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Comparison of Labetalol and Nitroglycerine's Effects on Deliberate Hypotension in Septo-Rhinoplasty Ssurgery, a Randomized Clinical Trial

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ABSTRACT

Introduction: Bleeding during ENT surgeries may contribute to impaired view. The less blood in surgical filed, the better quality and more surgeon's satisfaction is expected. Deliberate hypotension is a technique to achieve this goal. Current study aimed to evaluate effects of Labetalol andNitroglycerinein deliberate hypotension.
Methods: It is a double blind RCT,conducted on 68 septo-rhinoplastypatients in ENT ward, Imam Reza Hospital, Mashhad, during 2017 after obtaining written consent. Patients were assigned to receive Nitroglycerine (n=32) or Labetalol (n=36) randomly. Mean arterial pressure and HR monitored. Total blood loss was estimated and recorded at a Boezaart Surgical Field Grading Scale. Surgeon's satisfaction with surgical field condition was measured after the procedures using a questionnaire at a 5-point Likert scale.
Results: Two studied groups were similar in demographic characteristics. Heart rate was lower in Labetalol group (P <0.001) significantly, but there was no significant difference between two groups regarding mean arterial pressure variations (P = 0.12). Surgeon's satisfaction with the operation condition was not significantly different (P= 0.28). According to Boezaart scale, no statistically significant difference was found between groups with regard to bleeding volume (P= 0.75). Patients in Labetalol group received less additive drugs to maintain hypotension than another group (P=0.025).
Conclusion: Although Labetalol and Nitoglycerine are not much different in reducing blood loss or providing a better view of surgical field but Labetalol is superior in maintaining heart rate and hypotension and noneed toadditive drug.

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Introduction

Bleeding during surgery could lead to poor view of the surgical field. Many studies (1,2) have shown that using hypotensive drugs during general anaesthesia in small,bloodysurgical filed could reduce blood loss and make a better surgical field(3-6) especially in maxillofacial surgeries(7-9), without any threats to patient safety (10); even some studies indicated that deliberate hypotension caused shortened hospital stay (11). Hypotensive anaesthesia has shown a reduction by 30% in patient's baseline mean arterial pressure or its maintenance at

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60-70 mm Hg(4,5).

Labetalol is an alpha and,beta-adrenergic receptor blocking agent. It is 4 to 8 times more potent at beta than alphaadrenoceptors. Thus, it reduces the blood pressure by reducing the peripheral vascular resistance while preventing a reflex increase in heart rate. Labetalol can be administered in intermittent bolus doses or by infusion. It acts promptly, with peak effect occurring within 5 min. Contraindications include heart failure, bradycardia, hypovolemia, and atrioventricular block.

Intravenous Nitroglycerine has been used successfully to induce hypotension during orthognathic surgery (12,13). It directly acts on the vascular smooth muscle in a similar manner to that of Nitroprusside. However, its action is predominantly on capacitance vessels, resulting in decreased blood return to the heart, and therefore a reduced stroke volume (SV) and cardiac output (CO). However, especially in young patients, it may be hard to achieve the optimal degree of hypotension with Nitroglycerine(13).

Main goal of this study was to evaluate the effects of Labetalol and Nitroglycerinein achieving deliberate hypotensionin patients who underwent septo-rhinoplasty.

Methods

This randomized clinical trial study, approved by the ethics committee of Mashhad University of Medical Sciences. Participants included 68 candidates for septo-rhinoplasty surgery in ASA class I, II, with the age above 16 years. Exclusion criteria were any cardiac, renal or hepatic failure,unstable angina pectoris, heart block, asthma, previous history of hypertension, coagulopathies, and use of Aspirin or any other anti-coagulant or anti-platelet drugs, addiction, documented allergy to beta blockers or nitrates, and haemoglobin less than 10 mg/dl. The written consent was obtained from all patients.

At a tertiary referral hospital,in ENT ward, Imam Reza Hospital, Mashhad, during year 2015 participants selected using a convenience sampling method, and assigned into two groups of Nitroglycerine (group 1) and Labetalol (group 2) randomly. Patients' group was obscured for surgeon and anesthesiologist. An informed consent was obtained from all individuals.

