ORIGINAL RESEARCH PAPER

Anaesthesiology

KEY WORDS:

ATTENUATION OF CARDIOVASCULAR RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION BY A BOLUS DOSE OF INJ. ESMOLOL & PLACEBO IN LAPROSCOPIC CHOLECYSTECTOMY AND LAPROSCOPIC APPENDICECTOMY - A COMPARATIVE STUDY IN A TERTIARY HEALTH CARE CENTRE

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INTRODUCTION:-

Laryngoscopy and tracheal intubation are noxious stimuli that produce marked sympathetic response manifesting as tachycardia and hypertension.[1] These haemodynamic changes are generally transitory and without sequelae. However in patients with preexisting coronary artery disease, hypertension and cerebrovascular disease, an increase in the Heart rate & Blood pressure may precipitate myocardial ischaemia, arrhythmias, infarction and even cerebral haemorrhage.This response is exaggerated due to the narrow arterial lumen, blunted baro reflex response and increased sympathetic activity.[4]

Circulatory responses to laryngeal and tracheal stimulation were known since 1940 (Reid and Brace).The study by Tomori and Widdicombe 1969, showed that mechanical stimulation of the respiratory tract caused increased nervous system activity in cervical sympathetic efferent fibres.[2]

These haemodynamic changes stem from reflex sympathetic discharge resulting from epi-pharyngeal and laryngopharyn geal stimulation associated with increased plasma norepinephrine concentrations. Hence, to overcome this undesired response, the quest for an effective blockade of these responses has included the use of (Ebert and Pierson):[3]

I. Premedication

ii. Topical and systemic lidocaine

iii. Vasodilators e.g. Isosorbidedinitrate, sodium nitroprusside

iv. α and β adrenergic blocking agents

v. Angiotensin - converting enzyme inhibitors

vi. Opiates e.g. Fentanyl, Alfentanil

vii. Inhaled anaesthetic agents

viii. Thoracic epidural block.

Since tachycardia appears to be associated more frequently with myocardial ischaemia than does hypertension, interesting approach towards attenuating cardiac responses to laryngeal stimulation, is the use of β-adrenergic antagonists. However attenuation of pressor response to LTI is desirable, excessive negative chronotropic and inotropic action of the β-receptor blockers may reduce coronary perfusion and precipitate heart failure in susceptible patients.

Among the β-adrenergic antagonists **Esmolol**(Methyl 3-4-{2-hydroxy-3- (isopropyl amino) propoxy-phenyl} propionate hydrochloride) has been an effective option because of its -1 (cardioselective) adrenergic receptor blocking properties and its ultra-short duration of action. It has -distribution half-life of 2 min; β-elimination half- life of 9 min) &hydrolysed by Red blood cell esterase.

With Esmolol treatment, the difficulties of therapy with long lasting β-blockers are avoided. Sympathetic nervous system responses can be suppressed with a single dose i.v before tracheal intubation. In view of its pharmacokinetic profile, rapid onset, short elimination half-life and titrability, this study aims to evaluate the usefulness of Esmolol to deal with sympathetic activation at laryngoscopy and intubation.

AIMS & OBJECTIVES:

This clinical study is designed to evaluate and compare intravenous Esmolol in a bolus dose to a placebo regarding:

i. Haemodynamic responses to laryngoscopy and endotracheal intubation.
ii. Effect on ECG (arrhythmias)
iii. Any side effects

60 Patients satisfying below mentioned criteria will be considered for our study within the study period.

MATERIALS AND METHODS :

A study to evaluate and compare intravenous Esmolol in a bolus dose to a placebo will be carried out with patients posted for Laproscopic Cholecystectomy and Laproscopic Appendicectomygeneral anaesthesia from Department of General Surgery, after taking informed consent from all the patients.

Inclusion criteria :

i. ASA grade I and II (Normal healthy patients & Mild systemic disease without any functional limitation)
ii. Age 20 to 60 years.
iii. Normotensive patients.

