



OPEN ACCESS



VENOUS THROMBOEMBOLISM WITH THE USE OF ASPIRIN VERSUS ENOXAPARIN AS PROPHYLACTIC AGENTS AFTER HIP ARTHROPLASTY

Department of Trauma & Orthopedics, Lady Reading Hospital, Peshawar - Pakistan

Address for correspondence:

Syed Imran Bukhari
Department of Trauma & Orthopedics, Lady Reading Hospital, Peshawar - Pakistan

E-mail:

syedimran78@outlook.com

Date Received:

20th August, 2022

Date Revised:

2nd March, 2023

Date Accepted:

3rd March, 2023

Syed Imran Bukhari[✉], Muhammad Basir Khan, Asif Zahir, Sajjad Alam, Farhad Ullah

ABSTRACT

Objective: To assess how often venous thromboembolism (VTE) occurs in patients on low dosage aspirin versus enoxaparin for VTE prevention after hip arthroplasty.

Methodology: This quasi-randomized controlled trial was conducted at the Department of Trauma & Orthopedics, Lady Reading Hospital, Peshawar. The study was conducted over a period of 6 months. Lottery method was used to collect data and the patients were divided into two groups. The chi-square test was used to compare the frequency of VTE between groups. Effect modifiers such as age, gender, and BMI were managed through stratification. The post-stratification chi-square test was used to determine whether there is a relationship between these impact modifiers and study results. P-value 0.05 was used to define a significant difference.

Results: A total of 74 patients undergoing total/partial hip arthroplasty in orthopedics surgery were observed, which were divided in two equal groups. Patients in Group A were managed by aspirin (75mg/day) and Group B patients received enoxaparin (0.5mg/kg). Group A had 2(5.4%) patients with VTE in follow-up and 35(94.6%) patients had observed no VTE. Group B had VTE in 4(10.8%) patients and no VTE in 33(89.2%) patients which shows that VTE was high in group B as compared to group A. The difference was insignificant with p-value=0.337. Incidence of VTE was seen to be higher in patients aged more than 50 years.

Conclusion: The difference in incidence of VTE after hip arthroplasty with use of either Aspirin or Enoxaparin as prophylactic agents was statistically insignificant.

Keywords: Venous thromboembolism; Aspirin; Enoxaparin

INTRODUCTION

Total and partial hip arthroplasty are both major orthopaedic procedures. Deep vein thrombosis (DVT), pulmonary embolism, and other types of venous thromboembolism (VTE) are all regarded to have a high chance of developing after these treatments, according to the American College of Chest Physicians (ACCP) (PE).¹ PE is regarded as a major cause of death following major orthopaedic surgery. There were no recommendations for the best prophylactic until recently.^{2,3} Given the increased prevalence of VTE, the Scottish Intercollegiate Guidelines Network and the National Institute for Health and Clinical Excellence (NICE) recommend using low molecular weight heparin (LMWH) such as enoxaparin as a preferred treatment for thrombosis prevention.^{4,5} Aspirin (acetylsalicylic acid) use for VTE prophylaxis until recently, is supported only in observational and registry studies.⁶⁻⁸ According to a study, aspirin has a relative risk of VTE after total hip and total knee replacement of 1.12 (95% CI, 0.78-1.62) when

compared to other anticoagulants. The review's evidence quality ranged from low to high.⁹ Another study compared aspirin with rivaroxaban for VTE prophylaxis after hip or knee Arthroplasty and reported VTE rate of 0.64% in aspirin and 0.70% in rivaroxaban group.¹⁰ There are very few studies on direct comparison of aspirin with enoxaparin for VTE prophylaxis in patients undergoing major orthopedic procedures involving the lower limb. A study compared aspirin with enoxaparin for VTE prophylaxis and reported VTE rate of 1.04% in aspirin and 1.04% in enoxaparin groups in patients undergoing major lower limb (knee/hip replacement) orthopedic procedures.¹¹ Another study reported that aspirin is superior to enoxaparin for VTE prophylaxis; they reported VTE in 16.7% patients in enoxaparin group versus in only 5.2% patients in aspirin group.¹² In contrast, a study comparing the efficacy of enoxaparin, aspirin, and continuous enhanced circulation treatment (CECT) combined with aspirin to prevent deep vein thrombosis in joint arthroplasties discovered that the DVT rate in the CECT combined with aspirin

This article may be cited as

Bukhari SI, Khan BM, Zahir A, Alam S, Ullah F. Venous thromboembolism with the use of aspirin versus enoxaparin as prophylactic agents after hip arthroplasty. *J Postgrad Med Inst* 2023;37(1): 64-68. <http://doi.org/10.54079/jpmi.37.1.3151>

group was 6.6% and 28.3% in the enoxaparin group.¹³ The aim of the present study is to address the deficiency in previous literature by comparing the frequency of VTE in patients undergoing hip arthroplasty and receiving either aspirin or enoxaparin post operatively for VTE prophylaxis. The study results will help us to decide whether aspirin can be used as an alternative to enoxaparin for VTE prophylaxis.

