Evaluation and Comparison the Effectiveness of Remifentanil, Nitroglycerin, Esmolol, and Nitroglycerin + Esmolol on Blood Pressure And Heart Rate During Rhinoplasty Surgery

Mohammad Aydin Abbas (PhD)¹, Orhan Uludag (PhD)²
¹ Raparin Teaching Hospital, Erbil, Iraq
² Faculty of Pharmacy, Gazi University, Ankara, Turkey

Abstract

Background: Rhinoplasty is still one of the top five aesthetic surgeries performed and is considered one of the most challenging procedures in otorhinolaryngology surgery. Bleeding is one of the most important factors affecting an operation's success. The controlled hypotension method reduces bleeding; therefore, it provides a satisfying bloodless surgical field during operation.

Objective: To evaluate and compare the effectiveness of (Remifentanil, Nitroglycerin, Esmolol, and Nitroglycerin + Esmolol) on hemodynamic parameters and the effectiveness of these drugs in providing a satisfactory bloodless surgical field during rhinoplasty surgery.

Patients and Methods: 200 adults aged 20 to 45 years were randomly divided into four groups: Remifentanil (R), Nitroglycerin (N), Esmolol (E), Nitroglycerin + Esmolol (N+E). Systolic blood pressure, diastolic blood pressure, mean blood pressure, and heart rate (SBP, DBP, MBP, and HR) were recorded before anesthesia induction until the operation's end. The bleeding score and the visibility of the surgical field were rated by the surgeon as follows: (0) No bleeding, (1) Mild bleeding - no aspiration required, (2) Mild bleeding - intermittent aspiration is required, (3) Moderate bleeding - frequent aspiration is required, (4) Severe bleeding - constant aspiration is required, (5) Severe bleeding, operation stopped because of surgical field invisibility.

Results: As a result, during operation, decreased values of (SBP, DBP, and MBP) were statistically significant in all groups. At the same time, the value of HR showed a statistically significant decrease in the (E) and (R) groups, while there was a statistically significant increase in the (N) and (N+ E) groups. Patients in the (E) and (R) groups had a statistically significantly lower bleeding score than the patients in the (N) and (N + E) groups.

Conclusion: Patients had better Hemodynamic stability and surgical field visibility after applying Esmolol and Remifentanil.
Keywords: Controlled hypotension, Rhinoplasty, Esmolol, Remifentanil, Nitroglycerin, and Nitroglycerin + Esmolol, Bleeding score, Surgical field visibility.

Introduction
Rhinoplasty is a surgical procedure that is used to reshape the nose. This surgery is one of the most challenging procedures in aesthetic surgery and otolaryngology [1-3]. The most important factor affecting the success of rhinoplasty operations under general anesthesia conditions is bleeding [4, 5]. Reduced intraoperative bleeding provides the surgeon with better visualization of the operative field, better analysis of tissues, and more comfortable use of preferred techniques [6-9]. Controlled hypotension anesthesia is a well-known and effective technique used to reduce blood loss and subsequently reduce the need for blood transfusions, as well as provide a satisfactory bloodless surgical field in many operations, allowing the surgeon to see the surgical area more clearly, better analyze the tissues, and apply their chosen procedures more efficiently [10, 11]. For this reason, many rhinoplasty surgeons prefer to operate with controlled hypotensive anesthesia [7].

There are many definitions for controlled hypotension, lowering systolic blood pressure to 80-90 mmHg, reduction in mean arterial pressure (MAP) to 50-70 mmHg, reducing MAP by 20-30% from baseline values, and maintenance at a reduced level throughout the surgery [4, 8, 12-14].

The main purpose of drugs used to achieve controlled hypotension is to provide the desired level of controlled hypotension without affecting the perfusion of living organs. This effect should be rapid and disappear quickly when the drug is discontinued without the formation of toxic metabolites. Also, hypotensive agents are used to preventing hemodynamic changes during endotracheal intubation [15-18].

Many pharmacological agents are available to achieve controlled hypotension, allowing the surgeon to observe the surgical region more clearly, study the tissues more thoroughly, and perform their selected operations more quickly and efficiently [19]. In addition to agents that can be used successfully alone, some can be combined with other agents to limit dosage requirements and decrease the adverse effects of each agent [20, 21]. Commonly used agents to provide Controlled hypotension anesthesia; are inhalation anesthetics [22], sodium nitroprusside [23], nitroglycerine [15], beta-blockers (especially esmolol) [24, 25], a competitive non-selective β-adrenergic and a selective postsynaptic α1-adrenergic receptor blocker, alpha- and beta-adrenergic antagonists such as labetalol [26], and narcotics (especially fentanyl and Remifentanil) [27, 28] are used to achieve controlled hypotension. In some operations like Arthroplasty and Caesarean and major trauma, intravenous antifibrinolytic is used to prevent or treat excessive blood loss during operation [29].

The aim of this study: To evaluate and compare the effectiveness of Remifentanil, Nitroglycerin, Esmolol, and Nitroglycerin + Esmolol on blood pressure and heart rate and to evaluate and compare the clinical effectiveness of providing controlled hypotension with Remifentanil, Nitroglycerin, Esmolol, and Nitroglycerin +
Esmolol. At the same time, to evaluate and compare these drugs to provide a satisfactory bloodless surgical field during rhinoplasty surgery to increase intraoperative visibility.

