



Efficacy of Oral Clonidine as Premedication on Intraoperative Bleeding and Consumption of Inhalational Agent in Patients Undergoing Functional Endoscopic Sinus Surgery

**Vivek Chakole¹, Shilpa Shankar^{1*}, Sneha Kota¹, Jayashree Sen¹,
Sheetal Madavi¹ and Devavrat Vaishnav¹**

¹Department of Anaesthesiology, Jawaharlal Nehru Medical College, AVBRH, Sawangi (Meghe),
Wardha, Maharashtra 442001, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i47A33041

Editor(s):

(1) Dr. Asmaa Fathi Moustafa Hamouda, Jazan University, Saudi Arabia.

Reviewers:

(1) Hagi Bogdan-Alexandru, Alexandru Ioan Cuza University, Romania.

(2) Marija Petrushevska, University of Ss Cyril and Methodius, North Macedonia.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/76001>

Received 12 August 2021

Accepted 23 October 2021

Published 28 October 2021

Short Research Article

ABSTRACT

Aim: To study the efficacy of oral clonidine on intraoperative bleeding and consumption of inhalational agent in patients undergoing FESS under general anesthesia.

Study Design: Prospective, comparative observational study.

Place and Duration of Study: Department of Anesthesiology, AVBRH, from June 2020 to May 2021.

Methodology: A total of 30 patients fulfilling inclusion criteria scheduled for FESS were randomly allocated into 2 groups of 15 each; GROUP C (Clonidine group, n=15) who received tab clonidine 5 mcg/kg, 90 minutes before surgery and GROUP M (Multivitamin group, n=15) who received multivitamin tablet. Mean \pm standard deviation (SD) or absolute values were used to indicate data; comparison of qualitative data were done using Chi-square test and Fisher's exact test and quantitative variables using the student 't' Test. P value < 0.05 was taken as statistically significant.

Results: Bleeding was considerably less in the group C [1.65 ± 0.4] as compared to group M [2.20 ± 0.6] and is statistically significant [P value = 0.006]. The mean MAC value (%) of sevoflurane consumption is lesser in the group C [1.25 ± 0.25] than the group M [1.30 ± 0.20] but not statistically significant (P value = 0.55). The mean dose (microgram) of fentanyl requirement was more in group M [120 ± 20] than the group C [100 ± 25] and this was statistically significant (P value = 0.02).

Conclusion: Oral Clonidine can be used as an excellent premedication and provides cost effective method to attain controlled hypotension as there is lesser requirement of costly inhalational agent and other analgesic drugs. Also, it maintains better hemodynamic stability with fewer side effects.

Keywords: Oral Clonidine; premedication; intraoperative bleeding; inhalational agent; functional endoscopic sinus surgery.

1. INTRODUCTION

Functional endoscopic sinus surgery (FESS) is a very popular minimally invasive procedure. It helps in re-establishing the paranasal sinus aeration and drainage without hampering the normal anatomy and muco-ciliary clearance mechanism [1]. The operative field in FESS is very small and the nasal mucosa is highly vascular. Excessive bleeding can hinder the visualization of the anatomical structures in the surgical field. Tissue damage can lead to the development of post-operative adhesions and surgical complications like dura puncture, CSF leak, orbital and optic nerve trauma, extensive hemorrhage and procedure failure are more likely to ensue due to poor visibility of the surgical field [2]. This is a major limitation of this surgery and can affect the surgical outcome.

Maintaining a clear surgical field during functional endoscopic sinus surgery (FESS) is important. FESS can be carried out either by using local anesthesia with topical or injectable vasoconstrictors like phenylephrine, epinephrine and cocaine or under general anesthesia with controlled hypotension. Local anesthetic agents can lead to tachycardia, hypertension, arrhythmias and cardiac arrest if systemically absorbed and therefore should be used with caution in patients of coronary heart disease, congestive heart failure, arrhythmias and uncontrolled hypertension [3]. General anesthesia with controlled hypotension is preferred by the surgeons to meet the more challenging surgical need.

