Int J Pharm Bio Sci 2013 Jan; 4(1): (B) 587 - 591

Research Article Pharmacology

International Journal of Pharma and Bio Sciences ISSN 0975-6299

COMPARATIVE EVALUATION OF ORAL CLONIDINE AND INTRAVENOUS CLONIDINE PREMEDICATION IN FUNCTIONAL ENDOSCOPIC SINUS SURGERY

BALARAJU TC[1],RAMDAS B[2], REEJA THOMAS[3],AMIT GARG[4], SREEKANTHA[5], YOGISH B[6], SHEETAL D[*7] AND AVINASH SS[8]

[1]- Assistant Professor,Department of Anaesthesiology, Navodaya Medical College, Raichur,Karnataka.
[2] Associate Professor,Department of Anaesthesiology, Navodaya Medical College, Raichur,Karnataka.
[3]Post graduate student,Department of Anaesthesiology, Navodaya Medical College,Raichur,Karnataka.
[4]Assistant Professor, Department of Anaesthesiology, Navodaya Medical College,Raichur,Karnataka.
[5]Associate Professor, Department of Biochemistry,Navodaya Medical College,Raichur,Karnataka.
[6]Post graduate student,Department of Pharmacology,KMC,Manipal University,Mangalore.
[7] Assistant Professor ,Department of ENT,AJIMS,Mangalore.
[8] Assistant Professor,Department of Biochemistry,FMMC, Mangalore.

ABSRTACT

Aim: This randomized single blind study was designed to assess the effect of oral and intravenous (IV) clonidine premedication on hemodynamic response to endotracheal intubation, per-operative hemodynamic stability and post-operative analgesic requirements. Materials and Methods: In this randomised single blind study, 60 ASA grade I and grade 2 patients were randomized into two groups. Group O received 3µg/kg oral clonidine 2 hours prior to induction and group I received 3µg/kg iv clonidine 15 minutes prior to induction. Anaesthesia was induced with thiopentone and maintained with oxygen and nitrous oxide with halothane. Heart rate and mean arterial pressure was noted prior to induction and 1 min, 5 min, 10 min, 30 min and every half hourly till the end of procedure. Post-operative sedation and the analgesic requirements were also assessed. Results: Perioperatively the mean heart rate was comparable between the two groups. The mean arterial pressure also was comparable between the two groups at all times except at 1 hr where the mean arterial pressure was higher in the oral group compared to the IV group. There was no difference between the two groups in VAS and sedation scores recorded at 30 min intervals till 2 h postoperatively. Time of requirement of first dose of analgesic was also similar between the groups. Conclusion: the administration of both oral clonidine and iv clonidine results in improved perioperative haemodynamic stability which are comparable in its effects.

Keywords: Clonidine,oral route,IV route& hemodynamic stability

SHEETAL D
Associate Professor,Department of Anaesthesiology, Navodaya Medical College, Raichur,Karnatak,India

**Corresponding author*

INTRODUCTION

Functional Endoscopic Sinus surgery(FESS) is used for treatment of patients with sinus pathology. Intra-operative bleeding reduces visibility in the operative field. This results in increased incidence of complications like orbital injury, optic nerve damage, penetration into the brain, nasolacrimal duct injury, hemorrhage requiring transfusions, intracranial infections etc. General anesthesia is the preferred technique as hypotensive anesthesia can be maintained and it provides better patient comfort and good operating conditions.[1]Clonidine an alpha 2 agonist has been used widely as a pre-anesthetic medication. Clonidine acts on the central alpha 2 adrenoreceptor to decrease the sympathetic outflow thereby causing bradycardia, hypotension and produces its sedative effect by its action on the locus coeruleus. Its potential advantages include anxiolysis, sedation, attenuation of sympathoadrenal response to laryngoscopy and intubation, cardiovascular stability [2,3]and post-operative analgesia.[4] Oral Clonidine has been used for many years as an anesthetic adjuvant [5] to maintain intraoperative hemodynamic stability. Parenteral form of clonidine has been introduced in the recent years which have offset the use of oral clonidine. Comparative studies of the two forms are lacking. We hypothesized that the oral and intravenous form of clonidine would provide adequate and comparable hemodynamic stability during the surgery. And this study was ascertained to compare the efficacy of oral and intravenous clonidine for attenuation of the stress response to laryngoscopy, intra operative hemodynamic stability and post-operative analgesia.