**Patients and Methods**

This study included two hundred adult patients who underwent rhinoplasty operations in the Plastic and Reconstructive Surgery Department.

After the patient entered the operating room, the heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP) values, ages, and genders of the patients were recorded. Anesthesia induction was achieved in all patients with 2 mg/kg propofol and 1 μg/kg fentanyl. After muscle relaxation was achieved with rocuronium (0.6 mg/kg), endotracheal intubation was performed, and anesthesia was maintained with sevoflurane (2-3%).

Following the administration of the anesthetic (induction of anesthesia) and the endotracheal tube placement, the patients were given five minutes of quiet rest before continuing with the procedure. Then, T5 (T 5 minutes) hemodynamic values (baseline values) were measured, and a routine treatment protocol was started for the patients.

Medications were started to be given to provide controlled hypotension, 0.25 μg/kg/min remifentanil to (R group), 5 μg/kg/min nitroglycerin to (N group), 200 μg/kg/min esmolol to (E group), and the same doses of nitroglycerin+esmolol to (N+E group) were given to the patient in each group and continued throughout the operation. The reduction in systolic arterial pressure was considered effective when the required pressure of 80-95 mmHg was obtained. Drug doses were adjusted to maintain the mean arterial pressure 20-30% below the baseline value. The specialist anesthetist adapts the infusion rate to protect hypotension, maintain the desired blood pressure level, and achieve controlled hypotension during surgery. The infusion rates of the study drugs were titrated to maintain MBP at 60-80 mmHg.

To monitor and record any changes during the operation. Changes in HR, SBP, DBP, and MBP levels were monitored and recorded in all cases before anesthesia induction, 5 minutes after endotracheal intubation, and every 15 minutes until the end of the surgery.

**Participants**

Rhinoplasty surgery was performed on two hundred normotensives (Healthy patient ASA I) patients. Patients aged between 20-45 years of both sexes were randomly divided into four groups by the specialist anesthetist.

- Remifentanil group (n=50).
- Nitroglycerin group (n=50).
- Esmolol group (n=50).
- Nitroglycerin+Esmolol (n=50).

The anesthesiologist determined the dose of the drug. The data included in the study were recorded from the monitor. Before surgery, all patients were asked to fast for at least 8 hours.

**Exclusion Criteria**

Uncontrolled hypertension, severe renal or hepatic diseases, anemia, patients aged <20 and > 45 years, patients who refused to participate in this study, who are pregnant or may be become pregnant, have psychiatric disorders, have cardiovascular system disease, were not included in this study.
Visibility of the Surgical Field
During the operation, operative field bleeding amount and visibility of the surgical field was subjectively (personally) and visually graded by the surgeon from the beginning of the operation to the end of the operation in the following manner. Categories for evaluating the visibility of the intraoperative surgical field:
(0) No bleeding.
(1) Mild bleeding - no aspiration required.
(2) Mild bleeding - intermittent aspiration required.
(3) Moderate bleeding - frequent aspiration required.
(4) Severe bleeding - constant aspiration is required.
(5) Severe bleeding, operation stopped because of surgical field invisibility.

Statistical Analysis
The results were statistically evaluated using [Statistical Package for the Social Sciences (SPSS) version 24.0]. "Shapiro – Wilk" test was used to determine the normal distribution of the data. Patient characteristics, hemodynamic variables (Systolic blood pressure, diastolic blood pressure, mean blood pressure, and heart rate), and visibility of the intraoperative surgical field were compared among four Groups. All data obtained are expressed as Mean ± Standard Deviation. Comparisons between groups were made with the "Duncan test." The mean and standard deviation of the bleeding score were statistically analyzed with the "Friedman test" to compare individual group pairs; the "Wilcoxon test" was used. When the results were (p>0.05), the changes were considered statistically insignificant; changes were considered statistically significant when the P-value was 0.05 or less.

Results
Demographic Data of Patients
This study included 200 patients, 48 male (24%) and 152 female (76%); as shown in Table (1), there is no statistically significant difference between the four groups regarding gender distribution and average age.

<table>
<thead>
<tr>
<th>SEX (no.&amp; %)</th>
<th>Remifentanil</th>
<th>Nitroglycerin</th>
<th>Esmolol</th>
<th>Nitroglycerin + Esmolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>M F</td>
<td>M F</td>
<td>M F</td>
<td>M F</td>
<td>M F</td>
</tr>
<tr>
<td>13 37</td>
<td>12 38</td>
<td>12 38</td>
<td>11 39</td>
<td></td>
</tr>
<tr>
<td>26% 74%</td>
<td>24% 76%</td>
<td>24% 76%</td>
<td>22% 78%</td>
<td></td>
</tr>
<tr>
<td>AGE</td>
<td>30.86±6.47</td>
<td>30.96±6.43</td>
<td>30.92±6.43</td>
<td>31.10±6.20</td>
</tr>
</tbody>
</table>

Ages are given as Mean±Standard Deviation (M: Male, F: Female, n=50, p>0.05).

