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Original Research Article

Efficacy of Labetalol versus Fentanyl for Attenuation of Haemodynamic Stress Response to Laryngoscopy and Endotracheal Intubation

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Abstract:

Background and Aim: A special type of anti-hypertensive medication called labetatol primarily used for perioperative blood pressure management and hemodynamic stability. Due to its great strength and quick start of effect, IV fentanyl is used as a pre-medication to inhibit physiological response during laryngoscopy. present study was aimed to attenuate the haemodynamic response of laryngoscopy and intubationin adult patients posted for surgery under general anaesthesia with IV dose of Lobetalol 0.5 mg/kg and Fentanyl 2µg/kg over 5 minutes before induction and to compare effects of both the drugs.

Material and Methods: The present study was done at GMERS Medical College and Civil Hospital. The approval from Institutional Ethical committee was obtained prior to the start of the study. This Study was conducted on 60 patients in age group 18 - 60 yrs. Patients are to be randomly allocated into two groups, Group F (for fentanyl) and group L (for Labetalol). Group-F (N=30): Intravenous Fentanyl 2µg/kg in 10 ml Normal Saline was given over 5 minutes, 5 minutes prior to induction. Group-L (N=30): Intravenous Labetalol 0.5 mg/kg in 10 ml Normal Saline to be given over 5 minutes, 5 minutes prior to induction. HR, SBP, DBP, MAP were recorded at Base line (Before Injecting study Drug), Pre induction (After 5 minute of injecting study drug), immediately after larygoscopy at 1 min ,3 min, 5 min, 10 min, 15 min, 30 min of post intubation then every 30 min till end of surgery.

Results: Group L showed a significant fall in HR, SBP, DBP and MAP after injecting the drug, after induction, post intubation. When compare both the group, Labetalol 0.5mg/kg significantly attenuates the haemodynamic response to laryngoscopy and intubation. Fentanyl 0.5 µg/kg group attenuates the pressor response to laryngoscopy and intubation but not as effective as labetalol 0.5 mg/kg.

Conclusion: Labetalol (0.5 mg/kg) is a better agent than fentanyl (2 µg/kg) in attenuating the sympathomimetic response to laryngoscopy and intubation. There was no increased risk of bradycardia or hypertension.

Keywords: Fentanyl, Hypertension, Labetatol, Laryngoscopy.

Introduction

Translaryngeal intubation of the trachea is known as endotracheal intubation. Since Rowbotham and Magill first described them in 1921, laryngoscopy and endotracheal intubation have become the most crucial components of anaesthetic management.[1] A laryngoscope is used to perform tracheal intubation, which is regarded as the gold standard of airway management when administering general anaesthesia due to its many benefits, including the delivery of anaesthetic gases and oxygen and the isolation of the respiratory tract from the gastrointestinal system, which reduces the risk of aspiration.[2]

During general anaesthesia, direct laryngoscopy and tracheal intubation cause sympathetic activation and the release of plasma catecholamines, which clinically present as tachycardia, hypertension, and increased intraocular and intracerebral pressure. The stimulation of the epipharynx and laryngopharynx causes a sympathetic reflex that causes the circulatory response to laryngoscopy and intubation. The reflex that is mediated by the afferent Vagus (X) and Glossopharyngeal (IX) cranial nerves activates the vasomotor centre, resulting in a peripheral sympathetic adrenal response and the release of adrenaline and noradrenaline from the adrenal medulla.[3]

Usually, these hemodynamic reactions reach their greatest effect 1-2 minutes after intubation and return to normal 5–10 minutes later. However, in co-morbid patients with ischemic heart disease (IHD) and hypertension (HTN), this transient response can elicit life-threatening conditions like myocardial ischemia, arrhythmias, stroke, left ventricular failure, and cerebral haemorrhage. These hemodynamic responses are brief and well tolerated in otherwise healthy individuals.[4]

A special type of anti-hypertensive medication called labetatol contains both selective and non-selective beta-adrenergic blocking agents. The half-life of IV labetalol is 4-6 hours, with an action beginning of 5 minutes and a peak effect of 5-15 minutes. It is primarily used for perioperative blood pressure management and hemodynamic stability. Laryngoscopy and \7*tubation responses have been mitigated by low dosage IV labetalol (0.25–0.5 mg/kg).[5,6]

In comparison to morphine, phenylephrine, and alfentanil, fentanyl citrate has a stronger analgesic potency. It is primarily a (mu) receptor agonist. The characteristics of fentanyl citrate include its extreme potency, high lipophilicity, quick onset (4–10 min), and brief duration of action (30 min–1 hr). Due to its great strength and quick start of effect, IV fentanyl is used as a pre-medication to inhibit physiological response during laryngoscopy.7,8 With the above background the present study was aimed to attenuate the haemodynamic response of laryngoscopy and intubationin adult patients posted for surgery under general anaesthesia with IV dose of Lobetalol 0.5 mg/kg and Fentanyl 2µg/kg over 5 minutes before induction and to compare effects of both the drugs.

