Trauma Monthly 2024; 29(5): 1255-1261

10.30491/tm.2024.457307.1733

Trauma Monthly

Research Article

Evaluating Desmopressin Spray for Surgical Wound Drainage in Femoral Surgery Patients in Taleghani Hospital

Amir Mehrvar [1], Ahmadreza Ahmadi Abdashti [2], Akbar Ehsani [2], Samareh Heydari [3], Mohammad Kazem Emami Meybodi [4], Reza Zandi [5*]

[1] Assistant professor of Department of Orthopedics, Taleghani Hospital Research Development committee, Medical school, Shahid Beheshti University of medical sciences, Tehran, Iran.

[2] Resident of Orthopedic Surgery, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[3] Faculty of Medicine, Shahid Beheshti University of Medical Science, Tehran, Iran.

[4] Trauma Research Center, Clinical Sciences Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran.

[5] Associate professor of Musculoskeletal Injuries Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

*Corresponding Authors: Reza Zandi: Associate professor of Musculoskeletal Injuries Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran; Tel: (+98)2123031633; E-mail: reza.zandi@sbmu.ac.ir

Received 2023-04-06; **Accepted** 2024-08-24; **Online Published** 2024-10-29

Abstract

Introduction: Prolonged wound drainage (PWD) increases the risk of infection by compromising the skin barrier and promoting bacterial growth. Desmopressin, known for its hemostatic properties, has demonstrated the potential to reduce bleeding and accelerate wound healing in various surgical procedures.

Methods: In this study, 50 patients aged between 18 and 65 undergoing total joint arthroplasty and any femoral fractures were divided into intervention and control groups. Desmopressin spray with a daily dose of 80 micrograms for two days was prescribed for the intervention group. Wound discharge volume, hospitalization, and postoperative complications were compared between the two groups.

Results: There was a notable reduction (P=0.016) in discharge volume observed within both the control (14.4 ± 14.3 milliliters) and desmopressin-administered (6.5 ± 7.8 milliliters) groups on the second day postoperative. Also, discharge volume decreased significantly in both groups (p<0.001), and a significant discrepancy emerged in the efficacy of discharge reduction between the two groups (p<0.001). However, hospitalization was significantly (P=0.008) lower in the intervention group (3.64 ± 2.51 days) than in the control group (6.36 ± 3.1 days).

Conclusion: Patients receiving desmopressin exhibited significantly reduced discharge and shorter hospitalization periods than controls.

Keywords: Desmopressin, Prolonged Wound Drainage, Femoral Fractures, Total Joint Arthroplasty.

Introduction

Surgical site infections (SSI) are a significant complication in orthopedic surgeries, influenced by different factors such as patients' characteristics, surgical intervention, and perioperative care. These are associated with prolonged hospital stays, increased mortality, and scars. Despite multiple prevention strategies, including perioperative and postoperative approaches, the SSI rate in orthopedic surgery remains a problem [1].

PWD can create a pathway for pathogens to enter the wound and contaminate the organs by bypassing the skin's natural barrier. The risk of PWD is higher in patients with certain factors, including age, obesity, malnutrition, diabetes, anemia, inflammatory arthritis, smoking, and blood group O [2]. The first stage of wound healing is hemostasis. Any disruption to this stage can result in hematoma formation, a rich medium for

bacterial growth due to increased incision tension and decreased tissue perfusion [2,3].

Desmopressin, known as 1-deamino-8-D-argininevasopressin, is a lab-made version of L-arginine vasopressin. It has antidiuretic and anticoagulant properties that help increase the secretion of plasma factor 8 and von Willebrand factor (VWF). This makes it an effective treatment option for mild to moderate hemophilia, von Willebrand's disease, and other acquired platelet deficiencies [4]. As VWF is essential and crucial for platelet adhesion and aggregation at the site of endothelial damage, we thought of using these properties of desmopressin to help heal the surgical site faster and reduce the rate of SSI following it. Additionally, Desmopressin has been used to reduce intraoperative blood loss in patients without known coagulation disorders, especially during procedures like spine surgery, facial plastic surgery, open heart surgery, functional endoscopic sinus surgery (FESS), and septorhinoplasty [4]. One of the other benefits of desmopressin, which was significant before our study, is that it had been used as a pain reliever after orthopedic surgeries as an intranasal arginine vasopressor (AVP) [5].

