Original Article

Comparing the Effect of Labetalol versus Morphine on Controlling Blood Pressure and Pulse Rate during Emergence from Anesthesia after Craniotomy

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Abstract

Background: Emergence from anesthesia is associated with sympathetic stimulation, increase in pulse and blood pressure. There are different methods, but the most appropriate method should be selected regarding the differences in nationalities. This study aimed to compare the efficacy of morphine and labetalol in controlling blood pressure and pulse during emergence from anesthesia in brain tumors craniotomy. **Materials and Methods:** This study was conducted at Al-Zahra Hospital of Isfahan - Iran on 60 patients suffering from brain tumor candidated for craniotomy and randomly classified into two groups of 30. One group received labetalol with dose of 10 mg over 10 min from 45 min before finishing dressing and then 0.75 mg/min until 35 min later; another group received morphine in bolus dose of 0.1 mg/kg during 2–3 min. Blood pressure and pulse were measured every 10 min over 40 min. After operation, they were measured every 5 min over 15 min. **Results:** The morphine group had higher systolic (133.3 ± 18.8) and diastolic blood pressure (87.1 ± 13.6) (P = 0.021 and 0.028, respectively) at extubation and during 45 min before dressing, the diastolic blood pressure was significantly higher in compares with labetalol (75.3 ± 10.5) ($P < 0.05$). And extubation time was significantly shorter in labetalol group (7.7 ± 0.84) ($P < 0.001$). Pulse had no significant difference in both groups. In labetalol group, blood pressure and pulse fluctuations were more stable. **Conclusion:** Administration of labetalol 45 min before finishing dressing can significantly control blood pressure during emergence from anesthesia and also shorten the time of extubation during emergence in patients undergoing craniotomy.

Keywords: *Craniotomy, labetalol, morphine*

Introduction

Anesthetic complications and emergencies can occur during any of the four phases of premedication, induction, maintenance, and recovery from anesthesia. These are including central nervous system, respiratory and cardiovascular complication.[1] Emergence from anesthesia is associated with sympathetic stimulation and, therefore, may result in tachycardia, hypertension, and arrhythmia.

Closed control of blood pressure is very important during craniotomy. It is assumed that the brief periods of hypertension during emergence from anesthesia may result in the occurrence of postoperative bleeding and cerebral edema. It is generally preferable to avoid the occurrence of hypertension by preemptive therapy. There are many drugs that can be used to control emergence hypertension such as diltiazem, lidocaine, labetalol, esmolol, and intravenous opiates such as morphine, alfentanil, and remifentanil are used. But there is no single or commonly accepted method.[2]

Kross *et al*. compared the efficacy of the combination of enalapril/labetalol with that of enalapril/nicardipine to prevent emergence postcraniotomy hypertension and reported that systolic blood pressure was similarly controlled in both groups. There was a marginally smaller incidence of failures and adverse effects with labetalol. Blood pressure profiles were similar for both groups.[3] Goma and Ali, also compared the anti-hypertensive effects of both remifentanil and esmolol infusion in control of emergence hypertension after craniotomy for brain tumor surgery, they concluded that remifentanil can be used to control blood pressure during emergence of anesthesia after craniotomy for brain

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tumors. It has higher rapid recovery score than esmolol and other narcotics.[4] However, there have been no studies concerning the comparison of the effect of labetalol and morphine on blood pressure and pulse rate in patients undergoing craniotomy.

