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Comparison of intravenous and transtracheal lidocaine on hemodynamic changes in patients with hypertension following tracheal intubation: A double blind clinical trial

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ABSTRACT

Background: Hemodynamic changes following intubation can be reduced by lidocaine at the time of induction of anesthesia and during laryngoscopy to prevent complications such as myocardial ischemia, infarction and brain damage. The aim of this study was to compare the effects of intravenous lidocaine and transtracheal lidocaine on hemodynamic changes in patients with hypertension under medical treatment following tracheal intubation.

Materials and methods: In this prospective double-blind randomized clinical study, patients aged 40–70 years with hypertension who were candidates for general anesthetic surgery were randomly divided into three groups: A (intravenous lidocaine), B (transtracheal lidocaine) and C (placebo). Blood pressure and heart rate were record at 30 s after induction of anesthesia, 30 s after intubation and 3, 6 and 9 min after intubation.

Results: The results showed that the mean systolic blood pressure varied significantly between 3 groups at 30 s after induction (group A: 127.08 ± 10.08, group B: 134 ± 9.77 and group C: 123 ± 1.55 mmHg) ($P = 0.007$) and 30 s after intubation (group A: 154.42 ± 15.75, group B: 142.58 ± 8.63, group C: 158 ± 17.37 mmHg) ($P = 0.001$). The mean diastolic blood pressure was significantly different between 3 groups in 30 s after intubation (group A: 93.23 ± 13.7, group B: 87.92 ± 4.22 and group C: 98.09 ± 9.29 mmHg) ($P = 0.003$). The mean heart rate was significantly different between 3 groups in 30 s after intubation (group A: 81.65 ± 8.06, group B: 74.65 ± 6.22 and group C: 82.5 ± 7.16 bit/minutes) ($P < 0.001$).

Conclusion: Our results showed that use of lidocaine in hypertensive patients following tracheal intubation can results in a more stable systolic and diastolic blood pressure as well as heart rate. It should be noted that the use of lidocaine for the presence or absence of cardiac dysrhythmias showed no difference among the study groups.

1. Introduction

Hypertension, tachycardia and arrhythmia following laryngoscopy and tracheal intubation are very risky for people with brain trauma, brain tumors, ischemia and heart failure, glaucoma and high ocular pressure. Most of hemodynamic changes occur in laryngoscopy, and if the laryngoscopy time lasts longer than 15 s, it will have a significant effect on increasing these hemodynamic changes [1]. Complications of laryngoscopy include cardiovascular events such as high blood pressure, myocardial ischemia and myocardial infarction and stroke [2–4]. In addition, increased sympathetic activity causes myocardial ischemia in patients with underlying disease [5].

Hemodynamic instability is a tachycardia-arrhythmia with hypertension that can increase oxygen consumption and result in ischemic myocardial infarction, heart failure, acute pulmonary edema, increased intracranial pressure and increased intraocular pressure [6]. Intravenous lidocaine can suppress cough reflux and also control hemodynamic responses during intubation [7,8]. Lidocaine blocks the voltage-dependent sodium channel and lowers the entry of sodium ion into the cell leading to reduction in

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the impulse [9,10].

Intravenous injection of lidocaine 60–90 s prior to laryngoscopy and intubation of the trachea is usually effective but can lead to complications of the central nervous system or the cardiovascular system. Spraying of topical lidocaine on the trachea significantly reduces the hemodynamic response to laryngoscopy and intubation [11,12].

Some studies have demonstrated the positive effect of lidocaine sprays on reducing hemodynamic effects during intubation [13,14]. High-speed stimulus receptors exist in the upper and lower airways and their number is higher in the trachea. It seems that stimulation of these receptors by the cuff of a tracheal tube has an important role in coughing [15]. During general anesthesia, these stimuli are blocked [16]; therefore, a logical solution to reduce this stimulation is the use of local anesthetics such as lidocaine in the trachea [17].

