



Comparative Evaluation of Oral Clonidine and Oral Atenolol as Premedication in Functional Endoscopic Sinus Surgery (FESS) Under General Anaesthesia

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Abstract

Aim and Objectives: To assess the effect of oral clonidine and oral atenolol as premedication on hemodynamic stability, blood loss, quality of the surgical field and side effects in patients undergoing FESS.

Material and Methods: The study included total 100 patients of (age 15 – 50 years) ASA grade I and II were randomly divided into two groups of 50 each. Patients received oral clonidine 5mcg/kg in group C and oral atenolol 1mg/kg in group A, 90 minutes prior to induction. Induction and maintenance of general anaesthesia was performed by the same standard protocol for both groups. Various study parameters i.e. hemodynamic effect (PR, SBP, DBP & MAP), amount of total blood loss, quality of surgical field, sedation score and side effects were recorded and statistically analyzed.

Results: The hemodynamic stability, less amount of blood loss and good quality surgical field was obtained in clonidine group compared to that of atenolol group & there were no serious side effects both in the groups.

Conclusion: We conclude that oral clonidine is better than atenolol in terms of hemodynamic stability, lesser blood loss & quality of surgical field without any side effects.

Keywords: Atenolol, Clonidine, hemodynamic stability, Functional endoscopic sinus surgery (FESS).

Introduction

Functional endoscopic sinus surgery (FESS) was introduced in the 1960s by Professors Messerklinger and Wigand^[1]. Although major blood loss during FESS is rare, bleeding during functional endoscopy sinus surgery remains a main consideration. Even a small amount of blood may disturb the endoscopic view, increasing the likelihood of complications. To avoid such complications, FESS can be performed under local anesthesia or general anaesthesia depending

upon the choice of surgeon but general anaesthesia is a safe and viable option for FESS^[2]. Several methods have been designed & intravenous agents have been used to reduce bleeding during surgery but none of these techniques have proved to be reliable and without any side effects. So we designed the present study to compare the effects of oral premedication with tablet clonidine and tablet atenolol by as both of them possess nearly similar pharmacokinetic and pharmacodynamic profile. Oral route is

considered as safe option, because hypotension and bradycardia are major adverse effects with intravenous administration of clonidine and beta blockers^[3,4]. So, we decided to compare clonidine and atenolol as oral premedication for functional endoscopic sinus surgery and study their merits and demerits.

Materials and Methods

After getting ethical committee approval a prospective, randomised, double blind study was conducted at tertiary care hospital on 100 patients of ASA grade I & II of either sex with the age and weight between 15-50 years and 45 to 70 kg respectively, undergoing functional endoscopic sinus surgery. After taking informed written consent, patients were randomly divided into two groups, of 50 patients each using a computer generated randomization schedule. In group C, patients received single dose oral clonidine 5mcg/kg and in group A patients received oral atenolol 1mg/kg, 90 minutes before induction of anaesthesia. Patients with age less than 15 years and more than 50 years, patients preferring local anaesthesia, patients with major systemic diseases like rheumatic heart disease, ischaemic heart disease, hypertension, heart blocks, diabetes mellitus, anaemia, sick sinus syndrome, sinus bradycardia, respiratory diseases like chronic obstructive pulmonary disease, bronchial asthma, renal and hepatic derangements, disease of central nervous system, allergic fungal sinusitis, patients on clonidine or beta blockers, agents influencing autonomic nervous system and blood coagulation were excluded from the study.

A detailed case history, clinical examination and all relevant investigations were done for all the patients. Baseline parameters like pulse rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were noted, 90 min before surgery and all patients received oral premedication clonidine 5mcg/kg or atenolol 1mg/kg on the day of surgery 90 minute before operation with sips of water. On operation table, standard monitoring devices ECG, NIBP, SPO₂

