RESEARCH ARTICLE

A Comparison between Enoxaparin and Aspirin in Preventing Deep Vein Thrombosis after Spine Surgery: A Randomized Clinical Trial

Amir kavian, MD; Hamid Rezaee, MD; Seyedeh Fatemeh Darvari, MD; Hassan Mehrad-Majd, PhD; Hossein Mashhadinejad, MD

Research performed at Shahid Kamyab Hospital, Mashhad, Iran

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Abstract

Objectives: Deep Vein Thrombosis (DVT) is a significant medical concern characterized by the formation of blood clots within the venous system. Surgical procedures are known to increase the risk of DVT. While enoxaparin has proven to be highly effective in treating DVT, concerns about bleeding and accurate dosage regulation may restrict its application. Recent research has focused on aspirin's potential in preventing DVT after various surgeries. This study aimed to determine whether aspirin was as effective as enoxaparin in preventing DVT after spine surgery.

Methods: This randomized controlled trial enrolled study patients who underwent spine surgery at Shahid Kamyab Emergency Hospital in Mashhad, and had a Caprini score > 5, indicating a higher risk of DVT. In the control group, patients received subcutaneous injections of enoxaparin at a dosage of 40 mg, while the intervention group received oral aspirin tablets with a daily dosage of 81 mg. An experienced radiologist performed a Doppler ultrasound of the lower limbs' veins seven days after surgery to diagnose DVT. The outcomes of the two groups were then compared.

Results: A total of 100 patients participated in the clinical trial and were equally assigned to the aspirin and enoxaparin groups. Both groups were homogeneous regarding the basic and clinical characteristics. The incidence of postoperative DVT was 4.0% in the aspirin group and 10.0% in the enoxaparin group (p=0.092). The incidence of hemorrhage was 2.0% in the aspirin group and 4.0% in the enoxaparin group (p=0.610).

Conclusion: These findings indicate that aspirin may be a promising alternative to enoxaparin for DVT prevention after surgery, but additional research is essential to validate these results and further assess the benefits and risks associated with aspirin usage in this context.

Level of evidence: II

Keywords: Aspirin, Deep vein thrombosis, Enoxaparin, Prophylaxis, Spine surgery

Introduction

Deep Vein Thrombosis (DVT) and subsequent risk of pulmonary embolism are frequently observed complications in patients who have undergone spinal cord injury or spinal surgeries.[1] DVT is particularly prevalent in neurosurgical procedures and can result in considerable morbidity and mortality rates in spinal surgeries.[2,3] It is widely recognized that venous thromboembolic events (VTE) are preventable occurrences in spinal surgeries, with their presence significantly affecting morbidity and mortality rates.[4-8] Hence, it is recommended to implement preventive strategies, including mechanical and pharmacological methods.[9,10]

In studies conducted on orthopedic surgeries such as total hip and knee replacements, a comparison was made between aspirin and rivaroxaban for DVT prevention. In most cases, both aspirin and rivaroxaban were found to have similar efficacy in preventing DVT. However, aspirin

Corresponding Author: Hossein Mashhadinejad, Department of Neurosurgery, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. **Email:**mashhadinejadh@mums.ac.ir / Hassan Mehrad-Majd, Orthopedic Research Center, Mashhad University of Medical Sciences, Mashhad, Iran; Clinical Research Development Unit, Ghaem Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. **Email:** Mehradmajd.h@gmail.com; Mehradmajdh@mums.ac.ir

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was associated with fewer incidences of surgical site bleeding and was more cost-effective for patients compared to rivaroxaban.[11-13] According to the findings of a meta-analysis conducted in 2019 aspirin exhibited a lower efficacy in preventing DVT compared to rivaroxaban in hip joint replacement surgery. However, rivaroxaban had a higher incidence of hemorrhagic complications.[14] The advantage of prescribing aspirin is that it is significantly less expensive for patients, it can be taken orally, it is easily accessible, and patients are likely to comply with the treatment without the need for routine laboratory monitoring, unlike enoxaparin.[13]

Currently, there are no comprehensive studies specifically comparing aspirin with other anticoagulants, including enoxaparin, in spinal surgeries. Given the high prevalence and complications associated with DVT, as well as the lower cost of aspirin compared to other medications, it is necessary to conduct a study comparing the effectiveness of aspirin with other anticoagulants. If positive results are obtained, the use of aspirin could have more advantages for patients due to its lower cost, oral administration, and higher compliance.

Materials and Methods

Study design and patients' selection

This randomized controlled parallel arm trial study was conducted to investigate the efficacy of aspirin compared to enoxaparin as a prophylactic drug in a parallel randomized controlled trial. The study included 100 patients aged 18 to 70 who were undergoing spinal cord surgery at Shahid Kamyab Emergency Hospital in Mashhad between February 2023 and July 2023. The inclusion criteria were patients with a Caprini score greater than 5 for the occurrence of DVT. Patients who did not have follow-up visits and ultrasonography did not receive DVT prophylaxis medications, had a history of DVT or pulmonary embolism, had bleeding or hematoma requiring intervention at the surgical site, or had no willingness to participate were excluded from the study. Informed consent was obtained from the patients.