Labetalol is an adrenergic receptor blocking agent that has an effect on both selective alpha-1 and nonselective beta receptors, with the ratio of alpha to beta of 1/7 which is used for hypertension treatment and control. It has a rapid onset of action. Its maximum action begins within 5 min and has the duration of 5 h. Its initial dose is 10–20 mg in 2 min and then 40–80 mg in 10 min until the total dose of 300 mg, and then the infusion of 2 mg/min.[5] This drug does not increase intracranial pressure and improves cerebral perfusion pressure.[5]

Morphine is an opioid analgesic drug, a recreational drug and the main psychoactive chemical in opium. In clinical medicine, morphine is regarded as the gold standard, or benchmark, of analgesics used to relieve intense pain and suffering. Relative contraindications of morphine are acute respiratory depression, raised intracranial pressure, including head injury, renal failure, chemical toxicity, biliary colic.[3] However, in case of preventing unintentional complications, there is controversy over using the type of drug after craniotomy surgery.

The aim of this study was conducted to compare the efficacy and preventative effects of morphine and labetalol in controlling blood pressure and pulse during emergence from anesthesia in craniotomy for brain tumors as well as postoperative complications in these patients.

Materials and Methods

This is a double-blind clinical trial which was conducted at Al-Zahra Hospital in Isfahan - Iran in 2013. The study population consists of patients suffering from brain tumor who were candidated for craniotomy surgery in this hospital. After approval by our local ethic committee and obtaining informed written consent, 60 patients aged between 18 and 64 years old, American Society of Anaesthesiologists (1 and 2) undergoing craniotomy that were randomized with the use of randomization tables, included in this study.

Exclusion criteria included sensitivity to labetalol and morphine, smoking, alcoholism, opium addiction, asthma and history of arrhythmia, contraindications of consumption of labetalol and morphine, and brain stem tumors.

Sample size was calculated through the formula of sample size estimation to compare averages, and with respect to 95% confidence level and 80% test power. The postoperative variance of blood pressure was estimated 1.1, and the least significant difference between two groups was estimated 0.8, based on 30 patients in each group.

We studied 60 patients undergoing craniotomy, who were randomly allocated into two groups of 30. All patients had presurgery visit and after receiving premedication (All patients received midazolam 0.1 mg/kg 1 h before induction of anesthesia) were dispatched to the operating room. In order to start the induction of anesthesia, fentanyl (1.5 μg/kg), midazolam (5 mg), and propofol (2 mg/kg) and then atracurium (0.15 mg/kg) and lidocaine (1.5 mg/kg) were used. The maintenance of anesthesia was conducted using propofol (100 μg/kg/min). In case of fluid therapy, in addition to maintenance fluid which were NaCl 0.9% and ringer's lactate in alternate order, normal saline with 3 times the volume of blood was compensated for low bleeding and real blood was compensated for high bleeding. Diuretic fluid was compensated by 5 ml/kg of 5% NaCl and urine of patients was balanced by isotonic NaCl with an equivalent volume of urine. Furthermore, insensible water-loss was balanced using isotonic NaCl in each patient. If hypotension or bradycardia occurred, we administered Phenylephrine (100 μg) and atropine (0.5–1 mg), respectively. Nitroglycerin (5 μcg/min) was used to treat hypertension and if tachycardia occurred fentanyl 100 μg was administered. Hypotension and bradycardia are defined as more than 30% decrease in systolic blood pressure and heart rate, respectively, from the basic values.

Labetalol with dose of 10 mg over 10 min was injected into patients of the first group at 45 min before finishing dressing and then 0.75 mg/min until 35 min later. Morphine with bolus dose of 0.1 mg/kg was injected into the second group. The studied drugs were administered by the second anesthetist who was not aware of injected drugs. The extubation time (the time from discontinuation of anesthetic drugs till the tracheal extubation), blood pressure and pulse of the patients were measured at the beginning and then every 10 min up to 40 min, and then it was measured every 5 min up to 15 min after surgery. The results along with patient's demographic data were recorded by the second anesthetist in a special questionnaire which had been designed for this purpose. We did not find any side effects of labetalol and morphine in patients.

Our data were analyzed by using repeated measured design analysis of variance (ANOVA), *t*-test and chi-square test by applying SPSS version 22 statistical package (SPSS Inc., Chicago, IL, USA). A $P < 0.05$ was considered statistically significant.

