Original Article

Comparison the Effects of Intraoperative Labetalol and Lidocaine on Postoperative Blood Pressure and Heart Rate in Brain Surgeries

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Abstract

Background: Long-term anesthesia applied in some operations, especially in neurosurgical operations leads to unwanted complications. This study aimed to compare the effect of intraoperative labetalol and lidocaine injection on the rate of changes in postoperative blood pressure and heart beat in patients undergoing brain operation. **Materials and Methods:** This is a simple double-blind randomized clinical trial study conducted in Al-Zahra and Kashani Hospitals on 90 patients' candidate for craniotomy operation with the age range of 18–65 years, Glasgow Coma Scale (GCS) ≥13 before anesthesia, physical class of American Society of Anesthesiologists I, II, insensitivity to labetalol who were divided into two groups of 45 individuals in the random allocation method. To start anesthesia, fentanil 1.5 mg per 1 kg of body weight, midazolam 5 mg, propofol 2 mg/kg and then, atracurium 0.15 mg/kg and lidocaine 1.5 mg/kg were used. The rate of patients' bucking and blood pressure were checked at GCS time after operation and in patients' recovery in terms of 0, 5, 10, 20 and 30 min after arrival in the recovery room and 1 h later. **Results:** 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 bradicardia, hypotension, tachycardia or hypertension was observed in the patients of both groups. **Conclusion:** Using labetalol in craniotomy surgery is helpful for two main reasons that are the proper control of intraoperative and postoperative blood pressure and prevention of postoperative reactions, especially cough and if there is no contraindication for using it, it is recommended.

Keywords: *Heartbeat, intraoperative labetalol, lidocaine, postoperative blood pressure*

Introduction

Long-term anesthesia applied in some operations, especially in neurosurgical operations leads to unwanted complications both during intra-anesthesia and postoperation in patients that in some cases, such complications are serious and life-threatening and that the anesthesia time should be reduced to the minimum possible time.[1,2] On the other hand, anesthetic drugs can cause various complications for patients depending on the type, dose and duration of anesthesia as well as the method of anesthetic induction.[3] Therefore, in order to minimize the above-mentioned complications and for the patient to have a good general and hemodynamic condition after anesthesia, several methods such as using premedication or medications reducing complications are used after anesthesia[4] and since getting out of anesthesia is associated with stimulating sympathetic nervous system and increasing pulse rate and blood pressure in patient, a condition should be considered in which patients have minimal response to stimulation.[4] To that end, various methods such as the injection of diltiazem, labetalol, esmolol and injectable opioids such as fentanil, alfentanil and also lidocaine are used while there is no unified or generally accepted method for that work.[5]

Labetalol is a blocker of adrenergic receptors with the selective effect of alpha 1 receptors and nonselective effect of beta receptors. The ratio of alpha to beta, one to seven, is used to control and treat high blood pressure and is applied for the initiation of the effect which has the duration of 5 h. The initial dose of 10–20 mg and then 40–80 mg at 10 min up to the total dose of 300 mg are infused.[6,7] Labetalol is usually used in patients undergoing neurosurgery since it does not increase intracranial pressure (ICP).[7] Beta-blockers such as labetalol are not cerebral vasodilator and can be used as a prophylaxis in the

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reduction of supraventricular tachycardia and changes of ST-segment and T-wave in electrocardiogram.[5] Since the drug has mild side effects and can be used in craniotomy surgeries, it can be used as a drug for blood pressure control after extubation.[2] Lidocaine is one of the drugs commonly used to reduce postoperative complications including postoperative pain in all health centers. In addition to control and pain relief for patients, the drug also causes to decrease the blood pressure in patients.[3] However, to prevent unwanted complications, there is disagreement on the type of drug used after craniotomy operation. Therefore, according to the stated contents and the importance of the subject, the aim of this study was to evaluate the effects of intraoperative labetalol and lidocaine on postoperative blood pressure and heart rate in brain surgeries.

Materials and Methods

This is a simple double-blind randomized clinical trial study conducted in Al-Zahra and Kashani Medical Centers of Isfahan University of medical sciences in central part of Iran. The study population included patients with brain tumor candidate for craniotomy operation admitted to the hospital.

