Comparison of effectiveness and safety of labetalol and hydralazine on blood pressure during cataract surgery in patients with hypertension

Comparación de la efectividad y la seguridad de labetalol e hidralazina sobre la presión arterial durante la cirugía de cataratas en pacientes con hipertensión

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Abstract

Introduction: Cataract surgery is one of the most commonly performed surgeries, and patients over the age of 60 are major candidates for this procedure. Hypertension is one of the most commonly reported diseases in this age group. Since hypertension is associated with poor surgery outcomes, it is important to find appropriate medications for controlling the optimal blood pressure of patients. Therefore, the present study aimed to compare the effect of labetalol and hydralazine on blood pressure during cataract surgery.

Materials and Methods: A total of 63 patients undergoing cataract surgery in 2014-2015 were enrolled in this clinical trial, and randomly assigned to the hydralazine group (n=30) and the labetalol group (n=33). Systolic, diastolic, and mean arterial blood pressure and heart rate were recorded at 0, 5, 10, and 15 minutes.

Findings: Changes in the heart rate were similar in both groups and had an increasing trend from baseline to 15 minutes. In terms of changes in blood pressure after drug injection, labetalol resulted in a more rapid decrease in systolic, diastolic, and mean arterial blood pressures than hydralazine, so that their values were significantly lower in the labetalol group than the hydralazine group after 5 minutes.

Conclusion: Both labetalol and hydralazine seem to be suitable for controlling blood pressure during surgery. However, the more rapid effect of labetalol than hydralazine on lowering blood pressure and the reflex tachycardia, observed most often with hydralazine, should be considered when selecting them.

Keywords: labetalol, hydralazine, hypertension, surgery, cataract

Introduction

Cataract surgery is one of the most commonly performed surgeries, and patients over the age of 60 are major candidates for this procedure[1]. Non-ophthalmic complications of cataract surgery occur in 2% to 15% of cases. The most common complications are hypertension, bronchoconstriction, and arrhythmia which account for 90% of the cataract surgery-related non-ophthalmic adverse events[2]. Given the negligible physiologic effects of the eye, most of the eye surgeries, including cataract surgery, are considered low-risk surgical procedures[3]. However, two-thirds of patients undergoing cataract surgery have at least one chronic illness. Hypertension is one of the most commonly reported diseases occurring in about 50% of these cases. In fact, the high prevalence of hypertension in these patients can be justified by the increasing prevalence of hypertension with age[4].

Perioperative hypertension may arise from the following conditions:

- Induction of anesthesia
- Pain-induced sympathetic reflex resulting in general vasoconstriction during surgery
- Surgical pain, hypothermia, hypoxia, and overhydration-induced increase in intravascular volume after anesthesia
- Extracellular to intravascular fluid shift 24 to 48 hours after surgery
- Discontinuation of antihypertensive agents as one of the most important causes

Although the absolute cause of perioperative hypertension is unclear, the incidence of these events during cataract surgery can be associated with anxiety, pain, and the use of intra-ophthalmic vasoconstrictors such as epinephrine[5]. The existing evidence suggests that hypertensive patients, even with proper preoperative control of hypertension, are prone to hypertension in the preoperative period. It is also likely that blood pressure of known cases that are under antihypertensive therapy has not been controlled adequately before the operation, because evidence suggests that 50% of those who are aware of their hypertension are treated appropriately[6].

The data indicate that preoperative diastolic pressure of above 110 is a predictive marker for cardiac complications in patients with a history of chronic hypertension. In addition, patients with a history of uncontrolled blood pressure (>180/95) have a significant increase in postoperative neurologic deficits[7]. In multivariate analysis of preoperative risk factors in non-cardiac surgeries in men, preoperative hypertension increased the death rate to 2.8 times than those with normal blood pressure[8]. It has also been shown that high systolic blood pressure is associated with an increased incidence of silent myocardial ischemia in the perioperative period[9]. Given the mentioned complications, arterial blood pressure control during surgery is of great importance.

