Original Article

Desmopressin nasal spray reduces blood loss and improves the quality of the surgical field during functional endoscopic sinus surgery

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Abstract

Background and Aims: Making a dry surgical field during functional endoscopic sinus surgery (FESS) is a challenge for anesthetists. This study was conducted to evaluate the pre-emptive hemostatic effects of a single dose of an intranasal spray of desmopressin (DDAVP) in sinus surgery.

Material and Methods: Sixty consecutive patient's as first-time candidates for FESS due to chronic sinusitis were enrolled. They were randomly allocated to receive either a nasal spray of DDAVP 20 μg or sterile water before induction of anesthesia. Management of anesthesia was achieved with propofol and remifentanil infusions. Blood loss, quality of the surgical field, and surgeon's satisfaction were compared between the two groups.

Results: Blood loss in the DDAVP group was 147 ± 43 mL and in the placebo group 212 ± 64 mL (mean ± SD, $P < 0.01$). The quality of the surgical field in the DDAVP group was better than the placebo group. (median score, 1 (1–2) vs. 2 (1–3), $P = 0.017$). Surgeons were more satisfied with the surgical field in the DDAVP group than in the control group (median score, 4 (2.8–5) vs. 3 (2-3), $P = 0.04$).

Conclusion: Premedication with nasal spray DDAVP 20 μg effectively reduces bleeding and improves the surgical field during FESS.

Keywords: Anesthesia, blood loss, desmopressin, surgical, transanal endoscopic surgery

Introduction

Functional endoscopic sinus surgery (FESS) is increasingly used for surgical management of chronic rhinosinusitis. Although major blood loss during FESS is rare, a wet field with a small amount of blood prolongs the operation time, increases the likelihood of complications, and possibly results in incomplete surgery.[1] Several techniques have been suggested to improve the surgical field in endoscopic sinus surgery such as controlled hypotension, topical vasoconstrictors, premedication with alpha agonists, and use of antifibrinolytics.[2-4] However, none of these techniques has consistently provided an ideal bloodless field for the surgeon. Hemostasis during FESS remains a challenge for surgeons and anesthesiologists.

Desmopressin (1-deamino-8-D-argininevasopressin) is a synthetic analog of the antidiuretic hormone L-arginine vasopressin. It increases plasma concentrations of tissue plasminogen activator and endothelial factor VIII. Its use for mild-to-moderate hemophilia, von Willebrand's disease, and other acquired platelet deficiencies are well-known.[5] Desmopressin has been suggested to reduce intraoperative

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blood loss in patients without known coagulation deficiencies, namely, in spine surgery.[6,7] Earlier studies have shown the favorable effects of intravenous administration of desmopressin in facial plastic surgeries,[8] septorhinoplasty,[9,10] and FESS.[11] Nevertheless, the efficacy of its local administration in sinus surgery is unknown. This study was conducted to evaluate the pre-emptive hemostatic effects of a single dose of an intranasal spray of desmopressin (DDAVP) in sinus surgery.

Material and Methods

Sixty consecutive patients as first-time candidates for FESS due to chronic sinusitis were enrolled. Patients aged between 18 and 66 years with American Society of Anesthesiologists (ASA) physical status I–II were included in the study. Patients receiving anticoagulants or having a bleeding diathesis, those with known allergy to desmopressin, history of hypertension, ischemic heart disease, cerebrovascular disease, or drug addiction were excluded. The trial was registered (IRCT20101026005026N9) and the Institutional Ethics Committee of the Iran University of Medical Sciences approved the study protocol. Written informed consent was obtained from all patients.

Patients were randomly allocated to receive either nasal spray of DDAVP or sterile water before induction of anesthesia. Patients in the DDAVP group received one puff (desmopressin acetate 10 μg) in each nostril. (Desmex, Sina Darou Company, Tehran, Iran). The placebo group received a spray of sterile water prepared in the emptied nasal spray of Desmex. Assignment to the groups was performed by computer-generated random blocks which resulted in an equal number of patients in either group. The surgeon, anesthesiologist, and anesthetic technician who were involved in the patient care were blinded to the nature of the study assignments.

