



Effect of local desmopressin administration on intraoperative blood loss and quality of the surgical field during functional endoscopic sinus surgery in patients with chronic rhinosinusitis: a triple-blinded clinical trial

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Abstract

Background Bleeding during functional endoscopic sinus surgery always been a challenge for the quality of surgical field for surgeons. This study aimed to evaluate the effect of local nasal desmopressin premedication on blood loss and the quality of surgical field in functional endoscopic sinus surgery.

Methods This study was conducted on 90 patients with chronic rhinosinusitis who were candidate for endoscopic sinus surgery. They were randomly assigned to two study groups. One group received a single puff of local desmopressin (10 µg) in each side of nasal cavity 30 min before the surgery and the other received normal saline instead. Blood loss and the quality surgical field were determined in 15, 30, 60 and 90 min during the surgery (scoring by BOEZAART grading system). All data were analyzed.

Results Blood loss was significantly lesser in the desmopressin group (mean ± SD, 16.289 ± 5.605 ml) than in the control group (24.289 ± 5.2722 ml, $P < 0.001$). Surgeons were more satisfied with the surgical field in the desmopressin group than control group in all cutoff points (15, 30, 60, and 90 min during the surgery, $P < 0.001$). No side effects were observed using local desmopressin.

Conclusions Premedication with local desmopressin can reduce bleeding effectively and clear the surgical field during functional endoscopic sinus surgery.

Keywords Desmopressin · Blood loss · Surgical field · Endoscopic sinus surgery

Introduction

A common procedure for surgical management of chronic rhinosinusitis is functional endoscopic sinus surgery (FESS) [1]. Major bleeding during FESS is rare, even a minimal bleeding may blur the surgical view and this event may

lead to prolonged operation time, increases the probability of complications and possibly results incomplete surgery though [2]. Over time multiple techniques have been suggested to improve the surgical field in endoscopic sinus surgery, such as bipolar diathermy, topical vasoconstrictors, local injection of epinephrine and induced hypotension [3]. Although they are all used routinely, none of them permanently provide an ideal surgical field for the surgeon and bleeding in FESS remains a challenge for surgeons and anesthesiologists as well.

Desmopressin (1-deamino-8-D-arginine vasopressin) has been used as a treatment for neurogenic DI (diabetes insipidus), primary enuresis, mild-to-moderate type A hemophilia and von Willebrand disease. Hemostatic effects of desmopressin occurs through raising plasma concentrations of coagulation factor VII, von Willebrand factor and tissue

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plasminogen activator, improving platelet adhesiveness and probable effect on vascular stability [4]. This drug can be used in oral form, intranasal spray and intravenous injection [5]. The following side effects could be: nasal discomfort, headache, noncardiac chest pain, abdominal pain, oral bad taste, anorexia, increase of appetite and seizure (due to hyponatremia). However, all of them have been reported in taking therapeutical dose (at least 20 µg a day) and more than 10 weeks [4].

Hemostatic effects of desmopressin have been considered by surgeons in recent years. Several studies have been performed on patients undergoing various types of surgeries. A study in patients undergoing orthognathic surgery demonstrated a significant reduction in intraoperative blood loss using intravenous desmopressin [6]. A meta-analysis of randomized clinical trials noted that desmopressin reduces transfusion needs after surgery [7]. A study determine the effect of administration of intravenous desmopressin on intraoperative blood loss and the quality of surgical field in patients undergoing endoscopic sinus surgery and revealed that premedication with desmopressin effectively reduced intraoperative bleeding [8].

However, the effect of intranasal (local) desmopressin administration on intraoperative blood loss in endoscopic sinus surgery is unknown. This study aimed to determine the effect of administration of intranasal desmopressin on intraoperative blood loss and the quality of surgical field in patients undergoing endoscopic sinus surgery.

Methods

After IRCT registration (20130713013976N5) and approval by the Medical Ethics Committee of Hamadan University of Medical Science (IR.UMSHA.REC.1396.11), the trial was done between April 2017 and May 2018 in Besat medical education center, Hamadan, Iran. Written informed consent was obtained from the patients. All patients were 18–60 years old, and were candidate for two-side FESS due to chronic rhinosinusitis (with and without polyposis and no response to medical therapy). Exclusion criteria were as follows: patients with a history of bleeding disorders or taking medications that may affect surgical hemostasis during 1 month before the surgery, poorly controlled hypertension or cerebrovascular disease, a history of significant coronary artery disease or arrhythmias, compromised renal or hepatic function and hyponatremia. After inserting exclusion criteria, 93 patients were recruited in the study, 3 of them were out because of hypertension crisis during the surgeries.