Materials & Method

Study Setting

The present study was done at GMERS Medical College and Civil Hospital. The approval from Institutional Ethical committee was obtained prior to the start of the study.

Study Design

It was a Hospital based prospective, randomized, double-blind study conducted at Department of anaesthesia, GMERS Medical College and Civil Hospital.

Study Subject

This Study was conducted on 60 patients in age group 18 - 60 yrs, belonging to ASA I & II, scheduled for elective procedures under General Anaesthesia in GMERS Medical College and Civil Hospital.

Data Collection

All the patients came for elective surgery fulfilled the inclusion criteria and¬ the results were taken for our study purpose. After approval from the institution's ethical committee, written, informed, valid consent was obtained from all patients qualifying the inclusion criteria after explaining the study protocol and patients were divided in two groups. All selected subjects were approached and personally met¬& briefed about the study. After taking informed consent, a detailed questionnaire was administered toϖ the selected patient, at their convenience. Strict confidentiality was employed in carrying out the survey and use of information provided by each respondent.

Inclusion criteria: Patients undergoing surgical procedures under general anaesthesia, Patients aged 18-60 years of either gender, ASA physical status I, II, Patients weighing between 40-80 kg, were included in the study.

Exclusion Criteria: Pregnant patients, Patients allergic to any drug, Patients with coagulation abnormalities, Patients with poorly controlled hypertension, Patients with preexisting severe bradycardia and congestive heart failure (CHF), Patients with uncontrolled respiratory diseases, neuromuscular diseases, hematological disorders and severe hepatic or renal insufficiency were excluded from the study.

Sampling Technique

Purposive sampling method, which is a non-probability sampling technique, was used considering the patient inflow rate in this hospital during study period.

Randomization: Patients are to be randomly allocated into two groups, Group F (for fentanyl) and group L (for Labetalol). Randomization has been done by coin toss by the person not involved in the study for each patient. Patient getting heads has been allocated to group A and those getting tails has been allocated group B. Once the sample size of any one group is achieved, further allocation has been done by coin

toss for each patient, so that every patient gets the same probability to be allocated to either group. If the patient gets the completed group, he/she shall not be included in the study and the ones getting the still incomplete group has been included, until sample size for that group is achieved as well. Thus, maintaining randomization with each included patient getting equal chance of being allocated to either group. Sample size for group F was 30 patients and sample size for group L was 30 patients.

Blinding

The study drugs were prepared by hospital personnel who were not directly involved in the study and qualify to handle the study drugs. The person who is injecting the drug is blinded to the study drug. The observer who records vitals of the patient is also blind to the study.

Premedication

IV access was secured with a 20 G cannula and infusion of Ringer's lactate was started. Inj. Glycopyrrolate 0.004 mg/kg IV, Inj. Midazolam 0.02 mg/kgIV, Inj. Ondansetron 4 mg IV were given to the patients.

Study Drugs: The study drugs to be then prepared by qualified personnel not directly involved in the study. Group-F (N=30): Intravenous Fentanyl 2µg/kg in 10 ml Normal Saline was given over5 minutes, 5 minutes prior to induction. Group-L (N=30): Intravenous Labetalol 0.5 mg/kg in 10 ml Normal Saline to be given over 5 minutes, 5 minutes prior to induction.

Induction

Pre oxygenation was done with 100% oxygen for 3 minutes. Induction was done with Inj. Propofol 2mg/kg I.V and Suxamethonium 2mg/kg IV. laryngoscopy and tracheal intubation was done by Anaesthesiologist. Once tube position was confirmed, positive pressure ventilation had been started with tidal volume 6-8 ml/kg and respiratory rate 12-14/minute.

Maintenance

Anaesthesia was maintained with Sevoflurane, O_2 and Nitrous oxide (50:50) along with Inj. Atracurium 0.5 mg/kg loading dose and 0.1 mg/kg for maintenance.