Acute hypertension episodes are treated with intravenous esmolol, labetalol, nitroprusside, nitroglycerin, and hydralazine. Labetalol is a mixed alpha- and beta-adrenergic antagonist which is used for the treatment of hypertension[10]. This drug is a combination of the selective competitive blocking effect of alpha-1 adrenergic activity and non-selective competitive blocking effect of beta-adrenergic activity; the alpha-beta ratio in the intravenous injection is about 1 to 7[11]. The main physiological function of this drug arises from the blockage of beta-1 receptors in the myocardium, beta-2 receptors in the bronchus and smooth muscles of the vascular walls, and alpha-1 receptors of vascular muscle. This function ultimately results in lowering blood pressure and systemic vascular resistance without significantly reducing heart rate, cardiac output, or stroke volume[12]. Labetalol is administered through bolus intravenous injection or continuous infusion. Its effect starts in 2 to 5 min, reaches its peak in 5 to 15 min, and lasts 2 to 4 hours, and has a half-life of 5.5 hours. Labetalol can be prescribed at a dose of 20 mg and then increased to 20-80 mg every 10 minutes to achieve the desired blood pressure. It can also be infused at a dose of 1 to 2 mg per minute after the initial 20 mg[13].

Due to beta-blocking effects, the heart rate remains steady or decreases slightly. Unlike pure beta-blockers, the cardiac output does not change[15]. Hydralazine is an arterial vasodilator with a direct effect and is used as the first line medicine for the treatment of hypertension crisis in pregnancy and can cause a rapid decrease in arterial blood pressure. Hydralazine seems to affect diastolic blood pressure more than systolic blood pressure[14]. Its effect begins in about 5 to 15 minutes when administered intravenously, and lasts last up to 12 hours. However, its maximum effect is between 10 and 80 minutes when administered orally[14]. Although the circulating half-life of hydralazine is only about 3 hours, its effective half-life is estimated to be 10 hours[15]. Reduced resistance of peripheral vessels leads to a reflex tachycardia and can increase cardiac output[16]. Although these two drugs are extensively used, there is currently not enough evidence on their effectiveness and side effects during cataract surgery in people with hypertension. Therefore, the present study aimed to compare these medicines.

Materials and methods

Procedure

After approving the university's ethics committee and obtaining written consent for participating in the study, a total of 63 patients who visited the Farabi Hospital for cataract surgery were enrolled in this randomized, double-blind clinical trial. Inclusion criteria were candidacy for cataract surgery and a history of mild and moderate hypertension treatment. Exclusion criteria were a contraindication of the study drugs, not controlling hypertension before surgery, a history of severe asthma or severe COPD with a history of hospitalization, cardiac blocks I and II, severe bradycardia (heart rate <50/min), and having a pacemaker. Standard monitoring and sedation were identical in both groups. After entering the operating room and checking the vital signs under standard monitoring, sedative drugs including 1 mg midazolam and 1 µg/kg fentanyl were administered intravenously. Five minutes after administration of fentanyl and midazolam, the patient's vital signs including systolic and diastolic blood pressure, arterial blood pressure, heart rate, and arterial hemoglobin saturation were recorded. Written consent for participation in the study was obtained from patients with blood pressures of higher than 160/100. The intervention groups were:

Hydralazine group: In this group, 10 mg (half an ampoule) of bolus hydralazine was injected intravenously and the surgery was started 15 minutes later; if blood pressure was not controlled (or not declined more than 20%), 10 mg hydralazine was re-injected intravenously.

Labetalol Group: The patients in this group received 2 mL (equivalent to 20 mg) of bolus labetalol intravenously. The surgery was started 15 min later and the vital signs were recorded every 5 min (at 5, 10, and 15 min). If the patients' blood pressure was not controlled (or not declined more than 20%) after 10 min, an additional dose of 2 mL of labetalol was re-injected. If blood pressure was not controlled after re-injection, the patient was known to be resistant to labetalol and hence a bolus of 50-100 µg TNG was used to control blood pressure. In addition, if blood pressure was decreased by more than 40% or the patient had bradycardia (heart rate <50/min), sup-

portive measures, including serum therapy and injection of atropine and vasoconstrictor, were taken to increase blood pressure. The vital signs were also recorded during the recovery, after the end of the operation, and all data, demographic variables, and the need for re-injection were analyzed.

Measured variables

The variables measured in this study included systolic and diastolic blood pressure and mean heart rate. Other risk factors that were studied included the history of hypertension, diabetes, ischemic heart disease, kidney failure, heart failure, liver failure, thyroid disease, and asthma or mild COPD.

Data analysis

The data were analyzed in SPSS 20 through frequency percentage, central statistical indices such as mean, and dispersion indices such as standard deviation, and the desired charts were plotted. Chi-Square test was used to determine the relationship between qualitative variables. Differences between quantitative variables were assessed by independent sample t-test. Changes in the variables before and after each action were evaluated by paired samples t-test.