and ETCO₂ were applied to the patient. For all the patients standard protocol for induction of general anaesthesia was used, premedication with Inj. Glycopyrrolate 5µg/kg, Inj Pantoprazole 40mg, Inj. Ondansetron 0.08mg/kg, Inj. Midazolam 0.03mg/kg, Inj. Fentanyl 2µg/kg also given before induction of anaesthesia. General anaesthesia was induced with inj. Propofol 2mg/kg followed by injection succinylcholine 2mg/kg body weight and patients were intubated with appropriate sized cuffed portex endotracheal tube & throat packing done. Anaesthesia was maintained with oxygen (33%), nitrous oxide (66%), isoflurane 0.2%-0.8% and vecuronium 0.08 mg/kg as skeletal muscle relaxant. The tidal volume (VT) and the ventilator frequency was adjusted and intermittent positive pressure ventilation was continued by mechanical ventilation to maintain end-tidal carbon dioxide between 35-45 mm Hg. Any intraoperative hypertensive episodes were managed with rescue bolus doses of Propofol (10mg/bolus). At the end of the procedure oropharyngeal suctioning done, throat pack was removed & reversal of neuromuscular blockade was achieved using injection neostigmine 0.04 mg/ kg & injection glycopyrrolate 10 µg / kg. When patient started obeying commands, extubation was done and shifted to recovery room. Intraoperative hemodynamic variables i.e, PR, SBP, DBP, and MAP were recorded at the interval of 10 min till the end of surgery. After shifting to the postoperative recovery room, hemodynamic parameters (PR, SBP, DBP, and MAP) were again recorded at 15min interval for 2 hours and then 1 hourly till 8 hours. Intra-operative bleeding was measured by collecting blood in a suction bottles as well as weighing the gauge pieces (blood soaked by gauge pieces) before autoclaving and after the surgical procedure. Also side effects if any were observed such as bradycardia, hypotension, nausea, vomiting, shivering and sedation.

The surgeon, unaware of the groups, was asked to estimate the quality of the operative field using a pre-defined category scale with scores 0-5^[5].

0-No bleeding, 1-Slight bleeding; no suctioning 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 suction was removed, 5-Severe bleeding; constant suctioning required bleeding appeared faster than could be removed by suction surgical field severely threatened and surgery not possible. The detailed data was entered into the Microsoft excel sheet and subsequently analyzed by using appropriate statistical tests. Graphical display was done for better visual inspection.

Observation and Results

A total of 100 patients who underwent functional endoscopic sinus surgery were enrolled for the study and were randomly allocated to 2 groups of 50 patients each. In Group C, 50% patients were males and 50% patients were females, while in Group A, 54% patients were males and 46% patients were females. Table 1 show that mean age of patients in Group C and Group A was 36.60 ± 7.49 yrs and 37.10 ± 6.40 yrs respectively, mean weight in Group C was 59.40 ± 8.07 kg while mean weight in Group A was

60.14 ± 8.47 kg, the mean duration of surgery in group C was 77.94 ± 7.50 min and group A was 77.16 ± 7.06 min. Both the groups were comparable with respect to age, weight and duration of surgery,($P > 0.05$).

Table 1. Comparison of age(years), weight(kg) & duration of surgery and in group 1 and group 2

Variables	Group 1	Group 2	p-value
Age (years)	36.60 ± 7.49	37.10 ± 6.40	0.721
Weight (kg)	59.40 ± 8.07	60.14 ± 8.47	0.656
duration of surgery (min)	77.94 ± 7.50	77.16 ± 7.06	0.593

Figure 1 and figure 2 shows that comparison between PR and SBP, DBP, MAP respectively, we observed that oral premedication 90 minutes before induction with clonidine 5mcg/kg and atenolol 1mg/kg showed reduction in PR, SBP, DBP and MAP in both the groups. But on comparison the reduction in PR, SBP, DBP and MAP in clonidine group was more than that with atenolol group but without any significant bradycardia or hypotension. So, overall due to blunting of stress response & sympatho-adrenal stimulation hemodynamic stability was better in clonidine group compared to that of atenolol group.