Based on the background above, the administration of desmopressin may have a positive effect on the decrease in postoperative discharges. Hence, this study was performed to evaluate the impact of desmopressin administration on the reduction of postoperative wound discharges and the improvement of clinical outcomes in patients with traumatic femoral fractures, as well as total hip arthroplasties.

Methods

Design

The study was conducted in 2023 at the orthopedic ward at Taleghani Hospital in Tehran. It was carried out according to the Declaration of Helsinki of the World Medical Association.

Participants

The patients were enrolled on the Department of Orthopaedic Surgery waiting lists at Taleghani Hospital in Tehran, Iran. Eligible participants were patients aged between 18 and 65 undergoing total joint arthroplasty and any femoral fractures supposed to undergo surgery.

Exclusion criteria were applied to individuals meeting any of the following conditions:

1. Admission exceeding 3 days' post-injury
2. Presence of a pathological fracture
3. History of a prior fracture at the same hip
4. Concomitant extremity fractures
5. Patients with clear infectious discharge from the surgical site after 48 hours postoperative
6. Body mass index (BMI) below 18.5 kg/m2 or above 35 kg/m2
7. Abnormal vWF and factor 8 and electrolytes
8. Admission to the intensive care unit
9. Traumatic brain and spinal cord injuries
10. Abdominal organ injuries
11. Active malignancy
12. Malabsorption-related diseases

Interventions

All patients received the same preoperative and postoperative routine. At our referral surgery center, one surgical team performed all operations.

Patients were instructed to fast after midnight before the surgery. Additionally, patients were administered Cephazolin at a dose of 50 mg/kg intravenously within 30 to 60 minutes before the skin incision as a prophylactic approach against surgical site infections. To maintain cardiovascular stability during fasting, patients were prescribed a one-liter solution of dextrose (33.3%) and saline (0.3%). Postoperative medications were prescribed as follows: prophylactic antibiotics (1gr cefazolin every 6 hours) and 4000 units of subcutaneous low molecular weight heparin. The analgesics that were administered included acetaminophen, morphine, and pethidine.

For the first group, a desmopressin spray with a daily dose of 80 micrograms for two days was prescribed. The surgical site was only washed with normal saline for two days for the placebo group, the same as the first group. This dosage of desmopressin is higher than the usual dosage.

Following the start of the treatment, patients were examined daily regarding secretion from the wound site. The following indicators were evaluated:

1. The frequency of secretions at the wound site.
2. The type and nature of secretions, including serous secretions, bloody secretions, and infectious secretions.

3. The volume and intensity of secretions.

Patients were discharged from the hospital after controlling secretions, and sutures were removed two weeks after the operation. All patients were followed up one month after the operation while any evidence of infection was recorded.

Outcome

Wound discharge

The primary outcome was to measure the potential deceleration in wound discharge following desmopressin compared to the control group. A blind researcher monitored patients throughout their hospitalization. Assessments commenced on the first-day post-surgery (t1) and continued with scheduled multiple visits at the orthopedic ward each day. They were documented on day 2 (t2) and the day we decided to discharge the patient (t3). The volume of secretions was converted into milliliters based on the Gauze Visual Analogue [6].

Postop complication

The presence of complications was analyzed within a nine-month postoperative period.

- Delayed Union and Nonunion

The assessment of delayed union and fracture nonunion was conducted by two orthopedic surgeons at each postoperative visit, with confirmation based on the radiographic evidence of healing progression. Delay in union was defined as the inability to achieve a bony bridge after 6 months of injury incidence (7). Fracture nonunion was characterized by the failure of bone fragments to unite within 9 months of injury, with no signs of healing progression in the last three months (8). In this study, no instances of delayed union or nonunion were observed.

