Azhar and Gauhar, General Med 2015, 3:2
DOI; 10.4172/2327-5146.1000170

General Medicine: Open Access

Research Article Open Access

Haemodynamic Response to Tracheal Extubation: Verapamil versus Metoprolol

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Abstract

Background: Sympathetic response associated with tracheal extubation is recognized as a potential cause for a number of complications in surgical patients during the perioperative period. Various methods are used in normotensive patients to attenuate tracheal extubation response and all these methods are associated with adverse effects like hypotension and bradycardia. The aim of the study was to examine the effect of metoprolol in comparison with verapamil to attenuate the hemodynamic response at tracheal tube extubation.

Methods: A total number of 90 hypertensive patients with systolic blood pressure below 150 mm Hg and diastolic blood pressure below 90 mm Hg were randomly divided into three groups named as placebo (A), verapamil (B) and metoprolol (C). Heart rate and blood pressure trends were monitored at different time intervals.

Results: Hemodynamic responses at the time of extubation including heart rate, systolic blood pressure and diastolic blood pressure were well controlled in the metoprolol group as compared to placebo and verapamil groups. Adverse effects such as bradycardia and hypotension were not observed in metoprolol group.

Conclusion: Metoprolol is more effective as compared to placebo and verapamil in attenuating the hemodynamic response to tracheal extubation in hypertensive patients.

Keywords: Extubation; Hypertension; Metoprolol; Verapamil

Introduction

Emergence or recovery from general anesthesia is a stressful period and is often accompanied by a significant increase in arterial blood pressure and heart rate [1]. Tracheal intubation is associated with an increase in heart rate and blood pressure, however, at the emergence of anesthesia additional haemodynamic responses to pain makes tracheal extubation more complicated [2]. It is evident from the literature that these haemodynamic changes may cause an increase in myocardial oxygen demand resulting in myocardial ischemia and dysrhythmias in patients having coronary artery disease or hypertension [3]. In addition, disrupted vascular suture lines, elevated intra ocular pressure and intracranial pressure also have the potential to increase morbidities.

Patients with pre-existing hypertension exhibit an increase in blood pressure at the time of tracheal intubation and extubation due to non-compliant vasculature, elevated peripheral vascular tone, high level of baseline endogenous sympathetic nervous system activity and impaired baroreceptor control of heart rate. Several medications have been used to attenuate the extubation responses [4-6]. Verapamil has been used before extubation to control the hemodynamic responses; however, hypotension and bradycardia have frequently occurred with its use [7]. Significant hypotension following use of diltiazem has also been reported in the literature when used to attenuate extubation response [7].

Metoprolol, a β-blocker, has negative inotropic and chronotropic effects. This is readily available in our country and being frequently used by anaesthesiologists in the intensive care unit and perioperative period.

Methods and Materials

It was a randomized double blinded controlled trial. After approval from the institutional ethical review committee, and attaining the written informed consent, 90 ASA II hypertensive patients were recruited in this trial. Hypertensive patients, age between 35-65 years, arterial pressure <150/90 mm Hg and heart rate >60 beats/min undergoing total abdominal hysterectomy were included. Patients with known asthma and ischemic heart disease and having more than one anti-hypertensive medication were not included. Those who were treated intra-operatively (after induction until the start of the study) by antihypertensive/ vasopressor drugs were also excluded from the trial.

Patients were randomized for three treatment groups. Ninety slips of paper were taken and labeled as Group A placebo (5 ml), Group B verapamil 0.05 mg/kg (5 ml) and Group C metoprolol 0.02 mg/kg (5 ml). These slips were placed in an envelope. One slip was raised for each patient by an assistant who was not involved in taking observation during the study. Patients and the primary investigator (PI) injecting the drug and collecting the data were blinded about the drug being used. As for blinding purpose the medications were prepared beforehand by the pharmacist and the identities were unknown to the primary investigator (PI). Data was recorded in the proforma over a period of one year by the PI who was blinded to the drugs used. Statistical analysis was performed through SPSS version-12.0.