All patients were premedicated with oral oxazepam 10 mg 2 h before surgery and fentanyl 4 mg/kg 3–5 min before intubation. Anesthesia was induced with propofol 2 mg/kg and atracurium (0.5 mg/kg). Anesthesia was maintained with propofol, remifentanil, and atracurium. The bispectral index (BIS) was applied to adjust the maintenance of anesthetics. Acute increase in MAP above 70 mmHg was treated with incremental boluses of intravenous labetalol. Controlled mechanical ventilation with an initial tidal volume of 8 mL/kg and respiratory rate of 12 breaths/min was adjusted to maintain normocapnia. At the end of the surgery, muscle relaxation was reversed with neostigmine 0.04 mg/kg and atropine 0.02 mg/kg. For fluid management, patients were preloaded with isotonic crystalloids 3 mL/kg. Blood loss was replaced with Ringer's lactate solution in a 3:1 ratio. None of the patients required transfusion of the packed cell.

Patients were positioned 10–15 degrees reverse trendelenburg during the procedure. The same anesthesia and surgery teams performed all procedures using the same technique. To minimize bleeding in the surgical field, the surgeon left a mesh soaked in epinephrine 1:100,000 for 1 min at the beginning of the procedure.

Intraoperative blood loss was estimated by the attending anesthesiologist at the end of surgery by accounting for the loss of blood and irrigation fluid in the 25 mL-graded suction canisters and nasopharyngeal packing (measured weight of packing on the electronic scale). Approximately at 15th and 60th min of surgery, the quality of the surgical field was graded by the surgeon using the scale used by Boezaart *et al.* in 1995. The surgeon's satisfaction with surgical field quality was also graded in a 5-item Likert scale, where 1 = poor and 5 = excellent. Hemodynamic parameters, including systolic and diastolic arterial blood pressure (BP) and heart rate (HR) were recorded at 15-min intervals. Prothrombin time, partial thromboplastin time, and complete blood count were measured before surgery and 6 h postoperatively. The occurrence of possible side effects of treatment including nausea, vomiting, headache, convulsion, and epistaxis were evaluated in the postanesthesia care unit (PACU). Patients stayed in the hospital overnight and were discharged the following day if this period was uneventful. Participants were asked to return 3 days after surgery to remove the nasopharyngeal pack. The occurrence of the mentioned complications in the last 3 days was recorded.

Data were presented as mean (standard deviation), median (ranges), or percentages, as appropriate. Repeated measures of BP and HR were analyzed with repeated measures analysis of variance. Ranked data, including bleeding and satisfaction scores, were compared between groups with the Mann-Whitney U test. All comparisons were two-tailed. P values <0.05 were considered statistically significant. Statistical analyses were performed with SPSS version 19.0 software (SPSS, Inc., Chicago, IL, USA).

Results

Blood loss in the DDAVP group was 147 ± 43 mL and in the placebo group 212 ± 64 mL (mean ± SD, $P < 0.01$). Around 15 min after the beginning of surgery the median (25,75 percentile) score of the Boezaart scale in the DDAVP group was 1.5 (1–2.3) and in the placebo group, the median score was 2 (1–3) without statistically significant difference ($P = 0.14$). After 60 min this score

in the DDAVP group was much better than the placebo group. (1 (1–2) vs. 2 (1–3), $P = 0.017$). The data showed that in more than half of patients given DDAVP, no suctioning was required 1 h after the beginning of surgery, whereas 70% of patients in the placebo group had bleeding scores more than 1 and thus required suctioning [Table 1]. Accordingly, the surgeon was more satisfied with the surgical field in the DDAVP group than with that in the placebo group (median score, 4 (2.8–5) vs. 3 (2-3), $P = 0.04$). There were no significant differences between the two groups regarding the coagulation profiles of the patients [Table 1]. Figure 1 shows similar trends in systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate in two groups ($P > 0.05$). The frequency of possible adverse effects of treatment including nausea, vomiting, and headache was comparable between two groups [Table 2]. No case of convulsion was reported in our patients. The number of patients who experienced epistaxis in the follow-up period, was not significantly different in the two groups [Table 2].