Monitoring HR, SBP, DBP, MAP were recorded at Base line (Before Injecting study Drug), Pre induction (After 5 minute of injecting study drug), immediately after larygoscopy at 1 min, 3 min, 5 min, 10 min, 15 min, 30 min of post intubation then every 30 min till end of surgery.

Reversal: At the end of surgery, all anaesthetic gases were discontinued, and reversal of neuromuscular blockade was done after return of spontaneous respiration using Injection Neostigmine 50 µg/kg and Injection Glycopyrrolate 8 µg/kg Extubation was done after oral suction and deflating cuff after fulfilling the criteria for extubation.

Post Operative: All patients were kept in Post anaesthesia care unit (PACU) for two hours and vitals were monitored. Any complication was noted and treated accordingly.

Adverse effects: Adverse effects like bradycardia, tachycardia, hypotension, hypertension, nausea, vomiting, if any, noted during intra operative or post operative period and to be treated as follows: Bradycardia - (HR) 30% above baseline value): deepening plane of anaesthesia by increasing inhalation anaesthetic concentration or causative treatment. Hypotension – (SBP 140 mmHg): deepening plane of anaesthesia by increasing inhalation anaesthetic concentration or Inj. Propofol 20 mg IV. Post operative nausea and vomiting: Inj. Metoclopramide 10mg IV.

Data Analysis

Collected data was entered in the excel data sheet and data analysis was done with the help of Epi. Info.7.2 software. Data was cleaned, Validated and Analysed by Epi. Info 7 software. For continuous variable range, mean and standard deviation were calculated and for categorical variables proportion and percentage were obtained. Bi-Variate analysis:¬ To know the association between dependent and independent variable chi-square and student t test applied accordingly.

Results

Table 1: ASA status of physical health in both the groups

Gender	Group L	Group F	P value	Remark
ASA grade I	17 (56.7)	15 (50.0)	0.56	Not significant
ASA grade II	13 (43.3)	15 (50.0)		

Table 2: Side effects of drugs in both the study groups

Side effects	Group L	Group F
Bradycardia	2	1
Hypotension	1	0

In this study, patients of group L received intravenous Labetalol whereas patients of group F received intravenous Fentanyl as a loading dose over 5 minutes. The mean age in group L was 45.6 ± 11.9 years while the mean age in group F was 43.1 ± 13.1 years. The observed difference was statistically non-significant. Both Group L and group F had female preponderance as compared to males. This difference was found to be statistically non-significant. The mean weight did not differ significantly between the two study groups. Mean weight of patients in group L was 63.6 ± 10.4 kg, while mean weight of patients in group L was 64.6 ± 11.1 kg.

Both the groups had almost similar number of patients in ASA grade I and grade II. There was no significant difference in group L and group F with respect to ASA grade. Baseline HR in both groups were comparable. After intubation at 1 min the mean HR in group L was 71.3±4.9 bpm and group F was 75.1±7.3 bpm. The difference in HR was significant in both groups. (p 0.003).

At 3 min the mean HR in group L was 70.6±4.9 bpm and group F was 75.7±8.3bpm. The difference in HR was significant in both groups. (p 0.002) At 5 min the mean HR in group L was 72.7±4.2 bpm and group F was 79.4±9. 0bpm.The difference in HR was significant in both groups. (p 0.001) At 10 min the mean HR in group L was 74.9±4.1 bpm and group F was80.9 ±7.9 bpm. The difference in HR was significant in both groups. (p 0.001) Labetalol group has maintained lower heart rate as compared to fentanyl group in initial 15 minutes after intubation. This was found to be statistically significant. Baseline SBP in both groups were comparable.

After intubation at 1 min the mean SBP in group L was 111.0±9.9 mm of Hg and group F was 118.3±4.9 mm of Hg which was significant in both groups. (p 0.025) At 3 min the mean SBP in group L was 109±7.7 mm of Hg and group F was 116.7±2.9 mm of Hg which was significant in both groups. (p 0.001) At 5 min the mean SBP in group L was 114.2± 10.5 mm of Hg and group F was 121.7±5.1 mm of Hg which was significant in both groups. (p 0.001)

At 10 min the mean SBP in group L was 110.3± 9.4 mm of Hg and group F was119.8 ± 6.6 mm of Hg which was significant in both groups. (p 0.001) Labetalol group has maintained lower SBP as compared to fentanyl group in initial 15 minutes after intubation. This was found to be statistically significant.