Results

In this study, 60 patients who candidated for craniotomy surgery were randomly classified into two groups of labetalol and morphine. In labetalol group, 6 patients were excluded from the study due to arrhythmia ($n = 3$) and hypertension ($n = 3$). In Table 1, distribution of demographic and general variables of patients of the two groups is illustrated. According to *t*-test, the average of age, weight, duration of surgery, duration of anesthesia, and blood loss were not significantly different between the two

groups (P = 0.05). Also based on Chi-square test, the two groups did not differ in gender distribution (P = 0.21).

The most common type of tumor in the two groups was meningioma, with frequency of 13 cases in morphine group and 8 cases in labetalol group (43.3% vs. 33.3%). Also, 8 cases in morphine group and 6 cases in labetalol group suffered from gliomas (26.7% vs. 25%). Of these two groups, 2 and 1 cases suffered from hemangioendothelioma, respectively (6.7% vs. 4.2%). Three patients (12.5%) in labetalol group suffered from aneurysm [Table 1 and Figure 1]. According to the Figures 2-4, the average of hemodynamic parameters of patients before surgery and until extubation time in morphine and labetalol groups is illustrated. Based on these figures, blood pressure and pulse were more stable in labetalol group during the study.

In Table 2, the average and standard deviation of hemodynamic parameters before surgery, during surgery, during recovery, and at the time of extubation in the two groups, are shown. According to this table, patients receiving morphine had a higher diastolic blood pressure at the time of extubation (87.1 ± 13.6) (P = 0.021). Furthermore, in morphine group, during surgery (75.3 ± 10.5) and at the time of extubation (87.1 ± 13.6), diastolic blood pressure was significantly higher (P = 0.028 and 0.001, respectively), but in this period, the heart rate did not significantly differ between the groups (P > 0.05).

The time of staying in recovery in both groups of morphine and labetalol was 76 ± 4.4 and 61.7 ± 27.4 min, respectively, and according to t-test, no significant difference was observed between the groups (P = 0.37). Extubation time in both groups was 42.1 ± 10.7 and 7.7 ± 0.84 min, respectively, and according to t-test, no significant difference was observed between the groups (P < 0.001). It should be mentioned that during the study, no patient suffered from postoperative complications (bradycardia, hypotension, nausea and vomiting).

Table 1: Distribution of general and demographic variables in the two groups

Variable	Morphine group (n=30)	Labetalol group (n=30)	P
Age (year)	43.6±18	47.5±15.1	0.4
Weight (kg)	73.4±11.5	71.1±13.7	0.55
Operation duration (min)	228.8±48.4	218.1±44.4	0.41
Anesthesia duration (min)	246±64.7	258.1±51	0.46
Bleeding volume (ml)	523.3±427	550±379.2	0.83
Sex			
Male	11 (36.7)	8 (26.6)	0.21
Female	19 (63.3)	22 (73.3)	

Discussion

This study aimed at comparing the efficacy and preventative impacts of morphine and labetalol in