The involvement of paranasal sinuses was evaluated by CT scan and was scored based on the Lund–Mackay scoring system. Patients were randomly (using 6 blocks methods) assigned to one of two study groups: patients in the

desmopressin group received single puff (10 µg) of nasal desmopressin in each side of nasal cavity (20 µg totally) 30 min preoperatively and those in the control group received normal saline spray instead (nasal sprays had same shape but different content that was prepared by advisor pharmacist). Assignment to the groups was performed by computer-generated random numbers. All patients had a normal preoperative platelet count and coagulation test results and a normal sodium level. Anesthetic management of all patients was standardized and conducted by a single attending anesthesiologist that induced a bolus dose of propofol 2 mg/kg and remifentanyl 2 µg/kg immediately followed by infusions of propofol at first 15 min 100 µg/kg/min, at 15–45 min 80 µg/kg/min and after 45 min 70 µg/kg/min and remifentanyl 0.5 µg/kg/min (TIVA). All the surgeries were performed by training assistants with the supervisions of the professor and all of them were blinded to the patients study groups.

The surgeries started with nasal packing that soaked with phenylephrine for 10 min and local control of bleeding in the surgical field was facilitated by submucosal single time injection of 3 ml epinephrine (1:100,000) and 5% lidocaine by the surgeons in all the patients. During the surgeries, MAP (mean arterial pressure) was measured in two cutoff points (15 and 90 min) and volume of bleeding was measured in cc with calculating the volume of fluid in the suction bottle after deduction of normal saline serum volume that was used for endoscopic scrub. The quality of surgical field based on BOEZAART grading system (0 no bleeding cadaveric conditions; 1 slight bleeding: no suctioning required; 2 slight bleeding: occasional suctioning required; 3 sight bleeding: frequent suctioning required, bleeding threatens surgical field a few seconds after suction is removed; 4 moderate bleeding: frequent suctioning required and bleeding threatens surgical field directly after suction is removed; 5 severe bleeding: constant suctioning required; bleeding appears faster than can be removed by suction; surgical field severely threatened and surgery usually not possible) were measured in 15, 30, 60 and 90 min after initiating the operation. The duration of surgeries were recorded in all the patients as well.

Results

Among the participants in the trial, 90 patients completed it, out of whom 45 received placebo (normal saline nasal spray) and the rest received medication (desmopressin nasal spray). All the demographic characteristics and characteristics of FESS were comparable and are noted in Table 1. There was a significant effect of desmopressin on blood loss and quality of the surgical field in all the intervals (15, 30, 60 and 90 min) that is noted in Table 2. The mean arterial

Table 1 Patient's demographic characteristics and comparable data of FESS

	Desmopressin (n = 45) Mean ± SD	Control (n = 45)	P value
Age (year)	40.27 ± 10.254	41.91 ± 8.849	0.418
Gender (F/M)	20/25	19/26	0.832
Baseline MAP (mmHg)	73.24 ± 3.655	68.86 ± 4.245	0.004
CT Score (0–24)	16.98 ± 3.078	16.58 ± 2.950	0.531
Polypoid disease (yes/no)	12/33	15/30	0.490
Revision surgery (yes/no)	8/37	7/38	0.780

Table 2 Comparison of quantitative characteristics

	Desmopressin (n = 45) Mean ± SD	Control (n = 45)	P value
Duration of surgery (min)	101.56 ± 13.264	102.00 ± 11.251	0.864
Bleeding volume in 15 min (cc)	3.911 ± 1.6524	5.678 ± 1.5081	0.000
Bleeding volume in 30 min (cc)	3.867 ± 1.5203	5.744 ± 1.3039	0.000
Bleeding volume in 60 min (cc)	4.200 ± 1.0996	6.378 ± 1.0561	0.000
Bleeding volume in 90 min (cc)	4.311 ± 1.3327	6.489 ± 1.4041	0.000
Quality of surgical field in 15 min (1–5 by BOEZAART)	1.60 ± 0.780	2.89 ± 0.745	0.000
Quality of surgical field in 30 min	1.69 ± 0.557	2.82 ± 0.535	0.000
Quality of surgical field in 60 min	1.91 ± 0.417	3.13 ± 0.405	0.000
Quality of surgical field in 90 min	2.02 ± 0.583	3.04 ± 0.638	0.000
Mean arterial pressure (mm Hg) in 15 min	71.64 ± 4.964	68.62 ± 4.589	0.004
Mean arterial pressure in 90 min	75.58 ± 7.482	71.93 ± 6.706	0.017