Figure 1. Graphical comparison of pulse rate in group 1 and group 2

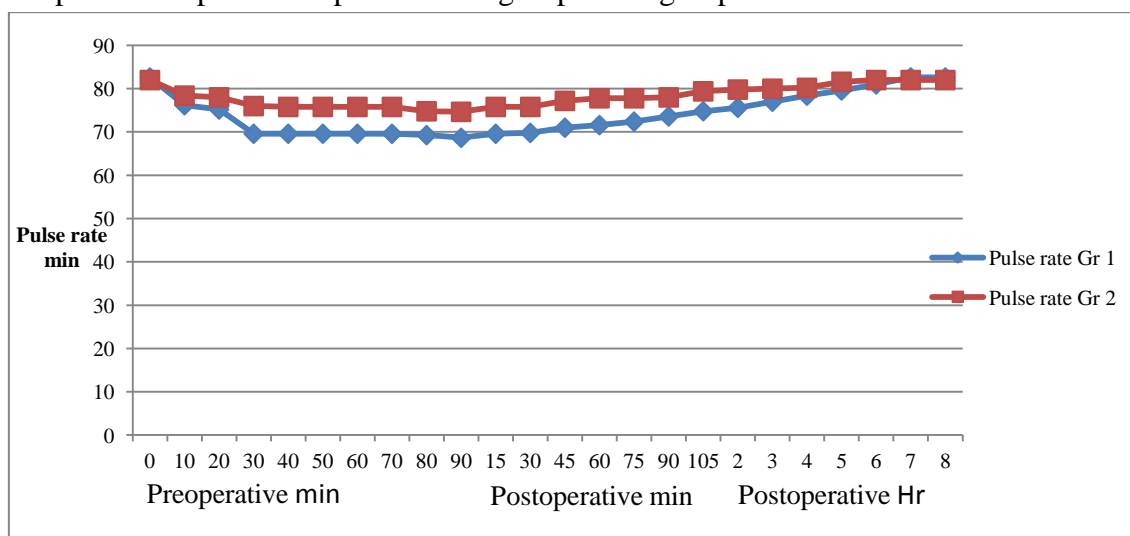


Figure 2. Graphical comparison of SBP, DBP, MAP in group 1 and group 2

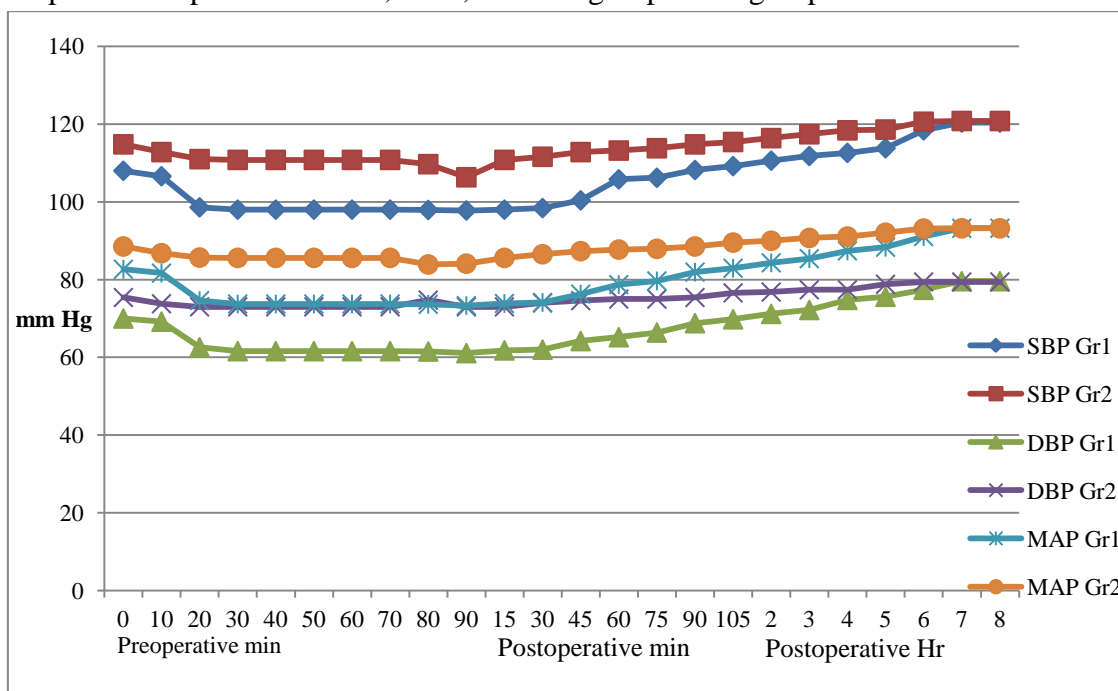


Table 2 shows that the comparison of intraoperative blood loss between group C and group A. The average blood loss in group C was 102.8 ± 6.07 ml while in group A was 130.2 ± 8.44 ml, ($P < 0.05$). The blood loss was less in clonidine group compared to atenolol group.

