

Comparison of Labetalol and Nitroglycerine on Intraoperative Bleeding in Patients Who Underwent Dacryocystorhinostomy

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Abstract- The bleeding during dacryocystorhinostomy (DCR) surgery is one of the main complications that led to the surgeon's dissatisfaction and increased the duration of the operation. The current study aimed at comparing the effects of labetalol and nitroglycerine (TNG) on blood loss and the surgeon's satisfaction during DCR. The current prospective and randomized study enrolled 60 patients candidate for DCR under local anesthesia and sedation and divided into two groups. When the surgeon dissatisfied with bleeding during the operation, patients in the labetalol group received labetalol infusion at a rate of 0.5-2 mg/kg and compared with the subjects in the TNG group that received TNG infusion at a rate of 0.1 µg/kg/min. Additionally, the surgical condition was assessed by the surgeon using the average category scale (ACS) and surgeon's satisfaction by a scoring system. The average bleeding in the labetalol group was 140.5±24.5 ml versus 170.4±24.6 ml in the TNG group, respectively ($P=0.001$). The average category scale for the labetalol group was better than the TNG group during all the time of operation. The surgeon satisfaction score during the operation was more in the labetalol group (3.4 in the labetalol group versus 2.8 in the TNG group, respectively). Labetalol was better than TNG for controlling bleeding during DCR procedure because of decreasing surgical blood loss and optimum operative condition.

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Introduction

Bleeding during dacryocystorhinostomy (DCR) is trivial, but because of the anatomical vessel variation and presence of tiny vessels in the field of DCR, it can obscure the surgical field and complicate the operation. Bleeding is one of the important complications during DCR, which dissatisfy ophthalmic surgeon, reduces surgical field visualization, and increases the duration of surgery (1). Thus, the management of this complication is a great consideration during this operation. Elevation of the patient's head during operation and injection of epinephrine in the mucosa field of surgery can be used to reduce blood loss as possible and improve the visibility of structures and prevent surgical complications (1,2). Another effective approach for controlling bleeding tendency during DCR is to reduce blood pressure in patients. To achieve this purpose, we can use beta-adrenergic blockers, calcium channel blockers, peripheral vasodilators, and a combination of anesthetic agents such as opioids, propofol, and inhalation drugs (3). Ideal

hypotensive medications administered to reduce blood pressure should has specific features such as easy to administration, being with rapid onset and offset without side effects, rapid elimination without any toxic metabolites, and having a predictable and dose-dependent action (4,5). Nitroglycerine (TNG) is a direct vasodilator agent, especially in veins and produces hypotension, and preferred by clinicians because of rapid onset and offset time and easy titration. However, as an adverse effect, TNG cause reflex tachycardia and venous congestion around the field of surgery and increase blood loss (6). Therefore, some anesthesiologists believe that this agent is not an optimal choice for controlling bleeding during surgery. Labetalol is a beta-adrenergic blocker agent with α_1 and beta-adrenergic receptors blocking action (α_1 : β ratio of 1:7 for intravenous administration). Labetalol reduces blood pressure through α_1 blockade by lowering systemic vascular resistance, but through beta-blockade decreases reflex tachycardia secondary to vasodilatation and leads to unchanged or increased cardiac output (7-9). The effect of labetalol presents after

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5 minutes, and the next dose of this agent can be used if the target blood pressure is not achieved (10,11). The current study aimed at comparing labetalol and nitroglycerine on intraoperative bleeding in patients who undergo DCR and evaluate their potential benefits or adverse effects in this regard.

