RESEARCH ARTICLE

A Comparison of Labetalol and Nitroglycerin for The Management of Intraoperative Hypertension in Ambulatory Surgical Patients Who Underwent Cataract Surgery

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Background: This is a prospective randomized blinded clinical trial comparing the efficacy and safety of labetalol and nitroglycerin for the management of intraoperative hypertension in ambulatory surgical patients who underwent cataract surgery.

Methods: A total of 80 hypertensive patients (systolic blood pressure> 200 mmHg or diastolic blood pressure> 100 mmHg) who had increased blood pressure during cataract surgery under topical anesthesia were reviewed. Patients were randomized to receive nitroglycerin (group N, n= 40) or labetalol (group L, n= 40). The initial dose of nitroglycerin was a bolus of 2 µg/kg and repeat dose of 1ug/kg intravenously every 5 minutes. Labetalol was administered as a bolus of 5 mg followed by 5 mg intravenously as needed every five minutes up to maximum dose of 1 mg/kg.

Results: Systolic blood pressure decreased from 21.4±8.6 mm Hg (200 to 260 mm Hg) to 18.8± 6.4 mm Hg with administration of nitroglycerin. Labetalol reduced systolic blood pressure from 21.4± 6.7 mm Hg (201 to 258 mm Hg) to 17.6± 11.6 (p= 0.02). Nitroglycerin increased baseline heart rate from 68±8 beats/min to 82±6 beats/min (p= 0.04), however, in the labetalol group heart rate reduced from control 72±6 to 64± 9 beats/min (P< 0.05). The hypotension episode was 18 (45%) cases in the nitroglycerin group and 2 (5%) cases in the labetalol group respectively (p<0.05). The mean of systolic blood pressure during their stay in the recovery room in nitroglycerin group was 20.7±9.6 mm Hg and in labetalol group was 18.5± 10.2 mm Hg (p< 0.05).

Conclusion: Nitroglycerin may produce reflex tachycardia and episode of hypotension especially in elderly patients intraoperatively. Labetalol is a safe and effective antihypertensive agent for management of increased blood pressure during cataract surgery with topical anesthesia.

Keywords: Labetalol; Nitroglycerin; Intraoperative hypertension; Cataract surgery

Cataract surgery is often performed using topical anesthesia [1]. The anesthesiologists prefer topical anesthesia for cataract surgery compared to regional anesthesia and general anesthesia [2]. A reduced length of hospital stay and decrease of nausea and vomiting can be experienced with topical anesthesia compared with general anesthesia [3]. Cataract surgery is usually carried out in on octogenarian patients. Many of these subjects have systemic illness and hypertension [4]. It was shown that blood pressure increases during cataract surgery especially in female patients and then reduces in the postoperative period [5]. The management of perioperative hypertension remains a therapeutic dilemma for anesthesiologist. Many antihypertensive agents use for management of intraoperative increased blood pressure. Vasodilator agents can elicit reflex tachycardia during surgery and can be deleterious in elderly patients particularly subjects with ischemic heart disease [6]. Nitroglycerin (TNG) is a direct vasodilator and has been used to management for intraoperative hypertension because of its rapid onset time, rapid offset time and easy titration. However, this agent elicits reflex tachycardia and venous congestion that leads to increase blood loss [7]. Labetalol which is an alpha1 and predominant non selective beta blocker agent (alpha1: beta blockade ratio of 1:7 for intravenously injection) does not induce reflex tachycardia but may induce prolonged hypotension [6]. Labetalol reduces blood pressure by lowering systemic vascular resistance (alpha1 blockade), however, reflex tachycardia because of vasodilator effect of alpha blockade is decreased by beta blockade effect and therefore, leads to unchanging cardiac output [8]. The purpose of this study was to compare the efficacy and safety of nitroglycerin with labetalol for the management of intraoperative hypertension in ambulatory patients who underwent cataract surgery.

