Review

Bleeding Management In Rhinoplasty Surgery: A Systematic Review Study On Clinical Trial Studies Conducted In Iran

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Abstract:

Introduction: Bleeding during rhinoplasty surgery is a complication that reduces the surgeon's vision and quality of surgery and causes multiple problems for the surgeon and anesthesiologist. So far, various methods have been performed to reduce bleeding during rhinoplasty. Therefore, this study aimed to evaluate the effectiveness of medications on the rate of bleeding during rhinoplasty surgery as a systematic review of clinical trial studies conducted in Iran.

Methods: In this systematic review study, SID, Magiran, Scopus, Science Direct, Medline, and PubMed databases and Google Scholar search engine were quarried from 2000 to 2020 using Persian and English keywords. The quality of the included articles was evaluated using a checklist related to clinical trial studies.

Results: Fourteen studies were included in this study. Among the studies, 4 studies were related to tranexamic acid, 3 studies on clonidine and Dexmedetomidine, 2 studies on nitroglycerin and labetalol, and one study on remifentanil, magnesium sulfate, dexamethasone, epinephrine, and lidocaine. In all studies performed in Iran, all medications except epinephrine reduced the amount of bleeding during rhinoplasty surgery. However, some studies did not show a significant difference in reducing bleeding between the compared medications.

Conclusion: It seems that tranexamic acid can be more effective in reducing or controlling bleeding during rhinoplasty surgery than other medications.

Keywords: Bleeding, Rhinoplasty, Iran, Clinical trial.

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Introduction

Rhinoplasty is a type of facial reconstructive surgery that enhances the appearance and function of the nose (1-2). Rhinoplasty is a procedure that reduces the size of the nose, changes the shape of the bridge or tip of the nose, and narrows the nostrils, or all of these things at the same time (3). One of the problems in the operating room for surgeons and anesthesiologists is bleeding during rhinoplasty. On the one hand, the surgeon needs a dry surgical site with little bleeding in order to execute delicate and sensitive procedures. The anesthesiologist, on the other hand, is concerned with minimizing intraoperative bleeding in order to preserve hemodynamic stability during the procedure (4). Bleeding during surgery may occur as a result of damage to any of the large vessels, such as the angular artery or small vessels (capillaries) in the subcutaneous network (5). Various techniques can reduce bleeding, such as controlled blood pressure-lowering methods, local vasoconstrictors, biological and chemical medications such as Desmopressin, Aprotinin (6), Tranexamic acid (7), Epsilon-aminocaproic acid (EACA), and Various medications such as clonidine (8), labetalol (9), nitroglycerin (10), Tranexamic acid (11), dexamethasone (12), dexmedetomidine (13), remifentanil (14), can reduce bleeding during rhinoplasty. Considering the effects of different drugs on the rate of intraoperative bleeding, the present study was performed to evaluate clinical trials of bleeding rate in rhinoplasty surgery in Iran.

Methods

This study was a systematic review. In this study, we performed a search in SID, Magiran, Scopus, Science Direct, Medline and PubMed databases and Google Scholar search engine from 2000 to 2020, with Persian/ English keywords of “Blood Loss”, “Rhinoplasty”, “surgery site” with all possible combinations using AND and OR operators, separately by 2 authors. Inclusion criteria were: clinical trial studies related to bleeding in rhinoplasty surgery from 2000 to 2020 in Iran and exclusion criteria were studies outside Iran and lack of full access to articles. Also, studies such as conference abstracts, letters to the editor, and case report studies were excluded from the study. To select studies and extract the data, first the titles of all the articles obtained by two researchers were reviewed and duplicates were removed. Then, the abstract of the remaining articles was carefully studied and the articles that did not seem relevant were excluded. Finally, the full text of possible related articles was reviewed and qualified articles were selected. In cases where there was disagreement between the two researchers, the article was reviewed by a third researcher. In the next step, the information related to the selected articles including the first author, the year of publication of the article, the title of the study, the sample size, the drug used, and finally the patients' outcome was recorded in the data extraction form. The quality of the reviewed articles was evaluated using the Jadad checklist of clinical trial studies.

