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Original Article

Efficacy of Isoflurane-Remifentanil versus Propofol-Remifentanil on Controlled Hypotension and Surgeon Satisfaction in Rhinoplasty: A Single-Blind Clinical Trial Study

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Abstract

Background: Rhinoplasty is a complex but popular surgery in Iran. The main complications of the surgery are post-operative bleeding and nasal septal hematoma due to poor intra-operative controlled hypertension. This study aimed to compare the efficacy of isoflurane-remifentanil (I-R) versus propofol-remifentanil (P-R) to induce controlled hypotension and to assess surgeon satisfaction with each of these combinations during rhinoplasty.

Methods: In 2020-2021, a single-blind clinical study was conducted on 98 patients aged 18-50 years undergoing rhinoplasty at Mother and Child Hospital (Shiraz, Iran). Patients were randomly divided into P-R (n=48) and I-R (n=50) groups. Changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) were assessed during surgery and in the recovery room. A questionnaire was used to evaluate the level of surgeon satisfaction. Data were analyzed using independent samples *t* test, Chi-square test, and repeated measures ANOVA with SPSS software. $P<0.05$ was considered statistically significant.

Results: Five minutes after anesthesia induction, the P-R combination had a greater effect on reducing SBP ($P=0.010$), DBP ($P=0.007$), MAP ($P=0.003$), and HR ($P=0.026$) than I-R. However, from the 40th minute to the end of surgery and after 30 minutes of recovery, the I-R combination had a slightly better effect on blood pressure reduction than P-R. There was no difference in surgeon satisfaction with either of the two drug combinations.

Conclusion: Both P-R and I-R combinations are recommended to induce hypotension during rhinoplasty. However, I-R is more effective than P-R in inducing the desired controlled hypotension.

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Keywords ● Hypotension ● Propofol ● Isoflurane ● Rhinoplasty ● Remifentanil

What's Known

- Controlled hypotension during rhinoplasty can directly affect surgical quality, especially in terms of bleeding and improvement of the surgical field.
- Remifentanil combined with propofol or isoflurane induces controlled hypotension.

What's New

- For the first time, the effect of isoflurane-remifentanil versus propofol-remifentanil on controlled hypotension during rhinoplasty is evaluated.
- None of the drug combinations had a significant effect on surgeon satisfaction.

Introduction

Iran has the highest rate of rhinoplasties worldwide.[1] Rhinoplasty is often performed for aesthetic rather than functional reasons.[2] It is one of the most popular cosmetic surgeries despite being a complex surgical technique.[3] Successful rhinoplasty depends on several factors.[3] Bleeding during rhinoplasty compromises the surgical field and may lead to various complications, such as blood loss, increased transfusion-related adverse reactions, postoperative edema, and ecchymosis.[4, 5] Patient dissatisfaction due to complications after rhinoplasty is estimated at 5 to 20%.[6] Intra-operative controlled hypotension using anesthetics can reduce bleeding and complications. During rhinoplasty, it can directly affect surgical quality, especially by reducing bleeding and improving the surgical field of view.[7]

Several medications that can successfully induce hypotension during surgery include beta-blockers, alpha-2 adrenoceptor agonists, calcium channel blockers, magnesium sulfate, sodium nitroprusside, and various inhalational anesthetics.[8] Isoflurane is a volatile anesthetic used to induce and maintain general anesthesia, which can also facilitate controlled hypotension.[9] Propofol is an intravenous anesthetic, which can be used to manage intra-operative hypotension.[10] A previous study showed that both propofol and isoflurane equally affect controlled hypotension.[11] Remifentanil, a short-acting µ-opioid agonist, has recently been introduced as a drug to facilitate controlled hypotension.[12] When combined with propofol or isoflurane, it induces controlled hypotension.[13] Some studies have compared these combinations in terms of hemodynamic parameters in other surgeries (e.g., eye surgery) or inhaled anesthetic with propofol without remifentanil in rhinoplasty.

Identifying the optimal agent for controlled hypotension during rhinoplasty is one of the main challenges of anesthesiologists and ENT surgeons. The present study, therefore, aimed to compare propofol-remifentanil (P-R) with isoflurane-remifentanil (I-R) to induce controlled hypotension and reduce bleeding during rhinoplasty. In addition, the level of surgeon satisfaction with these combinations was evaluated.

Patients and Methods

In 2020-2021, a single-blind clinical study was conducted on 98 patients who underwent rhinoplasty at Maternal and Child Hospital (Shiraz, Iran). The study was approved by the Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran (code: IR.SUMS.MED.REC.1398.511). The study was registered in the Iranian Registry of Clinical Trials (code: IRCT20141009019470N95). Written informed consent was obtained from the participants.