Inclusion criteria included patients with brain tumor candidate for craniotomy except for brainstem tumor, the age range of 18–65 years, Glasgow Coma Scale (GCS) ≥13 before anesthesia, physical class of American Society of Anesthesiologists (ASA) I, II, insensitivity to labetalol, the patient consent for participation in the study, nonhistory of hypertension (HTN) and heart rhythm disorders or asthma, not suffering from end stage renal disease and nonsevere respiratory disease. It was also decided that patient was excluded from the study in the case of the incidence of bradicardia (heart rate [HR] <40) intra-anesthesia, excessive hemodynamic changes (changes of more than 25%), heart block, extubation in the operating room and patient death before the intervention and need for massive transfusion (bleeding more than 100 cc per min or more than 2.5 L).

Using the formula of estimating the sample size, the sample size required for the study was estimated as 43 patients per group in order to compare means and by considering the confidence level of 95%, test power of 80%, variance of changes in postoperative blood pressure estimated as 1.33 in a similar study and also the least significant difference between two groups was considered as 0.8 that in order to increase the reliability, 45 patients were studied in each group.

The study was done in a way that after obtaining permission from the Department Research Committee and Medicine Ethics Committee and the written consent, 90 patients candidate for craniotomy operation were divided into two groups of 45 individuals in the random allocation method. Randomization method was in a way that patient was first placed in the labetalol group in the lucky draw and the next patients were sequentially distributed in the order of entering in the study and until the sample size reached to the sufficient number. For all patients, the preoperative visit was done and after receiving premedication of midazolam 2 mg, they were sent to the operating room. To start anesthesia, fentanil 1.5 μg/kg of body weight, midazolam 5 mg, propofol 2 mg/kg and then, atracurium 0.15 mg/kg and lidocaine 1.5 mg/kg were used. Using propofol 100 mg, anesthesia maintenance was per 1 kg of body weight per hour. Propofol was administered according to the Miller instruction and based on the patient age [Figure 1].

On the fluid therapy, the maintenance fluid of normal saline and ringer lactate was given as liter to liter. Little bleeding was compensated with a 3-fold of blood volume by normal saline and excessive bleeding by blood (according to miller instruction) that in all cases, the project executive was responsible for decision-making.

Diuretic fluid in the NaCl type 5% in the rate of 5 ml/kg and patients' urine was compensated with equal volume of urine in the isotonic crystalloid type. In each patient, insensible water loss was also compensated using isotonic crystalloid. However, hypotension and bradycardia of patients were compensated by phenylephrine 0.1 mg/kg every 1–2 h as needed and atropine 0.4 mg/kg, respectively. HTN and tachycardia were also compensated by labetolol 0.25 mg/kg. Extubation time was determined and the patient's blood pressure (mean arterial pressure [MAP], systolic pressure and diastolic pressure) and HR were measured and recorded at the onset of the operation and then, every 5–15 min. The rate of patients' bucking and blood pressure were checked at GCS time after operation and in patients' recovery in terms of 0, 5, 10, 20 and 30 min after arrival in the recovery room and 1 h later.

Blinding was in the way that patients were not aware of the types of drug used. Drug preparation and injection were done by the anesthetist who was not involved in the data collection. Data was collected by a physician who was unaware of the type of the studied group. All data were recorded on a check-list.

After collecting and eliminating defects, we entered the study data into computer and analyzed them using SPSS for Windows software (SPSS Inc., Chicago, IL, USA; version 22). The applied statistical tests included Chi-square and Fisher's exact tests for comparing qualitative variables between two groups, *t*-test for comparing quantitative variables between two groups and ANOVA for comparing the process of changes in the hemodynamic parameters in both groups and during stay in the recovery room.