Results:

In the initial stage of searching for studies, 558 studies were evaluated. The researchers then reviewed the searched articles and 544 studies were deleted due to not being relevant to the subject under study and duplication and lack of access to the complete article. Finally, 14 studies were used to write this study. Among the studies, 4 studies were related to tranexamic acid, 3 studies were related to clonidine and dexmedetomidine, 2 studies were related to nitroglycerin and labetalol, and one study related to remifentanil, magnesium sulfate, dexamethasone, epinephrine, and adrenaline lidocaine. In all studies performed in Iran, all medications used except epinephrine reduced the amount of bleeding during rhinoplasty surgery. However, some studies did not show a significant difference in reducing bleeding between the two medications (table 1).

Discussion:

Various methods and medications are used to reduce the amount of bleeding during rhinoplasty surgery. In this study, the drugs used in the articles were compared and compared with other studies.

Dexmedetomidine:

Dexmedetomidine has no side effects and has sedative and analgesic properties. As a result, it reduces bleeding during surgery and provides greater safety and patient satisfaction (21). Dexmedetomidine can possibly reduce bleeding during rhinoplasty with two effects. The first mechanism is likely to be the high ability of this

Table 1. characteristics of included studies

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Author /year of study	Study title	State	Sample size	The drug used	Consequences
Zamani / 2021	Comparison of the effect of Dexmedetomidine and remifentanil on the control of hypotension in rhinoplasty surgery	Arak	60	Dexmedetomidine - Remifentanil	Both Dexmedetomidine and Remifentanil reduce bleeding during rhinoplasty, but the effect of Remifentanil is greater than that of Dexmedetomidine (14).
Ghodrati / 2017	Comparison of labetalol and nitroglycerin in control blood pressure and bleeding loss in rhinoplasty	Tehran	60	Labetalol and nitroglycerin	There was no significant difference between the two groups in terms of bleeding volume (10).
Rok Tabnak / 2017	Control of hypotension in rhinoplasty surgery: Comparison of Dex Medomedin and Magnesium Sulfate	Tehran	50	Dexmedetomidine and Magnesium Sulfate	Dexmedetomidine significantly reduces bleeding compared to magnesium sulfate (15).
Berenjani / 2017	Comparison of the effect of tranexamic acid and dexmedetomidine on bleeding during rhinoplasty surgery	Tehran	76	Tranxamic acid - dexmedetomidine	In total, the efficacy of dexmedetomidine and tranexamic acid was equal (13).
Ghavami / 2017	The effect of tranexamic acid on the complications of rhinoplasty surgery: a double-blind randomized study	Tabriz	60	Tranexamic acid	Administration of 10 mm/kg tranexamic acid has a significant effect on reducing intraoperative bleeding ().
Beikaei / 2015	The effect of tranexamic acid on the rate of bleeding during rhinoplasty	Ahwaz	100	Tranexamic acid	Tranexamic acid can reduce bleeding during rhinoplasty (11).
Yari / 2015	Comparison of the effect of topical injection of lidocaine adrenaline with adrenaline alone on the bleeding rate of rhinoplasty surgery field	Kermanshah	56	Topical injection of adrenaline lidocaine vs. adrenaline	The effect of 2% lidocaine solution on bleeding during rhinoplasty is similar to that of normal saline solution (17).
Eftekharian / 2015	The effect of preoperative oral tranexamic acid on the rate of bleeding during rhinoplasty surgery	Shiraz	50	Tranexamic acid	The use of 1 g of tranexamic acid before surgery can reduce bleeding during rhinoplasty surgery (18).
Hadavi / 2015	Comparison of the effect of labetalol and nitroglycerin on bleeding during rhinoplasty surgery	Shiraz	60	Labetalol - nitroglycerin	There is no significant difference between the two groups of labetalol and nitroglycerin in the amount of bleeding during rhinoplasty surgery (9).
Tabrizi / 2014	Can Oral Clonidine Reduce Bleeding in Rhinoplasty?	Shiraz	66	Clonidine	The use of oral clonidine can reduce bleeding during rhinoplasty surgery (19).
Ghazipour / 2013	Can clonidine as a pre-anesthetic drug reduce bleeding during rhinoplasty surgery?	Tehran	80	Clonidine	Oral clonidine as a prodrug for anesthesia can reduce bleeding during rhinoplasty (8).
Kalantar-Hormozi / 2011	Can removal of epinephrine in rhinoplasty surgery reduce its complications: Introducing a new technique .	Tehran	111	Epinephrine	There was no statistically significant relationship between epinephrine injection and bleeding during or after surgery (20).
Dabirmoghaddam / 2007	Dexamethasone in reducing edema and ecchymosis around the eye and intraoperative bleeding in rhinoplasty	Yazd	90	Dexamethasone	The use of dexamethasone does not affect reducing the volume of intraoperative bleeding (12).
Sadri / 2007	The role of clonidine in reducing bleeding during rhinoplasty surgery	Tehran	40	Clonidine	Pretreatment with oral clonidine 3 micrograms per kilogram of body weight reduces the amount of bleeding in rhinoplasty (4).

