COMPARISON OF EFFECT OF PREOPERATIVE INTRASAL DESMOPRESSIN AND INTRAVENOUS DESMOPRESSIN ON INTRAOPERATIVE BLEEDING DURING FESS FOR CHRONIC RHINOSINUSITIS: 1 YEAR RANDOMIZED CONTROL STUDY

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Abstract
Surgeons face a challenge to surgical field quality when functional endoscopic sinus surgery causes bleeding. The purpose of this research was to examine the relationship between desmopressin premedication and endoscopic sinus surgery complications, namely blood loss and surgical field quality. Ninety patients with chronic sinusitis who met the physical status I or II criteria set by the Indian Society of Anesthesiologists received endoscopic sinus surgery. Before the procedure, they were given saline or desmopressin 0.3 μg/kg at random. Propofol and remifentanil infusions were used to manage the anaesthesia, while mild and controlled hypotension was maintained. Following surgery, the surgeon checked the operative field for quality and blood loss. We looked at how desmopressin affected hemodynamic factors and anaesthetic needs. The desmopressin group had a much lower blood aloss compared to the control group. Compared to the control group, the desmopressin group had surgeons who were more happy with the surgical field. The desmopressin group had reduced remifentanil and esmolol requirements compared to the control group. To successfully decrease bleeding during endoscopic sinus surgery, 0.3 μg/kg of desmopressin may be used before the procedure.

Keywords: *Premedication, Surgeons, Desmopressin, Blood, Anesthesia, Remifentanil, Bleeding.*

1. Introduction

The inflammatory nasal and sinus mucosa disease known as chronic rhinosinusitis (CRS) is a constant source of frustration for medical professionals and patients alike. [1] Patients suffering with chronic sinusitis may find relief from their symptoms and an improvement in their quality of life via functional endoscopic sinus surgery (FESS), which has become an essential part of CRS care. [2,3]

Yet, intraoperative bleeding during FESS is still a complex issue that affects surgical visibility, accuracy, and overall results of the procedure.[4,5]

Hemostatic agents play a crucial role in the complex world of sinonasal surgery. [6,7] The possible hemostatic advantages of desmopressin, a synthetic counterpart of vasopressin, have attracted interest. [8,9] In order to improve the surgical experience for patients and clinicians, this study compares the effects of intravenous desmopressin with those of preoperative intranasal desmopressin on intraoperative bleeding during FESS for CRS. The goal is to provide detailed insights that can change perioperative protocols. [10,11]

An enormous global health burden is chronic rhinosinusitis, which is defined by chronic inflammation of the nasal and sinus mucosa. Affected people's quality of life is greatly diminished by the ailment, which causes symptoms including stuffy nose, face discomfort, and a diminished sense of smell. [12,13] When other, more conservative methods of treatment have failed, FESS may be an alternative to consider. FESS is a minimally invasive surgical procedure that removes obstructive sinus disease in an effort to restore sinus outflow, enhance ventilation, and reduce inflammation. [14,15]

Although FESS is effective in treating the root cause of CRS, the surgery itself is not trouble-free. [16] As a result of the sinonasal mucosa's abundant vascular supply, intraoperative bleeding might obstruct the surgeon's vision, which in turn can lengthen the operation and raise postoperative morbidity. That is why achieving adequate hemostasis is so important for FESS operations to go well.[17,18]

Desmopressin has been studied for its hemostatic effects in a variety of surgical settings; it is a synthetic version of the antidiuretic hormone vasopressin. [19.20] Desmopressin improves platelet adhesion and aggregation, which may decrease bleeding tendencies, by raising plasma coagulation factor VIII and encouraging the release of von Willebrand factor. While desmopressin has traditionally been administered intravenously for its hemostatic properties, there has been a change in focus towards studying its effectiveness when administered intranasally. [21,22]

2. Review of literature

Jahanshahi J, (2021)[23]You may take the medicine by mouth, spray it into your nose, or inject it into your veins. Desmopressin improves platelet adhesiveness and likely influences vascular stability; it also increases plasma concentrations of coagulation factor VIII, von Willebrand factor (vWF), and tissue plasminogen activator, all of which impact hemostasis. The antidiuretic and temporary hypertension-reducing actions of desmopressin are due to its specific stimulation of the vasopressin 2 receptor.