Results

In the present study, 90 patients candidate for craniotomy surgery were selected and enrolled. The mean age of patients receiving labetalol and lidocaine was 64.16 ± 7.5

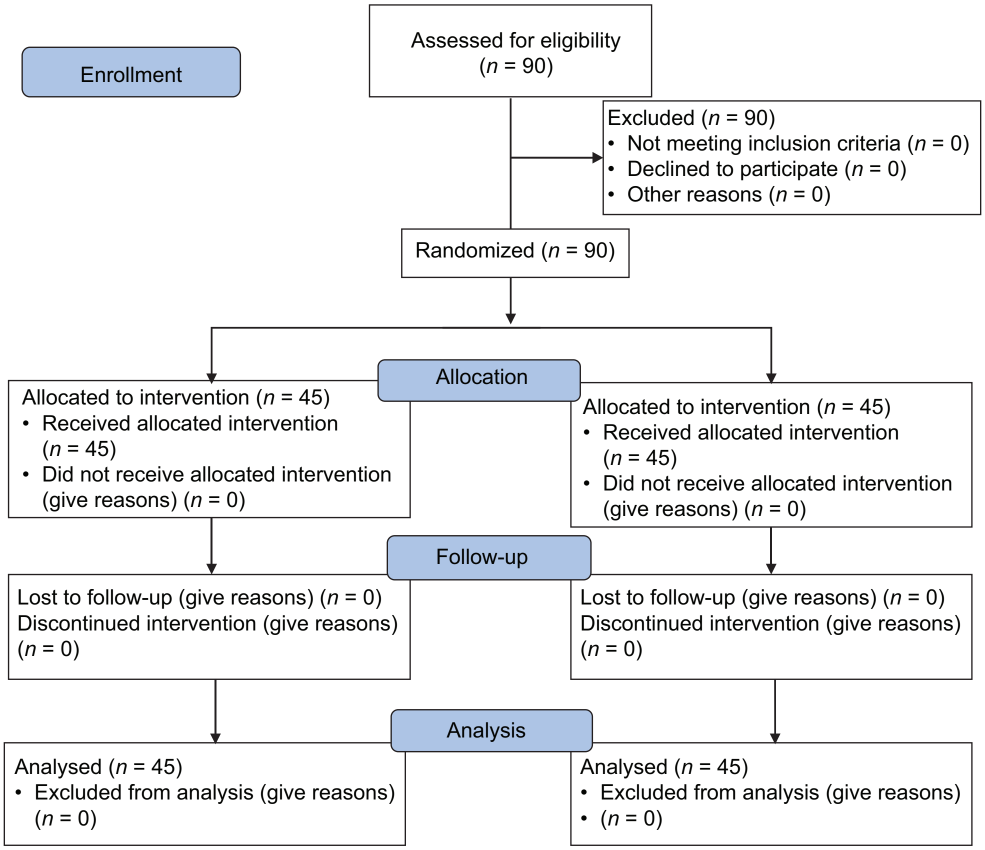

Figure 1: CONSORT 2010 flow diagram

and 64.04 ± 5.6 years, respectively and according to the *t*-test, there was no significant difference between two groups (P = 0.94). In two mentioned groups, 26 and 15 subjects, respectively were male and the rest were female (P = 0.21). In Table 1, the distribution of demographic and general variables in both groups has been shown. According to this table, mean weight, ASA, operation time, duration of anesthesia had no significant difference in the two groups ($P > 0.05$). Based on the obtained results, in the two mentioned groups, the most common operation site was frontal site (44.4% in the labetalol group and 40% in the lidocaine group) and according to Fisher exact test, the difference between two groups was not significant (P = 0.29).

Evaluation of hemodynamic parameters of the two groups revealed that the mean intraoperative systolic and diastolic blood pressure and HR had no significant difference in the two groups at the recovery- and extubation time and according to ANOVA with repeated observations, the process of changes in blood pressure and HR in both groups had no significant differences ($P > 0.05$) [Figures 2-5].

The mean duration of staying in the recovery room was 36.4 ± 8.1 and 41.8 ± 10.6 min in two labetalol and lidocaine groups, respectively and according to *t*-test, patients receiving labetalol stayed less in the recovery room (P = 0.009).