Ethical considerations

The information was recorded confidentially according to the principles of the Helsinki Declaration, and the patients were given the necessary explanations.

Results

The collected data were analyzed in SPSS 20. A total of 63 eligible patients were enrolled in this study. According to the randomized four-block table, 30 patients were entered in the hydralazine group and 33 in the labetalol group. In this study, the mean age was 67.80±7.31 years, ranging from 52 to 86 years. The mean age of patients was 67.54±7.54 years in the hydralazine group and 68.09±7.20 years in the labetalol group, and there was no statistically significant difference between them (p=0.752). In addition, 36 patients (57.1%) were male and 27 (42.9%) were female. The hydralazine group consisted of 15 male and 15 female patients and the labetalol group consisted of 21 male and 12 female patients with no significant difference (p=0.316). Comorbidity existed in 32 patients (50.8%) and 31 patients (49.2%) had no history of other diseases. Figure 4-4 shows the differences between the two groups for the presence of comorbidity. According to the analysis, there was no statistically significant difference between the two groups (p=0.904).

Table 1: Differences between hydralazine and labetalol groups in terms of parameters measured

Variables	Time	Drug				*P*-value
		Hydralazine		Labetalol		
		Mean	SD	Mean	SD	
PR	PR at 0 min	71.90	13.76	76.94	7.23	0.70
	PR at 5 min	75.67	14.01	76.33	8.12	0.816
	PR a 10 min	75.70	12.94	76.91	8.12	0.655
	PR at 15 min	79.17	19.40	77.61	6.96	0.667
Systolic BP	Systolic BP at 0 min	172.17	8.20	173.79	8.01	0.430
	Systolic BP at 5 min	155.20	17.62	136.52	5.93	<0.001
	Systolic BP at 10 min	146.10	15.09	134.09	6.18	<0.001
	Systolic BP at 15 min	143.17	15.21	132.88	6.25	0.001
Diastolic BP	Diastolic BP at 0 min	107.27	5.78	111.06	4.96	0.007
	Diastolic BP at 5 min	94.20	13.47	85.76	5.17	0.001
	Diastolic BP at 10 min	86.67	11.08	82.88	5.31	0.084
	Diastolic BP at 15 min	83.93	10.56	79.24	6.14	0.033
MAP	MAP at 0 min	128.90	5.51	131.97	3.98	0.013
	MAP at 5 min	114.53	13.90	102.68	3.63	<0.001
	MAP at 10 min	106.48	11.50	99.95	3.76	0.003
	MAP at 15 min	103.30	11.04	97.12	4.28	0.004

Discussion

Regarding the insignificant difference between the two groups in terms of demographic variables, an appropriate matching seems to exist between the groups in the present study and there are no confounding factors in terms of demographic variables. Changes in the heart rate of the patients of both groups were similar and the heart rate gradually increased from baseline to 15 minutes afterward. Differences between the two groups were not statistically significant and the changes observed in the heart rate of the patients may be justified according to the decrease in blood pressure after the injection of drugs and the release of catecholamines during surgery[17,18]. Regarding the reflex tachycardia following administration of hydralazine, other studies have also achieved similar results, but unlike the current study, some studies have reported a decrease in the heart rate due to the use of labetalol[16,19,20].

In addition, the mean systolic and diastolic blood pressure at baseline was slightly higher in the labetalol group than the hydralazine group, but after the injection of drugs, both systolic and diastolic blood pressures were decreased more rapidly in the labetalol group than the hydralazine group, so that their values were significantly lower in the labetalol group than the hydralazine group from the 5th minute afterward. Gradually, hydralazine also exerted its effect over time and reduced the observed difference in the mean blood pressure between the two groups. Dimich et al. had similar results and presented both compounds as appropriate drugs for controlling the pressure during surgery[16]. Vigil De Gracia et al. also found similar results on gestational hypertension[21]. Changes in arterial blood pressure were similar to changes in systolic and diastolic blood pressure.

Conclusions

Both labetalol and hydralazine seem to be suitable for controlling blood pressure during surgery. However, the more rapid effect of labetalol than hydralazine on lowering blood pressure and the reflex tachycardia, observed most often with hydralazine, as well as the surgery type should be considered when selecting them.

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