The sample size was calculated using the formula,[14]

$$2(Z_{\alpha/2}+Z_{\beta})^2/\Delta^2$$

assuming an effect size (Δ) of 0.60 for average systolic blood pressure (SBP) measurements during surgery, power (1-β) of 0.80, type I error (α) of 0.05, and a dropout rate of 0.15. Accordingly, a sample size of 50 patients per group was calculated. Patients were randomly assigned to P-R and I-R groups using block randomization in a block size of four (list blocks were extracted from www.sealedenvelope.com). All patients were blinded to group assignment. The inclusion criteria were patients aged 18-50 years, physical status class I or II according to the American Society of Anesthesiologists, and body mass index between 16 and 35. The exclusion criteria were patients with hypertension, cardiovascular disease, anemia, liver or kidney disease, central nervous system disorder, severe asthma, chronic obstructive pulmonary disease, and allergic to propofol, isoflurane, or remifentanil.

The P-R and I-R groups received propofol-remifentanil and isoflurane-remifentanil, respectively. Midazolam (0.03-0.06 mg/Kg) and fentanyl (2-4 µg/Kg) were administered as a prodrug. Anesthesia was induced using thiopental (5 mg/Kg), atracurium (0.6 mg/Kg), and morphine (0.1 mg/Kg). During the induction of anesthesia, the P-R group received propofol (50-100 µg/Kg/min) and remifentanil (0.1-0.4 µg/Kg/min). The I-R group received a maintenance dose of isoflurane (1.25% minimum alveolar concentration) and remifentanil (0.1-0.4 µg/Kg/min) with mechanical ventilation and controlled breathing with capnography of 30-35 mmHg. To prepare the drug infusion dose, remifentanil 2 mg powder was diluted with 50 cc of normal saline to obtain 40 µg of each cc. Drug combinations for each group were labeled as I-R and P-R and delivered to the anesthesiologist. Except for the patients, all others, who were involved with the study, were not blinded to group assignment.

SBP, diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) were measured before and after the induction of anesthesia, as well as at five-minute intervals throughout the surgery. These parameters were also measured every 15 minutes, while the patients were in the recovery room. Finally, at the end of the surgery, the level of surgeon satisfaction with the drug combinations was evaluated using a questionnaire.

Statistical Analysis

Data were analyzed using IBM SPSS software, version 21.0 (Armonk, NY: IBM Corp), and graphs were plotted using GraphPad Prism 9 (GraphPad Software, California, USA). Continuous variables were analyzed using independent samples *t* test and expressed as mean±SD. The Chi square test was used to examine the difference between the categorical outcome variables and expressed them as numbers and percentages. Repeated measures ANOVA (analysis of variance) was used to measure changes over different time points. P<0.05 was considered statistically significant.

Results

A total of 100 patients who met the inclusion criteria were included in the study. The patients were followed up during the surgery and during their stay in the recovery room. Two patients were lost to follow-up, and eventually, 98 were included in the analysis phase, namely the I-R group (n=50) and P-R group (n=48) (figure 1). The mean age of the patients was 29.28±7.642 years (range: 18-46 years), and the mean weight was 65.27±9.081 Kg. There was no significant difference in age, sex, and mean weight of the patients between the groups (table 1).

The results of ANOVA showed that the time effect and interaction effect between time and group were significant, however, the group effect was not significant for SBP, DBP, MAP, and HR. We used time as an independent variable to perform the independent samples *t* test, because the interaction effect was significant (figure 2). Furthermore, compared to the I-R group, SBP, DBP, and MAP levels were lower in the P-R group at a five-minute time point during the surgery, whereas they were higher at 50-, 60-, and 70-min time points. There was no significant difference between HR in the P-R and I-R groups throughout the surgery, except at the five-minute time point (figure 2).

While in the recovery room, the SBP of the patients in the P-R group was significantly lower than the I-R group at 15- and 30-min time points.

