ORIGINAL RESEARCH PAPER

Medicine

A CLINICAL STUDY OF COMPARISION OF CLONIDINE AND METOPROLOL IN ATTENUATION OF INTUBATION RESPONSE

KEY WORDS: Clonidine, Metoprolol, Attenuation, Pressor response, Laryngoscopy, Premedication.

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ABSTRACT

Background: The sequence of induction of anaesthesia, laryngoscopy and tracheal intubation are associated with marked haemodynamic changes and autonomic reflex activity which may be a cause of concern in many high risk patients. **Aim:** Objective of this study is to compare effectiveness of clonidine & metoprolol in attenuation of intubation response. **Methods:** In this study, 60 ASA I and II status normotensive patients scheduled for elective surgical procedure were selected randomly and divided into two groups of 30 each. All the patients received standard premedication Tab. Alprazolam 0.5 mg at bed time and were fasted for 12 hours. Group I received 3 µgm/kg I.V Clonidine and Group II 2 mg/ kg Metoprolol 90 seconds before intubation. **Results:** After intubation, Clonidine caused more better control in Heart rate than the pre-op value and was also very effective than Metoprolol in minimizing the rise in BP after intubation which is statistically significant and desirable. **Conclusion:** Though Clonidine, Metoprolol were effective in obtunding the raise in blood pressure (SBP, DBP, MAP), Clonidine was much better than Metoprolol in controlling blood pressure.

INTRODUCTION

Endotracheal intubation is translaryngeal placement of endotracheal tube into the trachea via nose or mouth. Endotracheal intubation and anaesthesia have become integral part of anaesthesiologist's contribution to the patient care.Laryngoscopy and endotracheal intubation are the most stressful conditions, the patient is subjected to, during general anaesthesia.The predominant response to laryngoscopy and intubation under anaesthesia are HTN, tachycardia and depression of LV ejection fraction.

The mechanical stimulation of upper respiratory tract induced reflex cardiovascular response associated with enhanced neuronal activity in cervical sympathetic fibers.[1] HTN seen in these patients is due to increased cardiac output rather than due to increased systemic vascular resistance and is associated with transient increase in central venous pressure .[2]

The usual circulatory response to laryngeal and tracheal stimulation are tachycardia, HTN and arrythmia.[2]These are associated with increased catecholmines .[3]

In normotensive patients there was a moderate increase in Nor-adrenaline levels where as in HTN patient's there was a three fold increase and also rise in adrenaline levels.[4]

Normal patients usually tolerate this sympathetic response but these changes can adversely effect the previously compromised cerebral and coronary circulations and can be catastrophic .So, attentuation of this haemodynamic response will be laudible objective and is clearly indicated to obtund this response. Hence various techniques have been used to attenuate this haemodynamic response to laryngoscopy and intubation.Pharmacological attempts included topical anaesthesia of oropharynx, IV Lignocaine, Beta blockers, Vasodilators, Opiods, deep plane of general anaesthesia,Isosorbide dinitrate, PG-E1, CCB, propofol, MgSo4, etc..

Attenuation of intubation was studied with various techniques like deep inhalational, deep general anaesthesia and with various drugs like midazolam, morphine, fentanyl, sufentanyl, remifentanyl , esmolol, propofol, lignocaine etc. and were proven to be effective.Though these drugs belong to different groups and have different mechanisms of actions like anxiolysis, analgesia, myocardial depression, suppression of airway reflexes, deepening the level of anaesthesia etc. they all can effectively attenuate haemodynamic response to laryngoscopy and intubation.

Our present study is to compare the effectiveness of Clonidine and Metoprolol in attenuation of intubation response.

AIM AND OBJECTIVES

The present study is under taken to evaluate the efficacy of clonidine and metoprolol in attenuating the haemodynamic response to laryngoscopy and intubation.

METHODOLOGY

This study is undertaken in 60 Normotensive patients aged 15-60 years of either sex belonging to ASA I & II, Mallampati class I & II undergoing various elective non cardiac surgeries conducted at MNR Medical college, sangareddy.

The patients are randomly selected and made into two groups of 30 each . Group I received clonidine and Group II Metoprolol to compare their action mentioned in the aim of study.

