Comparison Of Oral Clonidine And Intravenous Esmolol For Attenuation Of Stress Response To Laryngoscopy And Endotracheal Intubation In Middle Ear Surgeries

Dr Akash Chavda*, Dr Kashmira Pander, Dr Hemal Prajapati*, Dr M P Golwala*****

*MD Anesthesia, Consultant,**Assistant Professor, ***Retd. Professor, Dept of Anesthesiology, SSG Hospital, Vadodara

Abstract: Background: Induction of anesthesia is recognized as a hazardous phase in management of the patient during operative procedure. Laryngoscopy and intubation being noxious stimuli produce cardiovascular stress response, which result in an increase in cardiac work load, may terminate in pre operative myocardial ischemia and acute heart failure in susceptible individuals. So, this study was conducted with an objective to compare the efficacy of oral Clonidine and intravenous Esmolol for attenuation of cardiovascular stress response following laryngoscopy and intubation. Method: This study was conducted among 50 patients of ASA I & II who were scheduled for middle ear surgery at SSG hospital, Vadodara, Gujarat. All patients were divided in 2 groups of 25 patients each, depending upon drug they received - Group C: Patients received Tab. Clonidine 4 fxg/kg 90 min before induction with sips of water and Group E: Patients received Inj. Esmolol 1.5 mg/kg bolus intravenous 5 min before induction. All patients were premedicated with Inj. Glycopyrrolate 10 g/kg intramuscular 45 min before induction. Anesthesia were induced with Thiopentone sodium 2.5% (4-7 mg/kg) followed by Succinylcholine 1.5 mg/kg intravenously. All parameters like pulse rate, systolic BP, diastolic BP, MAP and RPP were recorded at regular intervals. Complications (if any) were also observed during perioperative period. Result**:** Pulse rate, SBP, DBP, MAP and RPP were comparable at baseline, at time of induction, during laryngoscopy and intubation and throughout whole study period it was not statistically significant in both groups. However In Intergroup comparison, SBP was comparable at base line and after 5 min of laryngoscopy and intubation in both groups, but SBP was significantly higher after 1 and 3 min of laryngoscopy and intubation in Group E than Group C. Also, there was statistically significant increase in MAP in Group E following laryngoscopy and intubation at one min in Group E than Group C. RPP was significantly higher after 1 and 3 min of laryngoscopy and intubation in Group E than Group C. Postoperative complications like dryness of mouth, excessive sedation, PONV, hypotension, Bradycardia, bronchospasm were not observed in any case in both groups. Conclusion**:** Oral clonidine and intravenous esmolol both controls rise in pulse rate following laryngoscopy and endotracheal intubation. Intravenous esmolol is not effective in obtunding hypertensive response following laryngoscopy and intubation and associated with significant rise in SBP, MAP and RPP. So, oral clonidine (4 μg/kg) is more effective in attenuating stress response than intravenous esmolol(1.5mg/kg). [Pander Kashmira B Natl J Integr Res Med, 2019; 10(6):66-71]

Key Words: Oral Clonidine, Intravenous Esmolol, Stress Response

Author for correspondence: Dr Kashmira B Pander, 103, Wings Villa Appt., 42, Arunoday Society, Near Arunoday Circle, Alkapuri, Vadodara, E-mail: drkashmira1379@gmail.com Mobile : 9099045151

Introduction: Laryngoscopy and tracheal intubation are noxious stimuli that produce marked sympathetic response manifesting as hypertension and tachycardia, increase in serum concentration of catecholamine and various arrhythmias ranging from ventricular ectopics, ventricular tachycardia, heart block etc.[1,2]

Some patients unquestionably require careful hemodynamic control during induction of anaesthesia and intubation of the trachea. Even a transient hyperdynamic response may cause serious complications in patients with symptomatic aortic aneurysm, recent myocardial infarction, cerebral aneurysm, or intracranial hypertension. Knowledge and studies of cardiovascular stress response has led to development of techniques, used to modify cardiovascular stress response.[3,4]

Various agents have been used to attenuate cardiovascular stress response during laryngoscopy and endotracheal intubation including oral clonidine (α-agonist),topical lignocaine, intravenous vasodilator like nitro glycerine, sodium nitropruside, β - adrenergic blockers - like esmolol, narcotics like fentanyl, sufentanyl, alfentanyl, inhalation anesthetics like isoflurane, desflurnae.