Table 2. Comparison of blood loss in both groups

Variable	Group 1	Group 2	P value
Blood loss (ml)	102.8 ± 6.07	130.2 ± 8.44	< 0.001

Table 3 shows the comparison of quality of surgical field in group C and group A, the median grade in group C was 2 and group A was 3. There was significant difference between median grades for quality of surgical field in both the groups, quality of surgical field was better in clonidine group compared to atenolol group.

Table 3. Comparison of quality of surgical field in group 1 and group 2

Quality of surgical field (grades)	1	2	3	4	Total
Group 1	15	35	0	0	50
Group 2	1	18	23	8	50

Groups	Median grade	p-value
Group 1	2	< 0.001
Group 2	3	

We did not observe the significant sedation which require any additional interventions in preoperative period and postoperative period in patients of both groups. There were no any serious side effects (like nausea, vomiting, hypotension, bradycardia, or shivering) observed after giving clonidine and atenolol as premedication in either groups.

Discussion

Although major blood loss during FESS is rare, bleeding during functional endoscopy sinus surgery remains a main consideration because the mucosa is highly rich in blood vessels [6]. Even a small amount of blood may disturb the endoscopic view, increasing the likelihood of complications as well as lengthening the operative procedure and possibly resulting in incomplete surgery [7]. The threat of serious complication from the poor visibility due to excessive bleeding in the surgical field and the possibility of neurological damage makes it important for anesthesiologists to produce optimal surgical conditions [8]. Several methods have been designed to reduce bleeding during surgery, none of these techniques have consistently provided a desirable bloodless field for the surgeon. So to provide optimal field

hypotensive agents given such as sodium nitroprusside, nitroglycerine, propofol, clonidine, esmolol, metoprolol & atenolol had been used individually to decrease blood loss in FESS^[9,10,11]. But none of the single agent proved to be best as each of them had their own advantages and disadvantages. So we decided to compare oral clonidine and oral atenolol as premedication, as both of them possess nearly similar pharmacokinetic and pharmacodynamic profile. We compare these two drugs as oral premedication, because hypotension and bradycardia are major adverse effects of intravenous administration of clonidine and beta blockers as compared with oral premedication, so oral premedication is considered as safe option^[3,4]. Clonidine is a centrally acting selective α_2 adrenergic agonist with α_2 : α_1 activity 200:1. Clonidine has gained popularity as an adjuvant drug in anesthesia for its sedative and analgesic effects^[12], as well as for its favorable effects on the hemodynamic profile of patients^[13]. It has been used to reduce intraoperative bleeding in major abdominal and orthopedic surgeries through its hypotensive effects^[14,15]. Clonidine as an α_2 agonist constricts peripheral blood vessels^[16], and has been suggested to reduce nasal mucous blood flow in animal models^[17]. Therefore, clonidine may reduce the bleeding associated with paranasal sinus endoscopy and other surgeries with similar vascular-rich environments. Atenolol is a β_1 selective (cardioselective) beta-adrenergic receptor blocking agent without membrane stabilizing or intrinsic sympathomimetic (partial agonist) activities. Atenolol was primarily used as an antihypertensive agent. All beta-blockers reduce the blood pressure and heart rate by reducing cardiac output through their negative inotropic effect and by reduction of sympathetic activity^[18]. Matot et al^[19], Singh and Arora^[20] and Gupta et al^[21] studied the hemodynamic stability after oral clonidine and oral atenolol premedication and reported decrease in pulse rate and blood pressure. In present study, there was a significant decrease