Considering the importance of this issue and novelty of the use of transtracheal injection of lidocaine in hypertensive patients during laryngoscopy and intubation, the aim of this study was to compare the effect of transtracheal and intravenous lidocaine on hemodynamic changes in patients with hypertension following intubation.

2. Materials and Methods

In this double-blind randomized clinical trial study, patients aged 40–70 years with controlled hypertension and candidates for general anesthetic surgery were recruited during 2017–2018 in Rasoul Akram hospital, Tehran. Exclusion criteria included emergency surgery, drug abuse, alcohol consumption, all cases of difficult intubation, diabetes, heart failure, kidney failure, taking beta blocker, initial dysrhythmia, systolic pressure more than 170 mmHg and diastolic more than 100 mmHg. Sample size ($n = 78$) was calculated according to the study of Rajan et al. [18]. The mean difference formula was used with alpha = 0.05 and power = 80%.

This study was approved by the ethics committee of Iran University of Medical Sciences (IR.IUMS.FMD.REC.1397.154) and the RCT code is: IRCT20141127020112N10. Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. A complete explanation of the treatment method for patients was described and the patients were assured that their information would be confidential and would be used only for the purposes of the research. No additional costs were incurred by patients in the implementation of this study.

The patients were randomly divided into three groups: A (intravenous lidocaine), B (transtracheal lidocaine) and C (non-use of lidocaine) by using a random allocation software. Data (blood pressure and heart rate) were recorded at 30 s after the induction. After 4 min, the patients were intubated with an appropriate tracheal tube and 30 s after the intubation, the blood pressure and heart rate were recorded again. Then, at intervals of 3, 6 and 9 min after intubation, the patient's blood pressure and heart rate were recorded as well. At the entrance to the operating room, blood pressure and heart rate were recorded. Then, in group A, fentanyl 2 mg/kg and intravenous lidocaine 2% 1.5mg/kg was injected and the patients were anesthetized by thiopental 4 mg/kg and cis-atracurium 0.2 mg/kg. Then, 30 s after the induction, blood pressure and heart rate were recorded. After 4 min, the patient was intubated by an appropriate tracheal tube and 30 s after the intubation, blood pressure and heart rate were recorded again, and then, at minutes 3, 6 and 9 after intubation, the patient's blood pressure and heart rate were recorded. In all monitoring registers, any incidence of dysrhythmia was recorded in the ECG.

In the group B, fentanyl 2 mg/kg was injected intravenously and the patients were anesthetized by thiopental 4 mg/kg and cis-atracurium 0.2 mg/kg. Then, 30 s after the induction of anesthesia, blood pressure and heart rate were recorded and lidocaine 2% 1.5mg/kg was injected as transtracheal. After 4 min, the patients were intubated by an appropriate tracheal tube and, similar to group A, at specified times, blood pressure and heart rate were recorded. Lidocaine was injected in both ways, 90 s before intubation.

In the group C, the only difference with other groups was the lack of use of lidocaine. In all groups, isoflurane was used to maintain anesthesia. To blind the study, all of patients and those who collected the data were blind to the method of intervention used. Our data saved on monitoring memory for each patient and after 30 min data was collected by an anesthesia nurse who was blinded to the kind of procedure noted.

2.1. Statistical analysis

Descriptive analysis are presented as Mean ± SD or frequency. To compare the two means, independent *t*-test was used and in case of skewed data distribution, the Mann-Whitney test was used. Repeated measures ANOVA and Least Significant Difference (LSD) were used to check quantitative values over time. A P value < 0.05 was considered statistically significant. All data were analyzed using SPSS version 21.

3. Results

The present study was conducted on 78 patients with hypertension candidate for elective surgery under general anesthesia and tracheal intubation. As shown in Table 1, there was no significantly difference among three groups regarding age and gender ($P > 0.05$). In addition, the results showed that the mean systolic blood pressure varied significantly among the three groups at 30 s after induction ($P = 0.007$) and 30 s after intubation ($P = 0.001$). The mean systolic blood pressure did not show any significant difference at other times ($P > 0.005$) (Table 2).