Materials and Methods

This was a prospective, single-blind randomized clinical trial study that was conducted in an educational center and was carried out on 60 patients from February to April 2019 after approval by the hospital ethical committee. The patients aged 42-65 years with American Society of Anesthesiologists (ASA) physical status I-II scheduled for DCR under local anesthesia and sedation were included in the current study. Exclusion criteria included known allergic reaction to nitrates, subjects who take sildenafil or other similar drugs, history of major psychiatric disorder, history of substances' abuse and opioids use, cases with compromised hepatic, renal, and cardiac function, subjects with coagulation disorders and cases on medications affecting coagulation system. Written informed consent was signed by each participant after admission to the ward. In our study, the participants' ophthalmic surgeons, and nurses of the anesthesia ward were blinded to study groups. The anesthetist who performed the sedation was aware of the agents being given, but the clinicians collecting data were blinded of groups or drugs received. All participants were randomized by a computer-generated random number list. Participants were randomly divided into two groups of 30 patients, according to the agent used. After the arrival of our subjects in the operating room, non-invasive blood pressure, three lead electrocardiography, and pulse oximetry monitoring was started. The characteristics recorded for all patients during surgery were heart rate, systolic, diastolic, mean arterial blood pressure, and oxygen saturation. These characteristics were recorded before the administration of sedation agents and every 5 minutes till the end of anesthesia. After securing the intravenous line, all patients received isotonic crystalloid (5 ml/kg) to replace compensatory intravascular expansion volume before injection of local anesthesia and administration of sedation agents. All patients were premedicated by midazolam 0.05 mg/kg and fentanyl 1

µg/kg before the operation. The surgeon infiltrated lidocaine-epinephrine (1:200,000) mixture at the surgical site for decreasing blood loss before the operation in all patients. All of the cases underwent DCR by the same surgeon, and head-up position to 30 degrees was applied to all of the subjects. Bleeding was estimated by the amount of blood loss from the surgical site by suctioning into the suction bottle. The operative field visibility was evaluated by the same surgeon according to the average category scale (ACS) (12) (Table 1). After starting of operation, if surgeon dissatisfied from bleeding during operation and mean arterial blood pressure of patients was more than 80 mm Hg, the anesthetist started infusion of labetalol or TNG in both groups, accordingly mean arterial pressure reduced 5 mm Hg till the surgeon told average category scale (ACS) of 2-3 or mean arterial pressure <65 mm Hg. In the labetalol group, patients received labetalol infusion at a rate of 0.5-2 mg/kg, and the upper limit of labetalol dosage was 300 mg. During labetalol infusion, if heart rate decreased below 50 beats/minute, the infusion was held transiently, and if heart rate dropped below 45 beats/min, 0.5 mg intravenous atropine was given. In the TNG group, the infusion of TNG administered with 0.1 µg/kg/min and increased up to 1 µg/kg/min if needed. After the infusion of TNG, if the heart rate exceeded 100 beats/minute, the dosing of agents decreased to ameliorate this adverse event. Hypotension (decrease of mean arterial pressure more than 20%) initially managed with a 50% reduction of infusion dose of agents and holding of infusion if no response was obtained in 5 minutes. For resistant hypotension, 5 mg ephedrine was injected. Five minutes before the end of the operation, the infusion of agents was discontinued. Any postoperative adverse events were observed and recorded. Surgeon's satisfaction was evaluated and recorded based on a 4 points scale (1=bad, 2=moderate, 3=good, 4=excellent) (13). All recorded data during the study were analyzed with SPSS software version 20. Based on the desired power of 80% and an α error of 0.05 to detect a between-group difference of 20% in the scale used to evaluate the amount of blood loss, 30 patients per group were established and included in this study. Data were summarized in the form of mean and standard deviation and were analyzed using student *t*-test and Chi-square test. *P* less than 0.05 was considered significant.

Table 1. Average category scale (ACS) for the assessment of bleeding in the surgical field

0	No bleeding
1	Slight bleeding (no suctioning of blood is required).
2	Slight bleeding (occasional suctioning is required). The surgical field is not threatened.
3	Slight bleeding (frequent suctioning is required). Bleeding threatens the surgical field a few seconds after suction is removed.
4	Moderate bleeding (frequent suctioning is required). Bleeding threatens the surgical field directly after suction is removed.
5	Severe bleeding (constant suctioning is required). The bleeding appears faster that can be removed by suction. The surgical field is severely threatened, and surgery is not possible,

Results

The demographic characteristics are depicted in table 2. No significant difference was identified between two groups for these characteristics. The intraoperative variables of the studied patients, such as duration of operation and duration of anesthesia, were similar in both groups. The surgeon satisfaction score during the operation was more in the labetalol group (3.4 ± 0.4 in the labetalol group versus 2.8 ± 0.6 in the TNG group, respectively). The average bleeding in the labetalol group was 140.5 ± 24.5 ml versus 170.4 ± 24.6 ml in the TNG group, respectively ($P=0.001$). The average category