Controlled hypotension means intended lowering of the systemic blood pressure to less than 20% of the baseline blood pressure in order to decrease the capillary hydrostatic pressure and capillary ooze thereby reducing the bleeding. Cerebrovascular insufficiency, coronary artery disease and decompensated heart failure are the

absolute contraindications and organ dysfunction (renal, hepatic, pulmonary), severe anemia and hypovolemia are the relative contraindications to controlled hypotension [4,5]. The ideal agent used for controlled hypotension should have short duration of action without its effect being extended into the post-operative period. Choice of agents include glyceryl trinitrate, β -blockers, α -agonists such as clonidine and remifentanyl [6,7].

In this study, we chose to use clonidine premedication as it is easily available and cheap compared to other agents. Sevoflurane was the inhalational anesthetic agent used in this study as it has advantages of less airway hypersensitivity, low pungency, low blood gas solubility which allows rapid smooth induction and quicker emergence as compared to other agents like isoflurane and halothane.

The aim is to study the efficacy of oral clonidine on intraoperative bleeding and consumption of inhalational agent in patients undergoing FESS under general anesthesia and to determine the incidence of clonidine side effects like bradycardia and hypotension. Fentanyl, a synthetic amine opioid drug and pure μ receptor agonist, which decreases blood pressure by its blocking effect on sympathetic nervous system is also used in this study if desirable hypotension is not achieved with the study drug clonidine and sevoflurane.

2. METHODOLOGY

- a) Study period: from June 2020 to May 2021.
- b) Study area: Department of anesthesiology, AVBRH.
- c) Research design: prospective, comparative observational study.
Inclusion criteria:
 - a) Patients willing to give informed written consent.
 - b) Patients aged between 18 to 50 years

- scheduled to undergo FESS under GA.
- c) Body weight 50 to 70 kg.
 - d) ASA class 1 and 2.
 - e) MPC grade 1 and 2
 - f) No comorbidities
- Exclusion criteria:
- a) Patients not willing for the study.
 - a) Patients below 18 years and above 50 years
 - b) Patients with body weight below 50 kg and above 70 kg.
 - c) ASA class III and above.
 - d) MPC grade III and IV.
 - e) Patients with hypertension/diabetes mellitus/ischemic heart disease/CVA/bronchial asthma/COPD/major respiratory problems/hepatic dysfunction/renal dysfunction and on medication for the above mentioned conditions.
 - f) Patients with coagulation disorders and on medications for the same.
 - g) Patients already on clonidine/beta blockers/opioids/TCAs/MAO inhibitors.
 - h) Patients with known allergy to drugs used in the study.

A total of 30 NPO patients fulfilling inclusion criteria scheduled for FESS were included in this study and were randomly put into 2 groups of 15 each, GROUP C (Clonidine group, n=15) who received tab clonidine 5 mcg/kg, 90 minutes before surgery and GROUP M (Multivitamin group, n=15) who received multivitamin tablet with similar color and shape to clonidine tablet.

In all the patients included in the study, detailed history and general examination was done and written consent was obtained after explaining the type of anesthesia, study being conducted and nature of surgery. Adequate fasting (6 hours for solids and 2 hours for clear fluids) was ensured. Vitals were recorded in the pre-operative room before giving oral clonidine/multivitamin tablet and again after shifting patient to OT, which was considered as baseline vitals.

Pre-medications were given [inj. Glycopyrrolate 0.004 mg/kg, inj. midazolam 0.05 mg/kg and inj. butorphanol 0.05 mg/kg]. Induction achieved using inj. propofol 2mg/kg till the loss of eye lash reflex and muscle relaxation with inj. vecuronium 0.1 mg/kg used to facilitate intubation after confirmation of ventilation. Patients were ventilated for 4 minutes before induction with 100% oxygen. Intubation was done using Macintosh blade with appropriate sized cuffed

endotracheal tube. Time limit for intubation was 30 seconds, done by senior anesthesiologist with experience for at least 3 years. After confirming bilateral air entry endotracheal tube was secured. Anesthesia was maintained using oxygen, nitrous oxide and sevoflurane (MAC value 1.8).