A Consort diagram depicting the flow of participant recruitment and intervention is presented in [Figure 1]. All 100 eligible patients were randomly assigned to either the control group (n=50) or the intervention group (n=50) using a computerized random sequence and random drawing of sealed, opaque envelopes. The control group received subcutaneous injections of enoxaparin with a dose of 40 mg for DVT prevention, while the intervention group received oral tablets of aspirin with a dose of 81 mg per day. The drugs were administered starting 24 hours after the surgical procedure and continued for 7 days. The consumption of the prescribed medication and the occurrence of side effects were monitored by the researcher for inpatients and by trained first-degree relatives for discharged patients. The prescribed drugs were sourced from the same brand for all patients. Doppler color ultrasonography of the lower limbs' veins was performed by an experienced radiologist 7 days after the surgery and following the medication intake to diagnose DVT. Thromboembolic stockings were prescribed for all patients to prevent confounding effects. All participants were aware of their assigned intervention during the trial, but the observer remained blinded when examining the outcomes. In addition, patients were instructed before each visit not to discuss the type of medications they had received with the observer.

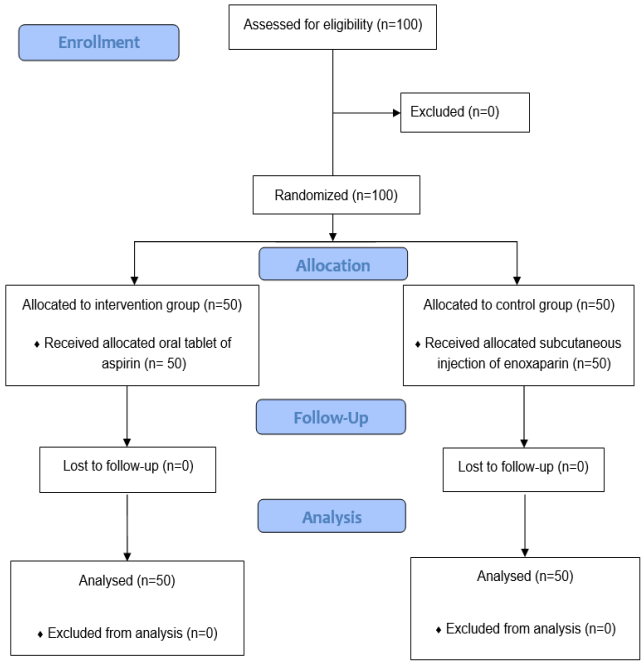

Figure 1. CONSORT diagram showing the flow of participant recruitment and intervention

Ethical considerations were taken into account by providing simplified and comprehensible informed consent forms, ensuring patient information confidentiality, and obtaining ethical approval from the Ethics Committee of the Mashhad University of Medical Sciences with the code of IR.MUMS.MEDICAL.REC.1401.515. The trial was registered in the Iranian Registry of Clinical Trials under the clinical trial code IRCT20221014056171N1. Patient information was kept and was not shared with anyone other than the primary investigator.

Outcome measures

The primary outcomes for this study were the occurrence of DVT and hemorrhage events using Doppler color ultrasonography within 7 days after surgery.

Statistical Analysis

The sample size was determined based on a previous clinical trial that compared major bleeding in patients who underwent hip or knee arthroplasty and were treated with either rivaroxaban or aspirin.[11] To ensure a power of 90% and type I error rate of 0.05, a minimum of 45 patients per group was calculated. To account for potential dropouts, the number of patients in each group was increased to 50. The normal distribution of the data was assessed using the Kolmogorov-Smirnov test. For parametric data, the mean and standard deviation values were calculated. For non-

parametric data, the median and interquartile range (IQR) were reported. The Mann-Whitney U test was employed for continuous non-parametric variables. The qualitative data were compared using the Chi-squared test (if needed Fisher exact-test). The Relative Risk (RR) was calculated with 95% confidence intervals (95% CI) to assess the risk difference between the two groups. A P-value less than 0.05 was considered statistically significant. The statistical analysis was carried out using SPSS software (version 26 for Windows. SPSS, Chicago, IL, USA).

Results

The demographic and clinical characteristics of the 100 patients who completed the trial are presented in [Table 1]. The mean age of the patients was 42.0±16.47 years. Regarding baseline clinical characteristics, the two groups were homogenous for various variables. The only variable with uneven distribution between the treatment groups was the frequency of underlying comorbidities (p=0.043). Since cardiovascular patients were only present in the enoxaparin group, the association between underlying comorbidities and the occurrence of deep vein thrombosis was adjusted and found to be independent (p=0.232). Therefore, the treatment groups were homogeneous for the comparison of the outcomes of interest.

