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A Comparative Study of Oral Clonidine and Intravenousesmolol for Attenuation of Pressor Response During Laryngoscopy and Endotracheal Intubation

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Abstract

Background: Endotracheal intubation and laryngoscopy are often associated with increased sympathetic response due to stimulation of laryngeal and tracheal sensory receptors. This can be harmful especially in patients who have cardiac issues, hypertension, etc. and can be associated with increased morbidity and mortality. Attenuation of pressor response can prevent sympathetic stimulation.

Aim: To evaluate and compare oral Clonidine and intravenous Esmolol for attenuation of pressor response during laryngoscopy and endotracheal intubation.

Materials and methods: 60 patients were divided into two groups after satisfying the inclusion and exclusion criteria. Group-A received clonidine orally at a dose of 150 mcg, around 75–90 minutes before elective surgery. Group-B received intravenous esmolol at a dose of 1.5mg/kg, 2 minutes prior to laryngoscopy. HR, SBP, DBP, MAP were recorded at time of shifting to operation theatre (T0), subsequent to administration of premedications (T1), prior to laryngoscopy (T2), subsequent to intubation (T3), at 1 minute (T4), 3 minutes (T5), 5 minutes (T6) and 10 minutes (T7) subsequent to intubation. Side effects if any were recorded.

Results: There was significant suppression of HR, SBP, DBP and MAP at T3, T4, T5, T6 and T7 in Group B that received Intravenous esmolol. There were no serious adverse events in either of the group.

Conclusion: Esmolol can be an effective pharmacological agent that can be used for attenuation of pressor response during laryngoscopy and endotracheal intubation. We suggest conducting similar study in patients with significant co-morbidities for a more comprehensive analysis.

Keywords: Pressor response; Esmolol; Clonidine; Endotracheal intubation.

Introduction

For maintaining a patent airway, laryngoscopy and endotracheal intubation are crucial procedures which an anaesthesiologist performs in day to day practice. Rield and brace in 1940,[1] were first to describe haemodynamic response to laryngoscopy and tracheal intubation. The pressor response to direct laryngoscopy (DL) and endotracheal intubation precipitating a significant increase in heart rate and systemic blood pressure is an established phenomenon and thus, a cause of concern for anesthesiologists all over.[2] King et al.[3] in 1951 described sympathetic hemodynamic response to laryngoscopy and endotracheal intubation. Direct laryngoscopy exerts a pressure over the tongue base that stimulates proprioceptors, resulting in a significant increase in sympathetic amines and hemodynamic parameters. Passage of the tube through the trachea further exaggerates this response by somato-visceral reflex followed

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by rapid regression of SBP and heart rate whereas plasma catecholamine concentrations regress more slowly.[3]

Clonidine is a partial agonist with high affinity and high intrinsic activity at alpha-2 receptors. It activates the alpha-2 receptor of the brain and spinal cord to decrease the sympathetic outflow, causing sedation, analgesia, hypotension and bradycardia without significant respiratory depression.[4] It is well absorbed after oral administration with peak plasma concentration in 75 to 90 minutes. Preoperative use decreases the intraoperative stress response by reducing the nociceptive transmission and decrease norepinephrine concentration in serum, provided haemodynamic stability.[5–6]

Esmolol is a Beta1-adrenoceptor blocker. It has a very short diffusion (2 minutes) and elimination half-life (9 minutes). Peak effects with bolus injections of esmolol are seen in 1–2 minutes.[7] Various workers have utilized esmolol to attenuate sympathetic vasopressor response associated with intubation.[8–9]

Considering both clonidine and esmolol have a suppressive action on activation of the sympathetic system, we evaluated their safety and efficacy in this study. We evaluated the attenuation of pressor actions by measuring and comparing heart rate, blood pressure and mean arterial pressure between two groups receiving either of the drugs at time of endotracheal intubation.

