Comparative Study Of The Effect Of Esmolol, Fentanyl And Their Combination For Attenuating Haemodynamic Responses Of Laryngoscopy And Intubation

***Dr.Manisha Bhagat, **Dr.Mukesh Kumar, ***Dr.Rajesh Khanna, ****Dr.Usha Suwalka**

* Resident 3rd year, **,*** Assisstant professor, **** Professor & HOD Department of Anaesthesia

Rajendra institute of medical sciencesRanchi-834009 India

Abstracts: **Background&Objectives:** Laryngeal, tracheal and bronchial receptors are stimulated by mechanical and chemical irritants during laryngoscopy, intubation and extubation. The reflex increases in sympathoadrenergic activity caused by these manipulations leads to an increase in catecholamine release, arterial blood pressure and heart rate. The aim of present study was to evaluate the efficacy of Fentanyl (2 mcg/kg), Esmolol (1mg/kg) and their combination in half the dose(fentanyl 1 mcg/kg +esmolol 0.5mg/kg) in attenuating the pressure response during laryngoscopy and tracheal intubation. **Methods:** This is a prospective double blind study comprising ninety patients between 21-60 yrs and ASA grade I and II scheduled for elective surgery under general anesthesia. Patients were randomly divided into group E (injection Esmolol 1mg/kg iv), group F (inj.Fentanyl 2mcg/kg iv) and group C (inj.Esmolol 0.5mg/kg and inj.Fentanyl 1mcg/kg). The study drug was given 2 minutes before induction of anaesthesia. All the vital parameters of patients were observed during intra operative and postoperative period .Values of heart rate and mean blood pressure were recorded at pre-induction, after giving study drug, after induction, immediately after intubation and at 1 min, 3 min, 5 min, 7 min and 10 min. after intubation. **Results:** Inter group comparison of groups E, F & C showed greater attenuation of heart rate in group F as compared to group C and group E. Inter group comparison of groups E, F & C in attenuating increase in MAP showed greater attenuation of MAP in group F as compared to group E (p=0.880) and group C (p=0.0005). **Conclusion:** Among the fentanyl (2 mcg/kg), esmolol (1 mg/kg) and their combination drug in half doses, injection fentanyl is best in attenuating haemodynamic responses to laryngoscopy and tracheal intubation. [Bhagat M NJIRM 2014; 5(3) :1-6]

Key Words: Haemodynamic responses, laryngoscopy, intubation, esmolol, fentanly

Author for correspondence: Dr.Manisha Bhagat, Road no.-1 hawai nagar, hatia, ranchi 834003;
M. 9386269477, Email: bhagatmanisha7@gmail.com

Introduction: Laryngoscopy and intubation is known to cause exaggerated haemodynamic responses. These responses manifest as tachycardia, hypertension and dysrrhythmias and it may have deleterious respiratory, neurological and cardiovascular effects[1]. Various pharmacological interventions (both intravenous and topical)[2,3,4,5,6,7,8] have been tried to obtund this haemodynamic responses to laryngoscopy and intubation with varying responses.

Both tachycardia and hypertension are transient responses and lasts for a little more than 10 minutes following laryngoscopy and intubation[9].

In 1977 lidocaine was used by Stoelting RK which was found to be inconsistently effective.[10] Then nitroglycerine was used by Fassouloki, A and Kaniaris P in 1979.[11] In 1989 Elbert J. P. et al compared the effects of fentanyl and esmolol during laryngoscopy and intubation[12]. Although higher doses of esmolol might blunt both heart rate and blood pressure responses, they may be associated with myocardial depression. Mikawaet al used calcium channel blocker in the year 1990[13]. Other important agents which have been used are lignocaine spray, clonidine, nifedipine, alfentanyl, diltiazem.[14,15,16,13.]

Fentanyl is a narcotic drug with no bronchospasm, cardiostability, rapid onset and short duration of action. Esmolol is ultrashort acting drug which causes bradycardia. There are studies which have shown that fentanyl and esmolol are effective in blunting pressor response to laryngoscopy and intubation. But fentanyl and esmolol in higher doses are associated with respiratory depression and myocardial depression respectively. Search for an ideal agent is still on.

The aim of present study was to evaluate the efficacy of Fentanyl (2 mcg/kg), Esmolol (1mg/kg) and their combination in half the dose (fentanyl 1 mcg/kg + esmolol 0.5mg/kg) in attenuating the

pressure response during laryngoscopy and tracheal intubation and to evaluate any side effects and adverse reaction.

