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Comparison of IV fentanyl with iv clonidine for attenuation of the heamodynamic response to laryngoscopy and endotracheal intubation

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***Abstract*---**Aim: To compare the efficacy of IV fentanyl with IV clonidine with regards to attenuation of haemodynamic changes during laryngoscopy and endotracheal intubation. Methodology: This study was undertaken in Mamata Medical College, Khammam from August 2018 amongst 90 ASA grade I and II patients in the age group of 18 to 45 years. Patients were allocated into three groups with the sample size of 30 each after a detailed pre-anesthetic evaluation was done. Group A was control with normal saline, Group B had Inj. Fentanyl 2µg/Kg, and Group C had Inj Clonidine 2µg/kg anesthesia. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients. Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups. Results: Intergroup comparison of change in heart rate in first min between the study groups (Group B & Group C) showed no clinical or statistical significance (p=0.5). Statistical evaluation between the groups showed

that the increase in Mean arterial pressure (MAP) observed in Group A (control group) was statistically highly significant when compared to increase in MAP in Group C but not Group F. Conclusion**:** Clonidine was superior to fentanyl in the attenuation of the pressor response and that the ideal time for its administration would be about 5 min before laryngoscopy and an intubation.

***Keywords*---**anaesthesia, endotracheal intubation, clonidine, fentanyl.

Introduction

Endotracheal intubation has become an integral part of anaesthetic management and critical care of the patient. It has been practiced since its description by Rowbottom and Magill in 1921. Prof. King et al., documented myocardial ischemic changes due to reflex sympathoadrenal responses immediately following laryngoscopy and intubation with a mean increase in systolic pressure of 40mmHg even in normotensive individuals. Laryngoscopy and tracheal intubation during induction of anaesthesia, are nearly always associated with sympathetic hyperactivity that is increase in the blood pressure and an increase in the heart rate due to the reflex sympathetic discharge that is release of catecholamines[1] which is caused by an epipharyngeal and laryngopharyngeal stimulation. This increased sympatho-adrenal activity may result in hypertension, tachycardia and arrhythmias. It starts within 5seconds, reaches a peak in 1–2 mins, and returns to baseline within 5mins. The rise in HR and blood pressure is usually transient, variable, and unpredictable. Average increase in HR has been reported to be 23 beats and increase in mean arterial pressure by 25 mmHg and decrease in the left ventricular ejection fraction by approximately 20%.[2] Though these changes are well tolerated by healthy individuals, they may be fatal in patients with hypertension, coronary artery disease or intracranial hypertension. To slow this pressor response, various pharmacological agents have been tried, which include adrenergic blockers, vasodilators, calcium channel blockers and lignocaine.[3] Various studies have shown that fentanyl is effective in 2 blunting the pressor response to laryngoscopy and endotracheal intubation.[4-6] If a small dose of fentanyl which is administered 5 mins before an intubation can prevent this haemodynamic response, it would be well worth it. Recently, clonidine, an alpha - 2 adrenergic agonist, was used.[7] A premedication with clonidine was shown to blunt the stress response to the surgical stimuli and the narcotic and anaesthetic requirements were also reduced. In addition, clonidine increases the cardiac baroreceptor reflex sensitivity to an increase in the systolic blood pressure, and thus it stabilizes the blood pressure.[8,9] Clonidine reduces sympathetic tone and the release of norepinephrine from nerve terminals. During general anaesthesia, clonidine reportedly enhances intraoperative circulatory stability by reducing catecholamine levels.[10] Therefore, the use of clonidine during surgery has been proposed as a way of improving hemodynamics, decreasing both the ICP and anaesthetic requirements. But very few studies have been done to compare the effects of clonidine and fentanyl on the haemodynamic response during laryngoscopy and tracheal intubation. The purpose of this study is to compare fentanyl and clonidine for the attenuation of the pressor response to an

intubation and to find the most favourable time for the administration of the same.

Aim of the present study

To compare the efficacy of IV fentanyl with IV clonidine with regards to attenuation of haemodynamic changes during laryngoscopy and endotracheal intubation also to assess changes in parameters namely heart rate, systolic blood pressure and diastolic blood pressure and mean arterial blood pressure and determine any side effects such as bradycardia, hypotension, miosis, nausea, pruritus etc.