- Other Clinical Outcomes

During postoperative visits, participants were evaluated for any signs of fixation failure, the necessity for revision surgery, SSI, pressure ulcers, pulmonary infections, UTIs, and DVT.

None of these were identified as complications in our patient cohort

Hospitalization

Days the patient stays at the hospital after surgery. The days before surgery that passed to stabilize the patient were not calculated.

Sample size

Since this is the first trial that elaborates on wound discharge, we used articles in which bleeding alteration was evaluated. The sample size was calculated based on the primary outcome, assuming that desmopressin usage decreases the wound discharge rate based on a previous study's results. According to Safaeian et al. (4), to achieve a statistical power of 95 %, considering an alpha error equal to 0.05, the required sample size was 20 subjects in each group (i.e., a total of 40).

$$n_1 = n_2 = \frac{(S_1^{\,2} + S_2^{\,2})(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2}{(\overline{X}_1 - \overline{X}_2)^2}$$

Considering a dropout rate of 25%, the sample size was adjusted to a minimum of 25 participants in each group (i.e., a total of 50).

Statistical methods

Data analysis was performed using R-4.4.0. The Kolmogorov-Smirnov test was applied to assess the normality of the data distribution. Quantitative data were presented as mean ± standard deviation (SD). For qualitative data, results are summarized as frequency (percentage). Student's t-test was employed to compare two groups, while the repeated measures ANOVA test was utilized to examine the group-by-time interaction for the discharge alteration.

Results

In this investigation, which spanned a trial of 50 patients, half of the participants, precisely 25 individuals, were allocated to the control group, while the remaining 25 patients were administered desmopressin daily. Statistical analysis revealed no significant disparities between the two groups concerning age (p=0.71) and gender distribution (p=0.64) as mentioned in Table 1.

According to the findings of this study, a notable reduction in discharge volume was observed within both the control and desmopressin-administered groups throughout the study period. Remarkably, these reductions in discharges were statistically significant, irrespective of the intervention employed. However, upon closer examination of Table 2, a considerable

discrepancy emerged in the efficacy of discharge reduction between the two groups. Specifically, the process of mitigating discharge within the desmopressin group demonstrated superior efficacy to the control group, as evidenced by several metrics, including reduced gauze consumption and fewer days required to cease discharges.

Employing an independent T-test to compare discharge frequencies between the two groups across various days revealed a significant disparity, except on the initial day when the effects of desmopressin had not yet manifested.

Notably, the control group exhibited a longer discharge duration, extending to 10 days, whereas the desmopressin group demonstrated a shorter duration, with only one day of secretion recorded. The mean hospitalization is 6.36 ± 3.1 and 3.64 ± 2.51 for control and desmopressin, respectively.

Table 1: patient characteristics

Variables		Control (n = 25)	Desmopressin (Dose:80 microgram) (n = 25)	P value
Age (year)		35.8 ± 14.7	12.8 ± 2.42	0.711
Gender	Male	17 (77.3)	20 (71.4)	0.64
	Female	5 (22.7)	8 (28.6)	
Hospitalization (Day)		6.36 ± 3.1	3.64 ± 2.51	0.008*

Table 2: The results of bleeding after surgery in two groups

	Time 1	Time 2	Time 3	P-value	P-value
Control	20.9 ± 16.5	14.4 ± 14.3	4.95 ± 4.31	<0.001	<0.001
Desmopressin (Dose:80 microgram)	21.3 ± 17.3	6.5 ± 7.8	2.37 ± 3.54	<0.001	
P-value*	0.925	0.016	0.025		

Discussion

In this study, we evaluated the desmopressin spray's efficacy in reducing secretion after osteosynthesis of the femoral bone and hip arthroplasties. According to the analysis, we reported a good response and limited side effects.

