

A randomized parallel design trial of the efficacy and safety of tranexamic acid, dexmedetomidine and nitroglycerin in controlling intraoperative bleeding and improving surgical field quality during septorhinoplasty under general anesthesia

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Abstract

In this blinded clinical trial, we attempted to compare the efficacy and safety of administering tranexamic acid, dexmedetomidine and nitroglycerin in preventing intraoperative bleeding and improving the quality of the surgical field during septorhinoplasty under general anesthesia. A total of 105 patients scheduled for septorhinoplasty were enrolled and randomly assigned into three groups based on the balanced-block randomization method. First group received 1 µg/kg intravenous injection dexmedetomidine, second group received 10 mg/kg intravenous injection tranexamic acid and third group received 0.5 µg/kg nitroglycerin, intravenously. The study sample was composed of 105 participants with the total mean age of 25.85 ± 6.52 years, and 59.05% of participants were female and the mean of body mass index was 24.34 ± 2.57 kg/m². The results showed that there was no statistically significant difference in terms of arterial oxygen saturation, mean arterial pressure, heart rate, bleeding rate, duration of surgery, and surgeon satisfaction among the three groups; however, there was a significant difference in the extubation time, recovery time and the dose of administered propofol among the three groups. Dexmedetomidine reduced the dose of administered propofol while increasing the extubation time and recovery time. In the tranexamic acid group compared with the other two groups, the recovery time was shorter. However, all the three drugs could reduce intraoperative bleeding and lead to surgeon satisfaction. It can be concluded that all these three drugs can be utilized to control bleeding and improve the quality of the surgical field but the ultimate decision lies with the anesthesiologist's judgment and the conditions of the patient. The study protocol was registered in the Iranian Registry of Clinical Trials (registration No. IRCT20141209020258N121) on September 24, 2019 and it was ethically approved by the Ethical Committee of Arak University of Medical Sciences (approval No. IR.ARAKMU.REC.1397.355) on February 24, 2019.

Key words: arterial oxygen saturation; bleeding; dexmedetomidine; general anesthesia; heart rate; mean arterial pressure; nitroglycerin; septorhinoplasty; tranexamic acid

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INTRODUCTION

Septorhinoplasty is one of the common neck and head surgeries especially among the youth. Surgeries on the nasal bone would often result in postoperative pain and the requirement for analgesic drugs. On the other hand, nasal obstruction along with the administration of common analgesics such as the opioids – especially in the early postoperative hours during which the anesthetic effects remain in the body – would weaken the immunity of the respiratory system, obstruct the airway and increase postoperative hypoxia in these patients.¹ Due to the high rate of septorhinoplasty, intraoperative bleeding and the limited surgical field, all of which have an impact on the result of the surgery,² it would be worthwhile to find methods to control intraoperative bleeding in septorhinoplasty. The most common and effective methods to reduce intraoperative blood loss are positioning of the patient's head (head-up), medications such as preoperative injection of epinephrine into the surgical

field, and relative reduction of mean blood pressure.³

Tranexamic acid reduces blood loss by the inhibition of fibrinolysis. It binds on lysine receptor sites in plasmin and plasminogen and thus, separates plasminogen from fibrin surface, leading ultimately to the inhibition of fibrinolysis. Topical application of tranexamic acid can reduce blood loss in surgical patients such as in gynecological (esp. postpartum) procedures, urological surgery, dental procedures for hemophiliacs and neuro-spinal surgeries.^{4,5} Tranexamic acid inhibits plasminogen as well as urokinase activators, which can be administered intravenously or orally.⁶ Urokinase is a physiologic thrombolytic agent that is produced in renal parenchymal cells and found in the urine. Urokinase binds directly to plasminogen and produces plasmin.⁷ Tranexamic acid is a synthetic analog of the amino acid lysine, which serves as an antifibrinolytic binding on plasminogen. This reduces the interaction of plasminogen and fibrin, preventing



fibrin clots.⁸⁻¹¹ Tranexamic acid is used to reduce intraoperative blood loss in cardiac surgery, liver transplantation, orthopedic surgery, arthroplasty and knee joint replacement, as well as reduce postoperative bleeding in prostatectomy and tooth extraction.¹²⁻¹⁴ Moreover, this drug is effective in treating idiopathic menorrhagia.¹²⁻¹⁴