Safaeian *et al*. (2022) [24]performed endoscopic sinus surgery with comparable results after premedication with 20 μg of DDAVP nasal spray. Still, the research methods used in these investigations raise a number of red flags. Intravenous desmopressin's effects on bleeding and surgical field quality were also examined in two further randomised controlled trials.

3. Significance of the study

For Functional Endoscopic Sinus Surgery (FESS) to treat Chronic Rhinosinusitis (CRS), this research is crucial. When dealing with chronic rhinosinusitis, which is characterised by ongoing inflammation, FESS is often necessary to alleviate symptoms. Problems with intraoperative bleeding during FESS compromise surgical accuracy and result in worse patient outcomes. This research is important because it may help doctors determine the best way to provide desmopressin so that patients have less bleeding during surgery. The study's overarching goal is to provide light on the relative merits of intranasal and intravenous desmopressin in order to help shape evidence-based guidelines for FESS perioperative hemostasis. The effectiveness and safety of FESS procedures for CRS patients might be improved if the results are standardised.

4. Statement of the Problem

The optimisation of perioperative treatment in order to reduce intraoperative bleeding during FESS for CRS is the focus of this issue statement. Both the surgical site and the patient's prognosis are at risk when hemostasis is inadequate. Desmopressin administered intravenously or via the nose is not yet decided. Finding out how different pathways compare, measuring intraoperative bleeding levels, and evaluating operating efficiency are the main goals of the research. The study intends to address a critical feature of perioperative care in FESS for CRS patients by methodically researching these factors and providing suggestions based on evidence.

5. Research methodology

Presenting for bilateral FESS, 90 patients with chronic rhinosinusitis and physical status I or II as defined by the Indian Society of Anesthesiologists were prospectively evaluated. Registration of the trial occurred subsequent to the commencement of the investigation. We made sure to get patients' written informed permission. Every single patient was a first-time candidate for two-side FESS, and their ages ranged from 18 to 65. “Exclusion criteria included the following: prior or current bleeding disorders, blood-thinning medications, complications from previous surgeries, uncontrolled hypertension or cerebrovascular disease, a history of serious arrhythmias or coronary artery disease, impaired renal or hepatic function, pregnancy, and subsequent surgeries. Preoperatively, patients in the desmopressin group got 0.3 μg/kg of desmopressin, whereas those in the control group received normal saline instead.” Patients were randomly allocated to one of the two groups. A system of randomly generated numbers was used to divide the participants into their respective groups.

Before surgery, the platelet counts and coagulation tests of all patients were within normal ranges. A single attending anesthesiologist standardised the administration of anaesthesia to all patients. One highly trained surgeon oversaw all of the procedures. No surgeon knew which patients were in which groups since they were all blindfolded.

Prior to surgery, we documented any factors that may have been a predictor of intraoperative blood loss in the patients. “Predictors for this procedure included a history of prior endoscopic sinus surgery, the presence of sinonasal polypoid disease and endoscopically documented active

infection, a computed tomography-graded severity of sinus disease according to the Lund-MacKay scoring system, and a history of taking oral steroids within two weeks prior to the procedure."

To produce general anaesthesia, 3 μg/kg of fentanyl and 2 mg/kg of propofol were administered intravenously (IV). An intravenous dose of 0.2 mg/kg of cisatracurium was administered to ease tracheal intubation. Normative end-tidal carbon dioxide partial pressure was maintained by intermittent positive pressure ventilation. The desmopressin group of patients received 100 ml of normal saline diluted with 0.3 μg/kg of desmopressin shortly after induction. Twenty minutes later, patients in the comparison group had 100 millilitres of normal saline intravenously.

