



Research Article

Remifentanil versus Nitroglycerin for Controlled Hypotensive Anesthesia During Primary Open Rhinoplasty: A Comparative Study

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Abstract

Background: Controlled hypotensive anesthesia is commonly utilized to reduce blood loss and provide a desirable surgical field during perioperative procedures, particularly in facial plastic operations. **Objective:** To assess the hypotensive effects of nitroglycerine and remifentanil for controlled hypotension anesthesia in primary open rhinoplasty. **Methods:** A prospective, comparative, randomized, double-blind study was carried out from June to October 2021 at Rizgary Teaching Hospital in Erbil, Iraq. Eighty patients were randomly divided into two groups and given either nitroglycerin or remifentanil to keep their mean arterial blood pressure between 50 and 60 mmHg. Heart rate, systolic and diastolic blood pressure, intraoperative blood loss, surgical field quality, and surgery duration are all measured and compared. **Results:** Patients in the nitroglycerin and remifentanil groups met the systolic, diastolic, and mean arterial pressure objectives with similar results. However, there is a statistically significant difference in operation duration between the remifentanil and nitroglycerin groups (135.3 and 145.3 minutes, respectively). The heart rate differed significantly between the two groups. The remifentanil group had decreased intraoperative blood loss, a higher surgical field quality, and significantly greater surgeon satisfaction. **Conclusions:** Continuous infusion of nitroglycerine and remifentanil is a dependable and effective method for achieving controlled hypotension by reaching the target mean arterial pressure. Remifentanil outperforms nitroglycerin in terms of limiting blood loss, reducing surgical time, and maintaining superior hemodynamics (particularly heart rate).

Keywords: Anesthesia, Controlled hypotension, Nitroglycerin, Remifentanil, Rhinoplasty.

ريميفنتانيل مقابل النيتروجليسرين للتخدير الخافض للضغط المتحكم فيه أثناء عملية تجميل الأنف المفتوحة الأولية: دراسة مقارنة

الخلاصة

الخلفية: يستخدم التخدير الخافض للضغط بشكل شائع لتقليل فقدان الدم وتوفير مجال جراحي مرغوب فيه أثناء الإجراءات المحيطة بالجراحة، خاصة في عمليات تجميل الوجه. **الهدف:** تقييم التأثيرات الخافضة للضغط للنيتروجليسرين والريميفنتانيل للتخدير الخافض لضغط الدم في عملية تجميل الأنف المفتوحة الأولية. **الأساليب:** أجريت دراسة مستقبلية ومقارنة وعشوائية مزدوجة التعمية في الفترة من يونيو إلى أكتوبر 2021 في مستشفى رزغاري التعليمي في أربيل، العراق. تم تقسيم ثمانين مريضاً بشكل عشوائي إلى مجموعتين وأعطوا إما النيتروجليسرين أو الريميفنتانيل للحفاظ على متوسط ضغط الدم الشرياني بين 50 و 60 ملم زئبق. تم قياس ومقارنة معدل ضربات القلب وضغط الدم الانقباضي والانقباضي وفقدان الدم أثناء الجراحة وجودة المجال الجراحي ومدة الجراحة. **النتائج:** حقق المرضى في مجموعتين النيتروجليسرين والريميفنتانيل أهداف الضغط الانقباضي والانقباضي ومتوسط الضغط الشرياني بنتائج مماثلة. ومع ذلك، هناك فرق يعبئ به إحصائياً في مدة العملية بين فئتي الريميفنتانيل والنيتروجليسرين (135.3 دقيقة و 145.3 دقيقة على التوالي). اختلف معدل ضربات القلب اختلافاً كبيراً بين المجموعتين. انخفض فقدان الدم في مجموعة ريميفنتانيل أثناء الجراحة، وجودة أعلى للمجال الجراحي، ورضا الجراح بشكل ملحوظ. **الاستنتاجات:** التسريب المستمر للنيتروجليسرين والريميفنتانيل هو طريقة يمكن الاعتماد عليها وفعالة لتحقيق انخفاض ضغط الدم المتحكم فيه من خلال الوصول إلى الضغط الشرياني المستهدف. يتفوق ريميفنتانيل على النيتروجليسرين من حيث الحد من فقدان الدم، وتقليل وقت الجراحة، والحفاظ على ديناميكا الدم الفائقة (خاصة معدل ضربات القلب).