Materials and Methods

Institutional ethics committee clearance was obtained prior to start of the study. This prospective, randomized study was conducted for duration of 3 months in a tertiary care hospital. 60 patients willing to give informed consent (explained in native language) who satisfied inclusion and exclusion criteria were recruited in to the study.

Inclusion criteria:

- ASA grade I or II
- Patients above 18 years and below 65 years of age
- Patients of either gender
- Mallampati class I and II
- Patients willing to give informed consent for the study
- Patients with normal hemodynamic parameters prior to surgery
- Patients undergoing elective surgeries under general anesthesia.

Exclusion criteria:

- Patients with a difficult airway or difficult intubation
- Patients with significant cardiac, respiratory, renal, endocrine, nervous system disorders
- Patients with allergy to either of the study drugs.
- Patients with malignancies.

Patients were randomized in to 2 groups of 30 subjects each.

Group A: Clonidine group (n=30) will receive oral Clonidine 150 mcg 75–90 minutes before surgery.

Group B: Esmolol group (n=30) received intravenous esmolol 1.5 mg/kg 2 minutes before laryngoscopy and ETT intubation.

All patients were kept nil per oral (NPO) for a period of at least 6 hours prior to surgery to avoid the risk of aspiration. After shifting the patient on the operating table, all the monitors such as NIBP, pulse oximeter, ECG, etc will be connected to the patient. Baseline vital parameters such as systolic blood pressure (SBP), diastolic blood pressure (SBP), mean arterial blood pressure (MBP), SpO2, respiratory rate and ECG were recorded (T0). The study drugs were administered prior to intubation. The vital parameters were recorded once again after premedication (T1). Patients were pre-oxygenated for 3 minutes. This was followed by Inj. Propofol (2 mg/kg) given slowly till the eyelash reflex is lost followed by Succinylcholine (2 mg/kg). Vital parameters were recorded as (T2). Patients were intubated with cuffed Endotracheal tube. Air entry equal on both sides of the lungs was checked, cuff was inflated and tube fixed. Loading dose of Vecuronium 0.1 mg/kg i.v. was given. Anaesthesia was maintained with 65% Nitrous Oxide and 35% Oxygen mixture along with Isoflurane 0.8%–1% in Bains breathing circuit and controlled ventilation with intermittent doses of Vecuronium (0.08 mg/kg) as and when required by the patient. Post intubation vitals at 0, 1, 3, 5, 10 minutes (T3 to T7) were be recorded.

Results

Table 1: Evaluation of age.

Age	Group-A	Group-B
Mean	46.17	44.5
Std dev	7.03	4.8
Range	32 to 57 years	36 to 56 years
P value	0.288 (P>0.05) (Student's t-test)	
Inference	Non-significant difference in age between two groups	

Table 2: Gender.

Gender	Group-A	Group-B
Male	15	15
Female	15	15
P value (Chi-sq)	1	1
Inference	Equal number of male and female participation in both the groups	

Table 3: Evaluation of heart rate.

Heart rate	Group-A mean	SD	Group-B mean	SD	P value	Inference
T0	82.70	5.64	81.07	4.08	0.204	NS
T1	81.90	5.90	83.27	2.88	0.26	NS
T2	82.40	5.05	80.13	4.69	0.076	NS
T3	93.90	5.10	79.33	3.40	<0.001	S
T4	92.30	5.27	82.87	4.35	<0.001	S
T5	92.77	3.40	84.70	3.91	<0.001	S
T6	89.43	5.04	84.43	3.64	<0.001	S
T7	86.50	4.86	80.33	4.57	<0.001	S

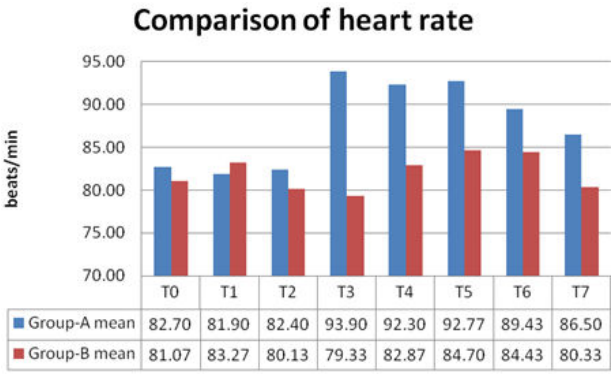


Table 4: Evaluation of SBP.