Pre-Operative HR and BP (SBP, DBP, and MBP) Values In Different Study Groups and Their Comparisons.
Before the operation, the HR and SBP values between different study groups were close to each other, and there was no significant difference between the DBP and MBP values of the various study groups.
In the pre-operative period, Heart Rate levels in the Remifentanil group were found to be significantly higher (with a small difference) when compared to the
Nitroglycerin+Esmolol group; however, no difference was found in the Remifentanil group when compared to the Esmolol and Nitroglycerin groups. At the same time, no statistical difference was observed in the Nitroglycerin+Esmolol group compared to the Esmolol and Nitroglycerin groups, and no statistical difference was observed between Esmolol and Nitroglycerin groups.

In the pre-operative period, SBP levels were significantly higher (with a small difference) in the Remifentanil group compared to the Esmolol and Nitroglycerin groups. In contrast, no significant difference was found when comparing the Remifentanil group to the Nitroglycerin+Esmolol group. No significant difference was observed between the Nitroglycerin+Esmolol group and the other groups, and no statistical difference was observed between Esmolol and Nitroglycerin groups.

There was no significant difference between the four study groups in the DBP & MBP measurements during the pre-operative period.

Table (2): Pre-Operative HR and BP (SBP, DBP, and MBP) Values in different study groups and their Comparisons

<table>
<thead>
<tr>
<th>Before Operation</th>
<th>Remifentanil</th>
<th>Nitroglycerin</th>
<th>Esmolol</th>
<th>Nitroglycerin + Esmolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>84.98±3.63*</td>
<td>83.64±4.07</td>
<td>82.84±5.12</td>
<td>82.30±4.80</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>131.70±3.66</td>
<td>128.44±4.34#</td>
<td>128.22±5.37#</td>
<td>130.04±4.31</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>80.62±3.96</td>
<td>80.26±4.77</td>
<td>81.8±4.58</td>
<td>81.13±4.23</td>
</tr>
<tr>
<td>MBP (mmHg)</td>
<td>97.64±3.66</td>
<td>96.30±4.28</td>
<td>97.26±4.40</td>
<td>97.88±3.34</td>
</tr>
</tbody>
</table>

Values are given as Mean±Standard Deviation (*Different from Nitroglycerin+Esmolol, # different from Remifentanil, n=50, p<0.05).

Intra-Group (within the same group) HR and BP (SBP, DBP, and MBP) Values at Scheduled Intervals (T5, T15, T30, T45, T60) and Their Comparisons During The Controlled Hypotension Period For Each Study Group.

**Remifentanil**

In the Remifentanil group, the decrease in HR, SBP, DBP, and MBP Values during the Controlled Hypotension at T15, T30, T45, and T60 after drug administration was statistically significant when compared to the T5 period.

In addition, HR and SBP values at the T30, T45, and T60 periods were statistically significantly lower than those at the T15 times.

The DBP value in the T45 period was significantly lower than the T15 values.

MBP values in the T45 and T60 periods were also significantly lower than T15 values.
Table (3): Remifentanil group HR and BP (SBP, DBP, and MBP) values at scheduled intervals (T5, T15, T30, T45, T60) and their comparisons during the Controlled Hypotension Period

<table>
<thead>
<tr>
<th>Remifentanil</th>
<th>T5</th>
<th>T15</th>
<th>T30</th>
<th>T45</th>
<th>T60</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>77.06±5.04</td>
<td>62.24±4.60*</td>
<td>59.00±5.20*#</td>
<td>57.92±5.53*#</td>
<td>57.68±5.00*#</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>104.54±5.12</td>
<td>94.92±6.62*</td>
<td>88.78±6.97*#</td>
<td>89.62±6.50*#</td>
<td>88.74±6.89*#</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>69.70±4.52</td>
<td>60.60±5.19*</td>
<td>59.22±5.96*</td>
<td>56.80±5.58*#</td>
<td>58.08±5.72*</td>
</tr>
<tr>
<td>MBP (mmHg)</td>
<td>81.38±4.57</td>
<td>72.06±5.50*</td>
<td>69.08±6.10* #</td>
<td>67.68±5.69*#</td>
<td>68.30±5.79*#</td>
</tr>
</tbody>
</table>

Values are given as Mean±Standard Deviation (* different from T5, # different from T15, n=50, p<0.05).

Nitroglycerine

In the Nitroglycerin group, HR values measured at T15, T30, T45, and T60 after drug administration was statistically significantly higher compared to the T5 time frame. In addition, HR values at T30, T45, and T60 intervals were statistically significantly lower than those measured in the T15 time frame. SBP, DBP, and MBP measurements in the Controlled Hypotension period after drug administration in the Nitroglycerin group were statistically significantly lower at T15, T30, T45, and T60 times compared to the T5 period. In addition, SBP values at the T30, T45, and T60 periods were statistically significantly lower than those measured in the T15 time frame. Also, DBP and MBP values at the T45 period were statistically significantly lower than those measured in the T15 time frame.

