ORIGINAL ARTICLE

Comparison of hemodynamic responses by IV labetalol and IV lidocaine at the time of tracheal extubation: A randomized controlled trial

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Abstract

Objective: The aim of this study is to compare the hemodynamic responses caused by labetalol and lidocaine during tracheal extubation.

Study design: Randomized controlled trial.

Place and duration of study: Jinnah Postgraduate and Medical Center, Karachi, from 5th September 2018 to 4th March 2019.

Material and Methods: This was conducted in neuro-surgical operative rooms. A total of 124 patients undergoing craniotomies for space-occupying lesions under general endotracheal tube anesthesia of age between 18–65 years of either gender were included. Patients with sinus bradycardia or heart block, congestive heart failure, and asthma were excluded. All patients had their pre and post-operative vital signs (BP, HR, and MAP) recorded. Upon discontinuation of the inhalational agent bolus of labetalol 0.1mg/kg or lidocaine (1.5 mg/kg) was given intravenously. Patients were followed for at least 30 min post-operatively.

Results: It was found that in group-A (IV lidocaine), the mean change in HR was 22.60±9.09, SBP of 20.96±10.53, DBP of 12.81±7.24, and MAP of 14.44±7.14 while in group-B (IV Labetalol), the mean change in HR was 24.11±0.12, SBP of 20.95±9.87, DBP of 12.13±5.31 and MAP of 13.37±5.26. Both groups have shown a significant reduction in mean hemodynamic parameters within groups. There is statistically significant reduction in heart rate in group-A (p-value= 0.0001) however for other hemodynamic parameters the difference between the two groups was not statistically significant.

Conclusion: This study concluded that mean changes in the hemodynamic responses by IV labetalol are not statistically different.

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Introduction:

Emergence and tracheal extubation after inhalational anesthesia carries high risk of cardiovascular complications. It often provokes significant early post-operative arterial hypertension and tachycardia, thought to be mediated by an increase in adrenaline concentration at the time of emergence.[1] These hemodynamic responses are often worrisome for an anesthetist as it causes an increase in intracranial pressure (ICP), myocardial after load and oxygen demand and peripheral vascular resistance; which may lead to increased chances of intracranial bleeding, myocardial infarction (MI), arrhythmia, post-operative bleeding from the site of surgery and prolonged duration in the post-anesthesia care unit (PACU) due to poor recovery. In 2012, Difficult Airway Society (DAS) identified extubation as a high-risk period, having an impact upon the patient's morbidity and mortality and issued guidelines for the management of tracheal extubation, which through algorithms is meant to help anesthetists plan and perform extubation.[2] Addressing these problems several new studies are being conducted either on the technique of exchange extubation with laryngeal mask airway[3] or on drugs that may blunt these hemodynamic changes. Various drugs have been used to

attenuate these hemodynamic changes and their efficacies compared. To name a few, remifentanil (opioid), dexmedetomide (alpha 2 agonists), verapamil (calcium channel blocker), and esmolol (beta 1 antagonist) have all been used, in different groups of patients.[4]

Lidocaine is a sodium channel blocker and a local anesthetic. It has long been known to help reduce hemodynamic changes and has come under study in several trials to compare the hemodynamic stability provided by various pharmacological interventions. It has been given in intravenous (IV) form at extubation, applied topically as a gel on the endotracheal tube (ETT) or as a spray directly on the vocal cords,[5] and even used to fill the ETT cuff. In a study conducted on 50 ASA I and II patients, undergoing craniotomies for the intracerebral space occupying lesion. Kothari et al,[6] demonstrated that the group (consisting of 25 patients) who received IV lidocaine for the control of hemodynamic responses at extubation had statistically significant mean change in HR of 5.93±5.80, SBP of 3.00±0.40, and DBP of 4.70±0.80. With a central neural blockade mechanism of action, these changes may be attributable to the blocking of autonomic fibers and a direct depressant effect on various components of the cardiovascular system.

Labetalol is a combined selective alpha 1 adrenergic receptor blocker and non-selective beta-adrenergic receptor blocker. It lowers the blood pressure primarily by blocking peripheral arteriolar alpha adrenoceptors thus reducing peripheral resistance and, by the concurrent beta-blockade, it also protects the heart from the reflex sympathetic drive that would otherwise occur.