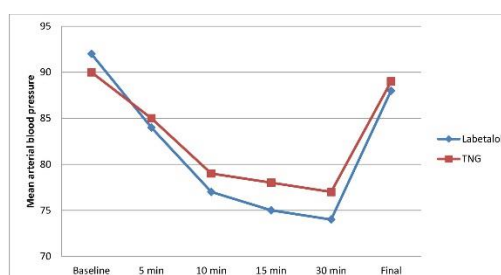
scale for the labetalol group was better than the TNG group during all time of operation (2.6 ± 0.5 in the labetalol group versus 3.5 ± 0.4 in the TNG group, respectively) (Table 3). Moreover, the intraoperative hemodynamic variables such as systolic, diastolic, and mean arterial pressure were similar in both groups (Figure 1). The intraoperative heart rate in the labetalol group was lower than the TNG group (Figure 2). Four patients had bradycardia during the administration of labetalol, and two cases needed injection of atropine. Therefore, Labetalol provided better surgical conditions about blood loss and surgical field visualization during operation compared to the TNG group.

Table 2. Demographic and baseline characteristics of labetalol and TNG groups

Variables	Labetalol group	TNG group	P-value
Age (years)	52.6 ± 8.4	54.3 ± 7.8	0.52
Sex (male/female)	16/14	18/12	0.26
Weight (Kg)	78.8 ± 8.2	79.6 ± 9.3	0.15
ASA class (I/II)	12/18	14/16	0.80
Systolic blood pressure (mm Hg)	135.8 ± 12.4	138.4 ± 10.6	0.92
Diastolic blood pressure (mm Hg)	76.4 ± 8.7	78.1 ± 9.5	0.67
Mean arterial blood pressure (mm Hg)	92.2 ± 10.4	90.8 ± 9.4	0.65
Heart rate (beat/minute)	78.7 ± 14.8	79.6 ± 12.4	0.41
Oxygen saturation (%)	97.8 ± 0.8	98.1 ± 0.6	0.82

Table 3. Comparison of intraoperative variables of labetalol and TNG groups

Variables	Labetalol group	TNG group	P
Duration of operation (min.)	32.2 ± 16.4	36.4 ± 18.2	0.09
Duration of anesthesia (min.)	42.2 ± 16.4	45.4 ± 18.2	0.12
Intraoperative bleeding (ml)	140.5 ± 24.5	170.4 ± 24.6	0.001
Average category scale (ACS)	2.6 ± 0.5	3.5 ± 0.4	0.01
Surgeon's satisfaction	3.4 ± 0.4	2.8 ± 0.6	0.001
Bradycardia (HR<50 beats/min) (%)	13.3	Zero	0.09

**Figure 1.** Comparison of intraoperative mean arterial blood pressure during operation between labetalol and TNG groups

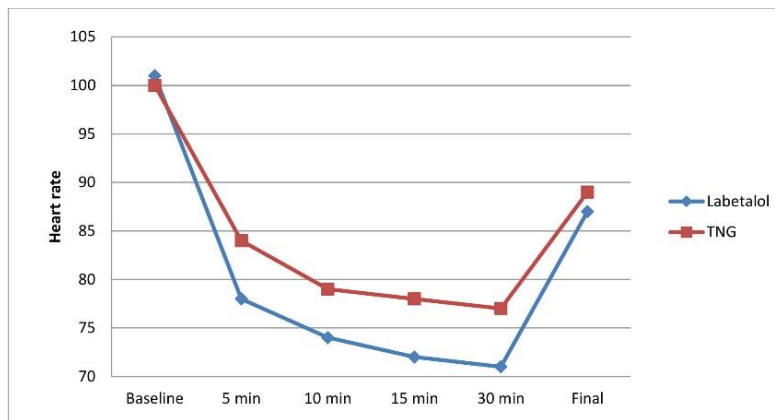


Figure 2. Comparison of intraoperative heart rate during operation between labetalol and TNG groups