Discussion

The results of this study suggest that DDAVP provides a drier operative field during FESS. This is in accordance with earlier studies recommending the use of intravenous desmopressin in nasal surgery.[8-10] Our finding was independent of hemodynamic variables and the suggested hypotensive effects of desmopressin.[12] Thus, the observed clinical effect may be attributed to the hemostatic effects of desmopressin, which include secretion of factor VIII and von Willebrand factor, increase in tissue plasminogen activator, and improvement of adhesiveness of platelets.[13,14]

The usual dose of desmopressin for intravenous administration is 0.3 μg/kg. It is given intravenously over 20 to 30 min. This dose is primarily suggested for patients with type 1 von Willebrand disease.[15] An earlier study tried to find out whether lower doses of desmopressin would be satisfactorily effective in making a bloodless field during rhinoplasty. The authors have suggested that even a dose of 0.1 μg/kg might be effective in some patients.[10] However, the retrospective nature of their study makes the conclusion somehow difficult. We used nasal spray one puff (10 μg) in each nostril that is approximately equivalent to the suggested intravenous dose for a midsize patient. It is not clear if the local use of desmopressin at the site of surgery would be more effective than its systemic use. But this route of administration is clearly more feasible and may eliminate some concerns surrounding its systemic use. Unfortunately, with spraying, the dose of the delivered drug could not be meticulously based on the weight of the

Table 1: Demographic data, coagulation profile, and outcome measurements in two groups

Variable	Desmopressin	Placebo	*P*
Age (year)	39 (13)	39 (12)	0.97
Male gender, *n* (%)	22 (73.3)	23 (79.3)	0.76
Platelet count (1000/mm^3)	258 (58)	231 (79)	0.74
Preoperative PT (s)	12.1 (1.3)	12.3 (1.1)	0.67
Preoperative PTT (s)	31.5 (2.9)	33.1 (3.2)	0.47
Postoperative PT (s)	12.3 (1.6)	12.5 (1.4)	0.89
Postoperative PTT (s)	33.9 (3.1)	34.2 (2.7)	0.76
Duration of surgery (min)	93 (24)	82 (17)	0.26
Bleeding score at 15th min, *n* (%)			0.14
1	15 (50.0)	9 (30.0)	
2	8 (6.7)	12 (40.0)	
3	6 (20.0)	5 (16.7)	
4	1 (3.0)	3 (10.0)	
5	0 (0)	1 (3.3)	
Bleeding score at 60th min, *n* (%)			0.01
1	16 (53.3)	9 (30.0)	
2	10 (33.3)	8 (26.6)	
3	4 (13.3)	10 (33.3)	
4	0 (0)	3 (10.0)	
5	0 (0)	0 (0)	

Data are presented as Mean (standard deviation)

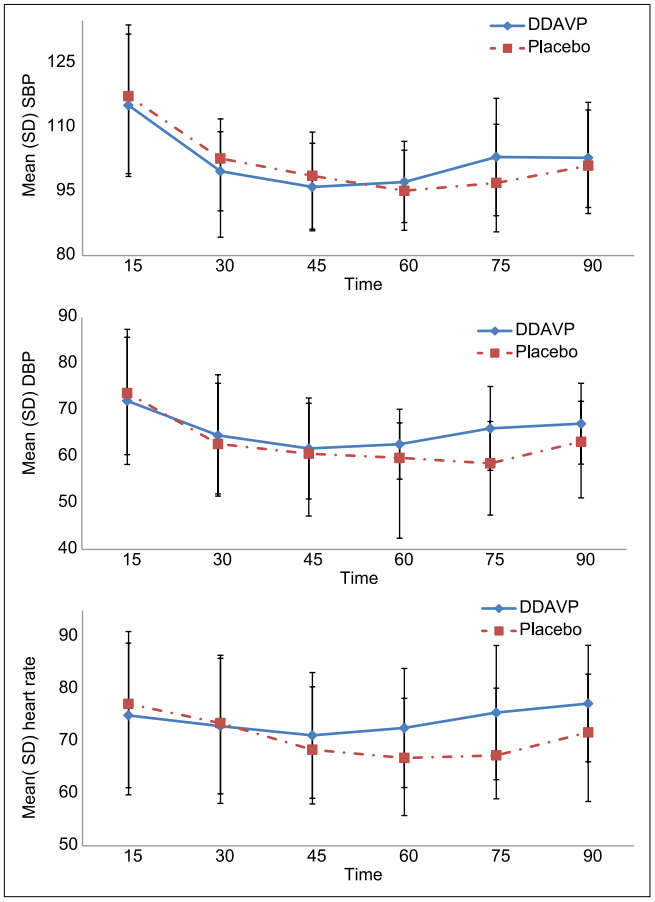

Figure 1: Trend of systolic blood pressure, diastolic blood pressure, and heart rate in two groups. Data are means (standard error). $P > 0.05$ with repeated measures analysis of variance