in PR, SBP, DBP and MAP in both the groups in spite of surgical stimulus. On comparison the reduction in PR, SBP, DBP, MAP was greater in clonidine group than atenolol group, which shows that hemodynamic stability was better in spite of intraoperative instrumentation in clonidine group. The amount of blood loss was less in both clonidine and atenolol groups but clonidine group had less amount of bleeding intraoperatively compared to atenolol group which proves that clonidine is better as premedication in FESS. Therefore, severity of bleeding was lesser in clonidine group compared to atenolol group. There was significant difference between median grade for quality of surgical field in group C and group A. Our findings were similar to the studies done by Jabalamelli^[16] in which patients undergoing endoscopic sinus surgery for chronic sinusitis were randomly allocated to receive either oral clonidine 0.2 mg or identical-looking placebo tablets 90 min before arrival at the operating room. Blood loss was less in clonidine group (214 ± 67 ml) compared to placebo group (276 ± 78 ml). The median (range) bleeding score in the clonidine group was significantly lower than that in the placebo group. Accordingly, the surgeon was more satisfied with the surgical field in the clonidine group than with that in the placebo group. Also Jabalamelli^[16] and Masood Mohseni et al^[11] reported that bleeding severity was significantly lesser in clonidine group. Similar to our study, they concluded that premedication with oral clonidine 0.2 mg can effectively reduce bleeding during FESS. Welfringer et al^[22] observed that comparative assessment of quality of surgical field was in favour of group C (no troublesome bleeding) as opposed to the control group (16% troublesome bleeding); there were also more bloodless surgical fields in the former group (73.7% vs. 48.7% in group T, p less than 0.05), this study therefore demonstrated that clonidine premedication before anaesthesia with isoflurane was helpful in decreasing bleeding during ear surgery. Also he found that in otologic surgeries clonidine premedication reduces the

pulse rate, blood pressure and provides better hemodynamic stability, good surgical field, their results were similar to our study. We did not observe the significant sedation in preoperative period and postoperative period in patients of both groups. This findings correlates with the study done by Gupta et al^[21] and he observed that postoperative sedation score were lower in clonidine and atenolol group compared to control group that might be due to reduced intraoperative anaesthetic drug requirement resulting in rapid and safe awakening. In present study there were no significant effect changes in respiratory rate, SpO₂ and EtCO₂ in either of the groups. There were no significant ECG abnormalities observed in either groups of patients perioperatively. During our evaluation it was observed that intraoperative anaesthetic agent requirement was less in clonidine group compared to atenolol group but it was not statistically analysed. Sedation may be associated side effect with the clonidine use, but none of the patient was sedated in intraoperative or postoperative period. As well as postoperative nausea and vomiting was less in clonidine group similar to study done by Shukla et al^[23].

Conclusion

So in the present study concluded that premedication with oral clonidine 5mcg/kg 90 min before the induction is better than oral atenolol 1mg/kg in terms of hemodynamic stability, lesser blood loss and quality of surgical field without any significant side effects. Though hypotension and bradycardia are known side effects of both clonidine and atenolol, but in our study there were no any obvious side effects observed in either group. Tablet clonidine is a cheaper drug so when used as preanaesthetic medication in FESS is cost-effective, also it has anxiolytic property, analgesic property, reduces the anaesthetic agent requirement without significant side effects.

Reference

1. Nasser A. Fageeh, Edilberto O. Pelausa, Adel Quarrington. Functional endoscopic sinus surgery: University of Ottawa experience and an overview. *Annals of Saudi Medicine*. 1996;16:(6): 711-714.
2. Paul D. Gittelman, Paul B Jacobs, Jane Scorina. Comparison of functional endoscopic sinus surgery under local and general anesthesia. *Ann Otol Rhinol Laryngol*. 1993;102:289-293.
3. Masood Mohseni, Amin Ebneshahidi, The effect of oral clonidine premedication on blood loss and the quality of the surgical field during endoscopic sinus surgery: a placebo-controlled clinical trial. *J Anesth*. 2011;25:614–617.
4. Engleman E, Lipszyc M, Gilbert E, Van der Linden P, Bellins B, et al. Effect of clonidine on anaesthetic drug requirement and hemodynamic response during aortic surgery. *Anesthesiology*. 1989;71:178-187.
5. Andre P. Boezaart. Comparison of sodium nitroprusside and esmolol- induced controlled hypotension for functional endoscopic Sinus surgery. *Can J Anesth*. 1995;42:(8):373-376.
6. Joseph MM: Anesthesia for ear, nose and throat surgery. In: Longnecker DE., Tinker JH, Morgan GE. *Principles and practice of Anesthesiology*, 2 nd ed. st Louis: Mosby, p 2210, 1998.
7. Wormald PJ. The surgical field in endoscopic sinus surgery. *Endoscopic sinus surgery—anatomy, three-dimensional reconstruction, and surgical technique*. New York: Thieme. 2005. p. 7–12.
8. Lindop MJ. Complications and morbidity of controlled hypotension. *Br J anaesth*. 1975;47:799-803.
9. M. Jabalameli MD, M. Hashemi MD, H. Soltani MD, J. Hashemi MD: Oral Clonidine Premedication Decreases Intraoperative Bleeding in patients undergoing