All patients were pre-medicated with tablet midazolam 7.5 mg one hour preoperatively. Routine antihypertensive medication was continued preoperatively. General anaesthesia with tracheal intubation and control mode of ventilation was delivered to all patients. In the operating room the standard monitoring was applied. Heart rate (HR) through ECG lead II, non-invasive blood pressure (NIBP), pulse oximetry, end-tidal carbon dioxide ($ETCO_2$) was monitored. Patients

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Received October 22, 2014; **Accepted** March 04, 2015; **Published** March 10, 2015.

Citation: Azhar R, Gauhar A (2015) Haemodynamic Response to Tracheal Extubation: Verapamil versus Metoprolol. General Med 3: 170. doi: 10.4172/2327-5146.1000170

were pre oxygenated for three minutes with a flow rate of 5-6 litres/min on the circle breathing system. Anaesthesia was induced with sodium thiopental 5-6 mg/kg, atracurium 0.5-0.6 mg/kg and fentanyl 2-2.5 µg/kg to facilitate tracheal intubation. The maintenance was then completed with O_2 and N_2O, 40% and 60% respectively. Intraoperative analgesia was maintained with morphine boluses while muscle relaxation was maintained by intermittent boluses of atracurium.

After surgery (last stitch) isoflurane and nitrous oxide was discontinued and muscle relaxation was reversed (2-3 on TOF) with neostigmine 2.5 mg and glycopyrrolate 0.4 mg. Two minutes later, metoprolol, verapamil or placebo was given i/v according to the randomization. The trachea was then extubated after the administration of the study drug while making sure that the patient was opening eyes on command and spontaneously breathing to maintain $ETCO_2$ less than 45 mm Hg.

Immediately, after tracheal extubation 100% oxygen was given via face mask for 3-5 minutes. Values of SBP, DBP, and HR immediately before induction (baseline), at the completion of surgery, time of reversal, one minute after reversal, time of study medication and ten minutes after extubation were recorded. Data were recorded on the proforma by the PI who was blinded to the drugs being used.

Statistical analysis was performed through SPSS version-12.0. Hemodynamic response including SBP, DBP and HR were presented by Mean ± S.D. These parameters at various time durations were compared by applying Repeated Measures Analysis of Variance (ANOVA) and post hoc multiple comparisons test between groups, bonferroni was used. P-value ≤ 0.05 was considered to be statistically significant.

Results

A total of 90 patients were enrolled in the study. There were found no demographic difference between the groups (Table 1). For pre-operative anti-hypertensive drugs the difference among all three groups was statistically insignificant (Table 2).

Heart rate at induction of anaesthesia, completion of surgery, time of reversal and study medication was not statistically significant, (p=0.25). In verapamil group (B), an increase in HR was observed until extubation. After extubation the HR started settling down towards the baseline. In metoprolol group (C), HR decreased after 1 min with maximum change observed at 4 minutes after extubation and HR did not decrease below the baseline at any point. In placebo group (A), HR started increasing at the time of reversal; the maximum increase observed at 1 min after extubation, and it remained at higher level until 10 minutes after extubation. This increase was significant when compared with the other two groups (Figure 1).

The systolic blood pressure (SBP) at the base line, time of reversal and study medication was statistically insignificant, among all three groups. SBP was found higher than the base line level in placebo and verapamil group after medication until 10 minutes of extubation. However, in metoprolol group, it was either dropped or remained near baseline SBP. This finding was statistically significant (p≤0.05). In verapamil group, the maximum drop in SBP was observed at 5 minutes after extubation. While in metoprolol group it was observed at the time of extubation and these changes were not below the baseline at any point (Figure 2).

The diastolic blood pressure (DBP) at base line, time of reversal and study medication was statistically insignificant in all three groups. After study medication, the mean DBP was well controlled in metoprolol group as compared to the other two groups. The difference was statistically significant (p=0.000) (Figure 3).

The time between giving a reversal to tracheal tube extubation in the placebo group was 5.77 ± (1.8) minutes, in verapamil group 5.57 ± (1.67) minutes and in metoprolol group 5.50 ± (1.66) minutes. The difference among the groups was statistically insignificant (p=0.18).