Along with their usefulness, they have some drawbacks which limit their application. A narcotic produces respiratory depression and fentanyl causes truncal rigidity, vasodilators produces reflex tachycardia and rebound hypertension. Lignocaine does not reliably obtund heart rate response. Non selective β - blockers may produce bronchospasm.

An ideal attenuating drug should have some of following properties like easy route of administration, sedative, anti-sialogouge effect, analgesic antiemetic, facilitates induction, reduces doses of anesthetic agents, post operative delirium. Clonidine and Esmolol possesses some of these properties.

Various studies have shown that Clonidine and Esmolol are effective in attenuation of cardiovascular stress response as well as in reducing the requirement of anesthetic drug, so hasten the recovery and making anesthesia safer and cost effective but very few comparative studies.[5-9] So, this study was conducted with an objective to compare the efficacy of oral Clonidine and intravenous Esmolol for attenuation of cardiovascular stress response following laryngoscopy and intubation.

Materials And Methods: This randomized controlled study was carried out at S.S.G.Hospital, Vadodara from May 2005 - June 2007 among 50 patients scheduled for middle ear surgery i.e. exploratory mastoidectomy, tympanoplasty.

Inclusion criteria: All patients undergoing middle ear surgery and requiring endotracheal intubation with ASA physical status -1, II only, i.e. patients had no other major illness were included in study.

Exclusion criteria: Patients with bradycardia (Heart rate < 60 beats/min), hypotension (Systolic blood pressure < 100 mmhg diastolic blood pressure < 50mmhg), H/o congestive cardiac failure, chronic obstructive pulmonary disease, bronchial asthma, peripheral vascular disease, H/o myocardial infarction in last 3 months, Impaired hepatic and renal function, Pregnant women, Patient receiving beta-blocker, alpha-agonist, AVblock were excluded from the study.

All patients underwent a pre-study evaluation which consisted of a medical history, physical examination and routine investigations including complete hemogram, urine examination and appropriate blood chemistry like blood urea, serum creatinine, random blood sugar, Serum electrolytes, X- ray chest PA view and Electrocardiogram. All patients were advised to remain nil orally from 10 pm and Tab. Diazepam (0.2mg/kg) was given orally on previous night of operation. A written informed consent was obtained from the patients.

All patients were randomly divided in two groups.
Group – C: Tab. Clonidine - 4 *ig/kg* orally 90 minutes before induction.
Group – E: Inj. Esmolol HC1 -1.5 mg/kg 5 minutes before induction.

Premedication was given 45 minutes before induction in each group in the form of Inj. Glycopyrrolate *(10\ig/kg)* intramuscular. After 45 minutes of premedication (PM), all patients were shifted to operation theatre from pre operative room. In operation theatre patients were monitored for pulse rate, SBP, DBP, MAP, RPP, ECG and oxygen saturation, with multiparameter monitor. All patients were cannulated with 20 gauze intravenous cannula and Inj. Dextrose 5% was started at 5ml/kg/hr.

Induction: Pre oxygenation was done with 100% oxygen with Bain's circuit for 5 minutes. Induction was done with Inj.Thiopentone sodium 4-7mg/kg (2.5%) intravenously till loss of eyelid reflex followed by Inj. Succinylcholine 1.5mg/kg intravenously. Lungs were ventilated with bag and mask with oxygen for 90 seconds. Laryngoscopy was performed and trachea was intubated with appropriate size disposable cuffed portex endotracheal tube. Bain's circuit was connected and after confirming position of endotracheal tube, it was fixed properly. All patients were observed for pulse, SBP, DBP, MAP, RPP and $Sp0_2$ at 1, 3, 5, 7, 10 and 15 min during study period.

Maintenance: Anesthesia was maintained with 0_2 + N_20 (50:50) + Inj. Vecuronium bromide O.lmg/kg as muscle relaxant in both groups.
In Group E during intra operative period patients were given Inj. Tramadol lmg/kg intravenously as analgesic and isoflurane inhalation and considering sedative, analgesic properties of clonidine patients were given only inhalation of isoflurane intraoperatively in Group C. Patients were monitored for vital sign till the end of surgery.

Reversal: After completion of surgery, residual neuromuscular blockade was antagonized with Inj. Neostigmine and Inj. Glycopyrrolate intravenously. Thorough oropharangeal toilet was done, trachea was extubated when clinical criteria for extubation were fulfilled. Post-

operative monitoring of various parameters like pulse, SBP, DBP, MAP, RPP, oxygen saturation, color of lips, tongue was observed. All patients were shifted to ward. Patients were observed for any complications.The data collected was analyzed in Microsoft Excel with appropriate statistical test like student's t-test. For intergroup comparison unpaired t-test is used. P Value>0.05 was considered as non significant, P value<0.05 was considered as significant and P value<0.001 was considered as highly significant.

