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Research article

Comparison of lidocaine and labetalol on the hemodynamic response patients with endotracheal intubation

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Abstract

Background: Comparison of lidocaine and Labetalol on the hemodynamic response patients with endotracheal intubation. **Introduction**: Poor physical condition, emergency intubation and use of drugs to induce anesthesia, cause complications such as hemodynamic instability. This study aims to investigate comparison of lidocaine and Labetalol on hemodynamic response in patients with endotracheal intubation. **Materials and Methods**: The clinical trial, randomized, single-blind study was performed with 192 patients with indication of elective non-cardiac surgery and endotracheal intubation. Patients were randomized into 3 equal groups; control group: received only anesthesia drugs; Group 1: 90 seconds before intubation received 1.5 mg/kg lidocaine, too; group 2:5 minutes before intubation received 0.4 mg/kg labetalol, too. Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) and mean arterial pressure (MAP) in all 3 groups at the time of intubation, 2 and 5 minutes after that were recorded. Data were analyzed by SPSS 18 software. **Results**: During 3-review process of the patients, SBP (lidocaine: p=0.001, labetalol: p=0.000), DBP (lidocaine: p=0.000, labetalol: p =0.01) and MAP (lidocaine: p=0.012, labetalol: p=0.05) in both lidocaine and labetalol groups, decreased significantly. HR decreased significantly only in the labetalol group (p=0.000). in control group, 2 min after intubation, all variables significantly increased and reached to baseline 5 minutes after intubation. **Conclusion**: Based on our results, lidocaine and labetalol can be good protection against hemodynamic changes. However, due to conflicting results among studies (especially in field of labetalol) further studies in the future are recommended.

Key words: lidocaine, Labetalol, endotracheal intubation.

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1. Introduction

Poor physical condition of the patient, emergency intubation and use of drugs to induce anesthesia during intubation, cause complications. one of these complications is stimulation of sympathetic system as hypertension and tachycardia. These complications can increase mortality and morbidity [1].

In order to relieve these stress-induced responses of the various drugs different methods have been proposed. Lidocaine is one of those drugs. Lidocaine is a local anesthetic and an anti-arrhythmic drug that can suppress this complication [2]. Lidocaine was used for spinal anesthesia and also injected around the dura-mater. Lidocaine intravenously was used in cardiac arrhythmias, ventricular arrhythmias, in particular applications. It is Class Ib anti-arrhythmic drug and is effective on the zero phase of cardiac cells action potential [3].

Another class of drugs that aim to protect the hemodynamic changes during intubation is beta-blockers such as labetalol. Labetalol is an adrenergic receptor blocker with effect on alpha-1 receptors and non-selective beta receptors, which are mainly used to treat high blood pressure. It also has a vasodilatory effect [4].

Not only hemodynamic response in patients, undergoing intubation is very important but also studies on the application of labetalol to maintain hemodynamic responses during intubation and comparison with the effects of lidocaine is limited.

2. Materials and Methods

This study is a randomized, single-blind clinical trial that was performed on 192 patients who filled consent form and undergoing elective non-cardiac surgery and indicated for general anesthesia with endotracheal intubations were examined for inclusion and exclusion criteria as well as other factors. The eligible patients randomized into 3 groups (with equal numbers: 64 cases) group 1, in addition to anesthesia drugs, 90 seconds before intubation, received 1.5 mg/ kg intravenous lidocaine, group 2, in addition to anesthesia drugs, 5 minutes before intubation received 0.4 mg /kg labetalol IV and group 3(control group) received only induction drugs

During endotracheal intubation, induction of anesthesia with fentanyl 2 mcg/kg, midazolam 2 mg, Atracurium 0.5mg/kg, thiopental 5 mg/ kg was made.

At the time of laryngoscopy, basic demographic data (age, sex, weight) were recorded.

During, 2 and 5 minutes after intubation, systolic blood pressure (SPB), diastolic blood pressure(DBP), heart rate(HR) and mean arterial blood pressure (MAP) in all 3 groups were recorded.