drug to reduce blood pressure (22) and the second mechanism is the same as adding to platelet

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aggregation (13). In Iran, three studies have been performed on the effects of Dexmedetomidine on the rate of bleeding in rhinoplasty surgery.

In their study, Zamani et al. (2021) compared the effect of Dexmedetomidine and Remifentanil on the control of hypotension in rhinoplasty surgery. The results of this study showed that both Dexmedetomidine and Remifentanil reduce bleeding during rhinoplasty, but the effect of Remifentanil is greater than that of Dexmedetomidine (14). Rokh Tabnak et al. (2017) in their study concluded that long-acting dexmedetomidine compared to magnesium sulfate significantly reduces bleeding (15). The results of the study of Baranjani et al. (2017) showed that the total effectiveness of the two drugs dexmedetomidine and tranexamic acid was equal. Tranexamic acid reduces bleeding in major surgeries, and dexmedetomidine may be a better option in rhinoplasty surgery where the amount of bleeding is not large (13). Overseas studies have also confirmed the effectiveness of Dexmedetomidine in reducing bleeding in septorhinoplasty (23-25). Overall, studies using Dexmedetomidine showed its potential to reduce bleeding during rhinoplasty surgery.

Remifentanil:

Remifentanil is one of the drugs that suppress the vasomotor system and reduce blood pressure by releasing histamine as well as centrally affecting vasoconstriction. Compared to other opioids such as fentanyl, remifentanil can improve hemodynamic stability in stressful surgical events and minimize changes in cerebral blood flow alternations (26). In Iran, a study was performed on the effects of remifentanil on the bleeding rate in rhinoplasty surgery. In their study, Zamani et al. (2021) compared the effect of Dexmedetomidine and remifentanil on the control of hypotension in rhinoplasty surgery. The results of this study showed that both Dexmedetomidine and Remifentanil reduce bleeding during rhinoplasty surgery, but the effect of Remifentanil was greater than that of Dexmedetomidine (14). Koşucu et al. (2014) in their study investigated the effects of intraoperative remifentanil with controlled hypotension on postoperative bleeding and postoperative edema and ecchymosis in rhinoplasty surgery. The results of this study showed that remifentanil reduces the amount of bleeding during rhinoplasty surgery (27). Overall, the studies showed that remifentanil was able to reduce bleeding during rhinoplasty surgery.