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INTRODUCTION

The incidence of cosmetic surgeries, including septorhinoplasty, has increased worldwide. A small amount of bleeding accompanies the surgery. Still, the presence of very small blood vessels in the nose, anatomical variations, and the closeness of the site of the operation to the orbits and the brain can black out the field of the operation and make the surgery difficult and complicated [1]. Thus, one of the most important

challenges of anesthesiologists in microscopic, cosmetic, and reconstructive operations is to minimize bleeding in the field of the operation and help the surgeon to see better [2]. Controlled hypotension is one of the most successful ways to decrease bleeding, which can be done by anesthetic drugs (volatiles and/or intravenous induction agents), beta-blocker drugs, and peripheral vasodilator drugs [3]. Other methods that can be used to reduce intraoperative bleeding are injection

of local vasoconstrictors and elevating the head of the bed during surgery [4]. Controlled hypotension is achieved by decreasing the baseline mean arterial pressure (MAP) by 30% or lowering the systolic blood pressure to 80-90 mmHg and the MAP to 50-60 mmHg [5]. Moderate hypotension can reduce about 40% of the average blood loss, decrease the need for blood transfusion by about 45%, and the average operating time can be decreased by about 10% [6]. Remifentanil is an ultrashort-acting opioid that has a 5- to 10-minute duration and a context-sensitive half-time of 3 minutes. It has an ester site, and nonspecific plasma esterase metabolizes it. Remifentanil is mostly used as a continuous infusion; it can also be administered as an intravenous bolus to facilitate endotracheal intubation, which may occasionally induce involuntary glottic closure, chest-wall rigidity, and bradycardia [7]. Patients having pseudocholinesterase deficiency have a normal response to remifentanil [8]. Doses of remifentanil include a loading dose of 1.0 µg/kg, maintenance infusion of 0.5–20 µg/kg/min, and postoperative analgesia/sedation of 0.05–0.3 µg/kg/min [9]. Nitroglycerin, also known as glyceryl trinitrate (GTN), is an organic nitrate compound with vasodilatory properties. It specifically targets the venous system and large coronary arteries, causing vasodilation and leading to decreased cardiac ventricular wall tension. Increasing the nitroglycerin dose also relaxes arterial vascular smooth muscle. Nitroglycerin leads to pulmonary vasodilation equivalent to the degree of systemic arterial vasodilation. This drug is mostly used in clinical settings to treat angina pectoris caused by atherosclerosis of the coronary arteries or intermittent vasospasm of the coronary arteries. It is given under the tongue or through an IV. Nitroglycerin can also be used to treat hypertension and ventricular failure. Controlled hypotension can also be achieved with the continuous infusion of GTN [10], diluted by a concentration of 100 µg/ml and given as a continuous intravenous infusion (0.5–10 µg/kg/min) [11]. Disadvantages of GTN include reflex tachycardia, rebound hypertension, hypoxic pulmonary vasoconstrictive impairment, and liability of cyanide toxicity at high-dose usage, which is characterized by metabolic acidosis and cardiac arrhythmia [12]. This study aimed to compare the effects of remifentanil and GTN when used to maintain controlled hypotension as primary medication in primary rhinoplasty operations. The comparison includes both drugs' effects on systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, severity of blood loss, duration of surgical time, quality of the surgical field, and surgeon satisfaction.

METHODS

Study design

This is a prospective, comparative, randomized, double-blind study that was performed from June to October 2021 at Rizgary Teaching Hospital in Erbil/Iraq.

Ethical approval

The study protocol was approved by the scientific council of the Arab Board for Medical Specialization (Anaesthesia and Intensive Care), and written consent was obtained from all participants.

Inclusion criteria

Patients fulfilled the American Society of Anesthesiologists physical status classification of ASA-I and aged 24-36 years with a BMI of 19-28 kg/m² were enrolled in the study.

Exclusion criteria

Patients with ASA II or higher, age less than 24 and more than 36 years, a BMI of less than 19 and more than 28 kg/m², a complicated rhinoplasty, surgery that took more than 180 minutes, hemoglobin levels below 10 g/dl, allergies to the medicines used, and those maintained on anticoagulant therapy were excluded from the study.