Baseline DBP in both groups were comparable. After intubation at 1 min the mean DBP in group L was 72.9± 6.1 mm of Hg and group F was 76.2±4.4 mm of Hg which was significant in both groups. (p 0.015) At 3 min the mean DBP in group L was 71.5±7.6 mm of Hg and group F was 75.3±4.1 mm of Hg which was significant in both groups. (p 0.001) At 5 min the mean DBP in group L was 73.2±10.6 mm of Hg and group F was 77.2±7.8 mm of Hg which was significant in both groups. (p 0.01) At 10 min the mean DBP in group L was 70.6±9.3 mm of Hg and group F was 74.6±6.9 mm of Hg which was significant in both groups. (p 0.001) Labetalol group has maintained lower DBP as compared to fentanyl group in initial 15 minutes after intubation. This was found to be statistically significant.

Baseline MAP in both groups were comparable. 57 After intubation at 1 min the mean MAP in group L was 99.3±0.4 mm of Hg and group F was 99.4±0.3 mm of Hg which was significant in both groups. (p 0.75) At 3 min the mean MAP in group L was 99.5±0.4 mm of Hg and group Fwas 99.5±0.4 mm of Hg which was significant in both groups. (p 1.000) At 5 min the mean MAP in group L was 99.4±0.4 mm of Hg and group Fwas 99.6 ±0.2 mm of Hg which was significant in both groups. (p 0.76) At 10 min the mean MAP in group L was 99.2±0.4 mm of Hg and group F was 99.3±0.4 mm of Hg which was significant in both groups. (p 0.84) Labetalol group has maintained lower MAP as compared to fentanyl group in initial 15 minutes after intubation. This was found to be statistically significant. In our study 2 patients of group L developed bradycardia, one patient developed bradycardia intraoperatively but did not need any treatment. Postoperatively there was bradycardia in one patient treated with inj. atropine 0.6mg IV successfully. In group F, one patient developed bradycardia postoperatively which was treated successfully. Hypotension was there in one patients of group L intraoperatively and treated successfully with IV fluids only. There was no hypotension in Group F.

Discussion

Laryngoscopy and endotracheal intubation are the most important integral part of anaesthesia management.[1,2] Direct laryngoscopy and tracheal intubation during general anaesthesia leads to sympathetic stimulation and release of plasma catecholamines which manifests clinically as tachycardia, hypertension along with raised intraocular and intracerebral pressure.[9,10]

These haemodynamic responses are transient and well tolerated in otherwise healthy individuals but in co-morbid patients having Ischemic heart disease (IHD), hypertension (HTN), this transient response can evoke life-threatening conditions like myocardial ischemia, arrhythmias, stroke, left ventricular failure and cerebral haemorrhage.[6] Traditionally used

drugs like lignocaine, clonidine, esmolol, etc., are either not fully effective or they are associated with considerable side effects at doses required to attenuate these responses.[10,11] Therefore, it has become imperative to develop a novel technique/drug to prevent these potentially hazardous responses. Fentanyl suppresses the hemodynamic response by increasing the depth of anesthesia and decreasing the sympathetic discharge. Low doses of fentanyl were employed in past studies because a large dose leads to muscular rigidity, bradycardia, nausea, and vomiting. Large doses may also cause postoperative respiratory depression.[12,13]

Labetalol is an antihypertensive drug that decreases the pressure response of intubation by α-1 and β-adrenergic receptor blockade. Presynaptic α-2-receptors are spared by labetalol so that the released norepinephrine can continue to inhibit further release of catecholamines via the negative feedback mechanism resulting from the stimulation of α- 2 receptors.[14,15]

It seems that when instrumentation stimulus is present Labetalol maintains the HR within normal range. When the effect of stimulus weans off, as occurs at 10 min post-intubation, the drug's effect takes over and pulse rates go below baseline values.[16]

Demographic Data

Age, Weight, Gender In the present study, the mean age in group L was 45.6 ± 11.9 years while the mean age in group F was 43.1 ± 13.1 years.

The observed difference was statistically non-significant. Both Group L had 14 male and 16 female patients and group F had 12 male 18 female patients. This difference was found to be statistically non-significant. Mean weight of patients in group L was 63.6 ± 10.4 kg, while mean weight of patients in group L was 64.6 ± 11.1 kg. The mean weight did not differ significantly between the two study groups. Babita et al[14] studied on 84 patients as per ASA grade I and II, either sex, aged 20-55 years, and scheduled for elective vascular surgeries. These group were comparable in patients characteristics with respected age, gender, mean weight, and ASA physical status.