Table (4): Nitroglycerin group HR and BP (SBP, DBP, and MBP) values at scheduled intervals (T5, T15, T30, T45, T60) and their comparisons during the Controlled Hypotension Period

<table>
<thead>
<tr>
<th>Nitroglycerin</th>
<th>T5</th>
<th>T15</th>
<th>T30</th>
<th>T45</th>
<th>T60</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>76.84±5.43</td>
<td>97.16±4.62*</td>
<td>92.98±3.72* #</td>
<td>91.92±2.43*#</td>
<td>94.28±2.03*#£</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>109.56±4.87</td>
<td>88.24±6.04*</td>
<td>82.82±7.90* #</td>
<td>81.48±9.34*#</td>
<td>82.14±9.38*#</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>72.18±5.14</td>
<td>58.68±5.72*</td>
<td>58.16±6.90*</td>
<td>54.56±8.16*#</td>
<td>56.26±8.53*</td>
</tr>
<tr>
<td>MBP (mmHg)</td>
<td>84.62±4.75</td>
<td>68.54±5.55*</td>
<td>66.36±6.86*</td>
<td>63.54±8.29*#</td>
<td>64.90±8.37*</td>
</tr>
</tbody>
</table>

Values are given as Mean±Standard Deviation (* different from T5, # different from T15, £ different from T45, n=50, p<0.05).

Esmolol

The decrease in HR, SBP, DBP, and MBP values in the Esmolol group during the Controlled Hypotension period was statistically significant at T15, T30, T45, and T60 intervals after drug administration when compared with the T5 period. In addition, SBP values at the T30, T45, and T60 periods were statistically significantly lower than those measured in the T15 time frame, and MBP values at the T45 period were statistically significantly lower than those measured in the T15 period.
Table (5): Esmolol group HR and BP (SBP, DBP, and MBP) values at scheduled intervals (T5, T15, T30, T45, T60) and their comparisons during the Controlled Hypotension Period

<table>
<thead>
<tr>
<th>Esmolol</th>
<th>T5</th>
<th>T15</th>
<th>T30</th>
<th>T45</th>
<th>T60</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>74.70±5.62</td>
<td>67.02±5.74*</td>
<td>64.82±5.20*</td>
<td>65.66±4.85*</td>
<td>64.32±4.41*</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>111.40±5.52</td>
<td>96.36±6.63*</td>
<td>92.04±6.30*</td>
<td>90.40±6.14*</td>
<td>91.42±6.13*</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>70.20±4.53</td>
<td>61.84±5.19*</td>
<td>60.58±4.78*</td>
<td>60.06±5.19*</td>
<td>60.92±5.16*</td>
</tr>
<tr>
<td>MBP (mmHg)</td>
<td>83.92±4.49</td>
<td>73.40±5.02*</td>
<td>71.06±4.87*</td>
<td>70.18±4.87*</td>
<td>71.06±4.67*</td>
</tr>
</tbody>
</table>

Values are given as Mean±Standard Deviation (*different from T5, # different from T15, n=50, p<0.05).

Nitroglycerin+Esmolol

In the Nitroglycerin+Esmolol group during the Controlled Hypotension period, the increase in HR measurements at T15, T30, T45, and T60 intervals after drug administration was found to be statistically significant when compared with the T5 period.

In the Nitroglycerin+Esmolol group, the decrease in SAB, DAB, and MAP measurements in the Controlled Hypotension period, after drug administration, at T15, T30, T45, and T60 intervals when compared with T15 time, was statistically significant.

DBP and MBP values were significantly lower in the T45 timeframes compared to the T30 timeframes.

Table (6): Nitroglycerin+Esmolol group HR and BP (SBP, DBP, and MBP) values at scheduled intervals (T5, T15, T30, T45, T60) and their comparisons during the Controlled Hypotension Period

<table>
<thead>
<tr>
<th>Nitroglycerin + Esmolol</th>
<th>T5</th>
<th>T15</th>
<th>T30</th>
<th>T45</th>
<th>T60</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>75.96±5.66</td>
<td>79.70±4.98*</td>
<td>81.14±3.29*</td>
<td>80.10±2.49*</td>
<td>80.74±2.42*</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>109.22±4.34</td>
<td>86.60±4.61*</td>
<td>81.52±3.44*</td>
<td>80.00±3.27*</td>
<td>80.36±3.38*</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>72.92±3.69</td>
<td>58.92±4.09*</td>
<td>56.42±3.89*</td>
<td>54.22±3.80*</td>
<td>54.62±4.10*</td>
</tr>
<tr>
<td>MBP (mmHg)</td>
<td>85.12±3.73</td>
<td>68.16±3.84*</td>
<td>64.78±3.33*</td>
<td>62.86±2.99*</td>
<td>63.18±3.17*</td>
</tr>
</tbody>
</table>

Values are given as Mean±Standard Deviation (*different from T5, # different from T15, £ different from T30, n=50, p<0.05).
In this study, statistically significant and important decreases were observed in SBP, DBP, and MBP levels in all study groups after administering hypotensive agents to provide Controlled Hypotension during surgery. Concerning Heart Rate data, statistically significant decreases in heart rate were identified in the Esmolol and Remifentanil groups. In contrast, statistically significant increases in heart rate were seen in the Nitroglycerin and Nitroglycerin+Esmolol groups. In general, hemodynamic changes in the intraoperative period during surgery were significantly different from baseline measures in all patients and all groups.

Heart Rate (HR) Values At Scheduled Intervals (T5, T15, T30, T45, T60) and Their Comparisons Between Study Groups

During The Controlled Hypotension Period

HR values in the Remifentanil group were statistically significantly lower than in the Esmolol group, Nitroglycerin group, and Nitroglycerin+Esmolol group.