Materials And Methods : This prospective, randomized double blind study was carried out after approval from Hospital Ethical Committee, and conducted in Department of Anaesthesiology at Rajendra Institute of Medical Sciences, Ranchi, Jharkhand. Ninety patients of either sex between age group of 21-60 years belonging to ASA grade I & II undergoing general anaesthesia for elective surgeries were selected.

All patients had undergone systemic examination in pre anaesthetic check up one day prior to the day of operation. Written and informed consent was obtained.

Besides a long and thorough clinical examination like history, general survey and systemic , routine investigations were done. Before induction of anaesthesia, all the patients were randomly assigned to either of the following groups. Randomization done by sealed envelope method. The study was done in a double blind fashion. The patients were numbered consecutively from 1 to 90. Only the leading author knew the drugs in the injectors and to which patient they were administered. The people who applied the drugs or who recorded the data did not know the contents of the injectors.

Group A : Received Esmolol 1 mg/kg body weight IV 2 minutes before induction.
Group B : Received Fentanyl 2 mcg/kg body weight IV 2 minutes before induction.
Group C: Received Esmolol 0.5 mg/kg body weight + fentanyl 1 mcg/kg body weight IV 2 minutes before induction.

Study drugs were prepared in a 10 ml syringe diluted with normal saline to be administered over 1 minute.

All patients were kept nil per orally overnight. On the day of surgery each patient was placed on a tilting table. Standard pre-operative procedure was followed and baseline vital parameters were recorded. All patients were premedicated with injection glycopyrrolate 0.2mg, injection ranitidine 50mg and injection metaclopramide 10mg IV, 30 minutes before induction.

After preoxygenation for 5 minutes, study drug was given according to the group allocated and then anaesthesia induced with 2.5%, inj. thiopentone sodium (3-5mg/kg IV) followed by 1-1.5 mg/kg succinylcholine 2 minutes after administration of study drug. Laryngoscopy and oral intubation was performed. Anaesthesiawas maintained with oxygen 40%, nitrous oxide 60%, isoflurane 0.5% and vecuronium with controlled ventilation. At the end of surgery residual neuromuscular blockade was antagonized with inj. Neostigmine (0.05 mg/kg) and in glycopyrrolate (0.02mg/kg) with PNS monitoring.

Values of heart rate and mean blood pressure were recorded at following stages: Pre induction, after giving study drug, after induction, immediately after intubation and at 1 min, 3 min, 5 min, 7 min and 10 min. after intubation.

The data were presented as mean ± standard deviation where appropriate. The values with normal distribution (BP, HR, weight and height) were analyzed using ANOVA and Dunnett test was used for post hoc comparison. Nonparametric data were analyzed using Chi square test. Intergroup comparison done by t test. $P \leq 0.05$ was regarded as statistically significant.

Observations And Results: In our study, the demographic data regarding age, sex, weight and ASA physical status were comparable.

Table 1: Patient's Demographics Profile

Variables	Group E (n=30)	Group F (n=30)	Group C (n=30)
Age	43.03±13.06	44.23±11.86	42.33±11.84
Weight	57.03 ± 9.68	54.86 ± 7.19	56.90±8.07
Height (cm)	168 ±15	165 ±12	166 ± 14
Sex(M/F)	15/15	16/14	17/13
ASA Grade(I/II)	22/8	15/15	13/17

Table 2: Types Of Surgeries

Type of surgery	Group E(n=30)	Group F(n=30)	Group C(n=30)
ENT/ORAL	8(26.67%)	5(16.67%)	10(33.33%)
GENERAL SURGERY	21(70%)	23(76.67%)	20(70%)
NEUROSURGERY	1(3.33%)	2(6.67%)	0(0%)

All three groups were comparable in baseline heart rate, the preinduction i.e. baseline heart rate was 81.20±7.32 in Group E, 82.96±4.24 in Group F and 80.16±7.38 in Group C.