Exclusion criteria:

i. Patient refusal
ii. ASA III & IV (moderate & Severe systemic disease making patient incapacitating)
iii. Pulse rate <60 beats/min, hypertensive patients.
iv. History of myocardial infarction in the past 6 months.
v. Conduction abnormality in ECG.
vi. Patients predicted to have difficult intubation like short neck,large tongue High arched palate.
vii. Clinically significant hepatic renal and metabolic dysfunction.

DISCUSSION:

60 Patients satisfying the above said inclusion and exclusion criteria were subjected to our study. They were enrolled in 2 equal groups (A &B). The study participants in each group were chosen by computer generated random numbers.This was a double blind study.

Group A received Inj.Esmolol with the standard regimen of general anaesthesia

Group B Received Normal Saline with the standard regimen of general anaesthesia.

The standard regimen for general anaesthesia In our set up includes Glycopyrolate, Analgesics (Nalbuphine, Paracetamol), Thiopentolsodium, Suxamethonium chloride, Vecuronium, Oxygen, Nitrous oxide, Isoflurane& Reversal agent(Myo-Pyrolate).

Intravenous cannulation were secured. All patients were premedicated with injection GLYCOPYROLATE 0.2 mg IV. Non-invasive blood pressure monitor, pulse oximeter probe and ECG were monitored. Baseline readings of heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and ECG were recorded.

All patients wiere pre-oxygenated for 3 minutes with 100% oxygen. Group A patients received inj. Esmolol 1.0 mg/kg IV bolus slowly over 15 seconds, whereas in group B equal volumes of Normal saline were given as placebo. This was soon followed in both the groups by induction with IV THIOPENTONE SODIUM 5 mg/kg (2.5%) and SUXAMETHONIUM CHLORIDE 1.5 mg/kg and ventilated with 100% oxygen. Laryngoscopy and intubation time were limited to less than 60 seconds.

Subsequently anaesthesia was maintained by IPPV with oxygen, nitrous oxide,Isoflurane, delivered through closed circuit with circle absorber. Muscle relaxation for the contemplated surgery was provided by VECURONIUM Patients will be extubated after reversal at the end of the procedure using MYO-PYROLATE on stable parameters.

The present study will focuss on events from the time of injection of the study drug/placebo upto 5 minutes after intubation. Surgery is to be carried out only after the study period. Analgesics(Nalbuphine,Paracetamol) and other adjuvants will also be administered after this period.

The following parameters were observed:

1. Baseline readings (pre-induction) of heart rate, systolic, diastolic, mean arterial blood pressure.
2. Reading of the above said parameters at 1, 3, and 5th minute after intubation.
3. Continuous ECG monitoring for arrhythmias, ST changes. [19]
4. Adverse effects namely burning on injection, bronchospasm, and postoperative phlebitis.

STATISTICAL ANALYSIS:

Table No. 1.0: Distribution of Age Group of Different Patients

Age Group	Esmolol	Placebo	Total (Percentage)
20-30	5	4	9(15%)
30-40	10	6	16(26.66%)
40-50	4	14	18(30%)
50-60	11	6	17(28.33%)
Total	30	30	60

RESULTS

From the above table 1.0 which gives the age wise distribution of the study participants from Esmolol group and placebo group. Maximum number of cases from age group 30-60(85%) and Minimum number of cases from age group 20-30. But in case of Esmolol group Maximum cases are from age group 30-40 (10), and Minimum number of cases from 40-50 age group. Similarly from placebo the Maximum age group from 40-50(14) and Minimum number of cases from the age group of 20-30 years.

Table no. 2.0 Distribution of weight of different treatment and placebo group

Weight Group	Esmolol	Placebo	Total
Below 50	2	0	2(3.33%)
50-55	4	6	10(16.66%)
55-60	6	2	8(13.33%)
60-65	6	8	14(23.33%)
65-70	5	7	12(20%)
70-75	6	5	11(18.33%)
Above 75	1	2	3(5%)
Total	30	30	60(100%)

RESULTS

From the above Table 2.0 and Figure 2.0, gives the weight wise distribution of the study participants from Esmolol group and placebo group. Maximum number of cases from weight group 50-75(92.66%) and minimum number of cases from weight of group below 50 (2.33%).