HR values in the Nitroglycerin group were statistically significantly higher than in the Remifentanil, Esmolol, and Nitroglycerin+Esmolol groups.

HR values in the Esmolol group were statistically significantly higher than in the Remifentanil group and significantly lower than in the Nitroglycerin and Nitroglycerin+Esmolol groups.

HR values in the Nitroglycerin+Esmolol group were statistically significantly higher than in the Remifentanil and Esmolol group while significantly lower than in the Nitroglycerin group.

Table (7): Heart Rate values at scheduled intervals (T5, T15, T30, T45, T60) and their comparisons between study groups during the Controlled Hypotension Period

<table>
<thead>
<tr>
<th>HR</th>
<th>Remifentanil</th>
<th>Nitroglycerin</th>
<th>Esmolol</th>
<th>Nitroglycerin + Esmolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>T 5</td>
<td>77.06±5.04</td>
<td>76.84±5.43</td>
<td>74.70±5.62</td>
<td>75.96±5.66</td>
</tr>
<tr>
<td>T15</td>
<td>62.24±4.60</td>
<td>97.16±4.62*#£</td>
<td>67.02±5.74*</td>
<td>79.70±4.98*£</td>
</tr>
<tr>
<td>T30</td>
<td>59.00±5.20</td>
<td>92.98±3.72*#£</td>
<td>64.82±5.20*</td>
<td>81.14±3.29*£</td>
</tr>
<tr>
<td>T45</td>
<td>57.92±5.53</td>
<td>91.92±2.43*#£</td>
<td>65.66±4.85*</td>
<td>80.10±2.49*£</td>
</tr>
<tr>
<td>T60</td>
<td>57.68±5.00</td>
<td>94.28±2.03*#£</td>
<td>64.32±4.41*</td>
<td>80.74±2.42*£</td>
</tr>
</tbody>
</table>

Values are given as Mean±Standard Deviation (*different from Remifentanil, £ different from Esmolol, # different from Nitroglycerin+Esmolol, n=50, p<0.05).
**Figure (1):** Mean heart rate (HR) values and comparisons between groups during the Hypotension period (Mean±Standard Deviation, *different from Remifentanil, £ different from Esmolol, # different from Nitroglycerin+Esmolol, n=50, p<0.05)

**Systolic Blood Pressure (SBP) Values At Scheduled Intervals (T5, T15, T30, T45, T60) and Their Comparisons Between Study Groups During The Controlled Hypotension Period:** SBP values in the Nitroglycerin and Nitroglycerin+Esmolol groups were found to be statistically significantly lower when we compared to the Remifentanil and Esmolol groups.

At the same time, there was no difference in SBP values between Remifentanil and Esmolol groups, and there was no difference in SBP values between Nitroglycerin and Nitroglycerin+Esmolol groups.

**Table (8):** Systolic Blood Pressure (SBP) Values at scheduled intervals (T5, T15, T30, T45, T60) and their Comparisons Between Study Groups during the Controlled Hypotension Period

<table>
<thead>
<tr>
<th>SBP</th>
<th>Remifentanil</th>
<th>Nitroglycerin</th>
<th>Esmolol</th>
<th>Nitroglycerin +Esmolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>T5</td>
<td>104.54±5.12</td>
<td>109.56±4.87*</td>
<td>111.40±5.52*</td>
<td>109.22±4.34*</td>
</tr>
<tr>
<td>T15</td>
<td>94.92±6.62</td>
<td>88.24±6.04**#</td>
<td>96.36±6.63</td>
<td>86.60±4.61*#</td>
</tr>
<tr>
<td>T30</td>
<td>88.78±6.97</td>
<td>82.82±7.90*#</td>
<td>92.04±6.30</td>
<td>81.52±3.44*#</td>
</tr>
<tr>
<td>T45</td>
<td>89.62±6.50</td>
<td>81.48±9.34*#</td>
<td>90.40±6.14</td>
<td>80.00±3.27*#</td>
</tr>
<tr>
<td>T60</td>
<td>88.74±6.89</td>
<td>82.14±6.38*#</td>
<td>91.42±6.12</td>
<td>80.36±3.38*#</td>
</tr>
</tbody>
</table>

Values are given as Mean±Standard Deviation (* different from Remifentanil, # different from Esmolol, n=50, p<0.05).
Figure (2): Change in Mean systolic blood pressure value and comparisons between groups during the Hypotension period (Mean±Standard Deviation, *different from Remifentanil, # different from Esmolol, n=50, p<0.05)

**Diastolic Blood Pressure (DBP) Values At Scheduled Intervals (T5, T15, T30, T45, T60) and Their Comparisons Between Study Groups During The Controlled Hypotension Period:**

No statistically significant difference was observed between Nitroglycerin, Nitroglycerin+Esmolol, and Remifentanil groups in the mean DBP level during periods of Controlled Hypotension (T15-T60).

During periods of the Controlled Hypotension (T15-T60), DBP values showed a statistically significant decrease in Nitroglycerin and Nitroglycerin+Esmolol group when compared to the Esmolol group.