Pre - anaesthetic checkup with detailed history and thorough examination was done a day before surgery. Basic investigations such as Complete blood picture, Blood sugar, Blood urea, Serum Creatinine, Chest X-ray, Complete urine examination was done. Patients with any abnormal reports were excluded from the study. An informed consent was taken from all the patients and institutional ethical committee's approval was obtained for the study. All the patients were given Tab. Alprazolam 0.5mg at bed time and were fasting for 12hrs. On the day of surgery patients were wheeled into the operation theatre & IV access was established. Blood pressure monitored by Non invasive BP monitor and SPO_2 by pulse-oximetry. ECG leads applied and connected to the monitor. All the medications like premedication, induction, Neuromuscular blockers except the study drug are

standardized. The patients were premedicated with Inj.Tramadol 2mg/kg. Inj.Glycopyrrolate 4µ/kg, Inj. Odansetron 4mg and Inj. Ranitidine 50mg IV. Pre-operative vitals including HR, SBP, DBP and MAP were noted in all patients. Patients in both the groups received Inj.Thiopentone sodium 5mg/kg & Inj.Vecuronium bromide 0.08mg/kg .After 1min of induction, the patients in Group I received clonidine 3µ/IV bolus and Metoprolol. 0.2mg/IV bolus in Group II. Controlled ventilation was continued manually with 67% Nitrous oxide and 33% Oxygen. Vitals were recorded 1min and 2min after the study drug was administered. After giving 4-5 breaths with 100% O2, laryngoscopy was done with Macintosh curved blade laryngoscope and intubation was done with appropriate sized ETT without lubrication. Anticipated difficult intubation cases were deleted from the study.The duration of laryngoscopy did not exceed 30 sec.

Vital data were recorded 1min, 3min & 5min after intubation. The patients were connected to closed circuit and controlled ventilation given with 67% Nitrous oxide and 33% O2 through out the surgical procedure. Monitoring was continued and patients were extubated and shifted after complete recovery. Patients were observed for 12 hrs post operatively.

OBSERVATIONS AND RESULTS

The anthropometric details of the patients of both the groups were:

Group I consisted of 30 patients with 15 male and 15 female patients with an average age of 39.14 years and average weight of 56.93 Kgs. Group II consisted of 30 patients with 14 male and 16 female with average age of 34.16 and average weight of 55.14 Kgs.

Anthropometric Details Of The Patients (TABLE- 1) :

AGE IN YEARS	GROUP I 39.14 (13.05)	GROUP II 34.16 (11.91)
Weight in Kgs.	56.93 (4.74)	55.14 (5.27)

- Mean values with standard deviation in brackets.
- There was no statistically significant difference between the 2 groups.

Pre Operative Vitals Are Shown In The Following Table (Table -2) :

	GROUP I	GROUP II
HR	88.54(7.00)	88.87 (9.47)
SBP	132.1 (13.85)	130.7 (11.65)
DBP	81.64 (7.47)	82.46 (6.99)
MAP	98.13 (6.94)	99.24 (7.08)

- Mean values with standard deviation in brackets.
- There is no significant statistical difference between the 2 groups.
- Calculated by unpaired student 't' test. ($p>0.05$).

Haemodynamic Parameters After The Study Drug Clonidine/Metoprolol Are Given In The Following Tables.

1 Minutes After Intubation (Table -3) :

	GROUP I	GROUP II	'p' value
HR	73.8 (7.09)	88.4 (11.19)	0.0001
SBP	106.3 (11)	137.3 (13.02)	0.0001
DBP	66 (9.90)	89.4 (8.76)	0.0001
MAP	79.7 (7.91)	105.7 (9.03)	0.0001

- Mean values with standard deviation in brackets.
- There is significant statistical difference between the 2 groups
- Carried out by unpaired student 't' test.
- $p < 0.05$ is statistically significant.

3 Minutes After Intubation (TABLE- 4) :

	GROUP I	GROUP II	'p' value
HR	77.3 (7.07)	82.2 (11.03)	0.0438
SBP	110 (11.2)	132.1 (15.26)	0.0001
DBP	69.3 (10.96)	82.3 (15.75)	0.0001
MAP	83.1 (8.76)	101.2 (8.46)	0.0001

- Mean with standard deviation in brackets.
- $p < 0.05$ is statistically significant.

5 Min After Intubation (TABLE – 5) :

	GROUP I	GROUPII	'p' value
HR	78.5 (6.92)	80.6 (9.96)	0.3396
SBP	111 (11.1)	127.7 (9.66)	0.001
DBP	68.5 (10)	82 (8.09)	0.0001
MAP	83.03 (7.95)	97.7 (7.64)	0.001

- Mean with standard deviation in brackets.
- $p < 0.05$ is statistically significant, except for HR .