Radwan et al, showed that out of the total 75 ASA I and II patients undergoing craniotomy for supratentorial tumors, the IV labetalol group (consisting of 25 patients) were found to have significant reductions in their hemodynamic parameters, at the time of extubation, with mean change in HR of 4.30±3.30, SBP of 1.00±1.75, DBP of 3.50±0.25 and MAP of 0.50±0.25.7

Since there are limited local and international studies done on labetalol and that in neurosurgery, hence, the purpose of this trial was to give either labetalol or lidocaine intravenously, as pharmacological intervention at the time of emergence, and to record HR, BP, and MAP, in our neurosurgical patient population, where avoiding hemodynamic changes is of utmost importance, so as to avoid catastrophic rises in intracranial pressures and post-operative intracerebral bleeding. The objective of this study was to compare the mean changes in the hemodynamic responses by IV labetalol and IV lidocaine at the time of tracheal extubation.

Material and Methods:

Study setting and design:
This was a single Centre, comparative study conducted over a period of six months from 5th September 2018 to 4th March 2019 in the neuro-surgical department, at Jinnah Postgraduate Medical Center, Karachi. It was hypothesized that a bolus of I/V labetolol (0.1 mg/kg) would be superior to a bolus of I/V lidocaine (1.5 mg/kg), in attenuating the hemodynamic responses occurring at time of extubation, in patients undergoing craniotomy for space occupying lesion.

Study population:
American Society of Anesthesiologists (ASA) class I and II patients, who were either male or female, ranging between the ages of 18-65 years, undergoing craniotomies for space-occupying lesions under general endotracheal tube anesthesia (GETA) were included in this study. ASA III and IV or patients with sinus bradycardia or any type of heart block (as seen on ECG) or patients presenting with history or clinical signs of congestive heart failure (on physical and cardiovascular system examination) or patients with a history or clinical signs of asthma/COPD or any other respiratory problems (on physical and respiratory system examination) were excluded.

Randomization and masking: Both lidocaine and labetalol dosages were prepared by an anesthetist, who was separate (blinded) from the anesthetist administering the drug and perform-

Table 1: Baseline characteristics of study participants by study groups

	Group A (n=62)	Group B (n=62)	Total (n=124)
Age (years)			
Mean±SD	42.1±9.8	42.3±9.4	42.2±9.6
18-40	32(51.6%)	32 (51.6%)	64 (51.6%)
41-65	30 (48.4%)	30 (48.4%)	60 (48.4%)
Gender			
Male	26 (41.9%)	21 (33.9%)	47 (37.9%)
Female	36 (58.1%)	41 (66.1%)	77 (62.1%)
ASA status			
I	30 (38.3%)	28 (45.2%)	58 (46.8%)
II	32 (51.6%)	34 (54.8%)	68 (53.2%)
Body mass index (kg/m²)			
≤ 27	21 (33.9%)	19 (30.7%)	40 (32.3%)
>27	41 (66.1%)	43 (69.35%)	84 (67.7%)
Type of surgery			
Frontal	21 (33.9%)	20 (32.3%)	41 (33.1%)
Temporal	25 (40.3%)	23 (37.1%)	48 (38.7%)
Parietal	16 (25.6%)	19 (30.6%)	35 (28.2%)

Table 2: Comparison of pre and post intervention heart rate, systolic and diastolic blood pressure and mean arterial pressure by treatment groups

	Group A (n=62)	Group B (n=62)	P-value
Heart Rate			
Pre-operative	100.79 ± 9.32	109.02 ± 6.91	0.0002
Post-operative	77.33 ± 9.20	83.40 ± 10.92	<0.001*
Change	22.60 ± 9.09	24.11 ± 0.12	0.552
Systolic BP			
Pre-operative	152.06 ± 14.76	157.40 ± 17.6	0.066
Post-operative	132.84 ± 13.21	136.45 ± 13.96	0.038
Change	20.96 ± 10.53	20.95 ± 9.87	0.995
Diastolic BP			
Pre-operative	87.46 ± 7.30	88.34 ± 7.3	0.508
Post-operative	75.96 ± 8.17	78.85 ± 9.35	0.069
Change	12.81 ± 7.24	12.13 ± 5.31	0.552
MAP			
Pre-operative	109.0 ± 7.99	111.31 ± 9.15	0.137
Post-operative	94.46 ± 8.25	98.06 ± 9.15	0.015
Change	14.44 ± 7.14	13.37 ± 5.26	0.335

**significant p-value<0.05*

ing the extubation. The Performa was filled by a third person (also blinded).