Discussion

The main target of this study was the comparison of labetalol and TNG for reducing blood loss during DCR operation. Reduction of blood loss in the operative field led to decreasing surgical manipulation and operation time and improved the quality of surgical conditions (14,15). Labetalol is a non-selective beta-blocker that induces vasodilatation by alpha’s receptor. It decreases blood pressure by reducing systemic vascular resistance without reflex tachycardia along with unchanged or increased cardiac output (1). TNG induces reflex tachycardia and hypotension due to vasodilatation by influencing vascular smooth muscle and leads to more oozing at the site of operation (16). One previous study evaluated the efficacy of the combination of sodium nitroprusside and labetalol during endoscopic sinus surgery and identified that induced hypotension with this combination induces satisfied synergic effect (17). Scott *et al.* assessed the efficacy of the combination of labetalol and halothane for safe, controlled hypotension during endoscopic sinus surgery and found that these agents have additive hypotensive action and induced satisfactory conditions during operation (18). It was shown that when blood pressure reduces during operation, the surgical time decreases because of better surgical field visualization and time lost in repeated suctioning (19). Nair *et al.*, found better surgical conditions during endoscopic sinus surgery with premedication beta blocker due to reduced heart rate during operation (20). N.S. EL.Shmaa *et al.*, assessed the efficacy of labetalol and TNG and showed that mean arterial blood pressure remained in a similar range during the time of controlled hypotension. He identified that optimum surgical conditions were achieved in the labetalol group compared to the TNG

group. Also, he demonstrated that there is a significant decrease in mean bleeding in the labetalol group compared to the TNG group, and the mean duration of surgery was slightly shorter in the labetalol group (21). Nagat *et al.*, compared labetalol and TNG and demonstrated that both agents were safe and effective, but labetalol was superior and improved the visualization of the surgical field and also with lower levels of blood loss due to less tachycardia compare to TNG (22). However, Sajedi *et al.*, evaluated the efficacy of labetalol and remifentanil administration and concluded that a higher measure of blood loss and other complications were identified in the labetalol group (1). In another study by Ghodraty *et al.*, regarding a comparison of labetalol and TNG concluded that hemorrhage is not significantly different between the two groups. Also, visualization of the surgical field and surgeon’s satisfaction was significantly higher in the TNG group than the labetalol group. He explained the paradoxical results compared to other studies because of the long onset time of labetalol in comparison with TNG in producing their hypotensive effects (23). Eltringham *et al.*, assessed the safety and efficacy of labetalol and TNG and demonstrated no significant difference in decreasing blood loss between two agents (24,25). Moreover, Yasameen *et al.*, compared the effects of labetalol and TNG in reducing blood loss in spinal surgery and found a significantly higher score for surgical field quality and less hemorrhage in the labetalol group (20,26). Hadavi *et al.* evaluated the efficacy of labetalol and TNG on intraoperative blood loss and surgical field quality in septorhinoplasty and concluded no significant difference in terms of hemorrhage or surgical field quality, but surgeon’s satisfaction was little more in the TNG group than labetalol group (27). In the current study, the mean

blood loss in the TNG group was significantly higher than the labetalol group, and optimum surgical condition and the surgeon's satisfaction were achieved in the labetalol group. We think the superiority of labetalol for the reduction of blood pressure during DCR is due to a decrease in the blood pressure along with lowering heart rate. Moreover, TNG by reflex tachycardia and venous congestion, especially around the field of surgery, led to increasing in bleeding during operation (28). We recommend the use of labetalol for intraoperative reduction of blood loss during DCR, especially in patients with cardiac diseases such as patients with ischemic heart disease or heart failure because of unchanged cardiac output in these subjects. Limitations of our study included: first, the maximum safe dosage of labetalol was 300 mg in 24 hours that reached 60 to 90 minutes with the administration of 4 mg/minutes infusion rate. Second, the estimation of hemorrhage in DCR surgery was inaccurate by the methods used in our study because of the small amount of blood loss during this procedure. Third, the better measurement for understanding the factors affecting hemorrhage during the operation was cardiac output and invasive mean arterial pressure monitoring. According to the results of the current study, labetalol was better than TNG for controlling bleeding during DCR procedure because of decreasing surgical blood loss, optimum operative condition, and more satisfaction of surgeons during the surgery.

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