Table 1: Distribution of general and demographic variables in both groups

Variables	Groups		*P*
	Labetalol	Lidocaine	
Age (year)	64.16±7.5*	64.04±5.6*	0.94
Sex ratio (male/female)	26/19	20/25	0.21
Weight (kg)	69.87±6.7*	67.11±7.15*	0.063
ASA**: I/II	38/7	43/2	0.08
Operation time (min)	197.6±46.0*	205.3±37.7*	0.39
Anesthesia time (min)	231±26.3*	238.7±39.8*	0.29
Recovery time (min)	36.4±8.1*	41.8±10.6*	0.009

*The data has been showed as mean±SD **: ASA: American Society of Anesthesiologists

Evaluation of postoperative complications such as cough, bradicardia, hypotension, nausea, vomiting and laryngospasm in two groups showed that 7 individuals of labetalol group and 17 cases of lidocaine group suffered from postoperative complications (15.6% vs. 37.8%) and according to the Chi-square test, the frequency distribution of the mentioned complications had a significant difference in both groups (P = 0.017). In Table 2, the frequency distribution of postoperative complications in the two groups is given. According to the mentioned table, the incidence of coughing in lidocaine group was significantly greater than that in labetalol group so that 8.9% and 33.3% suffered from coughing among from

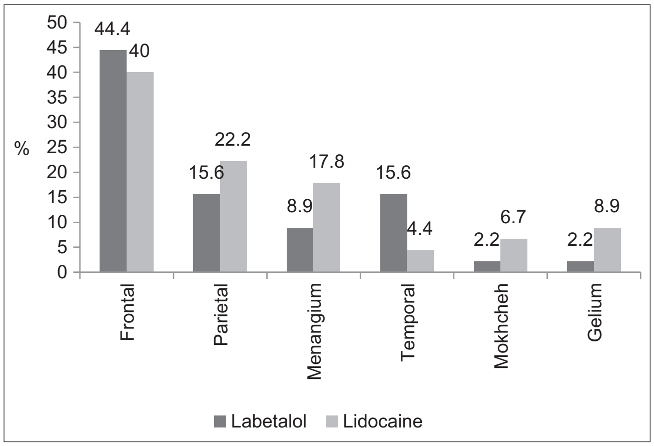

Figure 2: The frequency percentage of operation site in both groups (*P* = 0.29)

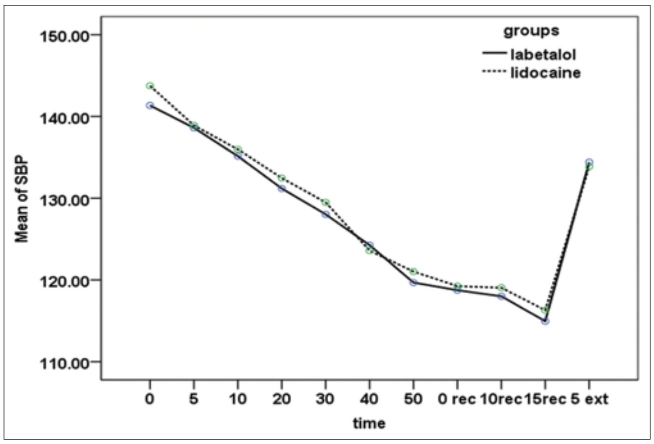

Figure 3: Mean systolic blood pressure from time zero to extubation time in both groups (*P* = 0.75)

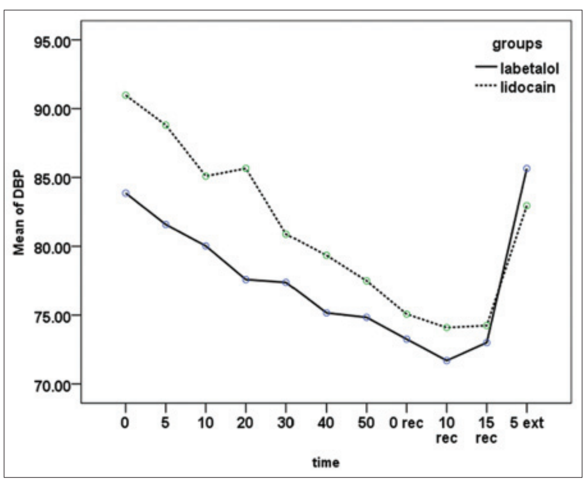

Figure 4: Mean diastolic blood pressure from time zero to extubation time in both groups (*P* = 0.08)

labetalol and lidocaine groups, respectively (P = 0.004). Also, the postoperative incidence of nausea and vomiting in lidocaine was more than that in the labetalol group while the difference between two groups was not significant (P > 0.05).