Despite several aspects of surgical site infection(SSI) prevention strategies that have been studied, including screening and treatment of asymptomatic bacteriuria in patients undergoing total joint arthroplasty, MRSA screening, nasal decolonization, preoperative bathing, hair removal, glycemic control, preoperative antibiotics prophylaxis, surgical site skin preparation, perioperative oxygenation and maintaining average body temperature, SSI rate in orthopedic surgery and its consequences including increased hospital length of stay which for instance in joint arthroplasty causing more complications and readmission rates, morbidity and mortality rates and higher hospital costs, remain a significant problem [1,9,10]. Periprosthetic joint infection (PJI) is one of the most dreaded complications that can occur after total joint arthroplasty (TJA), which is an example of a successful orthopedic procedure. It often requires multiple revision surgeries, extended courses of systemic antibiotics, prolonged periods of immobility, and can cause psychological distress. Despite our best efforts to prevent PJI, its incidence has yet to decrease [10,11]. Several risk factors have been identified for PJI in TJA, including post-traumatic osteoarthritis (OA), previous metal work in the joint, glucocorticoid use for

more than ten days, chronic liver disease, alcohol consumption, intravenous drug use (IVDU), prolonged surgical time, wound drainage for more than ten days, subsequent surgeries, urinary and respiratory infections, poor glycemic control, and a BMI greater than 35 [11]. It is crucial to diagnose and treat PJI promptly, as failure to do so can lead to sepsis, a life-threatening condition that can result in mortality (12).

Prolonged PWD following total hip arthroplasty as an orthopedic surgery using implants is associated with an increase in the risk of SSI [13]. PWD, a strong predictor of infection after total joint arthroplasty, can be related to pharmacological factors (prophylaxis against deep venous thrombosis), surgical time, estimated blood loss during the surgery, and patient-specific factors like body mass index, smoking, anemia, urinary tract infection, hepatitis C, and more [2]. Patel et al. confirmed that each day of prolonged drainage was associated with a 29% increase in the risk of postoperative infection [13]. The primary aim of managing patients with PWD is to minimize the duration of wound healing by preventing the mentioned risk factors. However, the available prevention strategies in many cases failed to prevent PWD, and antibiotic treatment alone in orthopedic device-related infections is only recommended if the patient fulfills the following criteria: a short duration of clinical symptoms (less than 5-7 days), a stable device, uncompromised soft tissue with the absence of a sinus tract or abscess. So, as Richard Peter et al. demonstrated, PJI is the most common reason for TKA revision and the third most common cause of THA revision [11]. Since the known prevention methods in many cases failed to prevent PWD, we decided to use a simple desmopressin spray due to its mechanism of action in accelerating wound healing and reducing revision procedures and prolonged courses of antibiotics and, as a result, decreasing long-term effects immobility, recurrent hospital encounters, and significant economic damage [1,14].

The hemostatic effects of desmopressin, which include secretion of factor 8 and von Willebrand factor, increase in tissue plasminogen activator, and improvement of adhesiveness platelets, all of which are essential parts of the first stage in wound healing, led us to use it after osteosynthesis and arthroplasties of the femoral bone [4].

According to Safaeian et al., even a small dose of 0.1 micrograms of Desmopressin acetate (DDAVP) can be effective in some patients undergoing FESS (Functional Endoscopic Sinus Surgery). This drug provides a drier and better operative field and helps reduce ecchymosis and edema [4,14]. It can also reduce bleeding and the need for blood transfusion in patients who have received aspirin and those with platelet dysfunction before open heart surgeries [15]. For patients undergoing flap reconstruction of pelvic pressure sores in spinal cord injury and surgeries that involve more than 1000 milliliters of blood loss, like lumbar fusions, taking a single dose of desmopressin (0.3 micrograms/kg) results in a smaller decline in hemoglobin and hematocrit, decreased intraoperative blood loss, and reduced need for transfusion [16,17]. In the research of Kobrinsky et al., desmopressin reduced blood loss by 32.5% during the surgery of spinal fusion with Harrington rod instrumentation and reduced the duration of treatment with analgesic agents by 13.1% by decreasing bleeding in the surgical wound [18]. In the review article of Alloussi et al. 10-80mcg intranasal DDAVP, which was applied in studies that put the review on desmopressin treatment regimen in enuresis, a very steep dose-response curve can be assumed for DDAVP. Also, there were no significant differences in adverse effects rate for the dosage range of 10-80 mcg for intranasal application [19]. In the study of Steiner et al., sublingual desmopressin with dosages of 20, 40,80,160,240 or 320mcg has been used instead of intranasal spray in patients with chronic rhino sinusitis and allergic rhinitis and proved to be safe and well tolerated by all volunteers [20].