Labetalol:

Labetalol is an antihypertensive drug that attenuates alpha and beta receptors while reducing heart rate and dilating blood vessels (28-30). In Iran, two studies have been performed on the effects of labetalol on the rate of bleeding in rhinoplasty surgery. Ghodrati et al. (2017) in their study compared labetalol and nitroglycerin in controlling blood pressure and the rate of bleeding in rhinoplasty. The results of their study showed that there was no significant difference between the two groups in terms of bleeding volume (10). Hadavi et al. (2020) in their study compared the effect of labetalol and nitroglycerin on the rate of bleeding during rhinoplasty surgery. The results of this study showed that there was no significant difference between the two groups of labetalol and nitroglycerin in the amount of bleeding during rhinoplasty (9). The efficacy of labetalol in comparison with other drugs does not seem to be sufficiently effective in reducing bleeding during rhinoplasty surgery and there is a need for further studies in this field to obtain the maximum effectiveness of this drug in reducing bleeding in Rhinoplasty surgery.

Nitroglycerin:

Nitroglycerin lowers blood pressure by dilating blood vessels in the arteries. However, this drug increases the heart rate as an undesirable side effect (31). In Iran, two studies have been performed on the effects of nitroglycerin on the rate of bleeding in rhinoplasty surgery. In both studies in Iran, nitroglycerin was not superior to other drugs in reducing bleeding during rhinoplasty surgery (9-10). More research in this area is needed to determine the drug's greatest efficacy in minimizing bleeding during rhinoplasty surgery.

Magnesium sulfate:

Magnesium sulfate causes hypotension by vasodilating effect (33-32). In Iran, a study was performed on the effects of magnesium sulfate on the rate of bleeding in rhinoplasty surgery. The results of the study of Rokh Tabnak et al. (2017) showed that Dexmedetomidine significantly reduced the amount of bleeding in rhinoplasty compared to magnesium sulfate (15). Kosucu et al. (2020) also concluded in their study that

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magnesium sulfate can reduce bleeding during rhinoplasty surgery (34). Due to the contradictory results in the studies, it is suggested that more studies be done on the effectiveness of this drug in reducing or controlling bleeding during rhinoplasty surgery.

Tranexamic acid:

Tranexamic acid is an analog of lysine and binds to plasminogen and plasmin, inhibiting their ability to bind to lysine residues in fibrin and thus inhibiting fibrinolysis (36-35). In Iran, four studies have been performed on the effects of tranexamic acid on the rate of bleeding in rhinoplasty surgery. In their study, Baranjani et al. (2017) compared the effect of tranexamic acid and dexmedetomidine on the rate of bleeding during rhinoplasty surgery. The results of this study showed that the total efficacy of dexmedetomidine and tranexamic acid was equal (13). Bikaei et al. (2015) in their study investigated the effect of tranexamic acid on the rate of bleeding during rhinoplasty. The results of this study showed that tranexamic acid can reduce bleeding during rhinoplasty (11). Eftekharian et al. (2015), in their study, investigated the effect of preoperative oral tranexamic acid on the amount of bleeding during rhinoplasty surgery. The results of this study showed that the use of oral tranexamic acid before surgery can reduce the amount of bleeding during rhinoplasty surgery (18). Ghavami et al. (2017) investigated the effect of tranexamic acid on the complications of rhinoplasty surgery. The results of this study showed that the administration of 10 mg/kg tranexamic acid has a significant effect on reducing intraoperative bleeding (16). Sara Juliana de (2018) evaluated preoperative tranexamic acid on the rate of bleeding, edema, and ecchymosis in patients undergoing rhinoplasty surgery, and the results showed that the use of tranexamic acid resulted in the reduction of bleeding during rhinoplasty surgery (37). Connor McGuire (2019) in his study systematically investigated the role of tranexamic acid in reducing intraoperative bleeding and postoperative edema and ecchymosis in rhinoplasty surgery. The results of this study showed that the use of tranexamic acid reduces the amount of bleeding during rhinoplasty surgery (38). The results of the above studies collectively indicate the effectiveness of tranexamic acid in reducing or controlling bleeding in rhinoplasty surgery.