The HR which was 88.5 in Group I has decreased to 73.8 in the 1st minute after intubation, then to 77.3 after 3rd minute and then to 78.53 after 5th minute. SBP, DBP, MAP which were 132.1 mm, 81.6 mm, and 98.1 mm have decreased to 106.3 mm, 66 mm and 79 mm after 1st minute ; 110 mm, 69 mm and 83.1 mm after 3rd minute and to 111 mm, 68.5 mm and 83 mm after 5 minutes after intubation respectively.

In Group II the heart rate after 1 minute was 88.4 and then decreased to 82.2 after 3 min and 80.6 after 5 minutes after intubation.SBP, DBP, MAP pre op are 130.7 mm, 82.4mm and 99.2 mm. They have increased to 137.3mm, 89.4 mm and 105.7 mm after 1st minute. After 3 minutes the values are 132.1 mm, 82.3 mm and 101.2 mm. After 5 minutes the values are 127.7mm, 82 mm and 97.7 mm respectively.

DISCUSSION

During the process of Ether anaesthesia, the last reflexes to be suppressed in stage III and plane III were laryngeal, carinal and sphincter reflexes. So, the trachea bronchial tree is the one of the most sensitive structures in the human body. It is natural that any stimulus at trachea could lead to intense sympathetic response.

Laryngoscopy and intubation are unavoidable events for a patient undergoing surgery under general anaesthesia for major cases and this laryngoscopy and intubation produces an increase of 25 -50 % in heart rate, blood pressure, dysrrhythmias peaking at 1 minute and returning to base line at 5 to 10 minutes.[5]

These sudden changes are not of great clinical significance in a normal individual with a good coronary vascular bed and no narrowing due to atheroma. But the sudden exaggeration of these haemodynamic changes can be detrimental in patients with hypertension, myocardial ischemia and infarction and in patients with increased intra cranial tension and altered blood gases.[6]

The methods advocated to suppress the response to laryngoscopy and intubation have utilized one of the following means.

They are :
Afferent blockade : Topical lignocaine, IV lignocaine
Central blockade : By deep planes of anaesthesia (IV Anaesthetics, Opiods, Midazolam etc).
By central autonomic blockade (Droperidol).
Efferent blockade : a) Peripheral vasodilators
- SNP, NTG, Hydralazine
b) Beta blockers
- Propranolol, Metoprolol, Esmolol
c) Calcium channel blockers

In our present study we have compared the effectiveness of Clonidine and Metoprolol in attenuation of hemodynamic response to intubation - after Clonidine 's established action on central blockade and Metoprolol's action on efferent blockade.

It is well known that clonidine decreases arterial blood pressure and heart rate by enhancing the parasympathetic nervous system activity and decreasing sympathetic nervous system activity at brain stem sites.

M Laisalmi et al used 4.5 μ/kg of intravenous clonidine or saline and studied the effects on haemodynamics, neuroendocrine response and renal parameters in patients undergoing laparoscopic cholecystectomy. They observed that clonidine decreased sympathetic tone, blood pressure and heart rate and also diminished the need for intra-operative analgesia. They conclude that clonidine enabled stable haemodynamics and prevented activation of RAAS.[7]

Malek et all used 0.15mg clonidine as infusion 15 minutes before laproscopic Cholecystectomy and 0.15 mg clonidine by intramuscular route 60-90 min before surgery and studied the haemodynamic changes and their suppression with clonidine premedication. They observed a significant drop in the incidence of both SBP, DBP during procedure after clonidine administration in both routes and recommend intravenous clonidine use as a routine procedure before laparoscopic cholecystectomy.[8]

Peter J Kulka studied the dose response effects of intravenous clonidine on stress response in CABG patients. They used 0, 2, 4, 0r 6 μ/kg clonidine as an intravenous infusion 30 min prior to induction of anaesthesia. They observed that clonidine 4 and 6 μ/kg significantly attenuated haemodynamic and adrenergic response to stress. They opined that clonidine 4microgm/kg intravenous was the appropriate dose to attenuate the stress response to laryngoscopy in CABG patients.[9]

Ghignone et al used clonidine 5microgm/kg per orally and studied the effects on perioperative haemodynamics and isoflurane requirements in elective surgeries. They observed clonidine pre treatment resulted in a reduction of pre operative SBP, DBP, and blunted the cardiovascular response to intubation. They opined that pre operative administration of clonidine results in improved perioperative haemodynamic stability in patients with mild to moderate arterial hypertension and in a reduction of anaesthetic requirement.[10]