Results: Age in both the groups varied from 15 - 55 years. The mean age in both the groups were comparable. The sex in both the groups was comparable. ASA physical status of patients were comparable in both the groups. (Table 1)

Table1: Age, Gender And ASA Status Wise Distribution Of Patients In Both Groups (N=50)

Variables	Group C (n=25)	Group E (n=25)
Age		
15-25	8(32%)	7(28%)
26-35	7(28%)	12(48%)
36-45	9(36%)	5(20%)
46-55	1(4%)	1(4%)
Mean	31.730	30.5
Gender		
Male	14(56%)	16(64%)
Female	11(44%)	9(36%)
ASA status		
I	15 (60%)	14 (56%)
II	10 (40%)	11(44%)

Pulse rate was comparable at baseline, at time of induction, during laryngoscopy and intubation and throughout whole study period it was not statistically significant in both groups.

In Intergroup comparison, SBP was comparable at base line and after 5 min of laryngoscopy and intubation in both groups, but SBP was significantly higher after 1 and 3 min of laryngoscopy and intubation in Group E than Group C. Moreover, DBP was significantly lower following premedication with clonidine, at time of induction in Group C. After that DBP was comparable in both groups. (Table 2)

Table2: Comparison of Pulse rate, SBP, DBP at various intervals in both group of patients

Stages	Pulse rate (beats/min) Mean±SD			Systolic BP (mmHg) Mean±SD			Diastolic BP (mmHg) Mean±SD		
	Group C	Group E	p VALUE	Group C	Group E	p VALUE	Group C	Group E	p VALUE
BL	87.9 ±18.26	90.48 ±13.4	> 0.05(NS)	121.04 ± 23.5	118 + 17.16	> 0.05(NS)	79.2 ±11.4	79.9 ± 11.4	> 0.05 (NS)
PM	81.68 ±6.62	91.52 ±16.30	< 0.05 (S)	108.88 ± 10.46	112 + 21.4	> 0.05(NS)	74.96 ± 11.43	80.6 ± 10.2	< 0.05 (S)
I	82.32 ± 10.4	82.72 ±8.16	> 0.05(NS)	108.56 ±20.14	102 ± 14.56	> 0.05(NS)	69.04 ± 13.57	78 ± 11.4	> 0.05 (NS)
L&I	85.2 ± 14.60	89.28 ± 14	> 0.05(NS)	117.28 + 15.6	106 ±21.26	< 0.05 (S)	78.44 ± 15.51	80 ±11.4	> 0.05 (NS)
T_1	87.08 ± 12.8	91.32 ±13.90	> 0.05(NS)	112.4 + 22.50	135 ±30.80	< 0.05 (S)	77.44 ± 15.51	83 ± 16.7	> 0.05 (NS)
T_3	87.8 ±11.90	88.68 ± 14.68	> 0.05(NS)	102 ± 22.62	129 ±20.58	< 0.05 (S)	76.64 ± 9.77	77 ± 11.6	> 0.05 (NS)
T_5	84.16 ±9.60	86 ±10	> 0.05(NS)	107.12 ± 17.16	119 ±17.6	< 0.05 (S)	76.64 ± 9.77	75 ± 10.2	> 0.05 (NS)
T_7	84.6 ± 7.6	87.08 ± 10.8	> 0.05(NS)	110.16 ± 18.60	111 ±16.84	> 0.05(NS)	78.56 ± 9.96	75.8 ± 13.2	> 0.05 (NS)
T_{10}	87.2 ±11.2	86.08 ±10.52	> 0.05(NS)	109.04 ± 19.66	112 ±19.2	> 0.05(NS)	77.28 ± 12.48	74 ± 10.5	> 0.05 (NS)
T_{15}	88.48 ±11.2	86.36 ±11.32	> 0.05(NS)	109.6 ± 17	114 + 18.42	> 0.05(NS)	75.04 ± 10.2	78.3 ± 7.63	> 0.05 (NS)

In all tables • BL - base line, • PM - 45 min after premedication, • I - at beginning of intubation, • T_n- time after laryngoscopy and intubation where n = 1,3,5,...15.