In the first group, hypotension was induced with Nitroglycerine 5 mcg/min, which would be repeated every 3-5 minutes for the mean arterial pressure to reach 60 mmHg. In the second group, hypotension was induced by using Labetalol 20 mg and was repeated 5-10 mg every 5 minutes. All patients were positioned 30 degrees head-up and pre-oxygenated, then underwent general anaesthesia with Midazolam 0.05 mg/kg , Fentanyl 2 microgram/kg , Lidocaine 1 mg/kg, Thiopental 5mg/kg, Atracurium 5mg/kg and endotracheal intubation. To maintain anaesthesia, we used Propofol infusion 100µg/min and Nitrous oxide in 50% Oxygen. MAP (Mean arterial blood pressure) and HR (heart rate) recorded every 5 minutes by a non-invasive technique (with a Philips M3929A device). If hypertension continued and/or tachycardia (MAP and HR20% above the base line) or surgeon's report of excessive bleeding, Isoflorane (1-1.5 %) was used. In some rare uncontrolled cases, we used Propranolol, as additive drug, in Nitroglycerine group and Hydralazine in Labetalol group.

Primary and secondary outcomes

All patients were checked for complete blood count (CBC), blood urea nitrogen(BUN), creatinine, PT and PTT. The Patients underwent septo-rhinoplasty with the same surgical technique. For all participants ECG, MAP (mean arterial pressure), HR (heart rate), peripheral oxygen saturation (SpO2) and end tidal CO2 were continuously monitored.

Surgeon's satisfaction with operation field quality [or conditions] measured after procedure at a 5-point Likert scale (1= too bad; 5= excellent). Total blood loss was estimated and recorded at a Boezaart Surgical Field Grading Scale (0= no bleeding; 5=severe bleeding).

Statistical analysis

All statistical analysis conducted using SPSS software program version11.0 (SPSS Inc., Chicago, IL, USA). Data normality was verified using the Kolmogorov-Smirnovtest. All measurements expressed as mean ± standard deviation, median (inter quartile range) or absolute number (percentage). Student t-test or Mann-Whitney U test was used to test for significant differences.

Fisher's exact test was used for qualitative variables. Clinical parameters were analyzed in groups by repeated measurement analysis of variance. This test was used to compare HR and MAP variations between baseline and the other time points in each group and the comparison of trends between groups. Statistical significance was set at P value < 0.05.

Result

Both studied groups were similar in terms of demographic characteristics; and no statistically significant differences observed regarding duration of surgery and primary clinical signs and symptoms (Table 1). No one excluded after randomization. The heart rate variations over time

in both groups of Nitroglycerine and Labetalol are shown in Figure 1. Repeated measurement analysis showed significant heart rate variations over time only in Labetalol group (P<0.001) and a significant difference in HR variations between groups (P<0.001).

Table 1: Patients' characteristics before surgery.

	Group		P value
	Nitroglycerine	Labetalol	
*Age	25.06 ± 4.98	27.08 ± 5.94	0.14
(%)Male	6(18.8)	7(19.4)	0.94
(%)Female	26(81.2)	29(80.6)	
Duration of anaes-&thesia	95(90-100)	100(90-110)	0.46
Heart rate before *induction	91.78 ± 18.28	90.97 ± 13.03	0.84
Mean arterial pres-*sure	90.31 ± 13.75	87.78 ±13.28	0.44

*mean ± SD, independent T Test; & median (IQR), Mann-Whitney U Test.

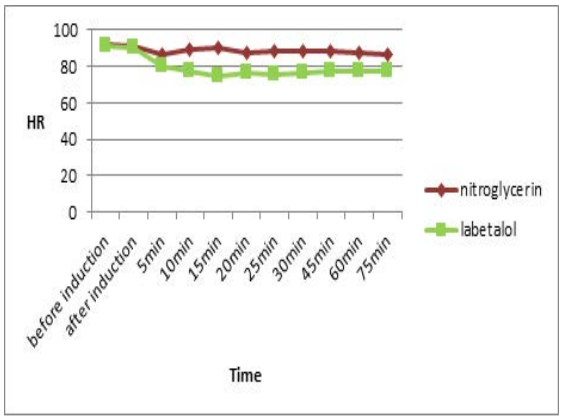

Figure 1: The trend of heart rate variations over time in nitroglycerine and labetalol groups.