Table No. 3.0 Descriptive statistics of the study participants

Category	Esmolol (Mean ± S.D.)	Placebo (Mean ± S. D.)	P-Value
Age	41.13±11.92	41.23±9.04	0.971
Weight	61.73±7.85	63.66±7.68	0.339

RESULTS

From the above Table 3.0 gives the descriptive statistics of the Demography variable of Age and Weight. The mean and standard deviation of age of esmolol group 41.13±11.92 years. The mean and standard deviation of age of placebo group 41.23±9.04 years.

The mean and standard deviation of weight of Esmolol group 61.73±7.85 kgs and the mean and standard deviation of weight of placebo group 63.66±7.68 years.

From the above test statistics p values (p=0.971) we conclude that the age group of Esmolol and placebo groups are statistically difference i.e. not significant.

From the above test statistics p values (p=0.339) we conclude that the weight group of Esmolol and placebo groups are statistically difference i.e. not significant.

Table 4.0 Distribution of Pre Induction Characteristics

Category	Esmolol				Placebo				p value
	Min	Max	Mean	S.D.	Min	Max	Mean	S.D.	
SBP	122	156	138.53	9.41	114	144	129.67	7.37	0.181
DBP	80	96	88.47	4.63	78	92	85	3.27	0.211
MAP	97	116	105.07	5.36	91	108	99.87	4.41	0.439
HR	64	96	83.6	9.43	68	92	79.27	8.31	0.195

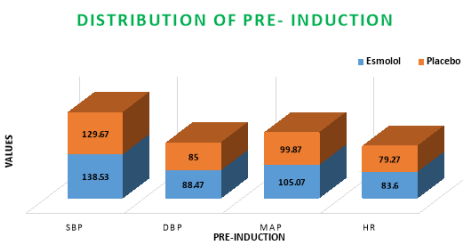

Figure No. 5.0 Distribution of pre induction

RESULTS

From the above table 4.0 and figure 4.0 gives the pre induction characteristics of different variables between the two groups (Esmolol and Placebo), statistically there is no significant different in pre induction stages.

Table No.5.0 Effect of Systolic Blood Pressure in the study with different times

SBP	Esmolol (Mean ± S.D.)	Placebo (Mean ± S.D.)	Test statistics	Effect size (%)

Pre-Induction	138.53±9.40	129.66±7.37	F=16.50, p<0.001	22.15%
1st Min	158.86±9.85	173.20±8.67	F=35.78,p<0.001	38.15%
3rd Min	152.20±7.60	165.93±8.05	F=46.109,p<0.001	44.28%
5th Min	145.20±7.03	158.53±7.00	F=54.074,p<0.001	48.24%

RESULTS

From the above table 5.0 which gives the 22.15% of the total variance is accounted for by the treatment effects case of pre induction stage. The change in SBP has been from placebo group 129.66±7.37 to 138.53±9.40 in Esmolol group at pre induction

The change in SBP has been from placebo group 173.20±8.67 to 158.86±9.85 in Esmolol group at 1St Minute , 38.15%of the total variance is accounted for by the treatment effects case of pre induction stage.

The change in SBP has been from placebo group 165.93±8.05 to 152.20±7.60 in Esmolol group at 3rd Minute , 44.28%of the total variance is accounted for by the treatment effects case of pre induction stage.

The change in SBP has been from placebo group 158.53±7.00 to 145.20±7.03 in Esmolol group at 5th Minute , 48.24%of the total variance is accounted for by the treatment effects case of pre induction stage.