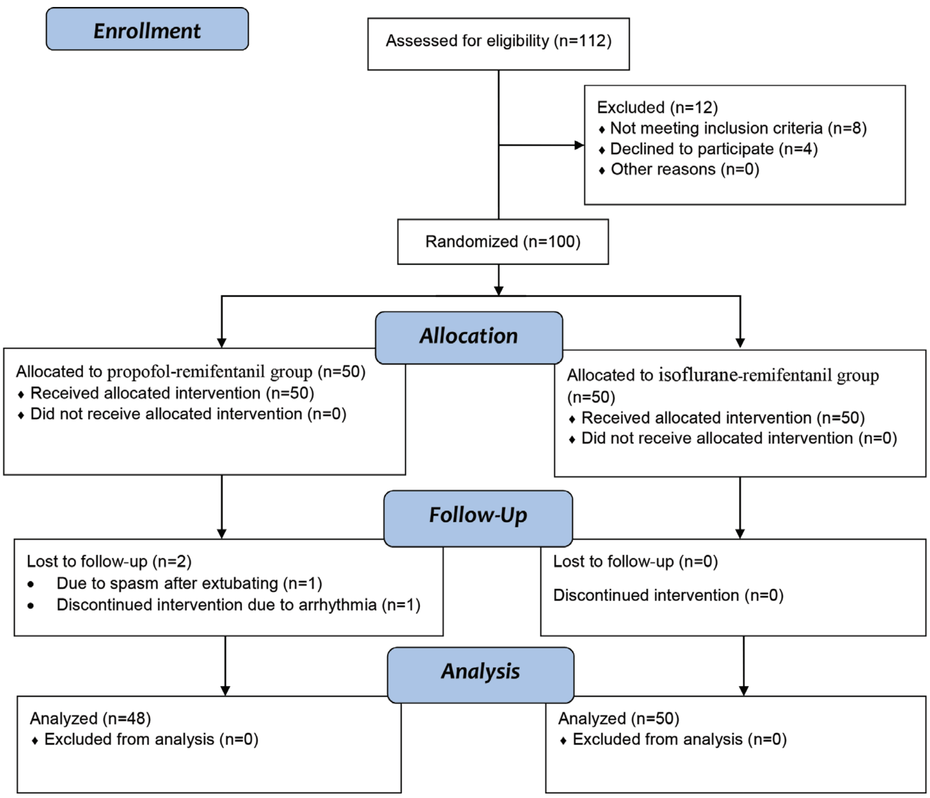

Figure 1: CONSORT flow diagram shows the participants recruitment process.

Table 1: Demographic characteristics of the patients in propofol-remifentanil and isoflurane-remifentanil groups

Variable		I-R group (n=50)	P-R group (n=48)	P value
Age (years)		27.92±7.43	30.64±7.68	0.075
Sex (n, %)	Female	41 (82)	40 (84)	0.790
	Male	8 (16)	8 (16)	
Weight (Kg)		65.88±10.44	64.71±7.72	0.555

Data expressed as mean±SD unless stated otherwise. I: Isoflurane; R: Remifentanil; P: Propofol; Independent samples *t* test is used for continuous variables and the Chi square test to examine the difference between categorical outcome variables. Statistical significance at P<0.05.