**Table (9):** Diastolic Blood Pressure (DBP) Values at scheduled intervals (T5, T15, T30, T45, T60) and their Comparisons Between Study Groups during the Controlled Hypotension Period

<table>
<thead>
<tr>
<th>DBP</th>
<th>Remifentanil</th>
<th>Nitroglycerin</th>
<th>Esmolol</th>
<th>Nitroglycerin+Esmolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>T5</td>
<td>69.70±4.52</td>
<td>72.18±5.14*</td>
<td>70.20±4.52</td>
<td>72.92±3.69*#</td>
</tr>
<tr>
<td>T15</td>
<td>60.60±5.19</td>
<td>58.68±5.72#</td>
<td>61.84±5.19</td>
<td>58.92±4.09#</td>
</tr>
<tr>
<td>T30</td>
<td>59.22±5.96</td>
<td>58.16±6.90</td>
<td>60.58±4.78</td>
<td>56.42±3.89#</td>
</tr>
<tr>
<td>T45</td>
<td>56.80±5.58#</td>
<td>54.56±8.16#</td>
<td>60.60±5.19</td>
<td>54.22±3.80#</td>
</tr>
<tr>
<td>T60</td>
<td>58.08±5.72</td>
<td>56.26±6.53#</td>
<td>60.92±5.16</td>
<td>54.62±4.10*#</td>
</tr>
</tbody>
</table>

Values are given as Mean±Standard Deviation (*different from Remifentanil, # different from Esmolol, n=50, p<0.05)
Figure (3): Change in Mean Diastolic arterial pressure value and comparisons between groups during the Hypotension period. (Mean±Standard Deviation, *different from Remifentanil, # different from Esmolol, n=50, p<0.05)

Mean Blood Pressure (MBP) Values At Scheduled Intervals (T5, T15, T30, T45, T60) and Their Comparisons Between Study Groups During The Controlled Hypotension Period:

During periods of the Controlled Hypotension (T15-T60), MBP levels were found to be statistically significantly lower in the Nitroglycerin and Nitroglycerin+Esmolol groups when compared to the Remifentanil and Esmolol groups. At the same time, there was no statistical difference between Remifentanil and Esmolol groups, and no statistical difference was observed between Nitroglycerin and Nitroglycerin+Esmolol groups.

Table (10): Mean Blood Pressure (MBP) values at scheduled intervals (T5, T15, T30, T45, T60) and their comparisons between study groups during the Controlled Hypotension Period

<table>
<thead>
<tr>
<th>MBP</th>
<th>Remifentanil</th>
<th>Nitroglycerin</th>
<th>Esmolol</th>
<th>Nitroglycerin + Esmolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>T5</td>
<td>81.38±4.57</td>
<td>84.62±4.75*</td>
<td>83.92±4.49*</td>
<td>85.12±3.73*</td>
</tr>
<tr>
<td>T15</td>
<td>72.06±5.50</td>
<td>68.54±5.55*#</td>
<td>73.40±5.02</td>
<td>68.16±3.84*#</td>
</tr>
<tr>
<td>T30</td>
<td>69.08±6.10</td>
<td>66.36±6.86#</td>
<td>71.06±4.58</td>
<td>64.78±3.33*#</td>
</tr>
<tr>
<td>T45</td>
<td>67.68±5.69</td>
<td>63.54±8.29*#</td>
<td>70.18±4.87</td>
<td>62.86±2.99*#</td>
</tr>
<tr>
<td>T60</td>
<td>68.30±5.79</td>
<td>64.90±8.37*#</td>
<td>71.06±4.67</td>
<td>63.18±3.17*#</td>
</tr>
</tbody>
</table>

Values are given as Mean±Standard Deviation (*different from Remifentanil, # different from Esmolol, n=50, p<0.05).
Figure (4): Change in Mean Mean Blood pressure value and comparisons between groups during the Hypotension period. (Mean±Standard Deviation, *different from Remifentanil, # different from Esmolol, n=50, p<0.05)

Bleeding Score Values and Their Comparisons Between Study Groups During The Controlled Hypotension Period.

In line with the data obtained from the study, the beneficial effect of Controlled hypotensive anesthesia is reflected in the surgical field visibility score. The patients in the Esmolol group and those in the Remifentanil group had similar bleeding scores without significant differences. In addition, these values were found to be statistically significantly lower when compared with the patients in the Nitroglycerin and Nitroglycerin+Esmolol groups. These results showed that patients had better surgical field image quality after applying Esmolol and Remifentanil to provide Controlled Hypotension during surgery.

Table (11): The difference in bleeding score values and their comparisons between study groups during the Controlled Hypotension Period

<table>
<thead>
<tr>
<th></th>
<th>Remifentanil</th>
<th>Nitroglycerin</th>
<th>Esmolol</th>
<th>Nitroglycerin + Esmolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding Score</td>
<td>1.98±0.68*</td>
<td>2.98±0.62</td>
<td>1.92±0.44*</td>
<td>2.14±0.49#</td>
</tr>
</tbody>
</table>

Values are given as Mean±Standard Deviation (*different from nitroglycerin group, # different from Esmolol group, n=50, p<0.05).
Table (12): Bleeding Score values Comparison Between Groups during the Controlled Hypotension Period