Methodology

This study was undertaken in Mamata Medical College, Khammam from August 2018 after obtaining institutional review and ethical board approval and with informed and written consent from the patients The study was conducted on 90 ASA grade I and II patients in the age group of 18 to 45 years of either sex scheduled for elective non cardiac surgeries done under general anaesthesia considering both inclusion and exclusion criteria's and taking written informed consent. Patients were allocated into three groups with the sample size of 30 each after a detailed pre-anesthetic evaluation was done.
Group A (n=30) received 4ml of normal saline 5mins before laryngoscopy and intubation (CONTROL GROUP)
Group B (n=30) received Inj. Fentanyl 2µg/Kg slow intravenous,5mins before laryngoscopy and intubation.
Group C(n=30) received Inj Clonidine 2µg/kg slow intravenous,5mins before laryngoscopy and intubation.

All patients were premedicated with Inj Midazolam 1mg IV. Induction was achieved with Inj. Thiopentone sodium 5mg/kg IV given in 2.5% solution. All patients were ventilated with 4 L/min of oxygen and 6 L/min of nitrous oxide. The heart rate, blood pressure, and SpO2 were recorded at the following time intervals (1, 3, 5, 7, 10 mins). At the end of the surgery reversal was done with Injection neostigmine 0.05 mg/kg and Injection glycopyrrolate 0.01mg/kg IV and extubated after recovery of adequate muscle power and consciousness. An observation was made related to adverse effects of drugs and anesthesia related problems and was attended to appropriately. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients. Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups. Kruska Wallis test has been used to find the significance of SPO2 between three groups. The Statistical software namely SAS 9.3, SPSS 16.0(2007) for windows were used for the analysis of the data.

Results

When mean change in heart rate in first min in group B and group C were compared with control (group A) group independently, there was no clinical or statistical significance between group A v/s group B (p= 0.09) and there was clinical or statistical significance between Group A v/s Group C (p = 0.02). (Table 1) Intergroup comparison of change in heart rate in first min between the study groups (Group B & Group C) showed no clinical or statistical significance (p=0.5). Statistical evaluation between the groups showed that the increase in Systolic blood pressure (SBP) observed in control group was statistically highly significant when compared to increase in SBP in Group C but not Group F. The increase in SBP in Group A and Group C were statistically highly significant compared to increase in SBP in GROUP F, ($p < 0.01$) at 1and 3mins, (p=0.006) at 5 and remained significant even up to 10min post intubation (p=0.03). Statistical evaluation between the groups showed that the increase in Diastolic blood pressure (DBP) observed in control group was statistically highly significant when compared to increase in DBP in group I but not group F. The increase in DBP in Group A and Group C were statistically highly significant compared to increase in DBP in group F ($p < 0.001$). (Table 2) Statistical evaluation between the groups showed that the increase in Mean arterial pressure (MAP) observed in Group A (control group) was statistically highly significant when compared to increase in MAP in Group C but not Group F. (Table 3)

Discussion

The anaesthesia and surgery are associated with a rise in plasma catecholamine concentration and subsequent increase in the blood pressure, HR and the cardiac dysrhythmias. These above mentioned effects may have serious repercussions on the high-risk patients like those with cardiovascular disease, high blood pressure, increased intracranial pressure, or anomalies of the cerebral vessels. Attenuation of such responses is of great importance in the prevention of the perioperative morbidity and mortality. In 1941, Burstein et al, found that the pressor response to laryngoscopy and endotracheal intubation was due to an augmented sympathetic activity which was provoked by the stimulation of the epipharynx and the laryngopharynx, which was further confirmed by Prys-Robert.[11] This was in contraindication to the finding of Reid et al, in 1940 who proposed that the stimulation of the upper respiratory tract provoked an increase in the vagal activity.[12] The findings of Burstein et al, was further confirmed by Prys-Roberts.[13] During laryngoscopy there is mechanical stimulation of upper respiratory tract which includes tongue, nasopharynx, oropharynx and most importantly the epiglottis. Afferents are carried by the glossopharyngeal nerve and vagus nerve. These afferents are carried to the cardioaccelerator or vasomotor centre. Sympathetic efferent from this centre results in transient rise in heart rate and blood pressure. It has been shown by Kaplan that stress due to sympathetic activation causes myocardial oxygen demand to exceed beyond its coronary supply resulting in parts of myocardium being rendered ischemic. Many drugs 51 have been reported to have beneficial effects in partially attenuating sympathoadrenal responses to endotracheal intubation. Injection lidocaine, esmolol, fentanyl, calcium channel blockers have been extensively studied by many authors. Alpha 2 agonist clonidine, though not extensively studied like