There are several limitations to this trial:

1. The single-center design affects the study's external validity; therefore, to get more reliable and generalizable evidence, future investigations should be carried out across multicenter.
2. While the sample size of 50 participants provides a high level of statistical confidence, more extensive studies are required before extrapolating general conclusions.
3. The relatively short duration of the intervention may have limited the outcomes, and a more extended intervention in the future may yield more substantial improvements and advantages for patients, particularly those who have undergone multiple traumatic events.

Conclusion

In conclusion study investigating the efficacy of desmopressin in reducing wound drainage following total joint arthroplasty and femoral fractures has yielded promising results. The administration of desmopressin spray, with a daily dose of 80 micrograms for two days, resulted in a notable reduction in wound discharge volume compared to the control group. This reduction was evident as early as the second day postoperative, underscoring the rapid onset of desmopressin's therapeutic effects. Importantly, patients receiving desmopressin demonstrated not only reduced wound discharge but also experienced shorter hospitalization periods compared to those in the control group. These findings suggest that desmopressin holds the potential as a valuable adjunctive therapy in promoting wound healing and mitigating postoperative complications in orthopedic surgical settings. Further studies with larger sample sizes and more extended follow-up periods are warranted to validate these findings and explore the broader implications of desmopressin in optimizing surgical outcomes and patient recovery.

Acknowledgments

None.

Conflict of Interest Disclosures

The authors have no competing interests to declare relevant to this article's content.

Funding Sources

None.

Authors' Contributions

All authors contributed to the study design, data interpretation, manuscript drafting, and critical revisions. They have all approved the final manuscript and agree to be accountable for the accuracy and integrity of the work.

Ethical Statement

The protocol confirmed by ethical committee by IR.SBMU.RETECH.REC.1403.053 code.

References

1. Tucci G, Romanini E, Zanoli G, Pavan L, Fantoni M, Venditti M. Prevention of surgical site infections in orthopaedic surgery: a synthesis of current recommendations. Eur Rev Med Pharmacol Sci. 2019 Apr;23(2 Suppl):224–39.

2. Almeida RP, Mokete L, Sikhauli N, Sekeitto AR, Pietrzak J. The draining surgical wound post total hip and knee arthroplasty: what are my options? A narrative review. EFORT Open Rev [Internet]. 2021 Oct 19 [cited 2024 Apr 16];6(10):872–80. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8559557/

3. Zeng W, Zhou K, Zhou Z, Shen B, Yang J, Kang P, et al. Comparison between Drainage and Non-drainage after Total Hip Arthroplasty in Chinese Subjects. Orthop Surg [Internet]. 2014 Feb 25 [cited 2024 Apr 16];6(1):28–32. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6583141/

4. Safaeian R, Hassani V, Ghandi A, Mohseni M. Desmopressin nasal spray reduces blood loss and improves the quality of the surgical field during functional endoscopic sinus surgery. J Anaesthesiol Clin Pharmacol [Internet]. 2021 [cited 2023 May 20];37(2):261–5. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8289654/

5. Yang FJ, Ma L, Yang J, Zhu ZL, Wang CH. Intranasal Vasopressin Relieves Orthopedic Pain After Surgery. Pain Manag Nurs. 2019 Apr;20(2):126–32.