Table1. Comparison of demographic and clinical characteristics of study participants between treatment groups

Variables		Enoxaparin group N=50	Aspirin group N=50	P-value
Age		39.48±18.02	44.5±14.51	0.128
BMI		25.42±2.41	25.87±2.38	0.357
Duration of surgery (hours)		4.16±1.05	4.24±0.89	0.683
Bleeding during surgery (ml)		449.0±183.9	417±141.3	0.332
Caprini score		12.3±2.70	11.96±3.67	0.599
Gender (%)	***Female***	18 (36.0)	14 (28.0)	0.391
	Male	32 (64.0)	36 (72.0)	
Comorbidities (%)	***No***	34 (68.0)	36 (72.0)	0.043
	Cardiovascular	6 (12.0)	0	
	Metabolic and others	9 (18.0)	14 (28.0)	
Detection mechanism (%)	***Traumatic***	40 (80.0)	38 (76.0)	0.582
	Degenerative/pathologic	10 (20.0)	12 (24.0)	
Neurological defect (%)	***Normal***	30 (60.0)	34 (68.0)	0.534
	paralysis	17 (34.0)	12 (24.0)	
	Plegia	3 (6.0)	4 (8.0)	
Surgical approach (%)	***Posterior***	42 (84.0)	40 (80.0)	0.603
	Anterior	8 (16.0)	10 (20.0)	
Place of taking medicine (%)	***In hospital***	29 (58.0)	21 (42.0)	0.110
	Out of hospital	21 (42.0)	29 (58.0)	

The effect of aspirin and enoxaparin prophylaxes on the incidence of postoperative DVT and hemorrhage events is depicted in [Figure 2]. The results revealed a higher incidence of DVT and hemorrhage events in the group receiving enoxaparin as compared to the aspirin group, although these differences were not statistically significant (p=0.092 and p=0.610, respectively).

To measure the effect size of the impact of different treatments on the outcomes, we calculated the relative risk with a 95% CI. The results showed a slightly elevated, yet statistically not significant, risk for the enoxaparin group when compared to the aspirin group (RR=1.09, 95%CI: 0.98-preventing DVT and potentially pulmonary embolism following spine surgery. However, additional research is necessary to confirm these findings and investigate the potential advantages of aspirin as a more accessible and 1.20 for DVT, and RR=1.02, 95%CI: 0.95-1.09 for hemorrhage events).

Discussion

The current study examined the protective effects of aspirin and enoxaparin prophylaxis on the incidence of postoperative DVT and hemorrhage events. While aspirin demonstrated a lower incidence of DVT and hemorrhage compared to enoxaparin, these differences were not statistically significant. These initial results indicate that aspirin could potentially be as efficacious as enoxaparin in cost-effective alternative to enoxaparin.

In a study conducted by Anderson et al., it was concluded that there was no significant difference in the prevention of DVT between aspirin and rivaroxaban in

patients undergoing hip replacement surgery.[11] Similar results were also reported by Azboy et al.[13] Our study similarly demonstrates that there is no significant difference in the prevention of DVT between aspirin and enoxaparin.

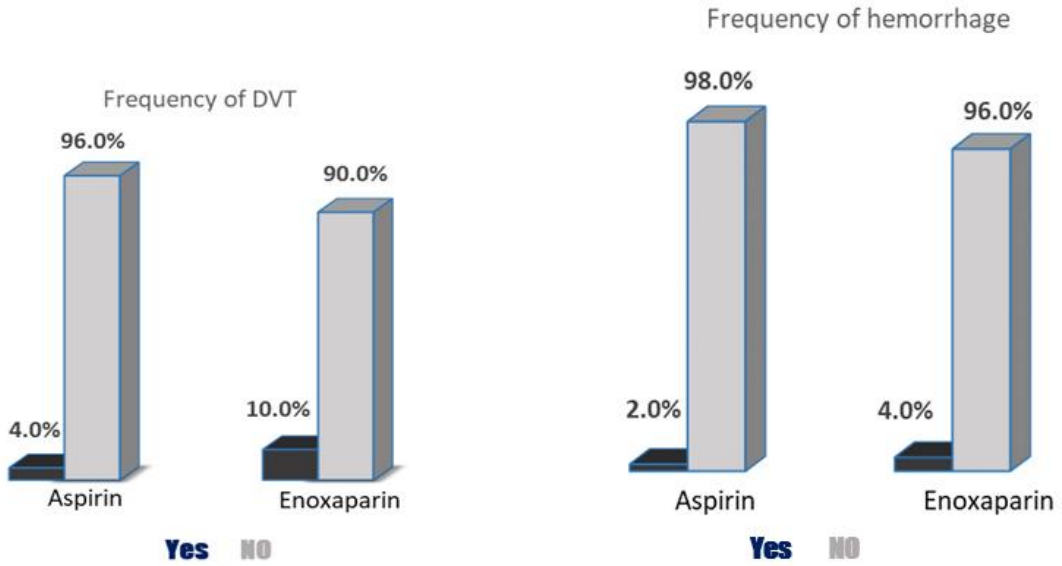

Figure 2. Comparison of the frequencies of DVT and hemorrhage events after surgery between treatment groups