Table 2: The frequency distribution of postoperative complications in both groups

Complication	Groups		*P*
	Labetalol *n* (%)	Lidocaine *n* (%)	
Cough	4 (8.9)	15 (33.3)	0.004
Bradicardia	0 (0)	0 (0)	1
Hypotension	0 (0)	0 (0)	1
Nausea	6 (13.3)	8 (17.8)	0.56
Vomiting	3 (6.7)	4 (8.9)	0.99
Laryngospasm	1 (2.2)	2 (4.4)	0.99

Discussion

The overall objective of the present study was to compare the effect of labetalol and lidocaine on changes in blood pressure and pulse during the extubation of anesthesia in craniotomy operation for brain tumors. In this study, two groups of 45 patients undergoing craniotomy operation were studied that two groups had no significant difference in terms of age- and sex distribution, duration of operation and anesthesia, operation type, weight and ASA and sine the confounding effect of the above factors was neutralized in the study, the obtained results are more likely related to the effect of the used drug type.

Patients in both groups had 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 bradicardia, hypotension, tachycardia or HTN was observed in the patients of both groups. Therefore, it can be concluded that using labetalol in craniotomy operation had no bad effect on hemodynamic in patients and it can be considered as a safe drug in the anesthesia for neurosurgery.[8] So far, the effect of labetalol on hemodynamic has been assessed in several studies and in most studies, no bad effects have been observed from this drug.[9] In the study by Kross *et al*., (2000) the combined effect of enalapril and labetalol with enalapril and nicardipine was compared to prevent HTN after craniotomy surgery. In the study, for 42 patients, intravenous enalapril with the dose of 1.25 mg and nicardipine of 2 mg were administered and in the other group, labetalol of 5 mg and nicardipine were used with the aim of systolic pressure below 140 that the result of systolic pressure in both groups was similar.[10] Also, in the study conducted by Do *et al*. in 2012, 54 patients aged between 20 and 60 years undergoing anesthesia with desflurane were randomly divided into two groups. Normal saline of 5 ml was injected to a group and labetalol 0.3 mg/kg was injected to other group. HR, MAP and systolic and diastolic blood pressure were measured at 5 min after the injection of saline and labetalol and then, every 1 min for 5 min after inhalation of dose of florent and 2 min after intubation. The result was that in group that saline was injected, inhalation of florent caused to increase HR and blood pressure while in labetalol group, HR and blood pressure dropped. In this study, it has been concluded that labetalol injection is effective in reducing hemodynamic responses in intubation and administration of desflurane.[11] In his study, Owens showed that given that sub-arachnoid hemorrhage is associated with aneurysm rupture, it can be prevented by keeping the systolic pressure <15 that nicardipine and labetalol have been proposed to treat the blood pressure during cerebrovascular accidents.[8]

Preventing increase or decrease in ICP is a common anesthesia requirement in neurosurgery. In an adult and healthy human, ICP is H_2O 120 mm that is fixed in internal space of skull and spine. When the skull is closed, cerebral perfusion pressure (CPP) is obtained by the formula of (CPP = MAP − ICP) and ICP is to the extent preventing brain herniation in intracranial spaces or through foramen magnum.[10] When the skull is opened, due to the relaxation of the intracranial contents, it is easily assessable for surgery; however, if the pressure is high, brain herniation may occur from craniotomy site. Cases considered for opened or closed skull is the same. Symptoms from increasing ICP include headache (especially headaches creating with changes in status or causing awakening from sleep at night), nausea, vomiting, blurred vision, and drowsiness.[11] In disease conditions, a slight increase in intracranial volume will cause a huge increase in ICP. Increasing ICP causes herniation of brain tissue from one part to the other.[12] This causes the mechanical damage or disorder in perfusion to brain tissue and as a result, ischemic brain[12] and physician should reduce the ICP for dealing with ICP increase and reducing it and after surgery, the control of postoperative ICP has a crucial importance. In order to achieve this objective, diuretics are usually and widely used in neurosurgery to reduce intra- and extra-cellular fluid.[9] In this respect, using labetalol is very helpful because of the proper control of blood pressure in patients. However, other studies have emphasized on the usefulness of lidocaine in the control of ICP. For example, in a study conducted by Messerer *et al*. in 2012, cerebral edema, increasing intracranial HTN, brain hypoxia and ischemia and tension are created as a result of failure to control ICP after brain surgery and doing a series of initial measures such as avoiding straining by patient, keeping the patient in Intensive Care Unit, taking antihypertensive medications and etc., are preventive measures that can be done in this field.[13] Also, in the study conducted by Samaha *et al*., the effect of esmolol and lidocaine on reducing MAP and ICP was assessed. Twenty-two patients with ASA I, II undergoing brain surgery were enrolled in the study and randomly assigned into two groups treated with esmolol and lidocaine. The obtained results revealed that the MAP was similar in both groups. Although the ICP was less in the group receiving esmolol, it became more in the group receiving lidocaine at the end of operation and after intubation. Beta-blockers are both tranquillizer and anti-HTN and cause to reduce brain ICP and as a result, backing by decreasing the blood pressure.[14]