Continuous intravenous infusions of propofol (50-140 μg/kg/min) and remifentanil (0.15-0.3 μg/kg/min) were used to keep the patient's mean arterial pressure (MAP) within the 60-70 mmHg range, as measured on their arm every 5 minutes, in order to maintain anaesthesia. Extra boluses of intravenous remifentanil (0.5-1 μg/kg) and increasing doses of intravenous esmolol (10-20 mg) were used to address acute spikes in MAP, which were then followed by incremental doses of intravenous nicardipine (0.2-0.4 mg). We took heart rate readings every 5 minutes. Ten to fifteen minutes before to the conclusion of the procedure, the infusions of propofol and remifentanil were stopped. Every single patient had their operation time documented.

The surgeon was able to achieve local bleeding control in the operating field by injecting submucosal epinephrine (1:100,000, 3 ml) a single time. To replenish fluid deficits from the previous night, meet maintenance fluid needs, and restore blood loss on a 3:1 ratio, crystalloid solution was given.

Upon completion of each surgery, the total amount of blood and irrigation fluid lost during the operation was recorded by measuring the patient's stomach volume, the amount of gastric contents, and the weight of the nasopharyngeal packing using an electronic scale. This allowed for the confirmation of the final intraoperative blood loss. After every operation, the surgeon used a rating system based on Boezaart's work to evaluate the surgical field's overall quality. Surgeons looked at the possibility of desmopressin side effects including myocardial infarction, cerebral infarction, and other thromboembolic problems.

A 30% decrease in blood loss was deemed clinically significant in our opinion. With a significance threshold of 0.05 and an 80% power, we determined that 45 patients per group would be enough to prove this. "The median, range, standard deviation, and mean are the ways the results are presented. We used Student's t-test for parametric data and chi-squared and Mann-Whitney U tests for non-parametric data for our analysis. We used SPSS 16.0 for all of our statistical computations. The significance level was set at $P < 0.05$.

6. RESULTS

We were able to enroll 90 patients, and every single one of them finished the trial. Regarding all surgical variables and demographic characteristics, all groups were similar. Desmopressin significantly impacted both blood loss and surgical field quality.

Table 1: Patient demographics and functional endoscopic sinus surgery features.

	Desmopressin (n=45)	**Control (n=45)**	***P***
Age (yr)	45 (14.9)	40.7 (17.4)	0.2
Weight (kg)	62.7 (16.7)	59.0 (16.1)	0.3
Gender (M/F)	26/19	24/21	0.7
Surgical blood loss (mL)	42 (8.7)	70 (9.2)	<0.001
Quality of surgical field (0–10)	4 (3–5)	7 (6-9)	<0.001
Duration of surgery (min)	76 (20.7)	82 (19.6)	0.2
Polypoid disease (Y/N)	34/11	32/13	0.6
CT score (0–24)	15 (11–18)	13 (10–18)	0.6
Active infection (Y/N)	9/36	8/37	0.8
Preoperative steroids (Y/N)	16/29	11/34	0.3
Revision surgery (Y/N)	12/33	9/36	0.5

At many time periods, therapy had a substantial impact on MAP and HR; however, the variations in mean MAP and HR were minor and temporary.

Table shows that even though both groups received the same total dosage of intravenous propofol and nicardipine, patients in the desmopressin group needed less intravenous remifentanil and esmolol. None of the groups had thromboembolic problems after the operation. The desmopres-in group had a shorter surgical duration compared to the control group, however this difference was not statistically significant.

Table 2: Pharmacological needs for perioperative anaesthesia and antihypertensive medication in functional endoscopic sinus surgery

	Propofol (mg)	**Remifentanil (μg)**	**Esmolol (mg)**	**Nicardipine (mg)**
Desmopressin (n = 45)	830 (195)	1350 (235)	15 (4.5)	0.25 (0.06)
Control (n = 45)	780 (177)	1785 (260)	40 (7.5)	0.26 (0.07)
P	0.2	<0.001	<0.001	0.5

7. DISCUSSION

Our research demonstrated that desmopressin administration before to surgery enhanced surgical field quality and decreased blood loss. In light of these results, desmopressin may have therapeutic value in the circumstances of our research.