In a meta-analysis conducted by Kohli et al., which included six studies comparing the effects of aspirin and rivaroxaban in preventing postoperative DVT after hip replacement surgery, they found that aspirin had a lower efficacy in preventing DVT compared to rivaroxaban. However, rivaroxaban was associated with more hemorrhagic complications. [14] In our study, there was no statistically significant difference between the treatment groups (enoxaparin or aspirin) for the outcomes under investigation.

In the study of Arti et al., the incidence of DVT after hip joint replacement surgery was reduced with the administration of enoxaparin for 20 days compared to heparin. Additionally, extending the administration of enoxaparin for 20 days compared to 10 days reduced the incidence of postoperative pulmonary embolism. However, there was no significant difference between heparin and enoxaparin in reducing the incidence of pulmonary embolism and postoperative mortality. Therefore, the study concluded that enoxaparin demonstrated superior efficacy over heparin in preventing venous thromboembolism and pulmonary embolism.[15] However, in our study, neither enoxaparin nor aspirin had a significant effect on the outcomes under investigation.

The study conducted by Michot et al. showed that the duration, type, and technique of surgery did not significantly affect the results. They found that DVT risk was notably higher in patients over the age of 53 and in female patients with an overall incidence of DVT in their study of 40%, indicating the necessity for prophylactic measures for criteria to calculate the risk of DVT. However, it is important to note that the drugs used in our study may potentially lead to bleeding complications in other areas of the body, although this aspect was not specifically explored. Therefore, it is strongly recommended that future studies incorporate a larger group of patients undergoing DVT.[16] In our study, the incidence of DVT was much lower. The incidence of postoperative DVT in the aspirin group was 3.8%, and in the enoxaparin group, it was 10.2%. Contrary to their findings, our study did not find any statistically significant difference in age and gender, as well as variables such as the duration, type, and technique of surgery, regarding the results.

A study conducted by Vulcano et al. revealed the significant benefits of DVT prophylaxis with aspirin in low-risk patients undergoing hip and knee arthroplasty.[17] In our research, we also observed the effectiveness of aspirin in reducing the incidence of post-surgery thrombotic events and hemorrhagic complications, with lower rates in the aspirin group compared to the enoxaparin group, albeit without statistical significance.

Given that DVT and its potentially fatal complication, pulmonary embolism, are prevalent among postoperative complications, there is a strong emphasis on the need for postoperative thromboprophylaxis. Currently, enoxaparin is the standard for DVT prevention following surgery.[18] However, due to aspirin's affordability, lower bleeding risk, and simplified dosage administration, surgeons increasingly prefer using aspirin for preventing deep vein thrombosis.[19] Considering the high prevalence and risks associated with thromboembolic events, conducting further detailed studies in this field is imperative.

One of the strengths of our study is that it focused on patients with spine problems and utilized the Caprini

preventive interventions, with varying consequences, to obtain more precise results regarding the optimal prevention method with minimal complications. Additionally, it would be advisable to implement longer follow-up periods for patients to compare the occurrence of delayed complications between the two groups.

Conclusion

In general, these findings suggest that aspirin may be as effective as enoxaparin in preventing DVT and possibly pulmonary embolism after spine surgery. Although the difference in DVT incidence between the two groups was not statistically significant, the lower incidence in the aspirin group is promising. The potential benefits of aspirin as a more accessible and cost-effective alternative to enoxaparin warrant further exploration. Further studies are needed to confirm these preliminary findings and fully understand the advantages and drawbacks of aspirin usage in this context.

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Authors Contribution:

Study concept and design: Mashhadinejad H. and Rezaee H.
Acquisition of the data: Kavian A. and Darvari SF.
Statistical analysis: Mehrad-Majd H.
Drafting of the manuscript: Kavian A. and Mehrad-Majd H.
Study supervision: Mashhadinejad H.

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Amir Kavian MD [1]

Hamid Rezaee MD [1]

Seyedeh Fatemeh Darvari MD [2]

Hassan Mehrad-Majd PhD [3,4]

Hossein Mashhadinejad MD [1]

1 Department of Neurosurgery, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

2 Department of Radiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

3 Orthopedic Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

4 Clinical Research Development Unit, Ghaem Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

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