Patients in all three groups remained hemodynamically stable without developing clinically significant hypotension, bradycardia or hypertension.

Patients who were on angiotensin-converting enzyme inhibitors (ACEI) as their routine antihypertensive medication, were significantly higher in metoprolol group (p=0.036).

Discussion

Tracheal and laryngeal receptors stimulation during tracheal tube extubation results in the release of catecholamines leading to increase in HR and BP. This sudden increase in hemodynamics following tracheal extubation may lead to harmful effects in patients with cerebral or cardiovascular diseases. Patients with hypertension shows exaggerated cardiovascular responses to airway management [2].

It is believed that extubation response is under treated which particularly in hypertensive patients may result in post-operative

Variables	Metoprolol n=30	Verapamil n=30	Placebo n=30	P-Value
Age (Years)	48.7 ± 6.99	46.2 ± 6.77	46.9 ± 5.77	0.33
Weight (Kg)	64.9 ± 9.9	68.1 ± 10.06	65.06 ± 11.6	0.26
Height (cm)	154.9 ± 5.2	155.06 ± 5.1	156.1 ± 4.9	0.21

Table 1: Comparison of demographic characteristics among the groups.

Name of antihypertensive medication	Placebo (n=30)	Verapamil (n=30)	Metoprolol (n=30)	P- value
β-blockers	15	15	16	0.231
Ca channel antagonists	05	05	03	0.201
ACE inhibitors	08	05	11	0.036
None	02	05	__	0.07

Table 2: Pre-operative antihypertensive medications in three groups.

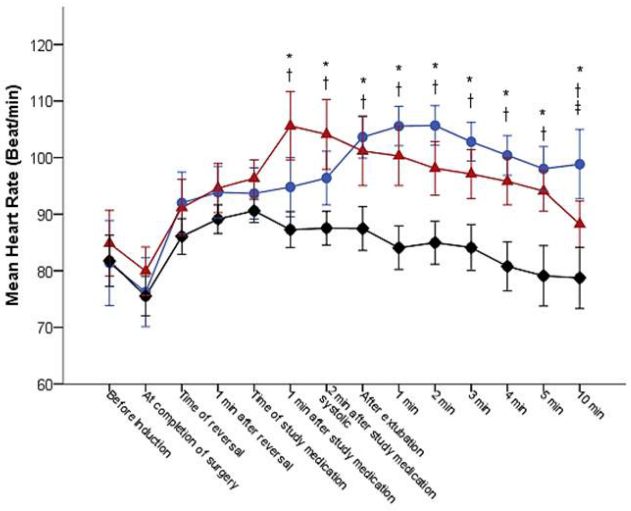

Figure 1: Comparison of mean Hear rate among Placebo (● ●), Verapamil (▲ ▲) and Metoprolol (◆ ◆). [Placebo vs. Metoprolol * p<0.05; Verapamil vs. Metoprolol †p<0.05 Placebo vs. Verapamil ‡p<0.05].

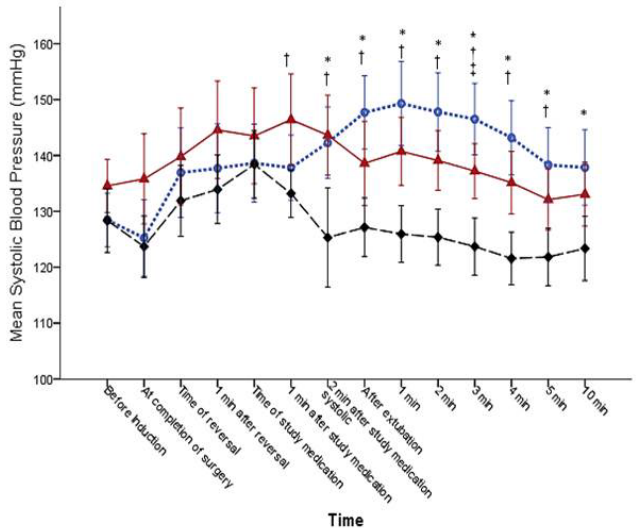

Figure 2: Comparison of mean systolic blood Pressure among Placebo (● ●), Verapamil (▲ ▲) and Metoprolol (◆ ◆). [Placebo vs. Metoprolol *p<0.05; Verapamil vs. Metoprolol †p<0.05 Placebo vs. Verapamil ‡p<0.05].

