONCLUSION:

both the tablet clonidine 100 microgram as well as 200 microgram, administered orally preoperatively1 hour 30 minutes before anaesthesia are effective as mainstay for circulatory manipulation and controlled hypotension to optimize the operating conditions in Functional endoscopic sinus surgery under general anaesthesia but there is higher risk of Bradycardia with 200 microgram clonidine. We thus infer that tablet 100 microgram oral clonidine is not inferior to 200 microgram oral clonidine for optimizing the operating conditions during Functional Endoscopic Sinus Surgery under general anaesthesia. Non inferiority of 100microgram oral clonidine compared with 200 microgram oral clonidine for induction of hypotension during FESS surgery with less side effects and creating a intraoperative blood less surgical field.

Source of support:
Nil.

Conflict of Interest:
None.

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