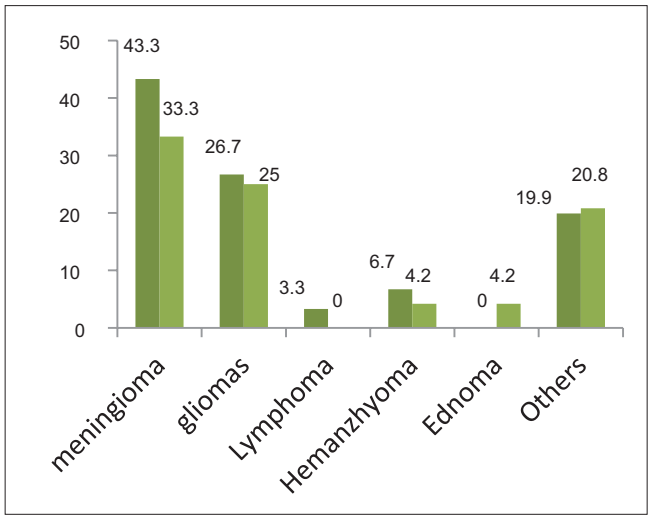

Figure 1: The frequency of tumor type in the two groups

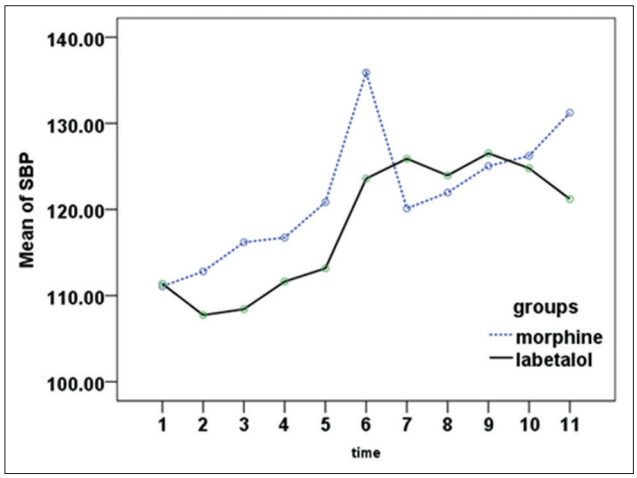

Figure 2: Changes in systolic blood pressure variations in two groups

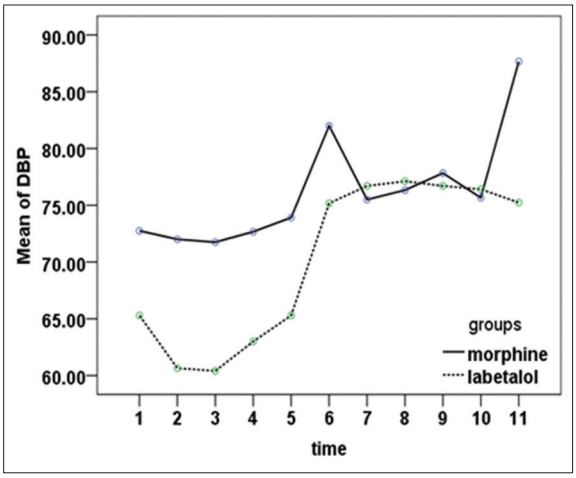

Figure 3: Changes in diastolic blood pressure variations in the two groups

Table 2: The average and SD of hemodynamic parameters in the groups during this period

Parameter	Groups(n=30)	Before operation	During 45 min before dressing	At recovery	At extubation
Systolic blood pressure (mmHg)	Morphine	110.6±12.5	121.1±13.1	124±17.1	133.3±18.8
	Labetalol	111.4±11.6	114.1±17.9	125.4±13.8	121.8±16.2
	P	0.83	0.11	0.74	0.021*
Diastolic blood pressure (mmHg)	Morphine	68.1±9.5	75.3±10.5	78.2±12.6	87.1±13.6
	Labetalol	65.2±12	65.9±7.6	76.5±9.9	77.2±11.7
	P	0.37	0.001*	0.59	0.028*
Heartbeat	Morphine	78.1±17.8	80.5±16.5	81.4±19	85.9±21.4
	Labetalol	76.4±11.2	78±10.3	78.9±12.9	80.5±12.2
	P	0.72	0.51	0.57	0.35