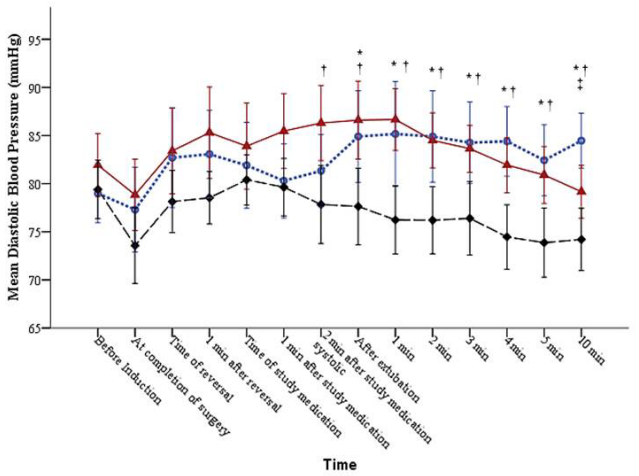

Figure 3: Comparison of mean Diastolic blood Pressure among Placebo (● ●), Verapamil (▲ ▲) and Metoprolol (◆ ◆). [Placebo vs. Metoprolol *p<0.05; Verapamil vs. Metoprolol †p<0.05 Placebo vs. Verapamil ‡p<0.05].

increase myocardial demand leading to myocardial ischemia. Based on these observations this trial was planned.

In the past two decades, several medications have been used to attenuate the hemodynamic response to tracheal tube extubation with varying level of success. These include narcotics, calcium channel & beta blockers and vasodilators, etc. Inhibition of norepinephrine release at postganglionic sympathetic nerve junctions is a well-established mechanism [8-13] of Metoprolol affecting SBP and HR however Verapamil, being a calcium channel blocker would not be expected to have this effect [14].

Metoprolol has been used for various anaesthetic purposes, including an antihypertensive agent, in the management of arrhythmias, in patients with alcohol with drawl syndrome and in hyperthyroid patients. The use of metoprolol to attenuate the haemodynamic responses to tracheal extubation has been studied in mixed sample population, [6] i.e. in non-hypertensive and hypertensive patients in previous studies. However, any study on metoprolol that aids in the reduction of haemodynamic responses exclusively in hypertensive patients is not in our knowledge yet.

In this study, metoprolol was used for the reduction of haemodynamic responses to tracheal extubation in hypertensive patients and less side-effect were observed and compared with other agents used in previous studies.

In this study the demographic data and duration from reversal to tracheal tube extubation were statistically insignificant in all three groups. However, it was found that the metoprolol is effective in decreasing the HR as compared to placebo and verapamil group, (p=<0.05).

We also found that metoprolol effectively controls the BP, both systolic and diastolic, at the time of extubation as compared to placebo and verapamil and this difference was statistically significant $p \leq 0.05$. In the study none of the patients developed hypotension or bradycardia as reported in a previous study [6]. It may be due to our patient population i.e. known hypertensive, whereas in the previous study the response was evaluated in non-hypertensive patients.

Another important finding of the study was the quick onset of metoprolol as compared to verapamil which in clinical scenario of extubation is very relevant. The dropping of heart rate towards the baseline in the verapamil group was noticed, though its delayed onset and peak effect might have missed the most desirable time in the extubation process.

Pre-operative anti-hypertensive medications types and requirements are statistically insignificant in this study. Nonetheless, it is obvious from the data that ACE- inhibitor use was higher in metoprolol group. This might also open the new area of thought that patients on ACE-inhibitors when treated with beta blockers at extubation have a more predictable and effective response as compared to other pre-operative anti-hypertensive medications.

Considering available erratic data in this area of tracheal extubation, it is strongly believed that the study findings are beneficial additions in common clinical scenario of tracheal extubation.

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