Fig. 1 shows the trend and error bar, the mean systolic blood pressure for the three groups at measured times. Post hoc test results were significantly different for mean systolic blood pressure between two groups of intravenous lidocaine and transtracheal lidocaine ($P = 0.027$), as well as transtracheal lidocaine and control ($P = 0.002$) at 30 s after induction. Also, these results were significantly different between the two groups of intravenous lidocaine and transtracheal lidocaine ($P = 0.004$), and the two groups of transtracheal lidocaine and control ($P < 0.001$) at 30 s after intubation. The results showed that the mean diastolic blood pressure was significantly different among the three groups at 30 s after intubation ($P = 0.003$). Diastolic blood pressure did not show a significant difference in other measured times ($P > 0.005$).

Table 3 shows the mean diastolic blood pressure for the three groups at the time of the study. Fig. 2 shows the trend, error bar and the mean diastolic blood pressure for the three groups at the measured times. The results of the LSD post-hoc for diastolic blood pressure at 30 s after intubation were significantly different between the two groups of transtracheal lidocaine and control ($P = 0.001$), and the mean diastolic blood pressure group was in the transtracheal lidocaine group. The results showed that there was no significant difference in the presence or absence of dysrhythmia between the patients in the three groups ($P = 0.249$). Fig. 4 shows flow chart of the study protocol.

The mean heart rate was not significantly different in other measured times ($P > 0.005$). Table 4 shows the comparison of the mean heart rate for the three groups at the measured times. Fig. 3 shows the trend, error bar and the mean heart rate for the three groups at measured times. The results of the LSD post-hoc for the mean heart rate at 30 s after intubation among the two groups of

Table 1
Distribution of age and sex in the three groups.

Variable		A	B	C	P value
Gender	Female	9 (34.6)	5 (19.2)	10 (38.4)	0.370
	Male	17 (65.4)	21 (80.8)	16 (62.6)	
Age (Mean ± SD)		64.85 ± 10.10	64.85 ± 8.40	65.32 ± 10.15	0.981

Table 2
Comparison of mean systolic blood pressure for the three groups at the time of study.

P Value	SD	Mean	Group	Time
0.858	15.286	158.35	A	Entrance
	12.093	160.35	B	
	11.796	159.00	C	
0.007	10.888	127.08	A	30 s after induction
	9.773	134.00	B	
	12.556	123.95	C	
0.001	15.754	154.42	A	30 s after intubation
	8.631	142.58	B	
	17.370	158.00	C	
0.599	16.239	137.77	A	3 min after intubation
	8.827	134.92	B	
	10.823	138.23	C	
0.468	26.680	128.04	A	6 min after intubation
	9.527	133.96	B	
	9.302	129.95	C	
0.530	11.813	132.96	A	9 min after intubation
	8.351	136.15	B	
	10.906	135.23	C	

Table 3
Comparison of mean diastolic blood pressure for the three groups at the time of study.

P Value	SD	Mean	Group	Time
0.719	10.190	97.92	A	Entrance
	7.556	96.15	B	
	6.905	96.41	C	
0.111	7.111	81.81	A	30 s after induction
	5.836	81.15	B	
	5.701	78.14	C	
0.003	13.706	93.23	A	30 s after intubation
	4.223	87.92	B	
	9.294	98.09	C	
0.694	10.760	84.88	A	3 min after intubation
	6.561	84.62	B	
	4.718	86.45	C	
0.329	8.741	84.38	A	6 min after intubation
	7.140	83.12	B	
	5.182	81.23	C	
0.266	10.076	86.38	A	9 min after intubation
	8.663	82.58	B	
	6.297	85.32	C	