Dexmedetomidine acts as an agonist of α_2 -adrenergic sedative which reduces blood pressure. Its infusion reduces heart rate (HR), systemic vascular resistance and blood pressure.¹⁵ Guven et al.¹⁶ observed that the HR and mean blood pressure were lower in patients who had received dexmedetomidine, suggesting it to be used to reduce intraoperative bleeding. Dexmedetomidine is a highly selective α_2 -agonist with sedative, amnestic and analgesic properties.¹⁴ This imidazole has also decongestant effects and may result in hypotension in various surgeries such as tympanoplasty.^{15,16} Dexmedetomidine is used in septoplasty operations and claimed to reduce bleeding score.¹⁷⁻¹⁹ It can reduce the need for the intraoperative and postoperative opioid requirement and has sympatholytic effects which can reduce the stress response to surgery and ensure hemodynamic stability.²⁰

Nitroglycerin is metabolized in the liver and converted to nitric oxide,¹⁷ which is a very potent vasodilator. Nitric oxide causes the dilation and relaxation of smooth muscle cells that line the vessels, by stimulating cyclic guanosine monophosphate and its accumulation inside the cells.¹⁸ Though nitrates have a great influence on the vessels, they cause vasodilation of smooth muscles in the arteries as well.¹⁸

In rhinoplasty surgeries, the surgical field must be without any or at least minimal bleeding so that the operation can be done with the highest visibility. Since there has been no study comparing the effects of tranexamic acid, dexmedetomidine and nitroglycerin in preventing intraoperative bleeding and the surgical field quality during septorhinoplasty, the current study conducted to compare the efficacy and safety of administering tranexamic acid, dexmedetomidine and nitroglycerin in preventing intraoperative bleeding and improving the surgical field quality during septorhinoplasty under general anesthesia.

SUBJECTS AND METHODS

Study design

This randomized clinical trial with parallel design was conducted on 105 patients 18–60 years scheduled for septorhinoplasty in Amir Kabir Hospital, Arak, Iran. The patient's recruitment effort lasted one year, from March 2019 to March 2020. The study protocol was registered in the Iranian Registry of Clinical Trials (registration No. IRCT20141209020258N121) on September 24, 2019 and it was ethically approved by Ethical Committee of Arak University of Medical Sciences (approval No. IR.ARAKMU.REC.1397.355) on February 24, 2019 (**Additional file 1**). The writing and editing of the article were performed in accordance with the CONSolidated Standards Of Reporting Trials (CONSORT) Statement (**Additional file 2**).

Subjects

After meeting the inclusion criteria and signing a written informed consent, the patients were included in the study. The inclusion criteria were: candidate for septorhinoplasty,

being within the age range of 18–60 years, American Society of Anesthesiologists class I or II,²¹ absence of coagulation disorders, having no history of cardiovascular conditions, appropriate control of blood pressure, not pregnant, absence of opioid addiction, having a body mass index of less than 35 kg/m², and absence of pulmonary chronic diseases (asthma). The exclusion criteria were; unwillingness to undergo surgery, allergy to the study medications, the need for administration of drugs inducing hypotension in addition to the administered ones in each group.