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Methods

This is a prospective randomized blinded clinical trial established at Farabi eye hospital, Tehran university of medical sciences and carried out on 80 hypertensive patients (systolic blood pressure> 200 mmHg or diastolic blood pressure> 100 mmHg) who had increased blood pressure during cataract surgery under topical anesthesia after approval by the hospital ethical committee. Subjects who underwent cataract surgery under topical anesthesia and developed intraoperative hypertension were included in our study. Patients with sick sinus syndrome, atrioventricular conduction block, a history of unstable angina or myocardial infarction within the past six months, asthma or chronic obstructive pulmonary disease, history of substance abuse and current opioid use, patients with compromised renal and hepatic function and patients preclude beta blocker and cases who received monoamine oxidase within the past six weeks were excluded from our study. All of subjects were evaluated in preoperative clinic which consisted of a medical history, physical examination, electrocardiogram and recording of blood pressure and heart rate as control values. Written informed consent was signed by each patient. The study participants, operation nurse, ophthalmic surgeons, anesthetist collecting data and keeping records of different parameters were unaware of groups or drug received. Therefore, blinding was property achieved. Randomization was done by a computer generated, random number list. We defined the perioperative hypertension as systolic blood pressure> 200 mmHg or diastolic blood pressure>100 mmHg from entering the operating room until leaving the recovery room demonstrated on two successive blood pressure reading taken five minutes apart. All subjects were monitored with electrocardiogram, noninvasive automatic blood pressure and pulse oximeter during operation. After securing IV-line preloading was carried out with lactated ringer solution 5 ml/kg. Premedication with midazolam, 1 mg iv and fentanyl 1µg/kg was given to all patients in our study. Systolic, diastolic and mean arterial pressure (MAP) and heart rate (HR) were recorded every 5 minutes during surgery in our cases. Patients who developed perioperative hypertension period were randomized to receive nitroglycerin (group N, n= 40) or labetalol (group L, n= 40). The initial dose of nitroglycerin was a bolus of 2 µg/kg and repeat dose of 1ug/kg intravenously every 5 minutes. Labetalol was administered as a bolus of 5 mg followed by 5 mg intravenously as needed every five minutes up to maximum dose of 1 mg/kg. The blood pressure was recorded every 10 minutes in the recovery room. We defined the therapeutic response as a 20% reduction in systolic blood pressure and or a diastolic blood pressure reduction to less than 100 mmHg. For prevention of orthostatic hypotension upon discharge, we determine the blood pressure and heart rate in the sitting and standing position. Sample size of our study was defined as power of 80% and an alpha error of 0.05 power to detect a significant difference of 10 mm Hg in the mean arterial blood pressure. Data were analyzed using multivariate analysis of variance (ANOVA). Data were expressed as mean± SD. A statistically significant difference was assumed when p-value was less than 0.05.

Results

Both groups were similar with respect to age and gender. The duration of operation was 15± 4 minutes and 16± 5 minutes in N group and L group respectively (p= 2.82). Both groups were similar respect to control systolic and diastolic blood pressure or heart rate. Systolic blood pressure decreased from 21.4± 8.6 mm Hg (200 to 260 mm Hg) to 18.8±6.4 mm Hg with administration of nitroglycerin during operation. Moreover, labetalol reduced systolic blood pressure from 21.4± 6.7 mm Hg (201 to 258 mm Hg) to 17.6± 11.6 intraoperatively (p= 0.02). Nitroglycerin increased baseline heart rate from 68± 8 beats/min to 82±6 beats/min (p= 0.04), however, in the labetalol group heart rate reduced from control 72± 6 to 64± 9 beats/min (P< 0.05). Two of our patients developed bradycardia (heart rate< 50 beats/min) after administration of labetalol. Both of these patients underwent beta blocker agent's treatment because of hypertension before operation. The mean time to onset of action in the nitroglycerin group was 3.8± 2.6 min (2 to 6 min) while the mean time to onset of the response in labetalol group was 4.6± 2 min (4 to 8 min) respectively. The hypotension episode (reduce mean arterial blood pressure more than 30% respect to baseline measurement) was 18 (45%) cases in the nitroglycerin group and 2 (5%) cases in the labetalol group respectively (p< 0.05). Five patients in nitroglycerin group needed intervention for management of hypotension such as head tilt position, administration of normal saline and ephedrine injection. The mean of systolic blood pressure during their stay in the recovery room in nitroglycerin group was 20.7±9.6 mm Hg and in labetalol group was 18.5± 10.2 mm Hg (p< 0.05).