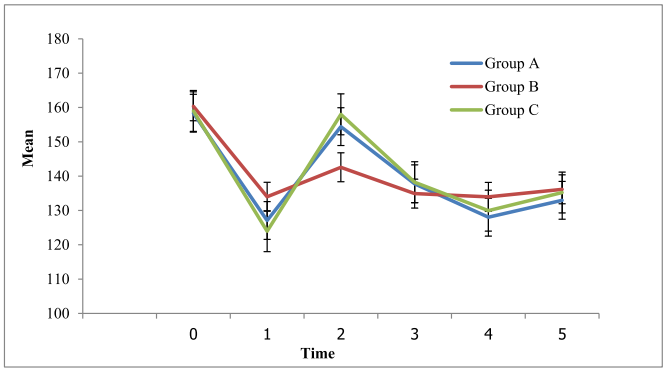

Fig. 1. Trend, error bar and mean systolic blood pressure for the three groups at measured times.

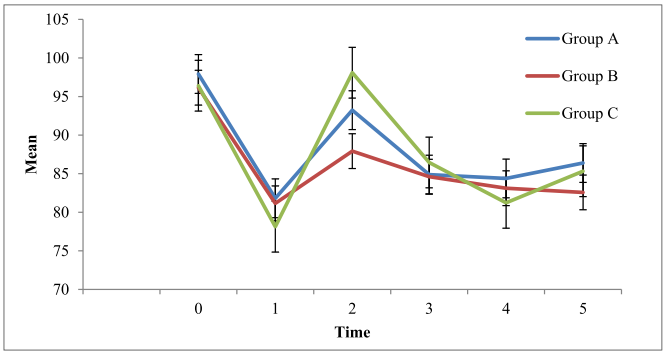

Fig. 2. Trend, error bar and mean diastolic blood pressure for the three groups at measured times.

intravenous lidocaine and transtracheal lidocaine ($p = 0.001$) and the two groups of transtracheal lidocaine and control ($p < 0.001$) were significantly different. In both cases, the mean heart rate was lower in the transtracheal lidocaine group.

4. Discussion

Results of this study showed that mean heart rate, systolic and diastolic blood pressures at 30 s after the induction and 30 s after the intubation, were significantly different among 3 groups and the lowest was transtracheal lidocaine. The mean heart rate, systolic and diastolic blood pressure did not differ significantly in other measured times. Results showed that there was no significant difference among the three groups in the presence or absence of dysrhythmia at different measured times. Thus, hemodynamic changes were significantly less in the group that used transtracheal lidocaine, which is probably due to the direct and local effects of lidocaine on the trachea and subsequent reduction of sympathetic

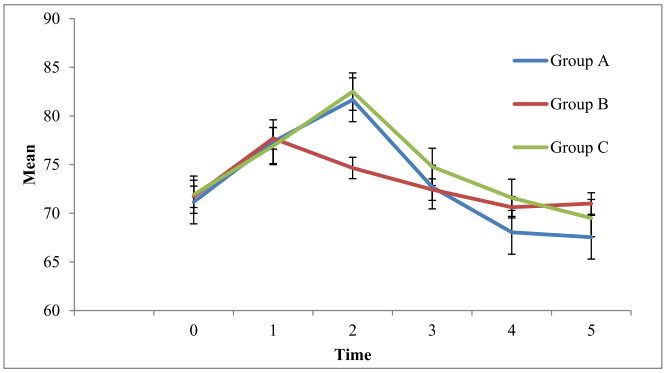

Fig. 3. Trend, error bar and mean heart rate for the three groups at measured times.