- Endoscopic Sinus Surgery. *J Research in Medical Sciences*. 2005;1:25-30.
10. Nair S, Collins M, Hung P, Rees G, Close D, Wormald PJ: The effect of B blocker premedication on surgical field during Endoscopic Sinus Surgery. *Laryngoscope*. 2004; 114(6): 1042-1046.
 11. Ankichetty SP, Ponniah M, Cherian VT, Thomas S, Kumar K, Jeslin L., Jaysheela K, Malhotra N. Comparison of total intravenous anaesthesia using propofol and inhalational anaesthesia using isoflurane for controlled hypotension in functional endoscopic sinus surgery. *Journal of anaesthesiology clinical pharmacology*, 2011;27(3): 328-332.
 12. Dahmani S, Brasher C, Stany I, Golmard J, Skhiri A, Bruneau B, Nivoche Y, Constant I, Murat I. Premedication with clonidine is superior to benzodiazepines. A meta analysis of published studies. *Acta Anaesthesiol Scand*. 2010;54:397–402.
 13. 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 Anaesthesiol Sin*. 2000;38:23–29.
 14. Toivonen J, Kaukinen S. Clonidine premedication: a useful adjunct in producing deliberate hypotension. *Acta Anaesthesiol Scand*. 1990;34:653–657.
 15. Lee J, Lovell AT, Parry MG, Glaisyer HR, Bromley LM. I.v. clonidine: does it work as a hypotensive agent with inhalation anaesthesia? *Br J Anaesth*. 1999;82:639–640.
 16. Maze M, Tranquilli W. Alpha-2 adrenoceptor agonist: defining the role in clinical anaesthesia. *Anesthesiology*. 1991;74:581–605.
 17. Folkow LP. Adrenergic vasomotor responses in nasal mucosa of hooded seals. *Am J Physiol*. 1992;263(6 Pt 2):R1291–7.
 18. Okopski JV. Recent advances in pharmaceutical chemistry review III, A new wave of beta blockers. *J Clin Pharm and Ther*. 1987; 12:369-388.
 19. Matot I, Sichel JY. The Effect of Clonidine Premedication on Hemodynamic Responses to Microlaryngoscopy and Rigid Bronchoscopy. *Anesth Analg*. 2000;91:828–833.
 20. Singh S, Arora K. Effect of oral clonidine premedication on perioperative haemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. *Ind J anaesth*. 2011; 55(1): 26-29.
 21. Gupta D, Srivastava S, Dubey RK, Prakash PS, Singh PK, Singh U. Comparative evaluation of atenolol and clonidine premedication on cardiovascular response to nasal speculum insertion during trans-sphenoid surgery for resection of pituitary adenoma: A prospective, randomised, double blind, controlled study. *Ind J Anaesth*. 2011;55(2):135-140.
 22. Welfringer P, Manel J, Garric J, Clonidine premedication and isoflurane anaesthesia to reduce bleeding in otologic surgery. *Ann Fr Anesth Reanim*. 1992;11(2):125-131.
 23. Shukla U, Malhotra K, and Prabhakar T. Comparative study of the effect of clonidine and tramadol in post-spinal anaesthesia shivering. *Ind J. Anaesth*. 2011; 55(3):242-246.