Surgical preparation and intervention

The patients were hospitalized 1 day before the surgery and were kept fasting for 8 hours. After recording the patients' demographic information, upon entering the operation room, two different sites were spotted on their veins, one of which was for injecting the study drugs and the other for intravenous injection of fluids and other drugs. At the beginning of induction, 5 mL/kg crystalloid liquid (normal saline) was injected and 100% oxygen was administered through masks to the patients in the first 3 minutes. As an anesthetic premedication, 30 μ g/kg midazolam (Caspian Tamin Pharmaceutical Company, Rasht, Iran) and 3 μ g/kg fentanyl (Caspian Tamin Pharmaceutical Company) were administered to the patients. Induction of anesthesia was performed with 2.5 mL/kg propofol (Fresenius Kabi Pharmaceutical Company, Homburg, Germany) and 0.5 mg/kg atracurium (Caspian Tamin Pharmaceutical Company). Endotracheal intubation was done with suitable spiral tubes. After that the patients underwent mechanical ventilation in order for the exhaled carbon dioxide concentration to remain within 35–40 mmHg and the percentage of arterial oxygen saturation at 98%. For maintenance of anesthesia, patients received 50% oxygen in addition to 50% nitrous oxide, 1% isoflurane (Piramal Critical Care, Bethlehem, PA, USA) and 10 mg atracurium (Caspian Tamin Pharmaceutical Company) every 20–30 minutes. Following this, the patients were randomly divided into three groups based on the balanced block randomization method. First group (dexmedetomidine group) received 1 μ g/kg dexmedetomidine (EXIR Company, Borujerd, Iran) ($n = 21$), second group (tranexamic acid group) received 10 mg/kg tranexamic acid (Caspian Tamin Pharmaceutical Company) ($n = 17$) and third group (nitroglycerin group) received 0.5 μ g/kg nitroglycerin (Caspian Tamin Pharmaceutical Company). All the study drugs were administered intravenously over 15 minutes for the three groups ($n = 27$). Besides, to achieve controlled hypotension and maintain mean arterial pressure (MAP) between 65–70 mmHg, 50–150 μ g/kg per minute, intravenous injection propofol was administered on a separate site and the administered dose for each patient was recorded. All surgeries were done by the same surgeon.

Measurements

The HR, MAP, and the percentage of oxygen saturation (SaO₂) after the induction of anaesthesia and during hypotension were measured and recorded every 15 minutes. Using a 6-point Likert scale,²² the quality of the surgical field in terms of bleeding was assessed by the surgeon, who was blinded to the group



assignments and the type of administered drugs. The points on the scale were as follows: 0 = no bleeding; 1 = very slight bleeding, which can be regarded as dry; 2 = slight bleeding which does not limit the visibility of the incision; 3 = moderate bleeding which limits the visibility of the incision; 4 = severe bleeding which can be controlled but threatens the visibility of the incision; 5 = very severe bleeding which cannot be controlled. In this study, points number 2 and below showed the appropriate surgical field quality in terms of bleeding in septoplasty. Furthermore, surgeon satisfaction was rated using a 3-point Likert scale including 0 = bad, 1 = moderate, and 3 = good. The inhalation of anesthetic agents and propofol infusion were stopped 5 minutes, before the end of the operation. The timing of extubation was determined and recorded based on appropriate tidal volume, the return of airway reflexes and the recovery time according to modified Aldrete score (having a score of 9 or more).²³ In case the patients achieved this score, they were discharged and then admitted to the hospital wards. Intraoperative side effects such as hypotension (MAP below 60 mmHg) were controlled first by reducing doses of anesthetics increasing the volume of crystalloid serum. In the absence of the desired response, 5 mg of ephedrine (BB Pharma, Lhotka Czech Republic) (intravenous injection) was administered and recorded. Furthermore, to control constant bradycardia (less than 50 beats/min), 0.5 atropine (intravenous injection) was administered and recorded. Postoperative complications such as nausea and vomiting, shivering, bronchospasm, headache, blurred vision and sore throat were recorded as well. If other hypotensive medications were used for a patient during the operation, it was recorded in the patient evaluation form and that patient was subsequently excluded from the study.

Randomization and blinding

Patients were allocated into three groups using a balanced block randomization method with block size 6. Random sequence was generated by an epidemiologist and kept with him. In terms of blinding, the surgeon, patients, outcome assessor and data analyzer were blinded.

Sample size

Taking into account the type 1 error of 5%, the power of 80%, the minimum clinically acceptable change in the mean bleeding volume equal to 15 mL and the standard deviation of^{22,24} the sample size of 33 people in each group was estimated, that considering the probability of attrition, 35 patients were

included in each group and a total of 105 patients in the study.