<table>
<thead>
<tr>
<th>Bleeding Score Values and comparison</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esmolol- Nitroglycerin</td>
<td>0.0001</td>
</tr>
<tr>
<td>Esmolol- Remifentanil</td>
<td>0.6</td>
</tr>
<tr>
<td>Esmolol- (Esmolol+ Nitroglycerin)</td>
<td>0.008</td>
</tr>
<tr>
<td>Remifentanil- (Esmolol+ Nitroglycerin)</td>
<td>0.19</td>
</tr>
<tr>
<td>Remifentanil- Nitroglycerin</td>
<td>0.0001</td>
</tr>
<tr>
<td>Nitroglycerin- (Esmolol+ Nitroglycerin)</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

Figure (5): Difference in bleeding score values and comparisons between groups during Controlled Hypotension Period (Mean±Standard Deviation, *different from nitroglycerin group, # different from Esmolol group, n=50, p<0.05)

Discussion

Rhinoplasty is a surgical procedure performed to alter the nose's appearance, enhance breathing, or both. Rhinoplasty is considered a very complex operation in both aesthetic and reconstructive surgery. However, despite the difficulty of obtaining the desired result, a high degree of patient satisfaction can also be achieved [30, 31]. In rhinoplasty surgery, even minor bleeding will make it challenging to work in the surgical field. Therefore, it is necessary to lower blood pressure in a controlled manner to obtain a bloodless surgical field [32, 33]. Controlled lowering of blood pressure to certain levels to reduce bleeding during surgery while maintaining good perfusion to organs is an important technique. These
procedures are the main event for controlled hypotensive anesthesia [34, 35].

In addition, it is of great importance in preventing severe complications that may occur and shortening the surgical time. For these reasons, controlled hypotensive anesthesia is one of the main methods to provide a suitable surgical field [36, 37]. Many studies have stated the advantages of using hypotensive anesthesia during rhinoplasty surgery [38].

Many studies have compared two medications to provide controlled hypotension, while research comparing three agents is limited. [39]. In our study, the evaluation and comparison of the effects of drugs from three different drug groups and their combination on 200 patients were discussed. No study with four groups covering such a large number of patients has been found in the literature.

Thus, considering the results of similar studies, in our research, the advantage of using Remifentanil, Nitroglycerin, and Esmolol separately and Nitroglycerin+Esmolol combination to induce controlled hypotension during rhinoplasty surgery was examined.

In this study, the efficacy of the three most used drugs [remifentanil (opioid receptor agonist), esmolol (short-acting-adrenergic receptor blocker), Nitroglycerin (vasodilator)] and nitroglycerin+esmolol combination, which are used to achieve controlled hypotension during rhinoplasty surgery and to provide visibility of the surgical field was evaluated and compared in terms of the hemodynamic response, operative field visibility, and the amount of bleeding during surgery.

When the demographic data of the patients participating in this study were examined, Gender distribution within all groups showed no statistical difference, and approximately 24% of the within-group distribution was male and 76% female. When the mean age was considered, it was approximately 30±2 without any significant difference between the different groups. This finding showed no difference between the patients would affect the study results.

The use of Remifentanil (in patients in the remifentanil group) has been shown to cause a significant decrease in SBP, DBP, MBP, and HR levels. The results of our study show that Remifentanil provides appropriate surgical field visibility and controlled hypotension in patients undergoing rhinoplasty. These results are in agreement with the results of previously published studies [7, 16, 19, 21, 27, 40, 41].

In our study results, it was observed that the patients in the Nitroglycerin group had a significant decrease in SBP, DBP, and MBP levels; at the same time, reflex tachycardia was observed, which is a disadvantage of Nitroglycerin. We concluded that Nitroglycerin could be used safely to provide controlled hypotension in patients without cardiovascular problems during rhinoplasty surgery. These findings are consistent with the results of previous similar studies [2, 3, 42-44].

In the results of our research, there was a statistically significant decrease in the levels of SBP, DBP, MBP, and HR in the patients in the Esmolol group. It has been determined that Esmolol can be used effectively to provide controlled hypotension for rhinoplasty surgery, as well as it has been
shown to be effective in providing ideal surgical field visibility. Findings from previously published similar studies also support these results [45-51].

In line with surgical site visibility in our research (Nitroglycerin+Esmolol) has been shown to provide better surgical site visibility than Nitroglycerin but lower surgical site visibility than Remifentanil and Esmolol.

It has been shown that the bleeding score is lower in patients after administering Esmolol and Remifentanil. These results mean better visibility scores were observed in patients after administering Esmolol and Remifentanil.

In the light of the data obtained with the results of our study, Esmolol and Remifentanil seem to give better results than Nitroglycerin and Nitroglycerin+Esmolol in terms of the effect of hypotensive anesthesia method on surgical site bleeding and increasing surgical field visibility at a satisfactorily high level during rhinoplasty surgery. These results may be due to the absence of reflex tachycardia in the Esmolol and Remifentanil groups, as in the Nitroglycerin group, which has been reported in many previous studies [52].

Esmolol and Remifentanil provide hemodynamic stability and ideal surgical field visibility, and Nitroglycerin can be considered alternatives during rhinoplasty surgery. These findings are similar to the results of previous studies [3, 13,16, 20, 21, 39, 42, 46, 53-58].