At baseline, MAP were comparable in both groups, but there was statistically significant increase in MAP in Group E following laryngoscopy and intubation at one min in Group E than Group C, after that MAP remained comparable to each other through out whole study period in both groups. RPP was comparable at base line and after 5 min of laryngoscopy and intubation in both groups, but RPP was significantly higher after 1 and 3 min of laryngoscopy and intubation in Group E than Group C. (Table 3)

Table3: Comparison Of Mean Arterial Pressure And Rate Pressure Product At Various Intervals In Both Group Of Patients (N=50)

Stages	MAP Mean±SD			RPP Mean±SD		
	Group C	Group E	p VALUE	Group C	Group E	p VALUE
BL	93.63 ± 13.20	92.51 ± 9.35	> 0.05(NS)	10681.12±3574.67	10654±2308.54	> 0.05(NS)
PM	83.27 ± 8.87	91.07 ± 9.17	> 0.05(NS)	8897.12±1244.254	10227±2430.99	< 0.05 (S)
I	82.31 ± 14.02	86.35 ± 8.56	> 0.05(NS)	8961.2±2389.396	8471.12±1478.839	> 0.05(NS)
L&I	88.05 ± 12.73	88.77 ± 9.41	> 0.05(NS)	10016.8±2592.26	9514.56±2602.87	> 0.05(NS)
T_1	86.43 ± 13.03	100.21±15.86	< 0.05 (S)	9791.68±2585.73	12335.3±3539.77	< 0.05 (S)
T_3	85.09 ± 11.60	94.24 ± 10.62	> 0.05(NS)	8972.4±2516.74	11491.52±3096.42	< 0.05 (S)
T_5	86.80 ± 9.18	89.73 ± 9.84	> 0.05(NS)	8996.64±1303.51	10241.76±1824.037	< 0.05 (S)
T_7	89.09 ± 9.64	87.44 ± 11.04	> 0.05(NS)	9313.44±1646.106	9643.20±1716.746	> 0.05(NS)
T_{10}	87.71 ± 12.85	86.59 ± 9.82	> 0.05(NS)	9529.6±2494.96	9630.72±2252.931	> 0.05(NS)
T_{15}	86.56 ± 8.85	90.05 ± 7.39	> 0.05(NS)	9675.36±1478.45	9803.12±2003.48	> 0.05(NS)

In all tables • BL - base line, • PM - 45 min after premedication, • I - at beginning of intubation, • T_n- time after laryngoscopy and intubation where n = 1,3,5,...15.

We have not observed any complication in any patients in any group during perioperative period. All patients in both groups were observed until they attained pre operative vital parameter

Discussion: Laryngoscopy and intubation are powerful noxious stimuli. Stimulation of supraglottic region by tissue tension induced by laryngoscopy and that of subglottic region by endotracheal intubation leads to reflex sympathoadrenal response. The circulatory response of this is hypertension and tachycardia.[1-4]

Hypertension and tachycardia are transient changes but have deleterious effects in patient with cerebral and cardiovascular disease.2 Persistence of these changes may be harmful in surgeries were hypotensive anesthesia is required or in surgeries where there is maximum chances of sympathoadrenal stimulation like head and neck surgeries, ear surgeries.

Numerous pharmacological methods have been recommended to obtund pressure response to laryngoscopy and intubation. They may be classified as non specific means achieved by deepening the plane of anesthesia or by specific means involving various pharmacological preparations. Various drugs used are either partially effective or may have deleterious side effects. Clonidin and Esmolol have already proved their efficacy as an attenuating agent in various studies done previously.

Comparing both the groups in our study HR was comparable at baseline, at time of induction, during laryngoscopy and intubation and throughout whole study period. It was not statistically significant. Similar findings have been observed by Miller et al, Wang et al and Zsigmond et al.[9-11]

SBP was comparable at base line and after 5 min of laryngoscopy and intubation. But SBP was significantly higher after 1 and 3 min of laryngoscopy and intubation. This suggest esmolol does not obtund the hypertensive response to laryngoscopy and intubation. Our findings were similar to studies of Donald Oxorn et al, Suman Sharma et al, Fuji Y et al. [4,5,12]

Moreover, DBP was significantly lower following premedication with clonidine, at time of induction & during laryngoscopy and intubation. DBP was comparable to esmolol after that during

whole study period. Our finding were similar to Donald Oxorn et al.[5]

On comparing both group we found statistically significant increase in MAP in esmolol group following laryngoscopy and intubation. Our findings were similar to Philip et al Carabin UA et al.[6,7] However, RPP was comparable at base line and after 7 min of laryngoscopy and intubation, but it was significantly higher after 1, 3 and 5 min of laryngoscopy and intubation. This suggests esmolol does not obtund the hypertensive response to laryngoscopy and intubation. Our findings were similar to study of Philip L. Liu.[6]