6. Ali Algadiem E, Aleisa AA, Alsubaie HI, Buhlaiqah NR, Algadeeb JB, Alsneini HA. Blood Loss Estimation Using Gauze Visual Analogue. Trauma Mon [Internet]. 2016 May 3 [cited 2024 Apr 16];21(2):e34131. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5003499/

7. Said GZ, Farouk O, Said HGZ. Delayed union of multifragmentary diaphyseal fractures after bridge-plate fixation. Int Orthop. 2009 Apr;33(2):549–53.

8. Nicholson JA, Makaram N, Simpson A, Keating JF. Fracture nonunion in long bones: A literature review of risk factors and surgical management. Injury. 2021 Jun;52 Suppl 2: S3–11.

9. Otero JE, Gholson JJ, Pugely AJ, Gao Y, Bedard NA, Callaghan JJ. Length of Hospitalization After Joint Arthroplasty: Does Early Discharge Affect Complications and Readmission Rates? J Arthroplasty. 2016 Dec;31(12):2714–25.

10. Frank RM, Cross MB, Della Valle CJ. Periprosthetic joint infection: modern aspects of prevention, diagnosis, and treatment. J Knee Surg. 2015 Apr;28(2):105–12.

11. Ahmed SS, Begum F, Kayani B, Haddad FS. Risk factors, diagnosis and management of prosthetic joint infection after total hip arthroplasty. Expert Rev Med Devices. 2019 Dec;16(12):1063–70.

12. Patel KM, Mears SC, Barnes CL, Stambough JB, Stronach BM. Sepsis and Total Joint Arthroplasty. Orthop Clin North Am. 2022 Jan;53(1):13–24.

13. Patel VP, Walsh M, Sehgal B, Preston C, DeWal H, Di Cesare PE. Factors associated with prolonged wound drainage after primary total hip and knee arthroplasty. JBJS. 2007;89(1):33–8.

14. Haddady-Abianeh S, Rajabpour AA, Sanatkarfar M, Farahvash MR, Khorasani G, Molaei H. The Hemostatic Effect of Desmopressin on Bleeding as a Nasal Spray in Open Septorhinoplasty. Aesthetic Plast Surg. 2019 Dec;43(6):1603–6.

15. Dilthey G, Dietrich W, Spannagl M, Richter JA. Influence of desmopressin acetate on homologous blood requirements in cardiac surgical patients pretreated with aspirin. J Cardiothorac Vasc Anesth. 1993 Aug;7(4):425–30.

16. Wingate GF, Lewis VL, Green D, Wiedrich TA, Koenig WJ. Desmopressin decreases operative blood loss in spinal cord injury patients having flap reconstruction of pelvic pressure sores. Plast Reconstr Surg. 1992 Feb;89(2):279–82.

17. Johnson RG, Murphy JM. The role of desmopressin in reducing blood loss during lumbar fusions. Surg Gynecol Obstet. 1990 Sep;171(3):223–6.

18. Kobrinsky NL, Letts RM, Patel LR, Israels ED, Monson RC, Schwetz N, et al. 1-Desamino-8-D-arginine vasopressin (desmopressin) decreases operative blood loss in patients having Harrington rod spinal fusion surgery. A randomized, double-blinded, controlled trial. Ann Intern Med. 1987 Oct;107(4):446–50.

19. Alloussi SH, Mьrtz G, Lang C, Madersbacher H, Strugala G, Seibold J, et al. Desmopressin treatment regimens in monosymptomatic and nonmonosymptomatic enuresis: A review from a clinical perspective. J Pediatr Urol. 2011 Feb;7(1):10–20.

20. Steiner IM, Kaehler ST, Sauermann R, Rinцsl H, Mьller M, Joukhadar C. Plasma pharmacokinetics of desmopressin following sublingual administration: an exploratory dose-escalation study in healthy male volunteers. Int J Clin Pharmacol Ther. 2006 Apr;44(4):172–9.