Table 2: Frequency of postoperative complications in the early and late recovery periods

Complication	Early recovery period			Follow-up assessment		
	Desmopressin	Placebo	*P*	Desmopressin	Placebo	*P*
Nausea	3 (10.3)	4 (13.3)	1.00	1 (3.3)	2 (6.6)	1.00
Vomiting	1 (3.3)	3 (10.0)	0.61	1 (3.3)	2 (6.6)	1.00
Headache	2 (6.7)	6 (20.0)	0.25	1 (3.3)	3 (10.0)	0.61
Epistaxis	0 (0)	1 (3.3)	1.00	0 (0)	4 (13.3)	0.11
Convulsion	0 (0)	0 (0)	1.00	0 (0)	0 (0)	1.00

patients. Further studies are required to find the optimal dose and route of administration.

We used DDAVP before induction of anesthesia. The quality of the surgical field after 15 min was not statistically different between the two groups but after 1 h the difference was remarkable. Our clinical experience was that we should wait for half an hour to observe the clinical effect. Thus, we suggest the use of DDAVP before induction of anesthesia to be effective from early minutes of surgery. Desmopressin causes a sustained increase in coagulation factors for approximately 4 h.[16] Considering the relatively short duration of FESS, it seems that a single dose of DDAVP before the beginning of surgery will fulfil our therapeutic goal.

There are potential side effects of desmopressin administration which include tachycardia, facial flushing, nausea, headache, and most important hyponatremia and seizure.[15] In this small size trial, the incidence of nausea, vomiting and headache were comparable between DDAVP and control groups. We did not measure serum sodium but none of our patients experienced visible clinical signs of hyponatremia or seizure. This is rare if excessive fluid intake is avoided. However, the risk of hyponatremia and following neurologic complications should not be neglected especially in the very young and elderly patients.

Desmopressin like other precoagulative agents may theoretically predispose patients to thrombotic events. Thus, its use in patients with the hypercoagulable state should be carefully justified. Contraindications of desmopressin include unstable coronary artery disease[17] and questionably type IIB von Willebrand disease.[18] We excluded those with a history of ischemic heart disease, hypertension, or cerebrovascular disease and we did not face any postoperative thromboembolic complications among the patients. Though statistically insignificant, the incidence of postoperative epistaxis in the DDAVP group was lower than the placebo group. This improvement in coagulation and local hemostasis may ameliorate the need for nasal packing and readmissions to the operating room in the nasal and sinus surgeries.

Study limitations

One limitation of this study is that we did not record the total dose of anesthetics and bolus doses of labetalol. One earlier study reported lower required amounts of remifentanil to maintain mean blood pressure at the desired level, possibly due to the suggested hypotensive effects of desmopressin.[11] Another limitation is that we did not address the severity of the sinus disease in our patients. However, all patients in this survey were first-time candidates for two-sided FESS due to chronic sinusitis. In this study, we used a subjective scale to evaluate the quality of the surgical field, as well as the satisfaction of the surgical team. We believe that the latter measurement modalities even more accurately reflect the efficacy of hemostatic interventions, seeing that the direct objective of the anesthesia in FESS is to make a clean surgical field rather than reduce the blood loss. The inter- and intraobserver reliability of this measurement has been verified in multicenter standardized reliability analysis.[19]

In conclusion, our limited data suggest the efficacy of DDAVP to acquire a much drier surgical field in sinus surgery. Our experience suggests that the safety and benefit of DDAVP outweigh its risks. Thus, its routine use in otherwise healthy candidates of sinus surgery could be considered. Desmopressin may have the potential to prevent postoperative epistaxis in nasal and sinus surgeries without the need for packing or alternative maneuvers. This likely advantage should be investigated in further studies.

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Conflicts of interest

There are no conflicts of interest.

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