Statistical analysis

Categorized and continuous data were described by number (percentage) and mean \pm standard deviation (SD), respectively. Likelihood ratio Chi-square test and one-way analysis of variance followed by Tukey's *post hoc* test used to analyze the data. Repeated measures analysis of variance test were used to compare the variables between three groups which were measured over time and also Tukey's *post hoc* test was used to further pairwise comparisons. To analyze the data, Stata statistical software version 13 (Stata Corp, College Station, TX, USA) was used at significant level less than 0.05.

RESULTS

As presented in **Figure 1**, 164 participants were screened to include in the trial. Among those, 59 patients (33 cases not met the inclusion criteria, 21 cases declined to participate in the study and 5 cases with other reasons) were not eligible and excluded and 105 cases were selected and randomly divided into three intervention groups.

The study sample was composed of 105 participants with the total mean age of 25.85 ± 6.52 years, with the minimum and maximum age being 19 and 45 years, respectively. In terms of gender distribution, 59% of participants were female and the mean of body mass index was 24.34 ± 2.57 kg/m². The MAP, HR and SaO₂ at baseline were reported in **Table 1** by groups.

Base on the results in **Table 2**, as the repeated measures analysis of variance test revealed, there was no significant difference in the overall MAP ($P = 0.490$), SaO₂ ($P = 0.171$) and HR ($P = 0.141$) across the three groups, while the time trend of aforementioned parameters were statistically significant ($P < 0.001$).

Using a 6-point Likert scale, the quality of the surgical field in terms of bleeding was assessed by the surgeon. No patient had a score of 0, 4 and 5 and as can be seen in **Table 3**, no significant difference was observed in bleeding rate among the three groups ($P = 0.463$).

As it was presented in **Table 4**, there was a significant difference in extubation time ($P = 0.001$), recovery time ($P = 0.001$), and the dose of administered propofol ($P = 0.001$) across the three groups. In the dexmedetomidine group, the extubation time and recovery time were longer than that in the other groups and the lowest means belonged to the tranexamic acid group. In the dexmedetomidine group, the

Table 1: Baseline demographic and clinical characteristics of septorhinoplasty patients with tranexamic acid, dexmedetomidine and nitroglycerin intervention

Item	Tranexamic acid (n=35)	Dexmedetomidine (n=35)	Nitroglycerin (n=35)	Total (n=105)
Age (yr)	25.94 \pm 6.90	25.77 \pm 7.10	25.85 \pm 5.70	25.85 \pm 6.50
Body mass index (kg/m ²)	24.40 \pm 2.90	24.48 \pm 2.40	24.14 \pm 2.50	24.34 \pm 2.60
Female	21 (60)	21 (60)	20 (57)	62 (59)
Heart rate (beat/min)	84.02 \pm 7.20	87.88 \pm 8.40	85.57 \pm 6.70	85.82 \pm 7.50
Mean arterial pressure (mmHg)	93.02 \pm 7.10	95.31 \pm 6.30	94.80 \pm 5.90	94.38 \pm 6.50
Percentage of oxygen saturation	97.02 \pm 0.74	97.25 \pm 0.65	96.94 \pm 0.63	97.07 \pm 0.68

Note: Data are expressed as the mean \pm SD, except sex, which are expressed as number (percentage), and were analyzed by one-way analysis of variance followed by Tukey's *post hoc* test.

Table 2: Comparison the heart rate, mean arterial pressure, and percentage of oxygen saturation among septorhinoplasty patients with tranexamic acid, dexmedetomidine and nitroglycerin intervention