Intervention and outcome measurements

Eighty patients were selected for elective primary open rhinoplasty with a controlled hypotension anesthesia technique. The same surgical team performed the procedures. They were randomly divided into 2 groups: the GTN group (G-group) and the remifentanil group (R-group). Induction of anesthesia was done by 2.0 mg/kg propofol and 0.6 mg/kg rocuronium, and anesthesia maintenance was obtained by oxygen and sevoflurane 1-2 MAC. All patients received pre-medications of 15-20 µg/kg midazolam and 1 µg/kg fentanyl, and an armored endotracheal tube size 7-7.5 mm ID was inserted 2-2.5 min after induction of anesthesia with laryngoscopy time <20 sec, and a wet throat pack was put in to prevent aspiration. The patient position was set, around 30 degrees head up, and the nasal mucosa was infiltrated by 2% lidocaine with epinephrine 1:80000. Before starting the surgery, patients received loading doses of 2.0 µg/kg GTN in the G-group and 1.0 µg/kg remifentanil in the R-group within 5 min through a syringe pump, the aim of which was to reduce MAP 20-25% before surgical incision to get started. The infusion of both medications was performed using a syringe pump. To get the mean arterial pressure (MAP) to 50 to 60 mmHg, we titrated the infusion of 10 mg GTN in 50 mL of normal saline and 5 mg remifentanil in 50 cc of normal saline. The infusion of GTN started at 0.25 to 1.0 µg/kg/min and remifentanil at 0.5 to 5.0 µg/kg/min. Baseline readings of hemodynamic parameters—systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR)—were recorded, which are mentioned as zero minutes in data and statistics, and a capnometer was attached to record EtCO₂, and then after induction, hemodynamic parameters (SBP, DBP, MAP, and HR) were recorded at times 5, 10, 15, 20, 30, 40, 60, 80, 100, 120, and 150

minutes perioperatively. The following 5-point scale was used to assess the amount of bleeding in the operative field: grade 1 = cadaveric condition with minimal suction required; grade 2 = minimal bleeding with infrequent suction required; grade 3 = brisk bleeding with frequent suction required; grade 4 = bleeding covers surgical field after removal of suction, before the surgical instrument can perform maneuver; grade 5 = uncontrollable bleeding. The idea was taken from Peter-John Wormald, and endoscopic sinus surgery was obtained in a questionnaire designed to the surgeons postoperatively. In cases of grade 4 and grade 5 bleeding, 250 mg of tranexamic acid (10 mg/kg) was given to the patients. After recovery, the patients were monitored for 30 minutes. BP for patients in the G-group was measured every 5.0 minutes in the recovery room, while for patients in the R-group, it was measured twice on arrival to the recovery room and before discharge from the recovery room, as in GTN, more time is needed to return blood pressure to normal baseline. Six cases were cancelled because of the requirement for emergency drugs and other medications to attenuate targeted MAP and heart rate, 4 from the G-group and 2 from the R-group. Regarding the GTN, 1 case needed a beta-blocker (metoprolol 2.0 mg) to decrease heart rate, two cases needed extra medication (propofol 0.1-0.2 mg/kg/min) to maintain target MAP, while the fourth case developed severe hypotension MAP decreased to 30 mmHg, in which phenylephrine (alpha-1 agonist) 150 mg was given until MAP reached back to the target. While in remifentanyl cases, one of them needed atropine because of bradycardia (HR < 40 beats/min), and the other case needed extra medication (propofol 0.1-0.2 mg/kg/min) to maintain target MAP.

Statistical analysis

Data of all patients in both groups were entered into a database software program; data was re-checked for any error and then analyzed using Minitab software version 17 for Windows. Descriptive statistics of variables were presented as mean and standard deviation; comparison between means and significant differences between both groups was done by using a student t-test for all continuous variables. A chi-square test is used for categorical variables. A p -value < 0.05 was considered statistically significant.

RESULTS

In this study, 80 patients underwent primary elective open rhinoplasty. Patients were divided into two groups randomly, the R-group for remifentanyl and the G-group for GTN; each group had 40 patients. In Table 1, there was no statistical difference in age and BMI between both groups. There was a statistically significant difference between the groups in how long surgery took and how much intravenous (IV) fluid was used. The R-group had shorter surgery and used less IV fluid. Regarding SBP, there was not any statistical difference between both groups at different time intervals, as

shown in Figure 1. Regarding DBP, there was no statistical difference between the two groups in the first two hours of operation ($p > 0.05$), while after two hours at 120 and 150 minutes, there was a statistical difference between the DBP measurement of both groups in which the R-group has lower readings ($p = 0.002$ and 0.006), respectively (Figure 2).

Table 1: Age, BMI, duration of surgery in minutes, and IV fluid usage (n=40 in each group)

Variables	Values	p -value
Age (year) R-group	29.6±4.32	0.488
Age (year) G-group	30.1±5.47	
BMI (kg/m ²) R-group	23.7±3.98	0.982
BMI (kg/m ²) G-group	23.2±4.23	
Duration of surgery (min) R-group	135.3±10.87	<0.001
Duration of surgery (min) G-group	145.25±11.36	
Total IV fluid (ml) R-group	766±75.3	0.001
Total IV fluid (ml) G-group	823±68.3	

Values were expressed as mean±SD. R-group: treated with remifentanyl; G-group- treated with nitroglycerin.