MATERIALS AND METHODS

This randomised prospective double blind studywas conducted on 60 adult patients of either sex, aged between 18 to 60 years, belonging to American Society of Anesthesiology physical status grade I& II undergoing FESS . Ethical committee approval was obtained and a written informed consent for participation in the study was also obtained from each patient. Patients were randomised to either Group O or Group I using a computer generated randomisation schedule. Patients with history of bronchial asthma, diabetes, hypertension, coronary artery disease, recent myocardial infarction, hepatic and renal disease, allergy to clonidine and patients on chronic clonidine, β blockers,antipsychotic drugs and chronic alcohol intake were excluded from the study. Group O patients were given 3µg/kg Clonidine orally 90 minutes before induction and to ensure blinding Group I patients were given vitamin C tablet 90 minutes before induction by the ward staff nurse .Group I patients were given 3µ/kg Clonidine which was drawn up in a 5 ml syringe intravenously 15 minutes before induction of anesthesia and to maintain blinding Group 0 patients were given 5 ml of normal saline. All the intravenous medications were prepared by the theatre anesthesia technician.All the patients received tab alprazolam 0.5 mg and tab ranitidine 150 mg the night before surgery. Perioperative monitoring consisted of pulse oximeter, non-invasive blood pressure, $EtCO_2$ and ECG. All patients were premedicated with intravenous ondansetron 0.08 mg/kg, glycopyrrolate 0.004mg/kg, midazolam 0.03 mg/kg and fentanyl 1µg/kg. General anesthesia was induced with thiopentone 5 mg/kg and vecuronium bromide 0.1 mg/kg to facilitate endotracheal intubation. Anesthesia was maintained with halothane in 60%N2O/ 40% O2. Controlled mechanical ventilation was done to maintain the EtCO2 between 30-40 mmHg. Hemodynamic variables i.e, heart rate(HR) and Mean arterial pressure(MAP) were recorded by a blinded anesthetist prior to induction, 1 min, 5 min, 10 min after endotracheal intubation and thereafter every half hourly till the end of surgery. Pain intensity was assessed using a 10-cm visual analog scale (VAS)[6]. Zero denoting no pain and 10 denoting intolerable pain. Sedation was assessed using Ramsay sedation score[7] from 1 to 6. The time when the first dose of analgesia was given at the request of the patient (VAS>4) after surgery that is the time

of analgesic requirement (TAR) was recorded. Rescue analgesia was given in the form of Inj. Diclofenac sodium 75 mg i.v. over 30 min 12 hourly.

STATISTICAL ANALYSIS

The results obtained from the study are presented in a tabulated manner. The results are expressed as mean (standard deviation [SD]). Within the group, comparison has been done with repeated measures of ANOVA followed by post hoc analysis Dunnett Multiple Comparison Test with basal. Comparisons between groups were performed with the Student's unpaired t test and for non-normally distributed data a non-parametric test, Wilcoxon rank sum test was used. p-value less than 0.05 was considered as significant and less than 0.01 as highly significant.

RESULTS

There were no differences between the clonidine and placebo groups regarding age, sex and weight [Table 1] The basal heart rate was not comparable. There was a rise in pulse rate post-intubation the difference being statistically significant only at 5 min after intubation. Perioperatively the mean heart rate was comparable between the two groups. Mean heart rate ranged from 71.90 ± 6.94 to 63.03 ± 3.81in group O, whereas it ranged between 73.13 ±6.49 to 62.06 ± 5.08 in group I.[Table 2] Perioperatively, the MAP was comparable between the two groups at all times except at 1 hr where the MAP was higher in the oral group compared to the IV group. MABP ranged from 89.48 ± 5.30 to 79.29 ± 4.64 in group O, whereas it ranged from 87.52 ± 3.62 to 77.06 ± 4.48 in group I. [Table 3] There was no statistically significant difference between the two groups in VAS and sedation scores recorded at 30 min intervals till 2 h postoperatively. TAR was also comparable between the two groups 168.45 ±15.40 min for Group I and 166.13 ±10.62 min for Group II.