Discussion

One of the most widely performed operations is the cataract surgery and most patients are over the age of 60 and accompanied by coexisting systemic diseases and approximately half of these subjects have hypertension [9-12]. It was shown that blood pressure tends to increase during cataract surgery [13]. The etiology of increase of blood pressure during cataract surgery is ocular pain, anxiety, discomfort and routine instillation of vasoconstricting ophthalmic agents such as epinephrine [14]. Moreover, twelve of our subjects developed intraoperative hypertension because of having failed to take their antihypertensive gents on the morning of surgery. Previous study established that rise of blood pressure in patients undergoing cataract surgery was related to stress response and associated with elevated plasma level of epinephrine and norepinephrine indicating sympathetic stimulation [15]. Elevated plasma constrictions led to hyperdynamic circulatory state manifested by increase blood pressure, heart rate and myocardial contractility. Singh et al. reported that patients with hypertensive episode during cataract surgery did not develop any increase in heart rate. This finding is consistent with the previous studies that identified minimal increase in heart rate in octogenarian patients. These findings established age related decreasing sensitivity of cardiac beta-adrenergic receptors especially in elderly patients [16]. Singh et al. found that one of the reasons that blunt increase of heart rate may be related to use of beta blockers for preoperative treatment of hypertension and the presence of autonomic neuropathy in diabetic patients [16].

According to previous studies we found that blood pressure increases during cataract surgery. However, we found the presence of reflex tachycardia in some of our patients who received nitroglycerin. Nitroglycerin produced increasing of the heart rate in our subjects (increase of baseline heart rate from 68± 8 beats/min to 82± 6 beats/min). Moreover, in our study blood pressure and heart rate reduced promptly and significantly with the use of labetalol. These data identified that elderly patients are less sensitive to the alpha and beta blocker effects of labetalol. This finding is according to previous studies which showed that with aging, alpha and beta responsiveness is not altered [16]. Labetalol blocks both alpha1 and beta adrenoreceptors and with blocking of alpha1 receptor, the peripheral vascular resistance reduces with little alteration in heart rate and cardiac output [17-18]. In our study we found reduction of blood pressure and heart rate after administration of labetalol and this effect was maintained for at least two hours. Moreover, we found that patients who received labetalol for management of hypertension during procedure had lower blood pressure during recovery period and needed less antihypertension agents after operation. Some studies showed that prolonged alpha1 blockade by labetalol may cause these findings [18-20]. Moreover, in the past anesthetist did not prefer to use labetalol in the perioperative period because of orthostatic hypertension especially in elderly patients who will soon be ambulatory [18, 21-22]. However, our study elicited that use of a small dose of labetalol intraoperatively avoided any precipitous reduction in blood pressure perioperatively and orthostatic hypotension prior to discharge. In the current study most of the subjects were discharged from the recovery room with no prolonged side effects of labetalol.

Conclusion

both nitroglycerin and labetalol administered for management of rising of blood pressure during cataract surgery in patients with hypertension and both agents are effective in controlling perioperative hypertension. However, nitroglycerin may produce reflex tachycardia and episode of hypotension especially in elderly patients. Labetalol offer advantages over nitroglycerin in the management of rising of blood pressure during cataract surgery under topical anesthesia. This agent produces prompt reduction of blood pressure and heart rate without episode of reflex tachycardia during operation and subjects have lower blood pressure in the recovery room. Labetalol is a safe and effective antihypertensive agent for management of increased blood pressure during cataract surgery with topical anesthesia.

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