Item	Tranexamic acid (n=35)	Dexmedetomidine (n=35)	Nitroglycerin (n=35)	P-value
Heart rate (beat/min)				$P_{Groups}=0.141$ $P_{Time}=0.001$ $P_{Interaction}=0.001$
Baseline	84.02±7.20	87.88±8.40	85.57±6.70	
5 min	84.63±6.95	83.69±7.95	87.11±6.48	
20 min	84.63±6.95	83.69±7.95	87.74±6.24	
35 min	85.49±6.72	85.43±7.23	88.43±5.92	
50 min	86.97±6.27	85.97±6.98	88.94±5.75	
65 min	87.54±5.78	86.26±6.76	89.49±5.33	
80 min	87.77±5.70	86.49±6.67	89.94±5.03	
95 min	87.97±5.57	87.03±6.34	90.20±4.92	
110 min	89.54±5.16	89.03±5.44	91.37±4.43	
125 min	93.40±4.73	90.69±4.90	94.51±3.99	
Mean arterial pressure (mmHg)				$P_{Groups}=0.490$ $P_{Time}=0.001$ $P_{Interaction}=0.001$
Baseline	93.02±7.10	95.31±6.30	94.80±5.90	
5 min	91.77±6.81	94.46±6.05	93.57±5.66	
20 min	91.46±6.27	93.37±5.19	92.94±5.21	
35 min	90.00±6.14	89.40±5.26	92.74±5.08	
50 min	83.14±6.12	83.11±4.86	85.89±5.00	
65 min	76.29±5.44	76.14±4.64	78.09±5.24	
80 min	69.69±3.35	69.46±3.06	70.89±3.82	
95 min	81.20±3.98	81.23±3.46	81.66±3.83	
110 min	90.91±4.13	91.77±4.02	90.09±3.13	
125 min	93.31±3.89	92.03±4.11	92.37±3.82	
Percentage of oxygen saturation				$P_{Groups}=0.171$ $P_{Time}=0.001$ $P_{Interaction}=0.639$
Baseline	97.02±0.74	97.25±0.65	96.94±0.63	
5 min	97.09±0.78	97.26±0.61	97.06±0.64	
20 min	97.03±0.79	97.26±0.70	97.03±0.75	
35 min	97.20±0.58	97.29±0.67	97.00±0.69	
50 min	97.03±0.71	97.29±0.62	97.03±0.62	
65 min	97.17±0.66	97.34±0.64	97.23±0.60	
80 min	97.14±0.69	97.43±0.61	97.26±0.66	
95 min	97.17±0.66	97.46±0.56	97.34±0.64	
110 min	97.11±0.68	97.40±0.65	97.29±0.67	
125 min	97.14±0.65	97.40±0.65	97.26±0.61	

Note: Data are expressed as the mean ± SD, and were analyzed by repeated measures analysis of variance followed by Tukey's *post hoc* test.

Table 3: Comparison of 6-point Likert scale among septorhinoplasty patients with tranexamic acid, dexmedetomidine and nitroglycerin intervention