Table 1
Demographic Data

	Oral Clonidine(n=30)	IV Clonidine(n=30)
Sex(M/F)	21(70%)/ 9(30%)	18(60%) / 12(40%)
Age(yr)	36.04 ± 10.3	33.78±7.83
Height(cm)	163.8 ± 3.42	162.8 ± 3.83
Weight (kg)	62.76 ±4.10	62.08 ± 3.25

Table 2
Heart rate given as mean (SD)

Heart rate	Group 0	Group I	95 % C.I. of difference	t-value	p-value
Basal	83.8 (12.67) **	87.4 (13.22) **	0.51 – 9.04	2.238	P>0.33
Bef Indc	67.23 (7.43) **	67.42 (7.52) **	-3.60 - 3.99	0.102	P>0.05
1 min	71.90 (6.94) **	73.13 (6.49) **	-2.19 - 4.64	0.718	P>0.05
5 min	69.61 (5.02) **	65.52 (6.43) **	1.16 – 7.03	2.79	P<0.007
10 min	65.13 (4.38) **	65.45 (6.57) **	-2.52 – 3.16	0.227	P>0.05
30 min	63.48 (4.12) **	62.06 (5.08) **	0.93 - 3.77	1.207	P>0.05
1 hr	63.03 (3.81) **	62.48 (4.73) **	1.63 – 2.73	0.503	P>0.05
1.30 hr	63.42 (3.24) **	62.16 (4.50) **	0.735 – 3.25	1.262	P>0.05
TAR	168.45 (15.40)	166.13 (10.62)	-9.043 – 4.398	0.691	P>0.05

P < 0.05, **P < 0.01, ***P < 0.001 compared with Basal

Table 3
Mean arterial pressure (MAP) given as mean (SD)

MAP	Group 0	Group I	95 % C.I. of difference	t-value	p-value
Basal	91.90 (3.96) **	89.58 (4.39) **	0.198 – 4.447	2.19	P<0.03
Bef Indc	86.71 (3.93) **	79.84 (4.49) **	4.725 – 9.017	6.41	P<0.0001
1 min	89.48 (5.30) **	84.61 (5.19) **	2.205 – 7.537	3.66	P<0.001
5 min	83.77 (5.78) **	79.52 (5.55) **	1.377 – 7.138	2.96	P<0.004
10 min	79.29 (4.64) **	78.81 (4.48) **	-1.835 – 2.803	0.42	P>0.05
30 min	79.55 (4.71) **	77.52 (4.94) **	-0.425 – 4.485	1.66	P>0.05
1 hr	79.52 (4.55) **	77.06 (4.48) **	0.156 – 4.747	2.14	P<0.037
1.30 hr	79.42 (4.13) **	78.32 (4.55) **	-1.113 – 3.307	0.99	P>0.05

DISCUSSION

This study was conducted on adult patients, to evaluate the effect of oral clonidine and intravenous clonidine premedication on haemodynamic response and post-operative pain. Orally administered Clonidine is completely absorbed and reaches peak plasma concentrations within 60-90 min and the maximum effect of intravenous clonidine occurs approximately 15 minutes after administration [6]. In our study, tablet clonidine was given 90 min before scheduled surgery and intravenous clonidine was administered 15 minutes before induction. A dose of 3µg/kg of clonidine has been used by other authors who have documented suppression of hemodynamic response to laryngoscopy and stable intra operative haemodynamics[7,8]. Dose of 3µg/kg was used in our study in both the groups. In our study the primary outcome measure was the hemodynamic stability of both the forms of clonidine. We found that both oral and intravenous Clonidine premedication effectively blunted the cardiovascular response to laryngoscopy and maintained cardiovascular stability peri-operatively. There was no significant difference between the two groups in terms of increase in heart rate and MAP compared to baseline measurements. Ray M et al compared the hemodynamic response to tracheal intubation, anaesthetic requirements and post-operative analgesia of intravenous clonidine with magnesium sulphate. Clonidine attenuated the stress response to intubation and was also found to have reduced the consumption of propofol and fentanyl[9] . In another study by Altan and colleagues where 3µg/kg clonidine was given iv followed by an infusion of 2µg/kg/hr clonidine effectively attenuated the hemodynamic response to intubation and reduced the consumption of anesthetic agents[10] . Gupta and colleagues studied the effect of oral clonidine and atenolol premedication on the cardiovascular response that occurs during nasal speculum insertion in trans-sphenoidal surgery. They found that oral clonidine premedication given 2 hours prior to surgery effectively prevented tachycardia and hypertension without causing significant post-operative sedation which is desirable in neurosurgical patients[11] , In our study, TAR was also comparable between the two groups. There was no significant difference between the two groups in terms of total cumulative analgesic requirement in 24 hr. The cumulative analgesic requirement (in 24 h) of diclofenac was ranging from 69 ± 40.82 mg in oral group vs 70 ± 50 mg in iv group for diclofenac, thus demonstrating a significant beneficial effect of clonidine. Singh et al found that oral clonidine pre-medication reduced the post-operative analgesic requirement compared to a placebo[12] . However, in a study comparing oral clonidine premedication with oral diazepam[13,14,15] no difference in the post-operative VAS scores for pain, number of analgesic requests was found. This is possibly due to the comparison with a different class of drug.