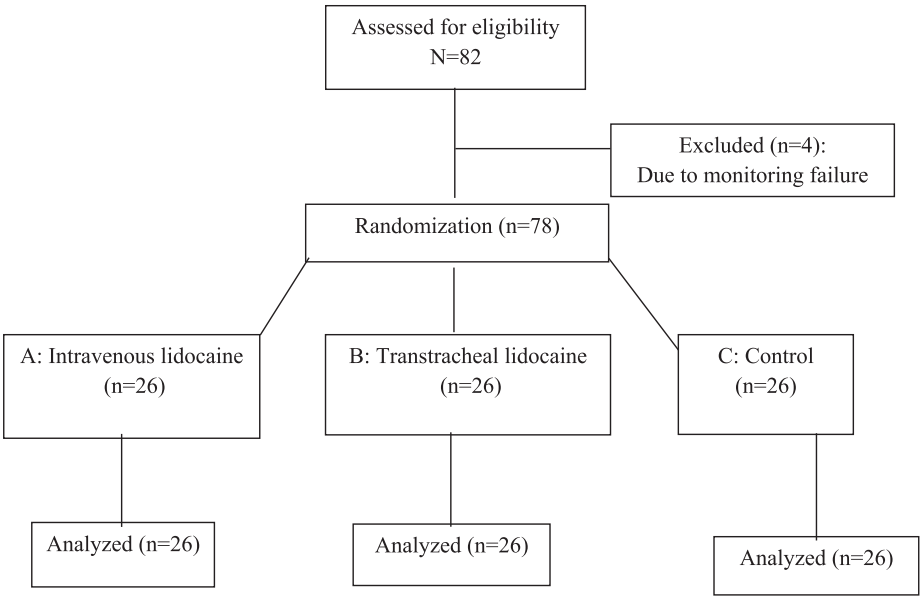

Fig. 4. Flow chart of the study protocol.

Table 4
Comparison of mean heart rate for the three groups at the time of study.

P Value	SD	Mean	Group	Time
0.950	8.346	71.15	A	Entrance
	8.498	71.69	B	
	8.766	71.91	C	
0.935	7.663	77.35	A	30 s after induction
	7.688	77.69	B	
	6.582	76.91	C	
<0.001	8.069	81.65	A	30 s after intubation
	6.229	74.65	B	
	7.163	82.50	C	
0.470	8.216	72.69	A	3 min after intubation
	6.506	72.42	B	
	6.264	74.77	C	
0.170	6.797	68.04	A	6 min after intubation
	6.700	70.62	B	
	6.766	71.59	C	
0.140	5.442	67.54	A	9 min after intubation
	6.747	71.00	B	
	6.435	69.50	C	

stimulation following intubation.

Results of Lee and Park's research indicated that use of lidocaine on the laryngoscopy blade would reduce cardiovascular responses following laryngoscopy during intubation with similar results to our findings, however our patients had known hypertension [20]. Some studies have demonstrated the proper effect of lidocaine sprays on reducing hemodynamic effects during intubation [13,19]. Transtracheal lidocaine is important on reducing hemodynamic changes and should be used at least 2 min before endotracheal intubation and these finding are consistent with our study [19,20].

In the study of Rajan et al., patients were randomly divided into two groups and received 4 ml of 4% solution of lidocaine intratracheal and group B received a routine combination with propofol 100 mg/hr. The use of lidocaine transtracheal can be considered as an alternative to infusion of propofol in surgical procedures without muscle relaxants, and lead to a reduction in hemodynamic changes. Transtracheal block is an appropriate and safe substitute for surgery in cases requiring muscle relaxant [21]. This study also was consistent with the results of our study.

5. Conclusion

The use of lidocaine, especially transtracheal, is one of the main options for maintaining hemodynamic status and preventing hypertension and tachycardia in patients with chronic under control hypertension during laryngoscopy and intubation. Further studies are required on high-risk patients with ischemic heart disease whose hemodynamic changes are important, along with an assessment of the degree of muscles relaxation and depth of anesthesia. We do not have any baseline data about BP and HR of patients in the home or in the rest without stress and it was a limitation of our study.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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None.

Authors' contribution

Pooya Derakhshan, Seyed Hamid Reza Faiz participated in the study concept and design. Azita Yazdi performed analysis and interpretation of data. Drafting of the manuscript was conducted by Pooya derakhshan and Masood Mohseni. Azita Yazdi and Pooya Derakhshan preformed the revision of the manuscript for important intellectual content, and statistical analysis.

Declaration of competing interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tacc.2019.09.002.

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