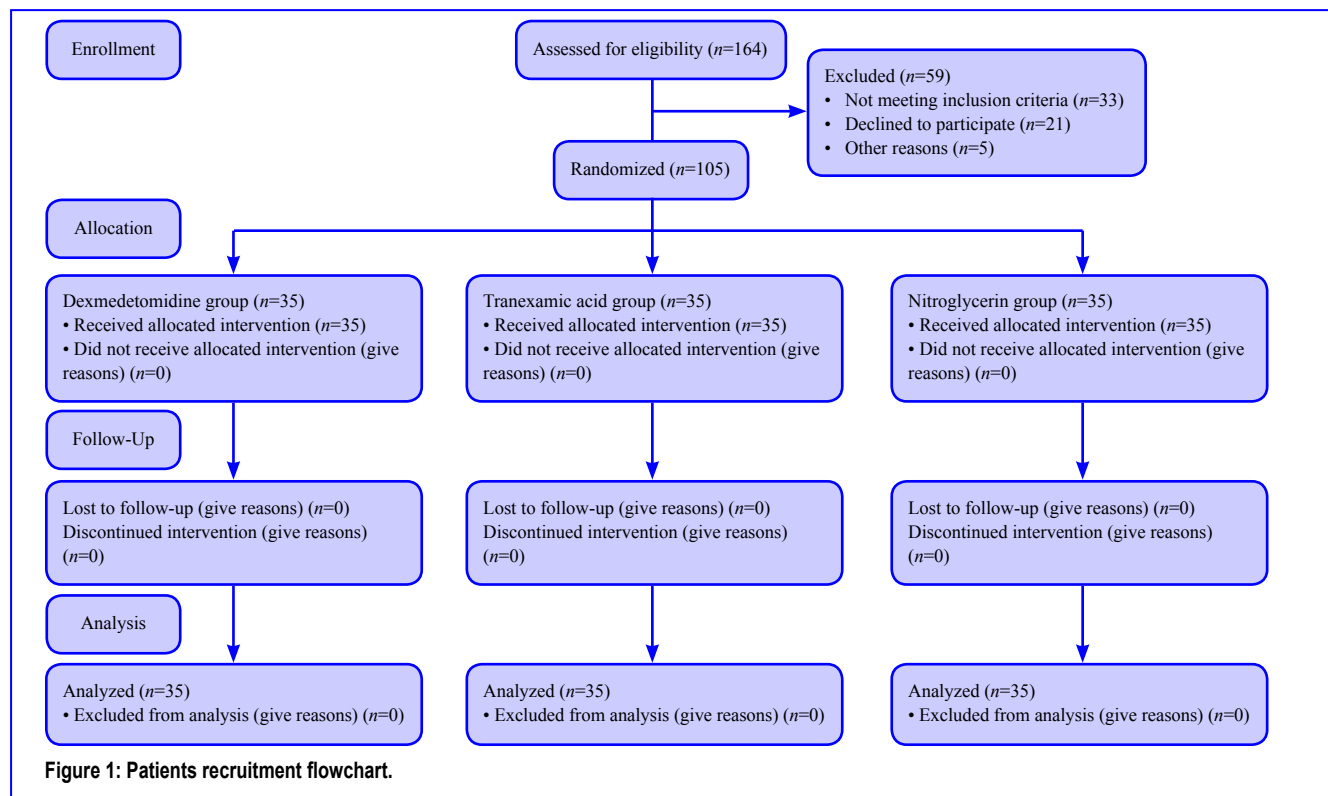
6-point Likert scale	Tranexamic acid (n=35)	Dexmedetomidine (n=35)	Nitroglycerin (n=35)
0	0	0	0
1	16 (46)	17 (49)	16 (46)
2	17 (49)	17 (49)	14 (40)
3	2 (6)	1 (3)	5 (14)
4	0	0	0
5	0	0	0

Note: Data are expressed as number (percentage).

Table 4: Comparison of bleeding rate among septorhinoplasty patients with tranexamic acid, dexmedetomidine and nitroglycerin intervention

Item	Tranexamic acid (n=35)	Dexmedetomidine (n=35)	Nitroglycerin (n=35)	P-value
Extubation time (min)	12.7±1.5	17.5±2.9	13.1±2.2	0.001
Recovery time (min)	21.8±2.2	26.8±2.9	22.2±2.1	0.001
The dose of administered propofol (mg)	552.4±10.2	550.7±7.2	687.7±26.3	0.001
Duration of surgery (min)	101.7±6.6	99.4±6.4	100.7±6.6	0.343
Surgeon satisfaction (3-point Likert scale)	1.45±0.50	1.48±0.50	1.45±0.50	0.963

Note: Data are expressed as the mean ± SD, and were analyzed by one-way analysis of variance followed by Tukey's *post hoc* test.



mean dose of administered propofol was shorter than that in the other groups and the highest mean of administered dose of propofol belonged to the nitroglycerin group. No significant difference was observed in duration of surgery ($P = 0.343$) and surgeon satisfaction ($P = 0.963$) among the three groups. No possible complication (i.e., nausea and vomiting, headache and dizziness, blurred vision, sore throat, bronchospasm, and hemodynamic changes) was observed in the three groups.