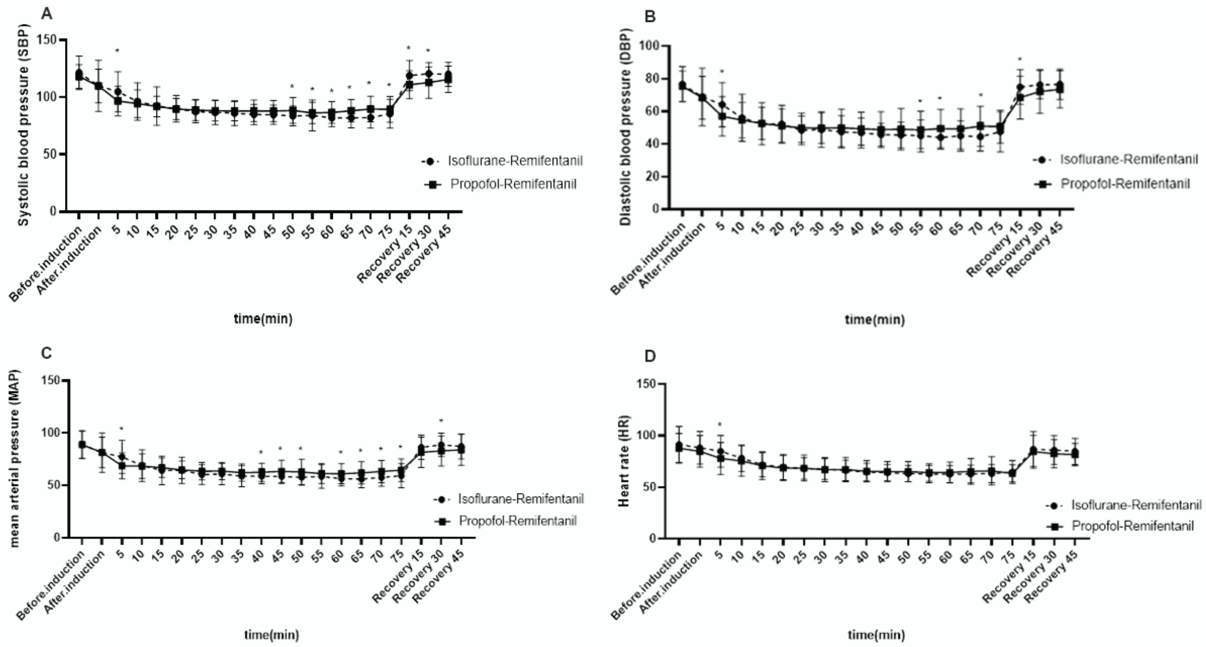

Figure 2: The results of analysis of variance (ANOVA) between the isoflurane-remifentanil and propofol-remifentanil groups for systolic blood pressure (A), diastolic blood pressure (B), mean arterial pressure (C), and heart rate (D) throughout the complete operation. *Statistical significance

Table 2: The results of the Chi square test for the level of surgeon satisfaction with the isoflurane-remifentanil and propofol-remifentanil drug combinations

Satisfaction level	I-R group (n=45)	P-R group (n=44)	P value
No satisfaction	2 (4.4%)	1 (2.3%)	0.111
Poor	0 (0)	1 (2.3%)	
Partial	3 (6.7%)	9 (20.5%)	
Complete	40 (88.9%)	33 (75%)	

I: Isoflurane; R: Remifentanil; P: Propofol; Statistical significance at P<0.05.

Moreover, DBP in the P-R group was lower than in the I-R group at 15- and 45-min time points. However, MAP was significantly lower in the I-R group than in the P-R group at the 30-min time point. While the patients were in the recovery room, there was no significant difference in HR between the groups.

At the end of the surgeries, the level of surgeon satisfaction with either of the drug combinations for 89 out of the 98 patients was evaluated using a questionnaire. The response to the questionnaire ranged from no satisfaction to poor, partial, and complete satisfaction levels. The results showed no significant difference in the level of surgeon satisfaction with either of the two drug combinations. However, the surgeon was completely satisfied with the result of rhinoplasty in 40 (89%) and 33 (75%) patients in the I-R and P-R groups, respectively (table 2).

Discussion

The results showed that the P-R combination decreased SBP, DBP, MAP, and HR more than the I-R combination at a five-minute time point after the induction of anesthesia. However, these hemodynamic parameters were significantly lower in the I-R group from the 40-minute time point to the end of surgery. While the patients were in the recovery room, we observed that these parameters were lower in the P-R group than the I-R group. In a previous study, Jouybar and colleagues showed that SBP, DBP, MAP, and HR were lower with the dexmedetomidine-propofol combination than remifentanil-propofol in rhinoplasty.[14] Montazeri and colleagues reported that SBP, DBP, and MAP were not different between the I-R and P-R groups in eye surgery. However, HR was significantly lower in the P-R than the I-R group.[15] Hyun and colleagues reported that P-R reduced SPB, DPB, MAP, and HR more than I-R during the first 10 min after the induction of anesthesia.[16]

In line with our study, Han and colleagues found that MAP decreased 30 minutes after anesthesia using isoflurane.[9] The study by Ankichetty and colleagues reported no significant difference between intravenous anesthesia using propofol and inhalational anesthesia with isoflurane for controlled hypotension in endoscopic sinus surgery.[11] Aboseif and colleagues concluded that the effect of remifentanil was similar to nitroprusside for controlled hypotension during rhinoplasty.[17] In contrast with our results, Wilhelm and colleagues found no significant difference in hemodynamic parameters between the use of I-R and P-R during the recovery phase.[18]

Our results showed that the level of surgeon satisfaction was similar with both I-R and P-R. However, in endoscopic sinus surgery, a previous study reported more satisfaction and effectiveness of P-R than inhalational anesthetics in reducing bleeding.[5] In a similar type of surgery, Tirelli and colleagues showed a significantly greater reduction in bleeding with total intravenous anesthesia compared to isoflurane with fentanyl. However, the hypotensive effect of these drugs was the same.[15] Jouybar and colleagues found that dexmedetomidine-propofol was associated with lower intra-operative bleeding and a greater level of surgeon satisfaction than the P-R combination.[14]

The main limitations of our study were the low sample size and not using a target-controlled infusion system. The latter would have allowed a user-defined target drug concentration in a specific body compartment or tissue of interest. Further studies are recommended with a larger sample size and the use of target-controlled infusion to substantiate our findings.

Conclusion

P-R and I-R combinations can both be used to control hypotension during rhinoplasty. Although I-R was more effective than P-R in controlling blood pressure, the level of surgeon satisfaction was not significantly different for either of the drug combinations.

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Authors' Contribution

All authors contributed to the study concept, project administration, formal analysis, research, data curation, methodology, writing of the original draft, and manuscript revision. They have read and approved the final manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest: None declared.

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