CONCLUSION

The administration of both oral clonidine and iv clonidine results in improved perioperative haemodynamic stability which are comparable in its effects. Oral clonidine is cost effective compared to its intravenous formulation. This emphasises the fact that oral clonidine is a simple and cost effective method for ensuring hemodynamic stability peri-operatively.

REFERENCES

1. Current Topics in Anesthesia for Head and Neck Surgery. Anesthesiology Clinics 2010;28:1-184
2. Ghignone M, Quintin L, Duke P C, Kehler C H . Effects of clonidine on narcotic requirements and hemodynamic response during induction of fentanyl anesthesia and endotracheal intubation. Anesthesiology 1986;64:36-42
3. Ghignone M, Calvillo O, Quintin L. Anesthesia and Hypertension: The effect of clonidine on perioperative hemodynamics and isoflurane requirements. Anesthesiology 1987;67:3-10
4. K Mikawa, K Nishina, N Maekawa and H Obara. Oral clonidine premedication reduces postoperative pain in children. Anesth Analg 1996;82:225-230
5. P. M. C. Wright, U. A. Carabine, S. McClune. Preanaesthetic medication with clonidine. Br J Anaesth 1990; 65(5): 628-632
6. Carlsson AM, Karolinska S. Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. Pain 1983;16:87-101
7. Schulte-Tamburen AM, Scheier J, Briegel J, Schwender D, Peter K. Comparison of five sedation scoring systems by means of auditory evoked potentials. Intensive Care Med. 1999 Apr;25(4):377-82
8. Dollery C T, Davis DS et al. Clinical pharmacology and pharmacokinetics of clonidine. Clinical Pharmacology and Therapeutics 1976;19:11
9. Marinangeli F, Cocco C et al. Hemodynamic effects of intravenous clonidine on propofol or thiopental induction. Act Anaesthesiol Scand 1998;44:150-6
10. Zalunardo MP, Serafino D et al. Pre-operative clonidine blunts hyperadrenergic and hyperdynamic responses to prolonged tourniquet pressure during general anaesthesia. Anesth Analg 2002;94:615-8
11. Ray M, Bhattacharjee DP, Hajra B, Pal R, Chatterjee N. Effect of clonidine and magnesium sulphate on anaesthetic consumption, haemodynamics and postoperative recovery. A comparative study. Indian J Anaesth 2010;54:137-41
12. Altan A, Turgut N, Yildiz F, Turkmen A, Ustiin H. Effects of magnesium sulphate and clonidine on propofol consumption, haemodynamics and post operative recovery. Br J Anaesth 2005;93:438-41
13. Gupta D, Srinivas S, Dubey RK, Prakash PS, 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 study. Indian J Anaesth 2011;55:135-40.
14. Singh S, Arora K. Effect of oral clonidine premedication on perioperative haemodynamic response and post-operative analgesic requirement for patients undergoing laparoscopic cholecystectomy. Indian J Anaesth 2011;55:26-30
15. Kumar A, Bose S, Bhattacharya A, Tandon OP, Kundra P. Oral clonidine premedication for elderly patients undergoing intraocular surgery. Acta Anaesthesiol Scand 2008;36:159-64