Mean arterial pressure (MAP) was maintained between 60 to 70 mm Hg. The direct control of MAP was attained with inspired concentration increments of sevoflurane up to MAC value 1.8 as needed. If failed to provide the desirable hypotension within 15 minutes, inj. fentanyl 2mcg/kg single bolus dose was given until MAP maintains between 60 to 70 mm Hg. Same surgeon performed all the surgeries to ensure consistency in the estimation of surgical field.

Intraoperative bleeding assessed according to a pre-defined category scale with scores 1-5.

Score 1: Slight bleeding. No suctioning of blood required.

Score 2: Slight bleeding. Occasional suctioning of blood required. Surgical field not threatened.

Score 3: Slight bleeding. Frequent suctioning required. Bleeding threatens surgical field a few seconds after suction is removed.

Score 4: Moderate bleeding. Frequent suctioning required. Bleeding threatens surgical field directly after suction is removed.

Score 5: Severe bleeding. Constant suctioning required. Bleeding appears faster than can be removed by suction. Surgical field severely threatened and surgery not possible.

At the end of surgery, bleeding volume (ml) was measured with scaled bottle. The number of gauze pieces (1 fully soaked gauze =10 ml blood loss) and mops (1 fully soaked mop =100 ml blood loss) used in the surgery, the amount of saline used for suctioning and field loss also considered while calculating the blood loss.

Intraoperatively consumption of sevoflurane (inhalational agent) was recorded from the completion of intubation till the closure of gases in both the groups. Continuous monitoring of vital parameters was done and recorded throughout the procedure. Total time of surgery also recorded and observed for side effects of bradycardia and hypotension. Intraoperative bradycardia is defined as heart rate less than 20% of baseline or absolute heart rate below 40 bpm in which iv atropine 0.6 mg is administered. Fall in MAP below 60 mm Hg will be treated with injection mephentermine 6 mg iv bolus.

Reversal attained with injection neostigmine 0.5 mg/kg iv after the procedure. End point of study was considered once the patient got extubated from GA and shifted to PACU.

The following parameters were observed and recorded:

- 1) intra-operative blood loss.
- 2) consumption of inhalational agent (sevoflurane) during the procedure.
- 3) side effects – bradycardia, hypotension.

Mean ± standard deviation (SD) or absolute values were used to indicate data; comparison of qualitative data were done using Chi-square test and Fisher’s exact test and quantitative variables using the student ‘t’ Test. P value < 0.05 was taken as statistically significant.

3. RESULTS AND DISCUSSION

Severity of bleeding is considerably less in the group C [1.65 ± 0.4] as compared to group M [2.20 ± 0.6] and is statistically significant [P value = 0.006]. Also, a significantly higher consumption of sevoflurane in group M with 13(86.6 %) of patients requiring MAC 1-1.5 % and 2 (13.3%) patients requiring ≤1% sevoflurane. The mean MAC value (%) of sevoflurane consumption is lesser in the group C [1.25 ±0.25] than the group M [1.30 ±0.20] but not statistically significant (P value = 0.55).

Better hemodynamic stability was observed with Group C. In group M, analgesic top-ups and sevoflurane increments were given for achieving hemodynamic stability. Also, blunted pressor response was noted in the clonidine group.

Fentanyl injection was used by 5 patients (33.3 %) of Group M whereas only 1 patient (6.7%)

required fentanyl injection in group C. Also, the mean dose (microgram) of fentanyl requirement was more in group M [120 ±20] than the group C [100 ± 25] and this was statistically significant (P value = 0.02).

1 patient in group C had bradycardia and hypotension which was managed using injection Atropine 0.6 mg IV and IV fluids and injection mephentermine 6 mg IV respectively.

WOODCOCK et al in their study conducted in 1987 observed mean concentration of isoflurane required to maintain hypotension in the clonidine group was 1.4% as compared to the requirement of 2.3% in the placebo group [8].