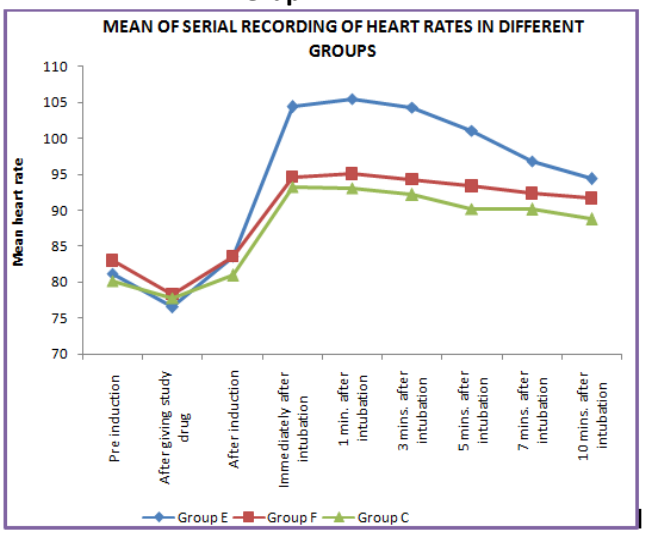
The group F showed lesser rise in heart rate (13.97%) compared to group C (16.3%) (p>0.05) and group E (28.57%) (p<0.0001) immediately after intubation. The maximum increase in heart rate was seen 1 minute after intubation in group E (29.83%) compared to group F (14.53%) (p<0.0001) and group C (16.09%) (p<0.0001).

The rise in heart rate persisted above basal value in all the three groups upto 10 minutes after intubation with group F showing least increase (10.4%) compared to Group E (16.16%) (p=0.157) and Group C (10.6%) (p=0.090). Inter group comparison of groups E, F & C showed greater attenuation of heart rate in group F as compared to group C and group E.

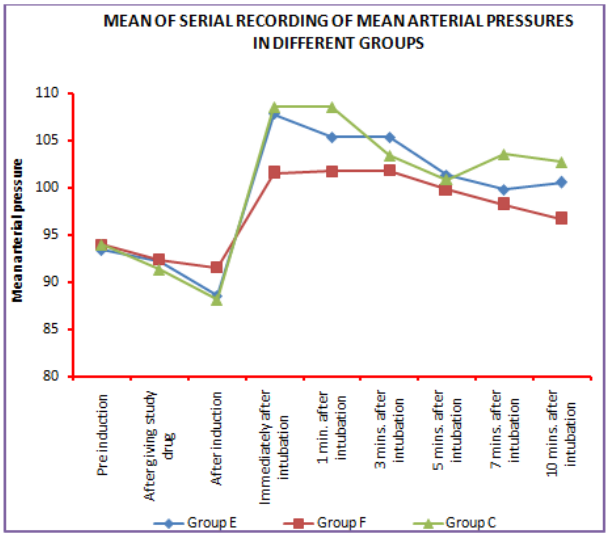
In our study the three groups had comparable baseline Mean arterial pressure i.e. pre-induction MAP in Group E was 93.40±4.39, in Group F was 93.93±4.84 and in Group C was 93.96±4.95.
All three groups showed slight decrease in MAP after administration of study drug and induction of anaesthesia. The group F showed minimum rise in MAP after intubation (8.02%) compared to group C (15.45%) (p=0.0005) and group E (12.7%) (p=0.880). The rise persisted up to 3 minutes after intubation and then began to regress. At 10 minutes post intubation, group F had 2.86% rise in MAP above basal value whereas in group E & C rise was 7.62% (p=0.019) and 9.3% (p=0.0002) above basal value.

Inter group comparison of groups E, F & C in attenuating increase in MAP showed greater attenuation of MAP in group F as compared to group E (p=0.880) and group C (p=0.0005).

Graph 1:



Graph 2:



Discussion: Tracheal intubation induces clinically relevant symapathoadrenal responses where plasma concentrations of catecholamines are increased. Hence direct laryngoscopy and tracheal intubation causes increase in blood pressure and heart rate. Reflex changes in cardiovascular system after laryngoscopy and intubation leads to an average increase in blood pressure by 40-50% and 26-66% increase in heart rate. King and Harris et al (1951)[1] first observed this circulatory response to laryngoscopy and tracheal intubation.
The present study confirms that there is a definite increase in heart rate and mean arterial pressure

following laryngoscopy and tracheal intubation in all three groups but this increase is attenuated following premedication with the study drug. We aimed to compare a beta blocker esmolol, an opioid like fentanyl and their combination drug in their half doses regarding their use during laryngoscopy, intubation to provide a smooth intubation and a safe perianesthetic period.