In this study Baseline HR in both group were comparable. After intubation at 1 min the mean HR in group L was 71.3±4.9 bpm and group F was 75.1±7.3 bpm. At 3 min the mean HR in group L was 70.6±4.9 bpm and group F was 75.7±8.3bpm. At 5 min the mean HR in group L was 72.7±4.2 bpm and group F was 79.4±9.0bpm. At 10 min the mean HR in group L was 74.9±4.1 bpm and group F was 80.9±7.9 bpm Labetalol group has maintained lower heart rate as compared to fentanyl group in initial 15 minutes after intubation. This was found to be statistically significant.

In our study Labetalol group has maintained lower SBP as compared to fentanyl group in initial 15 minutes after intubation. This was found to be statistically significant. In study conducted by Singh SP et al.[16] The preinduction values of SBP were comparable between groups with no significant difference. Post intubation SBP increased in both esmolol and control groups at all times. SBP was significantly lower at all time in the labetalol group at intubation, 1st and 3rd, 5 minute , 10 minute. conclusion of the study was SBP were significantly less in patients receiving labetalol compared to those who received esmolol. Baseline DBP in both group were comparable, After intubation at 1 min the mean DBP in group L was 72.9± 6.1 mm of Hg and group F was 76.2 ±4.4 mm of Hg. At 3 min the mean DBP in group L was 71.5± 7.6 mm of Hg and group F was75.3 ±4.1 mm of Hg, At 5 min the mean DBP in group L was 73.2± 10.6 mm of Hg and group F was77.2 ±7.8 mm of Hg, At 10 min the mean DBP in group L was 70.6 ± 9.3 mm of Hg and group F was 74.6 ± 6.9 mm of Hg. In our study Labetalol group has maintained lower DBP as compared to fentanyl group in initial 15 minutes after intubation. This was found to be statistically significant. In our study Baseline MAP in both group were comparable.After intubation at 1 min the mean MAP in group L was 99.3 ± 0.4 mm of Hg and group F was 99.4 ±0.3 mm of Hg , At 3 min the mean MAP in group L was 99.5 ± 0.4 mm of Hg and group F was 99.5 ±0.4 mm of Hg , At 5 min the mean MAP in group L was 99.4 ± 0.4 mm of Hg and group F was 99.6 ±0.2 mm of Hg , At 10 min the mean MAP in group L was 99.2 ± 0.4 mm of Hg and group F was 99.3 ±0.4 mm of Hg , In our study Labetalol group has maintained lower MAP as compared to fentanyl group in initial 15 minutes after intubation. This was found to be statistically significant.

In our study 2 patients of group L developed bradycardia, In group F one patient developed bradycardia. Hypotension was there in one patients of group L. There was no hypotension in Group F. 75 In the study done by Patel LP et al Bradycardia was observed in 28% of the patients after 10 minutes in labetalol group. Singh SP et al.[16] observed only the side effect of labetalol in the form of bradycardia, intraoperatively. Seven (28%) patients developed bradycardia (PR < 50 bpm) after the study period of 10 min. Bradycardia after Labetalol is due to Non-selective Beta blocking effect of the Drugs. In the study done by Amar D et al.[17] two patients receiving laletalol developed Hypotension intraoperatively.

This is due to alpha 1 adrenoreceptor blocking actions of the drugs. Present Study has few limitations like-Present study was conducted at single center and included small no of patients. The Age group in this study was 19-60 years, therefore we could not assessλ the effects of the study drugs at the extremes of ages. Only ASA I and ASA II, elective surgical cases were selected in this studyλ and therefore we could not assess the effect of the study drugs on high risk, haemodynamically compromised, critically ill and emergency patients.

Conclusion

We conclude that both fentanyl and labetalol effectively blunt the hemodynamic response to endotracheal intubation under general anesthesia and can be safely used. Labetalol (0.5 mg/kg) is a better agent than fentanyl (2μg/kg) in attenuating the sympathomimetic response to laryngoscopy and intubation. There was no increased risk of bradycardia or hypertension. According to this study and various other study it is advisable to use labetalol in patients to attenuate the hemodynamic responses of laryngoscopy and endotracheal intubation. This hemodynamic stability leads to better patient outcome.

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