Data collection:

Patients were selected through non-probability, convenience sampling. Patients fulfilling the eligibility criteria were included in the study after written informed consent before the procedure from the patient or care-taker. All patients had their pre-operative BP, HR, and MAP recorded, as soon as they entered the neurosurgical operative room. Pre-medication with metoclopramide 10mg and dexamethasone 8mg was done before induction. Standard general anesthesia was induced by propofol(2mg/kg), nalbuphine(0.1 mg/kg), and atracurium(0.5mg/kg), and after 4 minutes of intermittent positive pressure ventilation, via bag-mask on 100% oxygen, direct laryngoscopy, was done and an endotracheal tube of appropriate size was passed orally. After cuff inflation and confirmation via capnography, the patient was put on a ventilator (controlled mechanical ventilation). Thereafter anesthesia was maintained throughout the surgical procedure by inhalational agent isoflurane and 1-2 liters of oxygen. Atracurium top-up (10mg each every 20 min), Paracetamol 1gm, and mannitol 1gm/kg was also given. At emergence neostigmine/glycopyrrolate (2.5/0.5 mg) was given for complete reversal. After the return of spontaneous breathing, the inhalational agent was turned off 5 min before extubation. Upon discontinuation of the inhalational agent bolus of labetalol(0.1 mg/kg) or lidocaine(1.5 mg/kg) was given intravenously and BP, MAP, HR readings were recorded 15 min after extubation. Patients were followed for at least 30 min post-operatively.

Study outcome: The outcome of the study was measuring hemodynamic parameters such as a mean change in heart rate, and mean change in arterial pressure at baseline and 15 minutes after extubation.

Data analysis: The sample size was calculated using World Health Organization (WHO) sample size calculator, the calculated sample size is 62 patients in each group (a total of 124 patients) assuming test value of the population mean of 4.3, the anticipated population mean 5.9, population standard deviation 4.6 confidence interval 95%, power of 80%.

The data was entered and analyzed through SPSS version 22. The quantitative variables like age, HR, BP, MAP (pre-operative, post-oper-

ative, and change), and BMI were expressed as mean and standard deviation. The qualitative variables like gender, ASA status, and type of surgery. Mean HR, BP, and MAP were compared in both groups by using an independent t-test and p-value ≤0.05 was taken as significant. Effect modifiers like age, gender, BMI, type of surgery were controlled through stratification and a post-stratification independent t-test was applied. P-value ≤0.05 was taken as significant.

Ethical considerations: The study was conducted after obtaining approval from the ethical review committee of JPMC. A written informed consent was taken from all patients meeting the inclusion criteria before enrollment of patients.

Results:

The age range in this study was from 18 to 65 years with a mean age of 42.19±9.61 years. The mean age of patients in group-A was 42.05±9.79 years and in the group-B was 42.31±9.43 years. Table 1 showed the baseline characteristics of study participants by treatment group. The majority of the patients 64(51.61%) were between 18 to 40 years. Out of 124 patients, 47(37.90%) were males and 77(62.10%) were females with a male to female ratio of 1:1.6. ASA I patients were 46.77% and ASA II patients were 53.23 %. The mean BMI was 28.88±2.48 kg/m^2. Distribution of patients according to the type of surgery is shown in table I.

In this study, it was found that in group-A (IV lidocaine), the mean change in HR was 22.60±9.09, SBP of 20.96±10.53, DBP of 12.81±7.24 and MAP of 14.44±7.14 while in group-B (IV Labetalol), the mean change in HR was 24.11±0.12, SBP of 20.95±9.87, DBP of 12.13±5.31 and MAP of 13.37±5.26. Both groups have shown a significant reduction in mean hemodynamic parameters although reduction in HR was slightly more with IV lidocaine and is statistically significant (p-value = 0.001). Reduction in MAP was slightly more in IV labetalol group the comparison of the two groups has shown no significant change in hemodynamic parameters (Table 2).

Discussion:

Endotracheal extubation is one of the frequently performed procedures in the practice of anesthesia. Complications after tracheal extubation are 3 times more common than complications occurring during tracheal intubation and induction of anesthesia. Hypertension and tachycardia are well-documented events during extubation.[8] These hemodynamic responses reflect sympatho-adrenal reflex stimulation (epipharyngeal and laryngo-pharyngeal stimulation) with a concomitant increase in plasma level of catecholamine and activation of alpha and beta-adrenergic receptors.[9] This increase in blood pressure and heart rate (HR) is usually transitory, variable, and unpredictable.[10] The development of post-operative hypertension warrants immediate assessment and treatment to reduce the risks of myocardial infarction, arrhythmias, congestive heart failure, stroke, bleeding, and other end-organ damages.[11]

Tracheal extubation is associated with a 10%–30% increase in arterial pressure and HR lasting 5–15 min.[12] The response may be attenuated by pharmacological interventions including esmolol (1.5 mg/kg intravenous 2–5 min before extubation), glyceryltrinitrate, magnesium, propofol infusion, remifentanil/alfentanil infusion, I.V lidocaine (1.5 mg/kg over 2 min), topical lidocaine 10%, and peri-operative oral nimodipine with labetalol.[13] This study has been conducted to compare the mean changes in the hemodynamic responses by IV labetalol and IV lidocaine at the time of tracheal extubation.