Better and clearer surgical field achieved by the clonidine group were reported in similar studies done by WELFRINGER et al in 1992 and SUNG.C.S. et al in 2000 [9,10].

MARCHAL et al in 2001 found that clonidine group reduced hyperdynamic response to tracheal intubation and decreased requirement of isoflurane, fentanyl and urapidil for maintaining the target blood pressure [11].

N.M. Elsharnouby et al in 2006 used magnesium sulphate to induce hypotension in FESS and observed similar results [12].

Nitu Puthenveetil et al in 2013 in a prospective randomised study concluded that oral premedication with 300 mcg of clonidine is better than oral metoprolol 50 mg in maintaining a clear surgical field [13].

Shivinder Singh et al in 2011 conducted a study using oral clonidine 150µg and observed improved perioperative hemodynamic stability, a reduction in the intra-operative anesthetic and post-operative analgesic requirements in the clonidine group [14].

Table 1. Comparison of the demographic and clinical characteristics between the two groups

	Clonidine group C	Multivitamin group M	P value
N	15	15	
Age (years)	45 ± 10	40 ± 10	0.181
Weight (kg)	65 ± 10	60 ± 10	0.181
Sex (M: F)	1.75	1.62	
Pre-operative MAP (mm Hg)	88 ± 10	90 ± 10	0.588
Pre-operative PR (beats/minute)	85 ± 5	88 ± 7	0.187
Mean duration of surgery (minutes)	55 ± 20	60 ± 20	0.499

The P value following comparison of the demographic profile is not significant statistically.

Table 2. Comparison of the bleeding severity, requirements and adverse effects during FESS between the two groups

	Clonidine group C	Multivitamin group M	P value
<i>Bleeding severity</i>			
Grade 0	0	0	
Grade 1	6 (40%)	3 (20%)	
Grade 2	7 (46.6%)	7 (46.6 %)	
Grade 3	2 (12%)	3 (20%)	
Grade 4	0	2 (13.3%)	
Grade 5	0	0	
Mean	1.65 ± 0.4	2.20 ± 0.6	0.006
Sevoflurane consumption (MAC value)			
≤ 1 %	4 (26.6%)	2 (13.3%)	
1 – 1.5 %	11 (73.3 %)	13 (86.6 %)	
Mean (%)	1.25 ±0.25	1.30 ±0.20	0.55
Fentanyl consumption			
Use	1 (6.7 %)	5 (33.3%)	
No use	14 (93.3%)	10 (66.7%)	
Mean (microgram)	100 ± 25	120 ±20	.02
Adverse effects			
Bradycardia	1 (6.7%)	0	
Hypotension	1 (6.7%)	0	

Clonidine, a centrally acting α -2 adrenoreceptor agonist and exerts central sympatholytic effect which accounts for its antihypertensive property. After its oral administration, the plasma level peaks within 30 to 60 minutes and has plasma half-life of 9 to 12 hours. The hypotension effects peaks at 3 to 5 hours and lasts for 8 to 12 hours. Controlled hypotension with better hemodynamic stability, fewer side effects, lesser requirement of other analgesic drugs and sevoflurane intraoperatively was noted in this study using clonidine. The drug suppresses central noradrenergic activity with attenuation of perioperative hemodynamic fluctuations and stress response. Our study findings were similar to the study conducted by Pouttu et al and Quintin et al [15,16].

4. CONCLUSION

This study shows that oral Clonidine can be used as an excellent premedication and provides cost effective method to attain considerable reduction in bleeding as there is lesser requirement of costly inhalational agent and other analgesic drugs for the maintenance of controlled hypotension during FESS. Also, it maintains better hemodynamic stability with fewer side effects throughout the surgery.

CONSENT

All authors declare that informed written consent was obtained from the patient for publication.