DISCUSSION

This blinded clinical trial was conducted on 105 patients scheduled for septorhinoplasty in Amir Kabir Hospital in Arak, Iran. The patients were randomly assigned to three groups (namely, receiving dexmedetomidine, tranexamic acid and nitroglycerin). The results showed that there was no statistically significant difference in terms of SaO₂, MAP, HR, bleeding rate, duration of surgery, and surgeon satisfaction in the three groups. Also, no possible complication (i.e., nausea and vomiting, headache and dizziness, blurred vision, sore throat, bronchospasm, and hemodynamic changes) was observed in the three groups, but according to the results, there

was a significant difference in the extubation time, recovery time and the dose of administered propofol among the three groups. Based on the repeated measures analysis of variance test, there was no significant difference in the overall HR at different times among the three groups. In the dexmedetomidine group, the extubation time was longer than that in the other groups. In the dexmedetomidine group, the mean recovery time was longer than that in the other two groups, while the minimum recovery time was observed in the tranexamic acid group. In the dexmedetomidine group, the mean of the administered dose of propofol was less than that in the other groups. No significant difference was observed in bleeding among the three groups.

On the whole, dexmedetomidine was found to reduce the administered dose of propofol and increase the extubation time and recovery time. However, the mean recovery time was the lowest in the tranexamic acid group while all the three drugs reduced intraoperative bleeding and resulted in surgeon satisfaction. In a comparative study in 2008, Eghbal et al.²⁵ evaluated the effect of labetalol and dexmedetomidine on intraoperative blood loss and surgical conditions in endoscopic

sinus surgery. They observed that labetalol could reduce the bleeding during functional endoscopic sinus surgery more efficiently than dexmedetomidine, but complications including vomiting/nausea and chills were experienced more frequently in the labetalol group than the other groups. The results of our study revealed that dexmedetomidine reduced the administered dose of propofol and increased the extubation time. However, the mean recovery time was the lowest in the tranexamic acid group while all the three drugs reduced intraoperative bleeding and resulted in surgeon satisfaction.

Modir et al.²⁶ researched in 2018 to compare remifentanyl, magnesium sulfate, and dexmedetomidine for intraoperative hypotension and bleeding and postoperative recovery in endoscopic sinus surgery and tympanomastoidectomy. They concluded that dexmedetomidine seems to be a more effective choice than the other two drugs in preventing intraoperative bleeding, reducing HR and blood pressure, but it can lead to longer postoperative recovery time.²⁶ Though – in our study – dexmedetomidine caused reduced HR, blood pressure and increased recovery time, it functioned similarly with tranexamic acid and nitroglycerin in terms of blood loss management. In their study in 2017, Moshiri et al.²⁷ compared the effects of propofol and dexmedetomidine on controlled hypotension and bleeding during endoscopic sinus surgery. Their findings revealed that propofol could reduce HR more significantly than dexmedetomidine. However, no significant difference was observed in the groups with regard to the main outcomes of their study, i.e. bleeding reduction and improvement of surgical field quality. Their findings were in tandem with the results of our study. In their study conducted in 2017, Ghavimi et al.²⁸ maintained that tranexamic acid was very effective in reducing intraoperative bleeding rate, eyelid edema, and periorbital ecchymosis in the rhinoplasty. Their results lend support to the results of our study as well. In a study in 2012, Sankar et al.²⁹ found that tranexamic acid was effective in controlling blood loss and improving the quality of the surgical field.

In our study, no difference was obtained in the amount of bleeding and surgeon satisfaction among the three groups. Ghodrati et al.³⁰ stated that labetalol functioned more effectively than nitroglycerin in reducing intraoperative blood loss in rhinoplasty patients. In our study too, nitroglycerin resulted in better blood loss management but it also increased the administered dose of propofol as well as the extubation and recovery time. In a study conducted in 2016, Berenjian et al.²⁴ stated that on the whole, tranexamic acid and dexmedetomidine were both equally effective. Tranexamic acid reduces bleeding in major surgeries, but dexmedetomidine might be a suitable choice in rhinoplasty – in which bleeding volume is not considerable.²⁴ It is worth mentioning that in our study, dexmedetomidine and tranexamic acid had a similar degree of efficacy. Praveen et al.¹⁷ found that dexmedetomidine was more effective than nitroglycerin for hypotensive anesthesia in functional endoscopic sinus surgery.