Basu and Pramanik (1988)[5] observed that these circulatory changes are maximum from 1st to 3rd minute following laryngoscopy and intubation and lasts for up to 10 minutes. The present study confirms this and shows that maximum increase in pulse rate and blood pressure was from 1st to 3rd minute following laryngoscopy and intubation and these changes lasted for up to 10 minutes.

Guaubatz CL et al[17]and K Sam Chung et al (1992)[18] evaluated esmolol and fentanyl and their combination in controlling increase in heart rate and blood pressure during endotracheal intubation. Esmolol appear to attenuate increase in heart rate but not substantially. It seems that a dose in excess of 1 mg/kg esmolol was necessary for effective control of heart rate. They found that group which received fentanyl provided effective protection against the adrenergic responses to laryngoscopy and intubation followed by the combination drug group which was consistent with our study. Esmolol alone was not able to attenuate heart rate increases following intubation. Fentanyl was effective in attenuating increase in mean arterial pressure followed by esmolol group and then by combination group in half doses .

Our study also confirms that esmolol in low doses is only partially effective in blunting the haemodynamic responses to laryngoscopy and tracheal intubation. Although higher doses of esmolol might blunt both heart rate and blood pressure responses, they may be associated with myocardial depression. The above study also shows that the addition of esmolol in low doses allows the use of lower doses of respiratory depressants such as fentanyl.

Miller DR et al (1991)[19] found that esmolol combined with low dose of narcotic (fentanyl 2-3 mcg/kg) results in effective control of both heart rate and blood pressure responses while avoiding important side effects which is similar to our study. Similar results were found by Woo YC (1999)[20] who evaluated the effects of a combination of esmolol and low dose fentanyl on haemodynamic responses following laryngoscopy and tracheal intubation in hypertensive patients. He used the combination of fentanyl 2 mcg/kg and esmolol 1 mg/kg and concluded that in treated hypertensive patients, the use of combination of fentanyl and esmolol is a useful method to attenuate hypertension and tachycardia after endotracheal intubation. In our study also the combination of fentanyl (1 mcg/kg) and esmolol (0.5 mg/kg) in low doses is useful, results were very close to the fentanyl group to attenuate pressor response to laryngoscopy and intubation which could be used in a different dosage combination.

There are some other studies on esmolol for controlling haemodynamic responses to laryngoscopy and tracheal intubation[21,22,23]. They all used higher doses of esmolol (100-200 mg) which averages 2-4 mg/kg and found that esmolol was effective in this dose in controlling increase in heart rate and mean arterial pressure following laryngoscopy and tracheal intubation. In the present study esmolol was used in low doses. Very little attenuation in heart rate and mean arterial pressure was found. Perhaps esmolol in higher dosage is effective in controlling haemodynamic responses to laryngoscopy and tracheal intubation, but at the same time there is a risk of severe bradycardia and hypotension with high doses.

Although in our study fentanyl group had better control of heart rate and blood pressure than the combination drug group of esmolol and fentanyl in their half doses. Combination drug group results were very close to fentanyl group F,as we used a fixed drug dosage, might be a different dose combination would had been more effective in attenuating the haemodynamic responses. Therefore we recommend further study of different dose combination of esmolol and fentanyl.

Conclusion: This study showed that Fentanyl (2 mcg/kg), Esmolol (1mg/kg) and their combination in half the dose (fentanyl 1 mcg/kg +esmolol

0.5mg/kg) administered 2 minutes intravenously before induction of anesthesia decreases the hemodynamic responses to laryngoscopy and tracheal intubation.

Among these Fentanyl (2 mcg/kg), given 2 minutes before induction is more effective than Combination drug group and Esmolol group in attenuating haemodynamic responses to laryngoscopy and tracheal intubation.

References:

1. King BD, Harris LC, Greifenstein FE, Elder JD, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. Anesthesiology 1951;12:556-66.
2. Stoelting RK. Circulatory changes during direct laryngosocpy and tracheal intubation - influence of duration of laryngoscopy with or without prior lidocaine. Anesthesiology 1977;47(4):381-4.
3. Hamill JF, Bedford RF, Weaver DC, Colohan AR. Lidocaine before endotracheal intubation: Intravenous or laryngotracheal? Anesthesiology 1981; 55: 578-81.
4. Kautto UM, Heinonen J. Attenuation of circulatory response to laryngoscopy and tracheal intubation: A comparison of two methods of topical anaesthesia. Acta AnaesthesiolScand1982;26:599-602.
5. Vucevic M, Purdy GM, Ellis FR. Esmolol hydrochloride for management of the cardiovascular stress responses to laryngoscopy and tracheal intubation. Br J Anaesth1992;68:529-30.
6. Yaku H, Mikawa K, Maekawa N, Obara H. Effects of verapamil on the cardiovascular responses to tracheal intubation. BrJAnaesth1992;68:85-9.
7. Wig J, Sharma M, Baichoo N, Agarwal A. Nicardipine and verapamil attenuate the pressor response to laryngoscopy and intubation. Can J Anaesth 1994; 41: 1185-8.
8. Casati A, Fanelli G, Albertin A, Deni F, Daneili G, Grifoni F, Torri G. Small doses of remifentanil or sufentanil for blunting cardiovascular changes induced by tracheal intubation: A double blind comparison. Eur J Anaesthesiol 2001; 18: 108-12.
9. 9.Basu SM, Pramanik S. Duration and degree of circulatory changes following laryngoscopy and intubation and study of a method of attenuation of these changes. Indian J Anaesthesia 1988 Feb;36(1):29-31.
10. 10.Steolting RK. Circulatory changes during laryngoscopy and tracheal intubation: Influence of duration of laryngoscopy with or without prior lidocaine. Anaesthesiology 1977;47:381-3.
11. 11.Fassoulaki A, Kaniaris P. Intranasal nitroglycerine attenuates the pressor response to laryngoscopy and intubation of trachea. Br J Anaesth 1979;58:116-9.
12. 12.Elbert JP, Pearsonj JD, Gelman S, et al. Circulatory responses to laryngoscopy and endotracheal intubation: The comparative effects of placebo, fentanyl and esmolol. Can J Anaesth 1989;36:301.
13. 13.Mikawa K, Ikegaki K, et al. the effect of diltiazem on cardiovascular response to intubation. Anaesthesia 1990;45:289-93.
14. 14.AbouMadi MN, Keszler H, Yacoub JM. Cardiovascular reactions to laryngoscopy and tracheal intubation following small and large I.V. doses of lidocaine.Can AnaesthSoc J 1977 Jan;24(1):12-90.
15. 15.Prys Roberts C, Green LT, Foex P. Studies of anaesthesia in relation to hypertension II Hemodynamic consequence of induction and endotracheal intubation. Br J Anaesth 1971;43:531-47.
16. 16.Scheinin B, Scheinin M, Vourinen J, Lindgren L. Alfentanil obtunds the cardiovascular and sympathoadrenal responses to suxamethonium facilitated laryngoscopy and intubation. Br J Anaesth 1989;62:385-92.
17. 17.Gaubatz CL, Wehner RJ. Evaluation of esmolol and fentanyl in controlling increase in heart rate and blood pressure during endotracheal intubation.AANA J 1991 Feb;59(1):91-6.
18. 18.Chung KS, Sinatra RS, Halevy JD, Paige D, Silverman DG. A comparison of fentanyl, esmolol and their combination for blunting the haemodynamic responses during rapid-sequence induction.Can J Anaesth 1992;39(8):774-9.
19. 19.Miller DR, O'Brien H. Effect of alfentanil on the hemodynamic and catecholamine response to tracheal intubation. Anesthesia and Analgesia 1998;76:165-169.
20. 20.Woo YC. The effects of a combination of fentanyl and esmolol on hemodynamic responses after endotracheal intubation in

hypertensive patients.Korean J Anaesthsiol 1999 Dec;37(6):995-1000.
21. John P. Ebert, James D. Pearson, Simon Gelman, ConstanceHarris, Edwin L. Bradley. Circulatory response to laryngoscopy: the comparative effects of placebo, fentanyl and esmolol. Can J Anaesth 1989;36(3):301-6.
22. 22.Yuan L, Chia YY, Jan KT, Chen CS, Wang CH, HaungLH,Kang L. The effect of single bolus dose of esmolol for controlling the tachycardia and hypertension during laryngoscopy and tracheal intubation.ActaAnaesthesiol Sin 1994 Sep;32(3):147-52.
23. 23.Sharma S, Ghani AA, Win N, Ahmed M. Comparison of two bolus doses of esmolol for attenuation of haemodynamic response to tracheal intubation. Med J Malaysia 1995 Dec;50(4):372-6.

Conflict of interest: None
Funding: None