None of the patients experienced hypotension (MAP<50 mmHg) and bradycardia (HR<60); and no patient showed resistance to studied drugs, during anaesthesia or surgery, no one required additional atropine or ephedrine (for treatment of bradycardia or hypotension). No serious complications were observed during the surgery. In Nitroglycerine group, 10 patients (31.2%) didn't need additive drugs to reduce their blood pressure but 68.8% of patients in this group required Propranolol or Isoforane to achieve desired MAP. In Labetalol group, 15 patients (41.7%) needededditive drugs to control their blood pressure or heart rate. Significant differences found between two groups in terms of prescribed drugs (P value:0.025).

Surgeon's satisfaction with the operation field quality was not significantly different between groups (P value: 0.28). According to Boezaart scale, no statistically significant difference was found between the two groups with regard to bleeding volume (P value=0.75).

Discussion

Our study compared alpha and beta blocker drug (Labetalol) with a venodilator (Nitroglycerine) for deliberated hypotension in rhino-septoplasty surgery.

Bleeding during the surgery can lead to poor surgical field visualization which could be associated with weak surgical outcomes.

Many studies and meta-analyses have shown that using hypotensive drugs during general anaesthesia could reduce blood loss and make a better surgical field (1,3,4), especially in maxillofacial surgeries (7-9)without any threats tothe patient safety (10); even some studies indicated that deliberate hypotension caused shortened hospital stay (11).

Deliberate hypotension may lead to lower arterial pressure all over the body even in lungs

(Decreased pulmonary artery pressure), It may also reduce hypoxic pulmonary vasoconstriction, and rarely cause intrapulmonary shunts and increasedarterial pressure of CO2. Hypotension may decrease renal blood flow and stimulate renin-angiotensin system. As the arterial pressuredeclines below 70 mm Hg, the glomerular filtration rate declines. However, by the end of hypotensive anaesthesia, if patient is not dehydrated, urine excretion recovers.

There is no report of unwanted hepatic side effects after deliberate hypotension (13). Different drugs with wide range of effects like Esmolol, Labetalol, Remifentanil, Dexmedetomidine, Nitroprusside, and Nitroglycerine used to induce controlled hypotension. (14-18).

In another study Guney et al study compared Esmolol to Nitroglycerine regarding effectiveness in controlling hypotension during nose surgery. They recommended Esmolol as an effective alternative to Nitroglycerineas with hemodynamic stability and good surgical field visibility (15).

Sukhmindar et al compared Nitroglycerine, Dexmedetomidine and Esmolol to decrease blood pressure during endoscopic sinus surgeries and concluded that Dexmedetomidine and Esmolol were superior to Nitroglycerine, and even Dexmedetomidineprovided some benefits of reducing the analgesic requirements in postoperative period. (16).

Degoute et al used Remifentanil (a short acting opioid) combined with Propofol in middle ear surgery for controlled hypotension and concluded that it is as potent drug as Nitroprusside and

Esmolol in decreasing blood pressure. Remifentanil also reduced Blood flow of the middle ear and ensured a good operating field quality for tympanoplasty without use of other hypotensive drugs. (17).

In our study, all patients were in ASA class 1 without any risk factor for pulmonary, renal or hepatic disease. Monitoring during procedure revealed no sign of hypoxia or hypercapnia.

Our current study indicated that Labetalol is superior to Nitroglycerine to produce a "dry" surgical field which is desirable for surgeons. It could lower MAP rapidly after use and maintain deliberate hypotension without difficulties which is in accordance with previous studies. Labetalol has both alpha and beta adrenergic blockade activity. Alpha blockade induce decrease in systemic vascular resistance and beta blockade prevent tachycardia, but after induced hypotension with Nitroglycerine usually tachycardia occurs. This is because of peripheral vasodilation which could result in baroreceptor mediated sympathetic responses (increased HR & myocardial contractility) (14).

In both groups, oxygen saturation remained 97% or greater, with inspired 100% O2 indicating no clinically significant intrapulmonary shunting. Our findings were in agreement with previous researchers.

Limitations

We had no limitationsin conducting the study.

Generalizability

Future studies using larger sample size and inclusion of different types of surgeries are needed to illustrate the effectiveness and saftey of Labetalol for deliberate hypotension in ENT surgeries and confirm our results.

Conclusion

We concluded that Labetalol is an effective and safe drug with anesthetic benefits for deliberate hypotension. In comparison with Nitroglycerine, Labetalol can make better quality of surgical field and more satisfaction for surgeons with less variation in heart rate and blood pressure. It also decreased requirement for complimentary anesthetic/hypotensive drugs during the operation.

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Conflict of interest

The authors declare no conflicts of interest.

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