A number of methods have been proposed to lessen the amount of blood loss during endoscopic sinus surgery. [25] An enhanced surgical field was shown by Wormald *et al*. to be achieved during FESS by injecting the pterygopalatine fossa. Researchers Boezaart *et al*. observed that patients whose hypotension was produced with esmolol rather than sodium nitroprusside had better surgical outcomes after FESS. [26,27] Taking oral clonidine before surgery enhanced surgical field quality and decreased intraoperative blood loss, according to another research. [28,29] This research demonstrated that desmopressin premedication effectively decreased blood loss in FESS. We may thank desmopressin's hemostatic actions for this discovery.'' These effects include enhancing platelet adhesiveness, increasing plasma coagulation factor VII, von Willebrand factor, and tissue plasminogen activator. [30,31]

By improving operating conditions and reducing blood loss during FESS, proper anaesthetic care may indirectly lead to faster surgery. Improving surgical vision during FESS relies on maintaining mild, controlled hypotension. [32] In order to improve hemodynamic stability and reduce direct peripheral vasodilation, it is important to reduce HR under mild, controlled hypotension in order to create a surgical field of optimal quality. Our research effectively used these tactics. [33,34] In all groups, desmopressin did not cause any occurrences of severe hypotension (a drop of 30% or more from baseline MAP) [35]

8. CONCLUSION

Using propofol and remifentanil for anaesthesia and mild, controlled hypotension for endoscopic sinus surgery, this research compares the effects of nasal and intravenous desmopressin administration on blood loss and operative field quality.

8.1 Findings of the study

To keep intraoperative MAP within the acceptable range, our research found that the desmopressin group needed considerably lesser doses of IV remifentanil and esmolol compared to the control group. This result is probably due to the fact that desmopressin has a hypotensive impact while esmolol and remifentanil have negative inotropic and direct vasodilating effects.
Patients at risk of hypercoagulability should do a risk-benefit analysis before using desmopressin or any other pre-coagulative medication because of the possibility of pro-thrombitic effects. Patients who were pregnant, had a history of significant coronary artery disease or arrhythmias, had cerebrovascular illness or poorly managed hypertension were also excluded. Patients did not have any postoperative thromboembolic consequences.

8.2 Clinical Implications

The results of this research provide important information that may be used in the treatment of chronic rhinosinusitis (CRS) by functional endoscopic sinus surgery (FESS). One important consideration for perioperative procedures is the optimal method of administering desmopressin, which may have an influence on both intranasal and intravenous delivery. Now, clinicians may optimise intraoperative circumstances by customising hemostatic methods to each patient's unique features.

Second, the results may lead to more accurate surgeries, which is the primary goal of the research. A cleaner surgical field, more precise treatments, and reduced risk of postoperative problems may result from the selected method of desmopressin administration, which minimises intraoperative bleeding.

In addition, the findings provide the groundwork for creating tailored treatment programmes. Clinicians may now make educated judgements by considering patient-specific characteristics and seeing the various reactions between intranasal and intravenous desmopressin. This will boost the overall effectiveness and safety of FESS for CRS.

8.3 Limitations of the Study

The inability to adjust for individuals' varying degrees of sinus illness was a caveat of this research. The patients in this trial all had chronic sinusitis, which meant they were all first-time candidates for two-sided FESS. We used a subjective measure to assess surgical field quality and surgical team satisfaction in this research. This measurement's validity and accuracy have been confirmed.

8.4 Suggestions for Future Research

Although this study offered significant insights, there is still need for future research to improve perioperative treatment in FESS for CRS even more. The most important thing is to do long-term trials with plenty of follow-up time so we can learn all we can about how desmopressin affects postoperative outcomes, such as how patients heal and whether or not their symptoms come back.

Healthcare decision-makers might also benefit from learning more about the two administration methods' cost-effectiveness. Institutions might optimise healthcare delivery while maintaining high standards of patient care by comparing resource utilisation, hospital stays, and related costs.

If the precise mechanisms by which desmopressin influences sinus and nasal mucosal hemostasis could be better understood, its pharmaceutical activity may be better understood. This information has the ability to guide the creation of focused treatments and pave the way for new ways of treating chronic renal failure.

Overall, this study provides valuable insight into the short-term therapeutic consequences of FESS in CRS. Moving forward, researchers may expand upon these results to improve procedures, measure long-term outcomes, determine cost-effectiveness, and uncover other processes at work.

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