Systolic and diastolic blood pressure were measured using pressure NIBP (Noninvasive Blood Pressure Amplifier), using cardiac monitoring and arterial blood pressure was calculated using the following formula.

$$MAP= (SBP+2DBP)/3$$

The study hospital was Arak Valieasr hospital.

Inclusion criteria:

1. Patients aged 25 to 40 years for elective surgery and general anesthesia.
2. Patients without underlying disease such as diabetes, hypertension,

cardiovascular disease, kidney and liver diseases, and respiratory diseases and patients except 1 or 2 ASA classification.
3. Patients who filled consent from

Exclusion criteria:
1. Patients with a history of allergic reaction to treatment with lidocaine and labetalol (and other beta-blockers) or cardiac pulmonary disease, heart failure, asthma and insulin-dependent diabetes, angina were and hyper thyroid, There were excluded because of complications with β-blocker.
2. Patients with cardiogenic shock, severe bradycardia and CHF uncontrolled.
3. Trauma patients and patients with unstable hemodynamics.
4. Patient with life-threatening drug reactions.
5. Breastfeeding and Pregnant women.
6. Patient with concomitant use of monoamine oxidase inhibitors or TCA.

According to ASA Classification patients divided to 6 class rating based on sample size of 64 for each group was calculated based on its description of the patient's condition which is given in table 1. [5].
Sample size was based on significant level Alpha: 0.05, E-size: 10 and power: 80%.

$\alpha = 0.05$
$p_1 = 0.079$
$p2 = 0.5$
$power: 80\%$

$$n_1 = n_2 = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 [P_1(1-P_1) + P_2(1-P_2)]}{(p_1 - p_2)^2} = 64$$

After collecting data SPSS version 18 (version 18, SPSS Inc, Chicago, IL) and statistical methods were used to determine the frequency of variables.

However, for the analysis of quantitative variables, Student t-test and test for qualitative variables were used. It should be noted that the analysis of variance was used in the 3-step follow-up evaluation of the Friedman test.

3. Results

192 patients were divided into 3 groups of 64 to enter the study, 243 patients were studied. 51 patients withdrew from the study, 31patient (60.78%) and 20 patients (39.21%) respectively were excluded due to lack of filling consent form and underlying disease (ASA score higher than 2).
The mean age and weight of the total patients, respectively 36.91 ± 6.2 years and 68.14 ± 4.1 kg. 93 patients (48.43%) were male and 99 patients were female.
Basic patient demographic and clinical information were recorded in Table 2. The results of mean age (p =0.231), gender (p=0.246) and average weight of the patients (p =0.277), were not significantly difference between 3 groups.
The mean duration of intubation in the treatment group, labetalol and control, respectively, 16.1 ± 11.2, 15.8 ± 2.2 and 16.4 ±3h, difference between 3 groups were not significant. (p =0.12).
The frequency of ASA I patients in the treatment group, labetalol and control, were respectively, 46.87% 48.43% and 50%. (p =0.364). The frequency of ASA II patients in the treatment group, labetalol and control, were respectively, 53.12% 51.56% and 50% the difference between the 3 groups were not significant. (p =0.52)

Table 1. Classification of patients who are candidates for surgery based on physical condition and surgical procedure

ASA PS Category	Preoperative Health Status	Comments, Examples
ASA PS 1	Normal healthy patient	No organic, physiologic, or psychiatric disturbance; excludes the very young and very old; healthy with good exercise tolerance
ASA PS 2	Patients with mild systemic disease	No functional limitations; has a well-controlled disease of one body system; controlled hypertension or diabetes without systemic effects, cigarette smoking without chronic obstructive pulmonary disease (COPD); mild obesity, pregnancy
ASA PS 3	Patients with severe systemic disease	Some functional limitation; has a controlled disease of more than one body system or one major system; no immediate danger of death; controlled congestive heart failure (CHF), stable angina, old heart attack, poorly controlled hypertension, morbid obesity, chronic renal failure; bronchospastic disease with intermittent symptoms
ASA PS 4	Patients with severe systemic disease that is a constant threat to life	Has at least one severe disease that is poorly controlled or at end stage; possible risk of death; unstable angina, symptomatic COPD, symptomatic CHF, hepatorenal failure
ASA PS 5	Moribund patients who are not expected to survive without the operation	Not expected to survive > 24 hours without surgery; imminent risk of death; multiorgan failure, sepsis syndrome with hemodynamic instability, hypothermia, poorly controlled coagulopathy
ASA PS 6	A declared brain-dead patient whose organs are being removed for donor purposes	