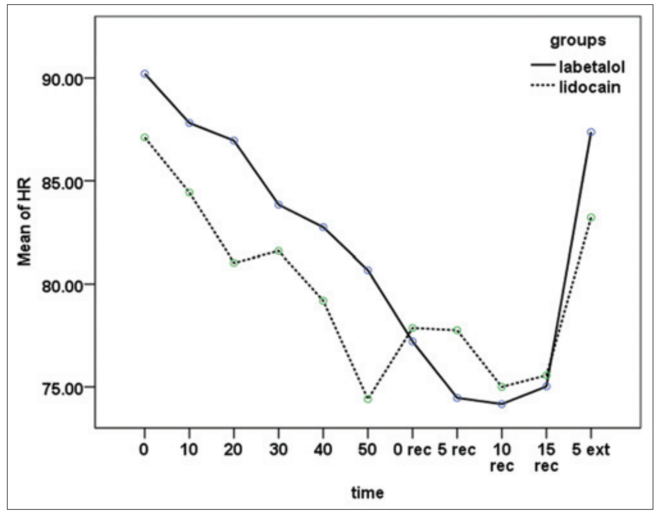

Figure 5: Mean heart rate from time zero to extubation time in both groups (*P* = 0.36)

Based on the results of our study, patients receiving labetalol had less postoperative complications that the difference was more visible in the incidence of postoperative cough so that 8.9% and 33.3% of patients suffered from postoperative cough in the labetalol and lidocaine, respectively. In craniotomy operations, extubation from anesthesia should be smooth and without straining or coughing. Increasing blood pressure causes bleeding.[15] If after extubation, the patient coughs, dura mater of skull space will open and there will be the possibility of entering air into brain and creating pneumocephalus. Cough also raises intra-thoracic, CSF and ICP and in the case of the incidence of HTN at the end of the operation, using labetalol is quite helpful and necessary. Also, coughing and vomiting cause CSF leakage and has a risk of meningitis.[13] On the other hand, suctioning into airway and ednotrachel tube and exubition cause to raise the blood pressure and increase the pressure into thorax. High blood pressure causes bleeding from ruptured arteries in the brain and raising pressure into thorax causes bleeding from ruptured brain venues during surgery and so, anesthesia should be continued until the end of the bandage and patient should not cough and strain during bandage.[16] Straining and bronchospasm are two serious respiratory disorders in existing from anesthesia. Straining is the contraction of skeletal muscles and bronchospasm results from the spasm of smooth muscles of brushing tree and both respond to chemical and physical stimulation and endotracheal tube and both can be prevented during the general anesthesia.[14-16] However, cough is dangerous hyperdinamic response in the postoperative course and can cause HTN and tachycardia and dysrhythmia and increase intracerebral hemorrhage and dehisens wound and bronchospasm that endanger the health of the patient.

Conclusions

Therefore, according to the results obtained from this study and compariing them with those of the other studies, using labetalol in craniotomy surgery is helpful for two main reasons that is the proper control of intraoperative and postoperative blood pressure and prevention of postoperative reactions, especially cough and if there is no contraindication for using it, it is recommended.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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