**P* values indicating significant change. SD: Standard deviation

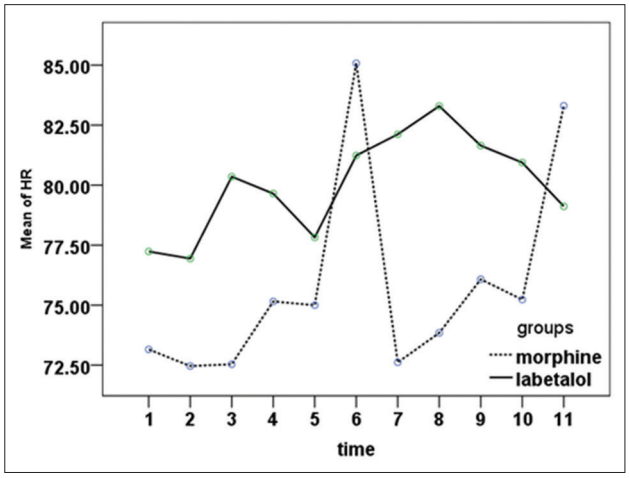

Figure 4: Changes in heart rate in the two groups

controlling blood pressure and pulse during emergence from anesthesia in craniotomy surgery for brain tumors as well as postoperative complications in craniotomy patients.

In this study, 60 patients who candidated for craniotomy surgery, were randomly classified into two groups, receivers of labetalol as well as receivers of morphine, and then analyzed. In labetalol group, 6 patients were excluded from the study, due to arrhythmia (n = 3) and hypertension (n = 3). Patients in two groups were similar in demographic variables including age, sex, weight, and also according to anesthesia duration and type of surgery. Since these factors can affect the results, their confounding effect was neutralized in this study, and the results are most likely related to the difference in the effects of morphine and labetalol.

By evaluating hemodynamic parameters of patients during surgery and recovery, it was found that patients receiving labetalol had lower systolic pressure at the time of extubation and had lower diastolic pressure during 45 min before dressing as well as at the time of extubation. Patients receiving labetalol had better hemodynamic stability, but in morphine group, some fluctuations in blood pressure and heart rate were observed.

In both groups, the duration of staying in recovery were similar, but extubation time was significantly shorter in labetalol group in comparison with morphine group. This difference may be due to the sedative effect of morphine which results in delayed awareness for extubation.

On the other hand, during the study, no postoperative complications were seen in both groups in terms of hemodynamic parameters. Other studies have revealed that using labetalol in craniotomy surgeries makes a better hemodynamic stability in patients after extubation.[3,6]

For example, Kross *et al*. compared the efficacy of the combination of enalapril/labetalol with that of enalapril/nicardipine to prevent emergence postcraniotomy hypertension and reported that systolic blood pressure was similarly controlled in both groups. There was a marginally smaller incidence of failures and adverse effects with labetalol. Blood pressure profiles were similar for both groups.[3]

In a study which was carried out in 2012, Do *et al*. studied the effect of intravenous labetalol administration on hemodynamic responses during desflurane inhalation. They reported that administration of intravenous labetalol is effective in attenuating tracheal intubation and desflurane-induced hemodynamic responses.[6] Moreover, in 2012, Owens studied the control of blood pressure in acute cerebrovascular disease. He recommended that nicardipine and labetalol are appropriate for rapidly treating hypertension during cerebrovascular emergencies.[7] The results of these studies were almost similar to our findings that in patients receiving labetalol, blood pressure was lower during emergence from anesthesia.

In our study, in labetalol group, complications of this drug were rare; it may be explained by the rapid distribution of labetalol in the body. In addition, the extubation time and the emergence from anesthesia were shorter, and the awareness of patients was rapider in this group. These findings are valuable for postoperative evaluation of neurological functions in patients undergoing craniotomy.

Moreover, labetalol reduces blood pressure and systemic vascular resistance, but keeps the cardiac output, therefore, cerebral blood flow is not endangered by this drug and it

may be an appropriate drug in treating uncontrolled blood pressure during craniotomy.

Conclusion

Administration of labetalol 45 min before finishing dressing can significantly control blood pressure and shorten the time of extubation during emergence from anesthesia in patients undergoing craniotomy for brain tumors.

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Conflicts of interest

There are no conflicts of interest.

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