ETHICAL APPROVAL

The study was conducted after approval of the ethics and screening committee of our institution. All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Gajanan Panjabrao Dhakne, Vaishali Gunwantrao Kotambkar. Role of oral clonidine premedication for decreasing intra- operative bleeding with respect to scoring system at tertiary health care centre. MedPulse International Journal of Anesthesiology. 2018;7(2):96-98. Available:<http://medpulse.in/Anesthesiology/index.php>
2. Pei Yu Tan, Ruban Poopalalingam. Anesthetic concerns for Functional endoscopic sinus surgery. Proceedings of Singapore Healthcare 2014;23(3).
3. Anderhyber W, Walch C, Nemeth E,

- Semmelrock HJ, Berghold A, Ranftl G et al. Plasma adrenaline concentrations during FESS. *Laryngoscope*. 1999;109(2):204-207.
4. Mandal P. Isoflurane anesthesia for functional endoscopic sinus surgery. *Indian Journal of Anesthesia*. 2003;47(1):37-40.
 5. Boezaart AP, van der Merwe J, Coetzee A. Comparison of sodium nitroprusside and esmolol-induced controlled hypotension for functional endoscopic sinus surgery. *Canadian Journal of Anesthesia*. 1995;42(5 Pt 1):373-376.
 6. Nair S, Collins M, Hung P, Rees G, Close D, Wormald PJ. The effect of beta-blocker premedication on the surgical field during endoscopic sinus surgery. *Laryngoscope*. 2004; 114(6):1042-1046.
 7. Cardesin A, Pontes C, Rosell R, Escamilla Y, Marco J, Escobar MJ et al. Hypotensive anesthesia and bleeding during endoscopic sinus surgery: an observational study. *European Archives of Oto-Rhino-Laryngology*. 2014;71(6):1505-1511.
 8. Woodcock TE, Millard RK, Dixon J, Roberts C. Clonidine premedication for isoflurane-induced hypotension, sympathoadrenal responses and a computer-controlled assessment of the vapor requirement. *British Journal of Anesthesia*. 1988;60(4):388-394.
 9. Welfringer P, Manel J. Clonidine premedication and isoflurane anesthesia to reduce bleeding in otologic surgery, *Ann Fr Anesth Reanim*.1992;111(2):125-131.
 10. Sung CS, Lin SH, Chan KH, Chang WK, Chow LH, Lee TY. Effect of oral Clonidine premedication on perioperative hemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. *Acta Anaesthesiologica Scandinavia*. 2000;38(1):23-29.
 11. Marchal JM, Gomez-Lugue A, Martos-Crespo F, Sanchez De La Cuesta F, Martinez-Lopez MC, Delgado-Martinez AD. Clonidine decreases intraoperative bleeding in middle ear microsurgery. *Acta Anaesthesiologica Scandinavia*.2001;45(5): 627-633.
 12. Elsharnouby NM, Elsharnouby MM. Magnesium sulphate as a technique of hypotensive anesthesia. *British Journal of Anesthesia*. 2006; 96(6):727-31. DOI: 10.1093/BJA/ael085. E-pub 2006 May 2. PMID: 16670112.
 13. Puthenveetil N, Rajan S, Kumar L, Nair SG. A comparison of effects of oral premedication with clonidine and metoprolol on intraoperative hemodynamics and surgical conditions during functional endoscopic sinus surgery. *Anesthesia Essays and Researches*. 2013;7:371-375.
 14. Singh S, Arora K. Effect of oral clonidine premedication on perioperative hemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. *Indian Journal of Anesthesiology*. January 2011;55(1):26-30. DOI: 10.4103/0019-5049.76583. PMID: 21431049; PMCID: PMC3057241.
 15. Pouttu J, Rouminen M, Rosenberg PH. Effects of oral clonidine premedication on concentrations of Cortisol And monoamine neurotransmitters and their metabolites in cerebrospinal fluid and plasma. *Acta Anaesthesiologica Scandinavia*. 1989;33:137-141.
 16. Quintin L, Bonnet F, Macquin I, Szekely B, Becquemin JP, Ghignone M. Aortic surgery: effect of Clonidine on intraoperative catecholaminergic and circulatory stability. *Acta Anaesthesiologica Scandinavia*. 1990;34 (2):132-137.

© 2021 Chakole et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:
<https://www.sdiarticle4.com/review-history/76001>