Table no. 6.0 Distribution of DBP in different time interval

DBP	Esmolol (Mean ± S.D.)	Placebo (Mean ± S.D.)	Test statistics	Effect size (%)
Pre-Induction	88.46±4.62	85±3.26	F=11.22, P<0.001	16.21%
1st Min	96.66±3.87	106.00±3.32	F=100.42, P<0.001	63.39%
3rd Min	94.93±3.92	96.60±2.83	F=3.55, P<0.064	5.78%
5th Min	89.93±4.37	92.73±2.89	F=8.52, P<0.005	12.82%

RESULTS

From the above table 6.0 which gives the 16.21% of the total variance is accounted for by the treatment effects case of pre induction stage. The change in DBP has been from placebo group 85±3.26 to 88.46±4.62 in Esmolol group at pre induction

The change in DBP has been from placebo group 106.00±3.32 to 96.66±3.87 in Esmolol group at 1St Minute , 63.39% of the total variance is accounted for by the treatment effects case of pre induction stage.

The change in DBP has been from placebo group 96.60±2.83 to 94.93±3.92 in Esmolol group at 3rd Minute , 5.78% of the total variance is accounted for by the treatment effects case of pre induction stage.

The change in DBP has been from placebo group 92.73±2.89 to 89.93±4.37 in Esmolol group at 5th Minute, 12.82% of the total variance is accounted for by the treatment effects case of pre induction stage.

Table No 7.0 Distribution of MAP

MAP	Esmolol (Mean ± S.D.)	Placebo (Mean ± S.D.)	Test statistics	Effect size (%)
Pre-Induction	105.06±5.36	99.86±4.40	F=16.83,P<0.001	22.5%
1st Min	117.33±5.21	128.43±3.83	F=88.14,P<0.001	60.31%
3rd Min	114.03±4.40	119.66±3.55	F=29.69,P<0.001	33.86%
5th Min	108.33±4.35	114.66±3.20	F=41.08,P<0.001	41.47%

RESULTS

From the above table 7.0 which gives the 22.5% of the total variance is accounted for by the treatment effects case of pre induction stage. The change in MAP has been from placebo group 99.86±4.40 to 105.06±5.36 in Esmolol group at pre induction

The change in MAP has been from placebo group 128.43±3.83 to 117.33±5.21 in Esmolol group at 1St Minute , 60.31% of the total variance is accounted for by the treatment effects case of pre induction stage.

The change in MAP has been from placebo group 119.66±3.55 to 114.03±4.40 in Esmolol group at 3rd Minute , 33.86% of the total variance is accounted for by the treatment effects case of pre induction stage.

The change in MAP has been from placebo group 114.66±3.20 to 108.33±4.35 in Esmolol group at 5th Minute, 41.47% of the total variance is accounted for by the treatment effects case of pre induction stage.

Table No. 8.0 Distribution of HR

HR	Esmolol (Mean±S.D.)	Placebo (Mean±S.D.)	Test statistics	Effect size (%)
Pre-Induction	83.60±9.43	79.26±8.30	F=3.56, P<0.064	5.79%
1st Min	94.83±6.84	102.10±5.43	F=20.72,P<0.001	26.32%
3rd Min	91.56±6.75	97.70±4.68	F=16.7,P<0.001	22.36%
5th Min	88.76±6.03	92.76±4.00	F=9.14,P<0.001	13.62%

RESULTS

From the above Table No. 8.0 which gives the 5.79% of the total variance is accounted for by the treatment effects case of pre induction stage. The change in HR has been from placebo group 79.26±8.30 to 83.60±9.43 in Esmolol group at pre induction

The change in HR has been from placebo group 102.10±5.43 to 94.83±6.84 in Esmolol group at 1St Minute , 26.32% of the total variance is accounted for by the treatment effects case of pre induction stage.

The change in HR has been from placebo group 97.70±4.68 to 91.56±6.75 in Esmolol group at 3rd Minute , 22.36% of the total variance is accounted for by the treatment effects case of pre induction stage.

The change in HR has been from placebo group 92.76±4.00 to 88.76±6.03 in Esmolol group at 5th Minute, 13.62% of the total variance is accounted for by the treatment effects case of pre induction stage.

RESULTS:

Esmolol significantly attenuates the sympathetic response to laryngoscopy and intubation.

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