pressure (MAP) in cutoff points 15 and 90 min were significantly higher in desmopressin group in comparison to control group (Table 2), even though they have higher MAP at the time of admission (a day before the surgery) as well (Table 1). The duration of surgery was a little shorter in the desmopressin group (101.56 ± 13.264 min) than in the control group (102 ± 11.251 min), but this difference was not significant (Table 2).

None of the complications and side effects of desmopressin administration were observed in the study and the comparison of sodium level of serum before and after the surgeries were not significant in both desmopressin (138.69 ± 2.712 mg/dl vs. 138.51 ± 2.817; *p* value: 0.938) and control (138.64 ± 2.715 mg/dl vs. 139.02 ± 3.361; *p* value: 0.436) groups. None of all 90 patients had complications of functional endoscopic sinus surgery.

Discussion

Various techniques have been suggested until now to reduce bleeding and improve the quality of surgical field visualization during functional endoscopic sinus surgery. Although the evidences that support the results of these methods are poor, most of them are used frequently to reduce

intraoperative blood loss such as the reverse Trendelenburg position, use of high doses of epinephrine, infiltration of phenylephrine and lidocaine into the pterygopalatine fossa, preoperative use of prednisone, and control of the heart rate (with dexmedetomidine or remifentanyl) [1, 9, 10].

In addition to these methods, receiving some other drugs as an oral premedication is under review. Nair et al. demonstrated that although satisfying conditions were present in the patients receiving premedicative β -blocker (metoprolol), the grading system was not discriminating enough to demonstrate a significant difference between β -Blocker and placebo [11]. Nuhi et al. showed that tranexamic acid premedication can decrease intraoperative hemorrhage during endoscopic sinus surgery and no coagulative complications were observed in their study [12]. Another study revealed that using oral clonidine as an endoscopic surgery premedication lead to less bleeding and better quality of surgical field in patient [13]. Ghorbani et al. compared oral clonidine and intravenous tranexamic acid premedication and experienced that they have the same effect on bleeding, surgical field quality and satisfaction of surgeons during endoscopic sinus surgery [14]. Khoshraftar et al. showed that dexmedetomidine is more beneficial for controlling hemodynamic status of sinus endoscopic surgery patients as it can provide a better operation field [15].

In recent years, hemostatic effects of desmopressin have been considered by surgeons. These hemostatic effects occurs through raising plasma concentrations of coagulation factor VII, von Willebrand factor and tissue plasminogen activator, improving platelet adhesiveness and probable effect on vascular stability. In 2015, Shao et al. worked on intravenous desmopressin and noted that premedication with 0.3 µg/kg IV desmopressin can efficiently reduce bleeding and clarify the field during functional endoscopic sinus surgery [8]. Their study also demonstrated that desmopressin could effectively reduce MAP in four cutoff point (10, 20, 30 and 40 min after starting the surgeries) which is not expected to happen by prescribing local desmopressin.

So far, as we have researched as a new experience, this study worked on local desmopressin (nasal spray) as a premedication and encountered reduction of bleeding, better quality of visualization and more surgeons satisfaction in comparison to placebo (saline nasal spray) in all cutoff points during the surgeries. In addition to coagulative effect of the drug, creating induced hypotension maybe cause of bleeding reduction although this effect was not seen in this trial because local desmopressin is not likely to have systemic effects and this is an advantage of this study. Despite these findings, there was no difference in the duration of two group surgeries although the patients had the similar CT score. This finding may be due to differences in surgeon skills. Even though there was no different in surgeries duration between IV desmopressin and placebo groups in Shao study too [8].

Since this study worked on low dose of local desmopressin, the probable risk of systemic complications is less. As mentioned, the biggest disadvantage of this study is that the surgeries were done by training assistants with the supervisions of the professor that could limit the study in some ways. Therefore, designing studies with a single surgeon is recommended.

Conclusion

Study ahead showed that administration of local desmopressin as a premedication could effectively reduce bleeding and clarify surgical field and increase surgical team satisfaction during endoscopic sinus surgery.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (IR.UMSHA.REC.1396.11) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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