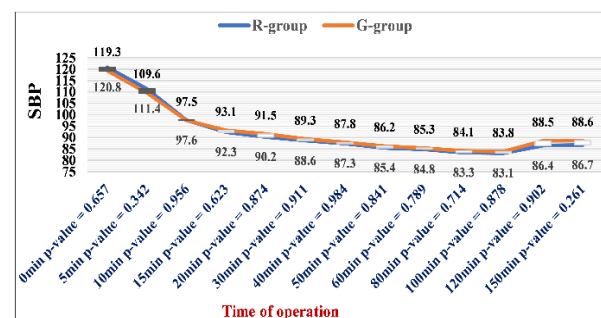


Figure 1: Comparison of systolic blood pressure (SBP) between groups.

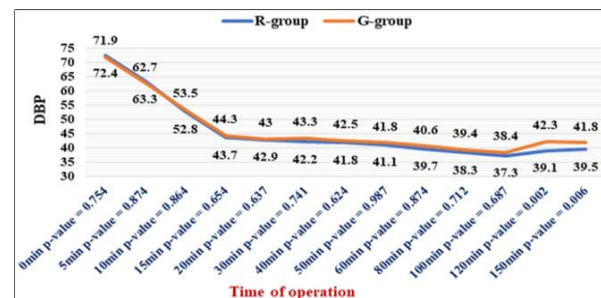


Figure 2: Comparison of diastolic pressure (DBP) between groups

Regarding the MAP, there was no statistical difference between both groups throughout the surgery, except in the 120th minute, in which there was a lower measurement in the R-group ($p = 0.015$) as shown in Figure 3.

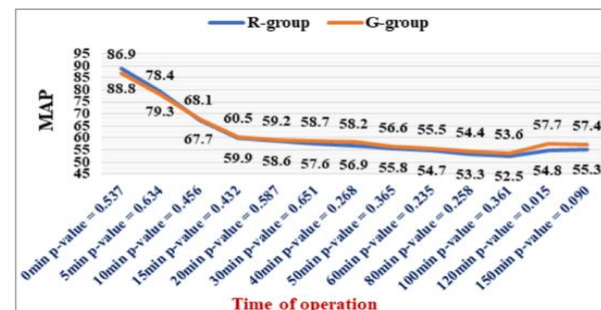


Figure 3: Comparison of mean arterial pressure (MAP) between groups.

Regarding the heart rate, there was an obvious significant difference between both groups ($p < 0.001$) as shown in Figure 4.

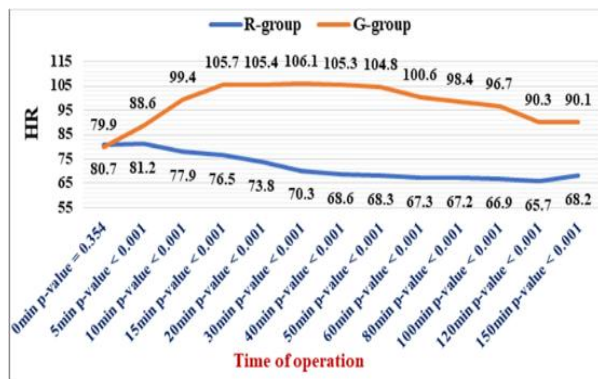


Figure 4: Comparison of heart rate (HR) between groups.

Concerning the severity of bleeding, surgical field, and surgeon satisfaction, there was an obvious statistical difference between the two groups; the R-group showed less severity in bleeding, more surgeon satisfaction, and better quality of surgical field ($p = 0.01$), as shown in Table 2.

Table 2: Comparison of bleeding, surgical site, and surgeon satisfaction (n=40 in each group)

Bleeding quality and surgeon satisfaction	Number of patients		Total
	R-group	G-group	
Grade 1	5(12.5)	0(0)	5(6.3)
Grade 2	23(57.5)	13(32.5)	36(45)
Grade 3	11(27.5)	18(45)	29(36.3)
Grade 4	1(2.5)	6(15)	7(8.8)
Grade 5	0(0)	3(7.5)	3(3.8)
Total	40(100)	40(100)	80(100)

Values were expressed as frequencies and percentages. R-group: treated with remifentanyl; G-group: treated with nitroglycerin.