other drugs, there are many reports stating its beneficial effects in attenuation of circulatory responses to endotracheal intubation. Batra YK, Indu B, Puri GD et al.,[14] studied the attenuation of circualatory responses to laryngoscopy and intubation by oral clonidine(5 mcg/kg) and concluded that oral clonidine attenuates This study result added more supports to earlier studies conducted by Ghignone et al.[15], and Pouttu et al. [16]. Carabine et al compared different doses of intravenous clonidine in attenuating intubating responses in 1991.[17] Clonidine is a centrally acting selective partial α2 adrenergic agonist which also has a sympatholytic effect.[17] More-over it attenuates stress induced sympathoadrenal response to painful stimuli, improves the intra-operative hemodynamic stability, reduces the incidence of peri-operative Myocardial Infarction episodes in patients with suspected or documented coronary artery disease & decreases anaesthetic requirements during surgery; So clonidine seems be well suited as premedication for attenuating hemodynamic response following laryngoscopy & intubation.[18] It is also beneficial in preventing postoperative nausea and vomiting (PONV) and shivering in the postoperative.[19] We conclude that minimal dose of IV clonidine 2 µg/kg cause maximum attenuation of pressor response with minimal side effects like hypotension and sedation, and also reduced anesthetic requirements. By providing improved haemodynamics, clonidine proved to be beneficial as compared to fentanyl in any clinical setup.

Conclusion

This study showed that clonidine was superior to fentanyl in the attenuation of the pressor response and that the ideal time for its administration would be about 5 min before laryngoscopy and an intubation. An intravenous bolus dose of clonidine 2µg/kg administered 5 mins before a laryngoscopy and an intubation can be recommended to attenuate the sympathetic response to the laryngoscopy and intubation without any side effects of the drug.

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Tables

Table 1- Changes in the mean heart rate

HR	GROUP A	GROUP F	GROUP C	SIGNIFICANT VALUE		
				GROUP A-F	GROUP A-C	GROUP F-C
0 min	80.2±6.8	77.8±5.6	75.5±7	0.84	0.71	0.85
POST INTUBATION						
1min	117±11	92.7±8.1	83.7±7	0.09	0.02*	0.50
3min	113±11	91.8±8.2	80.7±4	0.08	0.02*	0.56
5 min	109±11	88.6±6.1	77±6.3	0.35	0.04*	0.32
7min	100.8±10	84.8±4.0	75.5±5.3	0.24	0.04*	0.46
10min	95±8.7	77.3±4.5	71.8±5.1	0.17	0.07	0.65

Table 2- Changes in mean systolic blood pressure (SBP) and mean diastolic blood pressure (MBP)

SBP	GROUP A	GROUP F	GROUP C	SIGNIFICANT VALUE		
				GROUP A-F	GROUP A-C	GROUP F-C
0 min	124±9	118±6.9	118±6.8	0.80	0.75	0.95
POST INTUBATION						
1min	170±9.4	140±7.1	128±7	0.09	0.01**	0.46
3min	166±5	136±7.1	124±7	0.06	0.01**	0.62
5 min	162.7±10	133.3±5.2	117.5±7.6	0.08	0.006**	0.31
7min	155±9	126.2±7	111.8±6	0.09	0.008**	0.35
10min	144±11.1	116±6.8	108.6±6.3	0.08	0.03*	0.62

DBP mmHg	GROUP A	GROUP F	GROUP C	SIGNIFICANT VALUE		
				GROUP A-F	GROUP A-C	GROUP F-C
0 min	75.4±5	74.5±6.4	76	0.88	0.85	0.97
POST INTUBATION						
1min	108±10	85.8±7.7	80.1±5.5	0.11	0.04*	0.66
3min	102±8	82.2±7.6	74±5.5	0.14	0.03*	0.51
5 min	98±10	82.3±5.8	70.9±4.5	0.22	0.03*	0.32
7min	92±8.2	76.6±5.6	68±4.1	0.24	0.06*	0.47
10min	84±10.5	74.6±4.1	67.5±5.6	0.42	0.18	0.77

Table 3- Changes in the mean arterial pressure (MAP)

MAP mmHg	GROUP A	GROUP F	GROUP C	SIGNIFICANT VALUE		
				GROUP A-F	GROUP A-C	GROUP F-C
0 min	95.1±5	89±6.3	88.4±5.7	0.85	0.82	0.97
POST INTUBATION						
1min	123.4±10	101.5±7.2	96±5.7	0.12	0.04*	0.64
3min	121±7.0	97.1±7.0	91.9±5.6	0.09	0.03*	0.60
5 min	118±9.0	99.3±5.1	88.4±4.7	0.2	0.04*	0.43
7min	111.4±7.8	93.1±5.6	83.5±4	0.23	0.04*	0.35
10min	98.6±9	86±4.4	81.5±5.2	0.35	0.18	0.73