Table 2. Demographic and baseline clinical data of patients

p- value [4]	Control Group[3]	Labetalol Group[2]	Lidocaine group[1]	Variables
0.231	35.23±15	37.4±15	38.1±11	**age**(year) (mean±SD)
0.264	33(51.56)	29(45.31)	31(48.43)	**sex** (male) (%)
0.277	68.1±2	69.22±8.1	67.1±9.1	**weight** (mean±SD)
0.12	16.4±3	15.8±2.2	16.1±11.2	Laryngoscopic time (second)(mean±SD)
0.364	32 (50)	31 (48.43)	30 (46.87)	**ASA I**(%)
0.52	32 (50)	33(51.56)	34 (53.12)	**ASAII**(%)

Group 1 received induction drugs and lidocaine before intubation, group 2 received induction drugs and labetalol before intubation. Group 3 received induction drugs alone. [4]p-value less than 0.05 considered significant.

During the 3-stage (intubation time, 2 minutes and 5 minutes after intubation) systolic blood pressure(SBP) changes in the treatment group (p=0.001), labetalol (p=0.000) and control (p=0.008) were significant. SBP were significantly reduced in both lidocaine and labetalol groups. SBP in the control group, 2 min after intubation were significantly increased. (Table 3).

Table 3. Changes in mean systolic blood pressure in-patients with stage 3

p-value	SBP-5 [3]	SBP- 2[2]	SBP-0[1]	Group
0.001	96.33±14.08	112.3±14.08	130.4±16.38	Lidocaine group (SD±mean)
0.000	97.2±13.2	105.2±18.4	125.05±17.25	Labetalol (SD±mean)
0.008	105.8±84.7	138.2±14.3	117.88±84.6	Control Group (SD±mean)

1: at the time of intubation, 2: 2 min after intubation, 3:5 minutes after intubation

Changes in diastolic blood pressure (DBP) in the treatment group (p =0.000), labetalol (p =0.01) and control (p=0.023) were significant. So that lidocaine and labetalol DBP in both groups significantly decreased in the control group, DBP 2 min after intubation were significantly increased (Table 4).

Table 4. Changes in mean diastolic blood pressure in-patients with stage 3

p-value	DBP-5	DBP- 2	DBP-0	Group
0.000	87.2±23.2	90.6±97.8	98.76±14.66	Lidocaine group (SD±mean)
0.01	88.2±56.2	92.5±6.5	97.15±4.99	Labetalol (SD±mean)
0.023	91.1±2.3	102.3±7.2	98.14±4.3	Control Group (SD±mean)

Changes in heart rate (HR) in labetalol (p =0.000) and control (p =0.01), unlike lidocaine group (p =0.412) were significant. So that heart rate in 3 consecutive labetalol group study, showed significant reduction, and in the control group,HR 2 min after intubation were significantly increased. (Table 5).

Table 5. Changes in mean heart rate in 3 Patients

p-value	HR-5	HR - 2	HR -0	Group
0.412	87.5±13.2	88.6±14.83	93.12±97.8	Lidocaine group (SD±mean)
0.000	71.95±4.93	76.2±99	94.15±12	Labetalol (SD±mean)
0.01	91.2±14	103.3±11.57	93.15±13.2	Control Group (SD±mean)

In this study, mean arterial pressure (MAP) using the relationship between systolic and diastolic blood pressure were measured. Based on these results, changes in MAP in all 3 groups of lidocaine(p =0.012), labetalol (p=0.05) and control(p =0.001) were significant.

So that in the treatment and labetalol group mean MAP significantly decreased and in the control group, 2 min after intubation, increased significantly (Table 6).