DISCUSSION

In this study, we conducted a comparative analysis of the hemodynamic effects of remifentanyl and nitroglycerin (GTN) when used for controlled hypotension anesthesia. Both remifentanyl and GTN successfully achieved the target by reducing the SBP, DBP, and MAP with no significant difference between them. However, remifentanyl led to a more stable heart rate and prevented tachycardia significantly ($p < 0.001$). Additionally, remifentanyl resulted in less intraoperative bleeding and a better quality of the surgical field ($p = 0.01$), with a significantly shorter duration of surgical time ($p < 0.001$). Degoute *et al.* (2001) conducted a study to compare remifentanyl and propofol with esmolol and GTN for tympanoplasty; they showed that the combination of remifentanyl and propofol allowed for controlled hypotension, decreased middle ear blood flow, and created optimal surgical conditions for tympanoplasty without requiring the use of additional potent hypotensive agents [13]. Similarly, the result of the current study showed that there was a significant difference between remifentanyl and GTN in terms of the quality of the surgical field and severity of bleeding; also, this study had more cases from the GTN group

canceled because of the requirement of other medications to obtain targeted MAP compared with the remifentanyl group. In 2000, Dolman *et al.* demonstrated the effect of hypotensive anesthesia on blood loss and operative time during Le Fort I osteotomies; they reported the benefits of hypotensive anesthesia to decrease blood loss and improve the surgical field during Le Fort I osteotomies with easygoing and more intentional dissection without reducing operative time [14]. This result supports the outcome of the current study regarding the surgical field quality and severity of bleeding; however, there was a significant decrease in the duration of surgical time when using remifentanyl. In 2013, Tuncel *et al.* conducted a study on intraoperative bleeding, postoperative edema, and ecchymosis in rhinoplasty; they used dexamethasone and controlled hypotension anesthesia. They showed that the administration of three dexamethasone doses in combination with controlled hypotension resulted in a significant decrease in postoperative complications associated with rhinoplasty procedures involving osteotomy. Additionally, this approach has effectively minimized intraoperative bleeding [15], which supports the outcomes of the current study regarding the reduction of intraoperative bleeding in the R-group; however, in this study we depended only on controlled hypotension without dexamethasone. Koşucu *et al.* (2014) studied the effects of perioperative remifentanyl with controlled hypotension on intraoperative bleeding and postoperative edema and ecchymosis in open rhinoplasty and reported that the use of remifentanyl for controlled hypotension during rhinoplasty may decrease swelling and bruising of the upper and lower eyelids. This occurs by lowering the mean arterial pressure and decreasing the amount of bleeding during the procedure [16]. Similar findings were observed in this study, which revealed a significant difference in the severity of bleeding between the two groups. Tinker and Michenfelder used sodium nitroprusside, a similar nitrate vasodilator to GTN, which is used in this study, and reported that the mild hypotension induced by nitroprusside infusion leads to broad vasodilation, reflex tachycardia, and an increase in cardiac output, which is attributed to direct effects on the vascular smooth muscle. In the presence of nitroprusside, catecholamines have minimal influence on the arterioles' mucous membrane [17]. This finding supported the outcomes of this study in that using GTN to induce hypotension caused reflex tachycardia. Guney *et al.* performed a study to compare esmolol with nitroglycerin in controlling hypotension during nasal surgery. They reported that the average SBP, DBP, and MAP before inducing hypotension are not different between the drugs [18]. Their finding supported this study in that there was no difference between the two groups regarding SBP, DBP, and MAP, as there was a targeted MAP. Additionally, Modir *et al.* compared remifentanyl, magnesium sulfate, and dexmedetomidine for intraoperative hypotension and bleeding and postoperative recovery in endoscopic sinus surgery and

tympantomastoidectomy. They reported that remifentanil provided a superior balance of mild controlled hypotension with minimal reduction in blood pressure and heart rate, along with faster recovery time. On the other hand, dexmedetomidine reduced blood loss but was associated with lower blood pressure and heart rate [19]. In the current study, remifentanil showed good control of blood pressure but with a significant reduction in heart rate, associated with a significant reduction in blood loss and quality of surgical fields; these outcomes are superior to those reported with dexmedetomidine.

Conclusion

A dependable, secure, and efficient method of achieving the desired mean arterial pressure and managing low blood pressure is the continuous infusion of nitroglycerin and remifentanil. Remifentanil is more effective than GTN in open rhinoplasty for minimizing blood loss, decreasing surgical time duration, and sustaining superior hemodynamics, particularly in heart rate.

Recommendation

We highly recommend using remifentanil over GTN for controlled hypotension technique in patients undergoing primary open rhinoplasty.

Conflict of interests

No conflict of interest was declared by the authors.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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