In this study, the degree of surgeon satisfaction and bleeding was found to be similar too, which might be attributed to our larger sample size in comparison with that of the study by Praveen et al.¹⁷ in 2012, Jalali, et al.³¹ found the administered dose of tranexamic acid has a similar degree of efficacy in reducing postoperative edema and ecchymosis after rhinoplasty

and concluded that the selection of either of them depends on the other effects of the drug administration. In the current study, we found that tranexamic acid was similar to the other two drugs in blood loss management and surgeon satisfaction. In a study carried out in 2008, Ayoglu et al.³² concluded that dexmedetomidine reduced intraoperative bleeding and fentanyl consumption in septoplasty under general anesthesia. The results of the study are in agreement with those of Ayoglu et al.³²

There were some limitations to this study. The current study carried out on an Iranian sample and conducting a similar study in different population as a multicenter trials with larger sample size are recommended to better conclusion.

The results showed that there was no statistically significant difference in terms of SaO₂, MAP, HR, bleeding rate, duration of surgery, and surgeon satisfaction in the three groups. Also, no possible complication was observed in the three groups, but according to the results, there was a significant difference in the extubation time, recovery time and the dose of administered propofol among the three groups. Dexmedetomidine reduces the dose of administered propofol while increasing the extubation time. But in the tranexamic acid group, the recovery time is shorter, while all three drugs reduce intraoperative bleeding and lead to surgeon satisfaction. That is to say since in the dexmedetomidine group the overall dose of administered propofol for effective control of intraoperative bleeding was less than that in the other groups, it can be said that this drug is the most preferred one to control intraoperative bleeding. However, other factors such as the prolongation of extubation and patient's recovery times as well as the hemodynamic changes in this group must be duly considered. Therefore, based on the results of this study, it can be concluded that all these three drugs can be utilized in order to control bleeding and improve the quality of the surgical field but the ultimate decision lies with the anesthesiologist's judgment and the conditions of the patient.

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Author contributions

All authors conceived the study and drafted the manuscript. HM, EM, FF collected the data. AAH and HM analyzed the data and all authors revised the manuscript and approved the final version.

Conflicts of interest

All the authors declared no conflict of interest.

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Institutional review board statement

The study protocol was registered in the Iranian Registry of Clinical Trials (registration No. IRCT20141209020258N121) on September 24, 2019 and it was ethically approved by Ethical Committee of Arak University of Medical Sciences (approval No. IR.ARAKMU.REC.1397.355) on February 24, 2019.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for the images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published.

Reporting statement

The writing and editing of the article were performed in accordance with the CONSolidated Standards Of Reporting Trials (CONSORT) Statement.



Biostatistics statement

The statistical methods of this study were reviewed by the epidemiologist of Arak University of Medical Sciences, Iran.

Copyright transfer agreement

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Data sharing statement

Individual participant data that underlie the results reported in this article, after deidentification (text, tables, figures, and appendices). Study protocol and informed consent form will be available immediately following publication, without end date. Results will be disseminated through presentations at scientific meetings and/or by publication in a peer-reviewed journal. Anonymized trial data will be available indefinitely at www.figshare.com.

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Additional files

Additional file 1: Hospital ethics approval.

Additional file 2: CONSORT checklist.

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CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	Page 1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Page 1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	Page 1-2
	2b	Specific objectives or hypotheses	Page 1-2
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Page 2
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Page 2
Participants	4a	Eligibility criteria for participants	Page 2
	4b	Settings and locations where the data were collected	Page 2
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Page 2
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Page 3
	6b	Any changes to trial outcomes after the trial commenced, with reasons	Page 3
Sample size	7a	How sample size was determined	Page 3
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	Page 3
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Page 3
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Page 3
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Page 3
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	Page 3

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	Page 3
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	Page 3
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Page 3-4
	13b	For each group, losses and exclusions after randomisation, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Page 3
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Page 4
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Page 3-4
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Page 4-6
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Page 6
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Page 6
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Page 7
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Page 6-7
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Page 6-7
Other information			
Registration	23	Registration number and name of trial registry	Page 7
Protocol	24	Where the full trial protocol can be accessed, if available	Page 7
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Page 7

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.