Generally, for both lidocaine and labetalol groups SBP, DBP, HR and MAP had their maximum values at the time of Intubation, whereas for the control group the

maximum values were reached 2 min after intubation, and stayed unchanged afterward.

There was no evidence of arrhythmias, ischemic heart disease in any of the patients in the 3 groups during the study.

Table 6. Changes in mean arterial pressure in patients with stage 3

p-value	MAP-5	MAP - 2	MAP -0	Group
0.012	90.23±14.2	97.83±5.3	109.3±16.3	Lidocaine group (SD±mean)
0.05	91.2±9.4	96.73±8.4	106.45±11.5	Labetalol (SD±mean)
0.001	96±9.4	114.26±61.2	104.72±22.1	Control Group (SD±mean)

Discussion

The results of our study suggest that lidocaine and labetalol both can effectively reduce systolic blood pressure, diastolic blood pressure and mean arterial pressure during intubation. However, labetalol, unlike lidocaine is also effective in preventing increase in heart rate.

In 54 % of previous studies, poor physical conditions of the patients, emergency intubation and use of drugs to induce anesthesia during intubation cause a variety of side effects [6,7].

Based on our results, lidocaine, except for heart rate, could well prevent increase in systolic blood pressure, diastolic and mean arterial pressure is effective.

In a study to compare the effects of lidocaine and fentanyl on hemodynamic response to tracheal intubation, Splinter WM And colleagues did show lidocaine reduce systolic blood pressure more effective and side effects is less [8].

In contrast to our study, in FengCk et al.'s study, the effects of lidocaine on the hemodynamic response in patients undergoing intubation and laryngoscopy were not reported [9].

In a study, Ugur B. et al. evaluate the effect of esmolol, lidocaine and fentanyl in endotracheal intubation hemodynamic response. In this study, mean arterial blood pressure and heart rate, before intubation, immediately after intubation, and 1, 3, 5, 7, 10 min after intubation were assessed. Compared to the control group, in the group receiving esmolol, heart rate was significantly reduced immediately after intubation and 1 minute after. This effect was not seen in the lidocaine treatment group. It was also found that both lidocaine and esmolol can be effective in preventing an increase in the mean arterial pressure [10].

Hanci Vet al. did a study to evaluate the effect of esmolol, lidocaine and fentanyl on hemodynamic response during intubation. In this study, 80 patients, 18 to 60 years were examined in 4 groups.

The results showed that the use of esmolol 0.5 mg/kg before intubation can control tachycardia and increase protection against arterial blood pressure raise and the use of lidocaine can be a protective factor against increased arterial pressure during laryngoscopy and endotracheal intubation [4].

The results of our study about the benefits of lidocaine for prevention of arterial pressure rising during intubation is similar.

Except for few studies, comparison the use of labetalol and esmolol, and lidocaine (main purpose of our study) in the hemodynamic response in patients undergoing intubation is limited. Based on our study, labetalol can be good protection against hemodynamic changes in patients were intubated. Chung K S et al. [11], in their study, examined the labetalol impact on hemodynamics and blood pressure

response laryngoscopy and intubation. In this study, for the two groups of 18 patients who underwent elective surgery due to undergo intubation, intravenous labetalol under the administration of 0.4 mg /kg, 5 minutes before intubation was performed. Results showed that heart rate 1 minute after the intubation labetalol group was significantly lower. However, the effect of the dose of labetalol on blood pressure in this study was small.

Do HS et al. [12, under review], have studies the impact of 0.3 mg/kg labetalol in intubated patients, age 20 to 60 years. According to the results of this study, intravenous labetalol before the intubation effectively protect the hemodynamic changes in patients.

However, unlike our results, Chung CS [11] and the Do HS [12], Ryu JH [13] in their studies compared the use of labetalol and nicardipine in patients undergoing intubation and hemodynamic response. Whereas labetalol reduced patients' hemodynamic response, nicardipine did not changed this response.