Clonidine

Clonidine is a peripheral vasoconstrictor and reduces the blood flow to the nasal mucosa through its alpha-agonist property (39-40). In Iran, three studies have been performed on the effects of clonidine on the rate of bleeding in rhinoplasty surgery. Tabrizi (2014) in their study investigated whether oral clonidine can reduce bleeding in rhinoplasty surgery. The results of this study showed that the use of oral clonidine can reduce bleeding during rhinoplasty surgery (19). Ghazipour (2013) in their study examined whether clonidine as a pre-anesthetic drug can reduce bleeding during rhinoplasty surgery. The results of this study showed that oral clonidine as a prodrug for anesthesia can reduce bleeding during rhinoplasty (8). In their study, Sadri et al. (2007) investigated the role of clonidine in reducing bleeding during rhinoplasty surgery. Pretreatment with oral clonidine 3 micrograms per kilogram of body weight reduces the amount of bleeding in rhinoplasty (4). The results of the above studies together show the effectiveness of clonidine in reducing or controlling bleeding in rhinoplasty surgery.

Dexamethasone:

The anti-inflammatory effect of dexamethasone is linked to its potential in interrupting the macrophage inhibitory factor phase and preventing the accumulation of macrophages, reducing the dilation and permeability of inflamed capillaries and adhesion of white blood cells to the capillary wall, and, finally, slowing the onset of edema and Migration of white blood cells (41-44). In Iran, a study was performed on the effects of dexamethasone on the bleeding rate in rhinoplasty surgery. Dabiri Moghadam et al. (2007) investigated the effect of dexamethasone in reducing edema and ecchymosis around the eye and intraoperative bleeding in rhinoplasty. The results of this study showed that the use of dexamethasone does not affect reducing the volume of intraoperative bleeding (12). Bian (2020) evaluated the effectiveness of dexamethasone to reduce edema and ecchymosis after rhinoplasty surgery as a systematic review and meta-analysis study. The results of this study showed that dexamethasone reduces the amount of bleeding during rhinoplasty surgery (45). Due to the contradictory results in the studies, it is suggested that more studies be done on the effectiveness of this drug in reducing or controlling bleeding during rhinoplasty surgery.

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Adrenaline and lidocaine:

While adrenaline is mostly being used in acute care of arrested patients (46), one of the measures taken to reduce bleeding during rhinoplasty surgery is the injection of submucosal and intradermal adrenaline into the operation site. Usually, one to two percent lidocaine is used as an adrenaline booster when the adrenaline concentration is 1/200000 (46-47). The use of appropriate anesthetic drugs and vasoconstrictors in the surgical area reduces intraoperative bleeding (48). In Iran, a study was performed on the effects of adrenal+lidocaine on the rate of bleeding in rhinoplasty surgery. Yari et al. (2015) compared the effect of topical injection of adrenaline+lidocaine versus adrenaline alone on the bleeding rate of the rhinoplasty surgery field. The results of this study showed that the effect of lidocaine solution on the bleeding during rhinoplasty surgery is similar to the effect of normal saline solution. So, surgeons can use adrenaline solution with normal saline in rhinoplasty surgery (17). Gun et al. (2011) investigated the effect of lidocaine and adrenaline combination on postoperative edema and ecchymosis in rhinoplasty surgery. The results of this study showed that the combination of these two drugs reduces the amount of bleeding during rhinoplasty surgery (49).

Epinephrine:

Due to its vasoconstrictive effects, epinephrine increases heart rate, vasoconstriction, and airway dilation, and is effective in causing a sympathetic nervous system response (50). In Iran, a study was performed on the effects of epinephrine on the bleeding rate in rhinoplasty surgery. Kalantarhormozi (2011) and colleagues examined whether the removal of epinephrine in rhinoplasty surgery can reduce its complications as a new technique. The results of this study showed that there was no statistically significant relationship between epinephrine injection and bleeding during or after surgery (20) Fernández-Cossío et al. (2016) compared topical cocaine versus epinephrine. The results of this study showed that cocaine is more effective in reducing bleeding than epinephrine (51). Given the ineffectiveness of epinephrine in the study, it is suggested that further studies be performed to determine whether epinephrine has an effect on reducing bleeding during rhinoplasty surgery.

Conclusion:

It seems that tranexamic acid drugs can be more effective in reducing or controlling bleeding during rhinoplasty surgery than other drugs.

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