We have monitored for ECG changes but did not observe any arrhythmia during whole study period. We have not observed any complication in any group. Contrary to this, Suman sharma et al observed ventricular bigeminy in patients receiving esmolol 200 mg intravenously.[4] Marchal et al and Pilli G et al observed observed Bradycardia in patients receiving clonidine but did not require any treatment.[13,14]

Conclusion: Oral clonidine (4 μg/kg) attenuates stress response whereas Inj. Esmolol (1.5mg/kg) prevents rise in heart rate only. Oral clonidine and intravenous esmolol both controls rise in pulse rate following laryngoscopy and endotracheal intubation. Intravenous esmolol is not effective in obtunding hypertensive response following laryngoscopy and intubation and associated with significant rise in SBP, MAP and RPP. No significant changes in DBP was observed following laryngoscopy and intubation in any group. No adverse effects like dryness of mouth, excessive sedation, bradycardia, hypotension, post operative nausea vomiting, bronchospasm, ventricular arrhythmia observed in any patients. So, oral clonidine (4 μg/kg) is more effective in attenuating stress response than intravenous esmolol(1.5mg/kg).

References:

1. King BD, Harris LC et al: Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anaesthesia. Anaesthesiology 1951;12:556-566.
2. Miller Forbes et al: Acute hypertension during induction of anesthesia and endotracheal intubation in normotensive man. British Journal of Anaesthesia 1970;42:618-24.
3. Takeshima K, Noda K et al: Cardiovascular response to rapid anesthesia induction and endotracheal intubation. Anaesthesia Analgesia 1964;43:201
4. Suman sharma et al: Esmolol blunts haemodynamic response to tracheal intubation in hypertensive patients. Can J Anesthesia 1996 : 43-8 :778-782.
5. Donald oxorn, J W D Knox, Jerry Hill et al: Bolus dose of esmolol for prevention of perioperative hypertension and tachycardia. Can J Anesthesia:1990 : 37 - 2: 206-9.
6. Liu PL, Gatt S, Gugino LP, Mallampati SR, Covino BG: Esmolol for control of increases in heart rate and blood pressure during tracheal intubation after thiopentone and succinylcholine. Can Anaesth Soc J. 1986 Sep;33(5):556-62.
7. U.A.Carabin, P.M.C. Wright: Preanaesthetic medication with Clonidine: A dose response study. British Journal of Anaesthesia 1990;65:628-632.
8. Gong Z, Luo A.: Effects of alfentanil and esmolol on hemodynamic and catecholamine response to tracheal intubation. Chin Med Sci J. 1999Sep;14(3):189-92.
9. Miller PR, Martineau RJ, Wynands JE, Hill J : Bolus administration of esmolol for controlling the haemodynamic response to tracheal intubation: Can J Anaesth. 1991 Oct;38(7):849-58.
10. Wang SC WuCC Lin MS, Chang CF: Use of esmolol to prevent hemodynamic changes during intubation in general anesthesia. Acta Anaesthesiol Sin. 1994 Sep;32(3):141-6.
11. Zsigmond EK, Barabas E, Korenaga GM: Esmolol attenuates tachycardia caused by tracheal intubation: a double-blind study. Int J Clin Pharmacol Ther Toxicol. 1988 May;26(5):225-31.
12. Fujii Y, Saitoh Y, Tanaka H, Toyooka H: Pretreatment with oral clonidine attenuates cardiovascular responses to tracheal extubation in children. Paediatr Anaesth. 2000;10(l):65-7
13. J. M. Marchal, A. Gomez-Luque, F. Martos-Crespo, F. Sanchez De La Cuesta, M. C. Martinez-Lopez and A. D. Delgado-Martinez. Clonidine decreases intraoperative bleeding in middle ear microsurgery Acta Anaesthesiologica Scandinavica 2001; 45: 627

14. Pilli G, Guzeldemir ME, Bayhan N Esmolol for hypotensive anesthesia in middle ear surgery. Acta Anaesthesiol Belg. 1996; 47(2):85-91

Conflict of interest: None

Funding: None

Cite this Article as: Akash C, Kashmira P, Hemal P, M P G.Comparison Of Oral Clonidine And Intravenous Esmolol For Attenuation Of Stress Response To Laryngoscopy And Endotracheal Intubation In Middle Ear Surgeries
Natl J Integr Res Med 2019; Vol.10(6): 66-71