SBP	Group-A mean	SD	Group-B mean	SD	P value	Inference
T0	122.73	7.62	120.37	7.65	0.234	NS
T1	119.73	6.29	121.10	8.26	0.474	NS
T2	125.17	6.64	119.03	4.84	<0.001	S
T3	125.13	8.24	118.47	5.42	<0.001	S
T4	128.07	5.96	117.07	4.69	<0.001	S
T5	130.90	5.60	119.83	7.87	<0.001	S
T6	127.50	3.05	118.10	5.47	<0.001	S
T7	123.10	2.35	117.67	6.32	<0.001	S

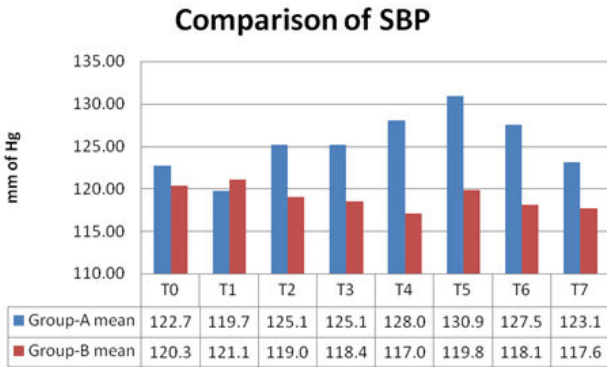


Table 5: Evaluation of DBP.

DBP	Group-A mean	SD	Group-B mean	SD	P value	Inference
T0	80.27	3.68	79.10	5.97	0.366	NS
T1	80.13	3.40	78.17	6.74	0.16	NS
T2	79.83	3.90	74.57	5.15	<0.001	S
T3	84.70	3.31	78.17	4.10	<0.001	S
T4	84.27	5.33	79.63	3.74	<0.001	S
T5	82.20	4.64	76.93	4.43	<0.001	S
T6	81.17	5.40	76.17	5.14	<0.001	S
T7	82.10	4.99	75.43	4.75	<0.001	S

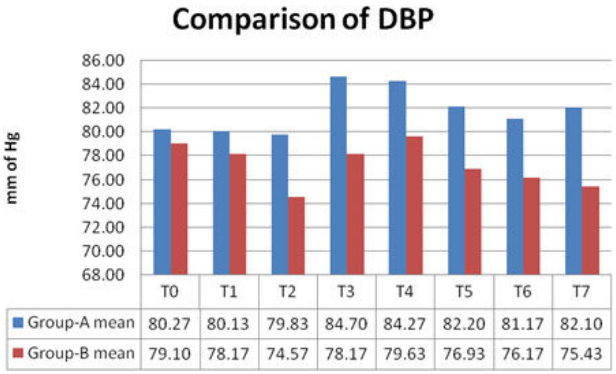
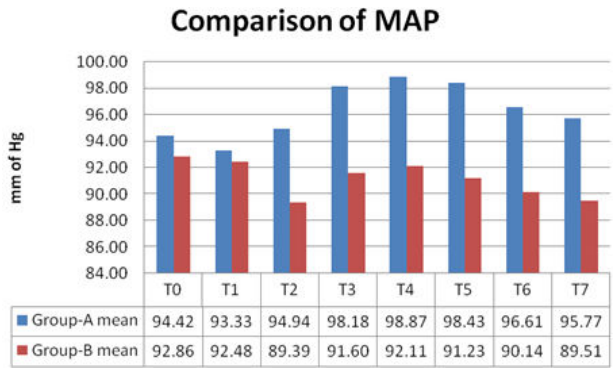


Table 6: Evaluation of Mean arterial pressure.