Dr. Dipek L Raval et al used tablet clonidine 4 microgram/kg and studied the attenuation of haemodynamic response to laryngoscopy and intubation. They conclude that premedication with oral clonidine produces less sedation and same level of anxiolysis as compared to diazepam with regards to its anti sialogague effect and blunting haemodynamic response during laryngoscopy and endo tracheal intubation.[11]

Metoprolol is a cardio selective Beta blocker with rapid onset and relatively short duration of action, (½ life 3-7 hrs).Coleman A and Jordanc shown that Metoprolol can effectively prevent rise in heart rate and blood pressure.[12]
Issur singh and GP Dureja compared oral Metoprolol with IV lignocaine and concluded that metoprolol is effective in attenuating cardiovascular response to laryngoscopy and intubation.[13]

Liu Y, Huang CL, He M, Zhang LN, Cai HW, Guo QL. Studied the Influences of perioperative Metoprolol on haemodynamic and myocardial ischemia in elderly patients undergoing noncardiac surgery and concluded that Intravenous administration of 0.5 mg and 1.5 mg Metoprolol before the induction of anesthesia and after the tracheal intubation has several advantages, including the decrease of myocardial oxygen consumption, the improvement of hemodynamic stability, and the lowering peri operative incidence of myocardial ischemia and damage.[14]

So, Metoprolol by virtue of its Beta receptor blockade attenuates intubation response.

HEART RATE

The HR which was in pre op period was 88.5 in group I. It has decreased to 73.8 in the 1st minute after intubation, then to 77.3 after 3rd minute and then to 78.53 after 5th minute .There was significant decrease in HR after intubation.

In Group II the heart rate in the pre operative period was 88.86. After 1 minute it reduced to 88.4 , 82.2 after 3 minutes and to 80.6 after 5 minutes after intubation. The fall in values of HR were lower than that of Clonidine.

The decrease in heart rate with clonidine was statistically significant after 1 minute and 3 minutes after intubation when compared to Metoprolol. At 5 minutes the fall in HR was not significant.

Blood Pressure Response

The SBP, DBP, and MAP in pre-operative period in group I were 132.1 mm, 81.64 mm and 98.13 mm respectively. They have reduced to 106.3 mm ,66 mm, 79.7 mm after 1 minute ; 110 mm, 69.3 mm and 83.1 mm after 3 minutes ; and then to 111 mm, 68.5 mm and 83 mm after 5 minutes after intubation.

There was significant decrease in SBP, DBP and MAP after intubation.

In Group II SBP, DBP and MAP in the pre op period were 130.7 mm, 82.46 mm and 99.23 mm respectively . They increased to 137.3 mm, 89.4 mm and 105.7 mm after 1 minute ; 132.1 mm , 82.3 mm, and 101.2 mm after 3 minutes ; then reduced to 127.7 mm, 82 mm, and 97.7 mm after 5 minutes after intubation. The fall in values of SBP, DBP and MAP were lower than that of Clonidine.

Though the raise in SBP, DBP, MAP was seen after intubation, it was only transient. However it was significantly lower than those without any attenuating agent.

Attenuation of blood pressure due to intubation was better with Clonidine than Metoprolol.

Side Effects

In both the groups, we have not encountered any complication like bradycardia, hypotension, delayed recovery etc.

Limitations Of Our Study

Our study was done on a small group of 60 patients in each of the groups, all patients studied belonged to ASA 1 and 2. Most patients were in the middle age group with oldest being 60 years. Patients with co-morbidities like hypertension and diabetes were well controlled before surgery. Hence the advantage of using clonidine in hypertensives with inadequate control could not be appreciated.

CONCLUSION

In our study of comparing Clonidine and Metoprolol in attenuation of intubation response, we concluded that:

- Clonidine and Metoprolol causes decreases in heart rate and blood pressure.
- Both Clonidine and Metoprolol were effective in attenuation of haemodynamic response to laryngoscopy and intubation.
- Clonidine caused more better control in Heart rate than the pre op value and was also very effective than Metoprolol in minimizing the rise in BP after intubation which is statistically significant and desirable.
- Though Clonidine, Metoprolol were effective in obtunding the raise in blood pressure (SBP, DBP, MAP), Clonidine was much better than Metoprolol in controlling blood pressure.
- Both drugs are safe without any side effects or

complications like bradycardia, hypotension etc., in the given dosages.

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