In our study, we have found that in group-A (IV lidocaine), the mean change in HR was 22.60±9.09, SBP of 20.96±10.53, DBP of 12.81±7.24, and MAP of 14.44±7.14 while in group-B (IV Labetalol), the mean change in HR was 24.11±0.12, SBP of 20.95±9.87, DBP of 12.13±5.31 and MAP of 13.37±5.26. Both groups have shown a significant reduction in mean hemodynamic parameters although the comparison of the two groups has shown there is statistically significant reduction in heart rate in IV lidocaine group. Whereas there is no significant change in other hemodynamic parame-

ters. Our results are comparable to other similar studies. Kothari et al,[6] demonstrated that, in the group (consisting of 25 patients) who received IV lidocaine for the control of hemodynamic responses at extubation had statistically significant mean change in HR of 5.93±5.80, SBP of 3.00±0.40 and DBP of 4.70±0.80.5 Whereas a mean change of MAP 2.07±0.53 was seen in a randomized controlled trial done on lidocaine; at the time of extubation by Savitha KS.[14] Radwan et al, showed that out of the total 75 ASA I and II patients undergoing craniotomy for supra-tentorial tumours, the IV labetalol group (consisting of 25 patients) were found to have significant reductions in their hemodynamic parameters, at the time of extubation, with mean change in HR of 4.30±3.30, SBP of 1.00±1.75, DBP of 3.50±0.25 and MAP of 0.50±0.25.[7] Tempe et al,[15] did comparative study between esmolol (loading dose of 500 μg/kg followed by an infusion of 50–300 μg/kg/min, mean = 160 μg/kg/min) and labetalol (incremental doses of 0.25, 0.5, 0.75, and 1.00 mg/kg, mean = 0.98 mg/kg/min) in treating increase in blood pressure during emergence and recovery from anesthesia after intracranial surgery and found both labetalol and esmolol were equally effective in controlling SBP on emergence and in the recovery room. However, decrease in HR was significantly more frequent in the immediate post-operative period in patients given labetalol. Singh et al,[16] compared esmolol 0.5 mg/kg and labetalol 0.25 mg/kg, 2 min and 5 min before intubation. He observed that labetalol was more effective in controlling HR and SBP than esmolol which was statistically significant $P < 0.05$. Labetalol also controlled diastolic and mean arterial pressure better than esmolol but statistically insignificant except 1 min post-intubation. The author also commented about bradycardia being only the side effect in his study, not hypotension.

In another study,[17] there was no significant difference in terms of hemodynamic parameters during the period of operation and recovery and at the time of extubation and during the study, no case of bradycardia, hypotension, tachycardia, or hypertension was observed in the patients of both groups. Roelofse et al,[18] found that labetalol of dosage 1 mg/kg given as an IV bolus 1 min before laryngoscopy was not effective in the attenuation of HR. This failure of the study can be explained by the different times of administration of the study drug because labetalol has a peak effect after 5-10 min.[19] Ramanathan et al,[20] used 20 mg labetalol to prevent the rise in SBP successfully. Inada et al,[21] found 10 mg (0.14 mg/kg) labetalol ineffective in attenuating the rise in systolic pressure. This difference might be because of the lower dose they used and the timing of giving of labetalol (2 min before intubation) because of which the peak effect of the drug was lost at intubation. Maharaj et al,[22] failed to blunt the blood pressure response with 0.25 and 0.5 mg/kg labetalol. However, they did not mention the timing of giving the drug.

Conclusion:
Mean changes in the hemodynamic responses by IV labetalol are less at the time of tracheal extubation as compared to IV lidocaine. The decline in heart rate is significantly seen more in IV lidocaine group although the difference in other hemodynamic parameters between these two drugs are statistically not significant. So, we recommend that IV labetalol should be used at the time of tracheal extubation and prevent patients from post-anesthetic complications of laryngoscopy.

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Role and contribution of authors:
Shoaib Malik, collected the data, references and did the initial writeuo.

Maida Muzaffar, helped in collecting the data and introduction writing.

Nadeem Munir, critically review the article and made final changes.

Lal Rehman, critically review the article and made useful changes in discussion, result and conclusion writing.

Shahneela Raza, collected the references and did the interpretation of data and also helped in discussion writing.

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