MAP	Group-A mean	SD	Group-B mean	SD	P value	Inference
T0	94.42	3.52	92.86	6.42	0.247	NS
T1	93.33	3.27	92.48	6.59	0.527	NS
T2	94.94	4.12	89.39	3.76	<0.001	S
T3	98.18	3.63	91.60	4.07	<0.001	S
T4	98.87	3.79	92.11	3.20	<0.001	S
T5	98.43	3.85	91.23	3.45	<0.001	S
T6	96.61	4.17	90.14	4.27	<0.001	S
T7	95.77	3.54	89.51	3.75	<0.001	S



Discussion

The patients were compared by age, gender and ASA groups. The mean age in group A was 46.17 years whereas it was 44.5 years in Group B (Table 1). The P value was non significant at 0.288 and hence Non-significant difference in age between

two groups was found. Equal number of patients had ASA grade 1 and 2 in both the groups at 17 and 13 respectively. Both the groups had equal number of gender participation at 15 males and 15 females in each group (Table 2). The baseline and T1 values of all vital parameters (heart rate, blood pressure, mean arterial pressure) was non significantly different when compared between the two groups. In group A that received oral clonidine the heart rate was significantly higher at time intervals T3 to T7 when compared to Group B that received intravenous esmolol (Table 3). The systolic blood pressure, diastolic blood pressure and the mean arterial blood pressure were similarly higher (significant $P<0.05$) at time intervals T2 to T7 in Group A that received oral clonidine when compared to Group B. These findings are suggestive of elevated vasopressor response in Group A when compared to Group B (Table 4-6). In our study Intravenous Esmolol in the dosage of 1.5 mcg/kg prior to laryngoscopy provided an adequate attenuation of pressor response to laryngoscopy and subsequent endotracheal intubation. No serious adverse events were noted in the study however, one patient in Group B had bradycardia (HR:58 bpm) that resolved without any intervention.

Various workers have utilized either of the drugs to suppress stress response in form of increase in heart rate and blood pressure at time of endotracheal intubation. Yadav S et al.[10] evaluated efficacy of single intravenous dose of esmolol hydrochloride in attenuation of hemodynamic response of laryngoscopy and endotracheal intubation. They noted that in dose of 1 mg/kg and 1.5 mg/kg drug effectively controlled post intubation rise in pulse rate whereas dose required to control MAP is higher (1.5 mg/kg) and without any serious side effects. We used a dose of 1.5 mg/kg in our study. Swargiri K et al.[11] noted attenuation of vasopressor response of at a higher dose of 3 mg/kg 3 minutes prior to laryngoscopy in form of intravenous bolus. On contrary, Gupta HB et al.[12] compared intravenous dexmedetomidine with esmolol (1 mg/kg dose) in suppressing vasopressor response at time of intubation and noted dexmedetomidine to be superior to esmolol. Rathore P et al.[13] compared oral pregabalin and clonidine for control of hemodynamic response to laryngoscopy and intubation. Authors noted that clonidine provided adequate control of hemodynamic response and it was superior to pregabalin. Singh S[14] noted that both oral and intravenous clonidine can be useful in attenuation of pressor response in patients undergoing elective surgeries with ASA grade I and II in general anesthesia requiring endotracheal intubation. The effect was more pronounced with intravenous clonidine without any adverse events.

Limitations

- Patients with ASA grade III and other co-morbidities were not included.
- Sample size was small and cannot be extrapolated.
- The study was not blinded with a chance of bias.
- The cost-effectiveness of the study drugs was not conducted.
- Effect beyond 10 minutes post intubation was not noted.

Conclusion

Esmolol can be an effective pharmacological agent that can be used for attenuation of pressor response during laryngoscopy and endotracheal intubation. Also no significant or serious side effects were identified in the study. We suggest conducting similar study with higher patient participation and also in patients with significant co-morbidities for a more comprehensive analysis. We also suggest comparing intravenous esmolol at various doses and in comparison with other drugs used for this purpose such as dexmedetomidine, labetolol, etc.

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