Conclusions
This study concluded that the application of controlled hypotension resulted in a beneficial reduction in blood loss and operative time and increased visibility in the operation field in patients undergoing rhinoplasty surgery.

In light of all these findings, it can be said that after administering Esmolol and Remifentanil to provide controlled hypotension, more stable blood pressure and heart rate values on hemodynamic changes and better surgical field visibility quality were achieved. In cases where controlled hypotension will be applied, Esmolol and Remifentanil administration is superior to Nitroglycerin and Nitroglycerin+Esmolol administrations due to the better quality and ideal surgical field visibility obtained after Esmolol and Remifentanil administration.

Recommendations
Administration of Esmolol and Remifentanil could reduce the bleeding during rhinoplasty surgery and improve the visualization of the operative field. For this reason, we recommend that Esmolol and Remifentanil applications be preferred first.

We think that further studies with larger patient groups will contribute to finding the most appropriate intraoperative application method and treatment protocols for patients undergoing rhinoplasty surgery.

Source of funding: The current study was funded by our charges with no other funding sources elsewhere.

Ethical clearance: The approval was taken from the Scientific Research Division, with code 11265, on September 21, 2016.

Conflict of interest: Nil

References


Archives of Anesthesiology and Critical Care, 5(1), 15-17.


تقييم ومقارنة فعالية الريميفنتانيل والنيتروجليسرين والإسمولول والنيتروجليسرين + الإسمولول على ضغط الدم ومعدل ضربات القلب أثناء عملية جراحة تجميل الأنف

د.محمد أيدين عباس ١، د. أورهان أولوداغ ٢

الملخص

خلفية الدراسة: تظل عملية تجميل الأنف واحدة من أفضل خمس عمليات تجميل يتم إجرائها وتتكرر واحدة من أكثر عمليات صعبة في كل من الجراحة التجميلية وجراحة الأنف والأذن والحنجرة. يتم إجراء عملية تجميل الأنف لتغيير مظهر الأنف أو تخفيض التنفس أو كليهما. و يعتبر النزيف من أهم العوامل التي تؤثر على نجاح عملية تجميل الأنف. لذا، فإن طريقة خفض ضغط الدم الخاضع للرقابة يقلل النزيف وكذلك يقلل من فقدان الدم. لذا، فإنه يوفر مجالًا جراحيًا غير دموي مرضي أثناء العملية.

أهداف الدراسة: لتقديم ومقارنة فعالية الريميفنتانيل، النتروجليسرين، الإسمولول، النتروجليسرين + الإسمولول على ضغط الدم ومعالجة ضربات القلب أثناء جراحة تجميل الأنف وتقييم ومقارنة فعالية هذه الأدوية لتوفير مجال جراحي غير دموي مرضي أثناء جراحة تجميل الأنف لزيادة الرؤية أثناء العملية.

المرضى والطريقة: تم تقسيم ٢٠٠ مريض تراوح أعمارهم بين ٢٠ و ٤٥ عامًا من كلا الجنسين بشكل عشوائي إلى أربع مجموعات متساوية: (الريميفنتانيل + الإسمولول)، (النتروجليسرين و الإسمولول)، (النتروجليسرين + الإسمولول)، و (النتروجليسرين + الإسمولول). تم تسجيل ضغط الدم الانقباضي، و ضغط الدم الانبساطي، و معدل ضربات القلب، و ومتوسط ضغط الدم في جميع الحالات قبل إعطاء التخدير و بعد الفحص الرغامي، وكل ١٥ دقيقة حتى نهاية العملية. خلال العملية الجراحية، تم تصنيف درجة النزيف في المجال الجراحي و إمكانية رؤية المجال الجراحي، بصرف النظر عن النزيف من قبل الجراح على النحو التالي: (٠) لا يوجد نزيف، (١) نزيف خفيف - لا يتطلب شفط، (٢) نزيف خفيف - يتطلب شفط متقطع، (٣) نزيف معتدل - يتطلب شفط متكرر، (٤) نزيف حاد - يتطلب شفط مستمر، (٥) نزيف حاد - توقف العملية في حالة النزيف.

النتائج: في فترة أثناء العملية انخفض ضغط الدم الانقباضي، و ضغط الدم الانبساطي، و معدل ضربات القلب، و ومتوسط ضغط الدم. كان ذلك من خلال تدخل مجموعة ضغط الدم المتتحكم فيه، تجميل الأنف، الإسمولول، النتروجليسرين، الريميفنتانيل، الإسمولول، النتروجليسرين، الإسمولول، الريميفنتانيل، رؤية المجال الجراحي بالإضافة إلى خفض ضغط الدم في مجال الجراحي.

الكلمات المفتاحية: انخفاض ضغط الدم، تجميل الأنف، الإسمولول، الريميفنتانيل، النتروجليسرين، الإسمولول، الريميفنتانيل، رؤية المجال الجراحي

البريد الإلكتروني: Pharmacistmuhamedaydin@gmail.com

تاريخ استلام البحث: ١٩ شرين الأول ٢٠٢٢
تاريخ قبول البحث: ١٥ شرين الثاني ٢٠٢٣

١ مستشفى راهين التعييمي - اربيل - العراق
٢ كلية الصيدلة - جامعة غازي - انقرة - تركيا