However, the results of this study and similar previous studies lidocaine can be used to improve the hemodynamic changes in patients undergoing intubation. However, there are not enough studies on the application of labetalol, as well as studies comparing the application of both Labetalol and lidocaine for patients with underlying diseases. Therefore, the use of lidocaine and labetalol prophylaxis in patients undergoing intubation requires further studies.

The limitations of our study are: the lack of Patients with underlying diseases and less frequent follow up (compared to similar studies). In order to achieve a more comprehensive conclusions, future studies for addressing these shortcomings are recommended.

References

1. Arasu M, Al-Dhabi N, Rejiniemon T, Lee K, Huxley V, Kim D, Duraipandiyan V, Karuppiah P and Choi K. Identification and characterization of *Lactobacillus brevis*P68 with antifungal, antioxidant and -probiotic functional properties. Indian Journal of Microbiology 2015; 55(1):19-28.
2. Min JH, Chai HS, Kum YH, Chae YK, Choi SS, Lee A, et al. Attenuation of hemodynamic responses to laryngoscopy and tracheal intubation during rapid sequence induction: remifentanil vs. lidocaine with esmolol. Minerva Anesthesiol 2010; 76:188-92.
3. Mann D. Zipes D, Libby P, BonowR. Braunwald's Heart disease, tenth edition, ELSEVIER 2015, 35(693).
4. Hancı V1, Yurtlu S2, Karabağ T3, Okyay D2, Hakimoğlu S4, Kayhan G5, Büyükuysal Ç6, Ayoğlu H7, Turan IÖ8. Effects of esmolol, lidocaine and fentanyl on P wave dispersion, QT, QTc intervals and hemodynamic responses to endotracheal intubation during propofol induction: a comparative study. Braz J Anesthesiol. 2013; 63(3):235-44.
5. American Society of Anesthesiologists. ASA Physical Status Classification System Accessed 10/5/2015.
6. DeWitt CR, Waksman JC. Pharmacology, pathophysiology and management of calcium channel blocker and beta-blocker toxicity. Toxicol Rev. 2004;23(4):223-38.
7. Reid C, Chan L, Tweed dale M. The who, where, and what of rapid sequence intubation: Prospective observational study of emergency RSI outside the operating theatre. Emerg Med J. 2004;21:296–301.
8. Splinter WM1, Cervenko F. Haemodynamic responses to laryngoscopy and tracheal intubation in geriatric patients: effects of fentanyl, lidocaine and thiopentone. Can J Anaesth. 1989; 36(4):370-6.
9. Feng CK1, Chan KH, Liu KN, Or CH, Lee TY. A comparison of lidocaine, fentanyl, and esmolol for attenuation of cardiovascular response to laryngoscopy and tracheal

intubation. ActaAnaesthesiol Sin. 1996; 34(2):61-7.
10. Ugur B1, Ogurlu M, Gezer E, NuriAydin O, Gürsoy F. Effects of esmolol, lidocaine and fentanyl on haemodynamic responses to endotracheal intubation: a comparative study. Clin Drug Investig. 2007;27(4):269-77
11. Chung KS, Sinatra RS, Chung JH. The effect of an intermediate dose of labetalol on heart rate and blood pressure responses to laryngoscopy and intubation. J ClinAnesth. 1992; 4(1):11-5.
12. Do HS, Kim SY, Heo SJ, Park SJ. The effect of intravenous labetalol administration on hemodynamic responses during desflurane inhalation. Korean J Anesthesiol. 2012; 62(3):245-50. doi: 10.4097/kjae.2012. 62.3.245. Epub 2012 Mar 21.
13. Ryu JH, Apfel CC, Whelan R, Jeon YT, Hwang JW, Do SH, Ro YJ, Kim CS. Comparative prophylactic and therapeutic effects of intravenous labetalol 0.4 mg/kg and nicardipine 20 μg/kg on hypertensive responses to endotracheal intubation in patients undergoing elective surgeries with general anesthesia: a prospective, randomized, double-blind study. ClinTher. 2012; 34(3):593-604. doi: 10.1016/j. clinthera. 2012.01.017. Epub 2012 Feb 24.