METHODOLOGY

This quasi-randomized clinical trial was conducted at the Department of Trauma and Orthopedics, Lady Reading Hospital, Peshawar. The study aimed to determine whether aspirin is superior to enoxaparin in preventing VTE in patients undergoing hip arthroplasty. The WHO sample size calculator was used to determine the sample size, based on the following parameters: 80% power of the test, 5% level of significance, p1 (estimated frequency of DVT in patients receiving aspirin) = 6.6%, p2 (estimated frequency of DVT in patients receiving enoxaparin) = 28.3%. The estimated sample size was 74 patients (37 in the aspirin group and 37 in the enoxaparin group). The study's inclusion criteria comprised all patients undergoing total hip arthroplasty (cemented and non-cemented) or hemiarthroplasty, both male and female, aged 18-70 years. Exclusion criteria included patients undergoing bilateral procedures, hypersensitivity to either LMWH or aspirin, long-term anticoagulation therapy, unfit for surgery (ASA III and above), family unwilling to give informed consent, and revision hip arthroplasty. After obtaining approval from the ethical review, 74 patients who met the study's inclusion criteria underwent hip arthroplasty at the Department of Trauma & Orthopedics, Lady Reading Hospital, Peshawar. All patients provided written informed consent before enrolling in the trial. Patient data, including age, gender, body mass index (BMI), and smoking history, were recorded.

The 74 patients were randomly divided into two equal groups using a lottery method. Non-transparent envelopes containing treatment options were placed in a jar, and a staff nurse on duty was asked to pick one envelope for each patient. Group I received aspirin 75 mg/day once daily for 14 days after hip arthroplasty at discharge, while Group II received enoxaparin 0.5mg/kg for 14 days after hip arthroplasty at discharge. Doppler ultrasound studies were conducted at two weeks by a radiologist to determine the rate of VTE. VTE was diagnosed if venous pulses disappeared, or clots were present in lower limb veins on Doppler studies. All gathered information was noted on a pre-designed proforma. SPSS v25 was used for data analysis. Quantitative values such as age, height, weight, and BMI were depicted using mean and standard deviation. Qualitative characteristics, including gender, smoking, and VTE, were displayed using frequency and percentage. The frequency of VTE was compared between the groups using the chi-square test. Age, gender, and BMI were managed as effect modifiers by stratification. The post-stratification chi-square test was used to determine if there was any correlation between these impact modifiers and study results. A difference was considered significant if the P-value was 0.05 or lower.

RESULTS

A total of 74 individuals underwent complete or partial hip arthroplasty; they were all observed. The patients were split into two equally sized groups. Patients in Group A were managed with aspirin (75mg/day) and Group B patients received enoxaparin

(0.5mg/kg). Gender wise distribution showed that 14(37.8%) were male and 23(62.2%) were female in Group A (0.6:1) while Group B had 17(45.9%) male and 20(54.1%) female (0.85:1). Overall Male to female ratio was 0.72:1. Gender distribution among the groups was insignificant with p-value=0.480 showing that gender distribution was equal in both the groups (Table 1). The average age was 48.4 years±12.72SD in Group A While Group B had an average age of 50.7 years ±10.8SD. The overall average age of the patients was 49.6 years ±11.8SD. The age distribution among the group was also insignificant with p-value 0.746 (Table 2). Group A had 2(5.4%) patients with VTE in follow-up and 35(94.6%) patients had no observed VTE. Group B had VTE in 4(10.8%) patients and no VTE in 33(89.2%). The difference was insignificant with p-value=0.337 (Table 1) Incidence of VTE was seen to be higher in patients aged more than 50 years. The effect of interventions on incidence of VTE was insignificant when stratified according to age (Table 2). There was an insignificant difference in incidence of VTE among the groups, when stratified on the basis of gender, BMI, and smoking (Table 3).

DISCUSSION

The findings of this study show that the incidence of DVT did not statistically differ when either aspirin or enoxaparin were used as preventative medications. This study partially supports our hypothesis, but further research is needed to address it. Aspirin and enoxaparin did not significantly lower overall VTE rates in a recent meta-analysis of 1507 patients having elective lower limb arthro-

Table 1: Venous thromboembolism wise distribution in both the groups

Variables		Group A	Group B	Total
Venous Thromboembolism	Yes	2	4	6
		5.4%	10.8%	8.1%
	No	35	33	68
		94.6%	89.2%	91.9%

Table 2: Age Wise distribution of venous thromboembolism in both the groups

Variables		Group A (Venous Thromboembolism)		Group B (Venous Thromboembolism)		Total
		Yes	No	Yes	No	
Age (in years)	<= 30.00	0	3	0	1	0.500
		.0%	100.0%	.0%	100.0%	
	31 - 40	0	9	0	8	0.500
		.0%	100.0%	.0%	100.0%	
	41 - 50	0	7	1	7	0.533
		.0%	100.0%	12.5%	87.5%	
	51 +	2	16	3	17	0.552
		11.1%	88.9%	15.0%	85.0%	

Table 3: Gender, BMI (kg/m) and smoking wise distribution of venous thromboembolism in both the groups

Variables		Group A (Venous Thromboembolism)		Group B (Venous Thromboembolism)		p-value
		Yes	No	Yes	No	
Gender	Male	2	12	1	16	0.425
		14.3%	85.7%	5.9%	94.1%	
	Female	0	23	3	17	0.092
		.0%	100.0%	15.0%	85.0%	
BMI (kg/m)	<25 Kg/m	0	16	1	13	0.467
		.0%	100.0%	7.1%	92.9%	
	>25 Kg/m	2	19	3	20	0.545
		9.5%	90.5%	13.0%	87.0%	
Smoking	Yes	1	8	2	11	0.642
		11.1%	88.9%	15.4%	84.6%	
	No	1	27	3	21	0.441
		3.6%	96.4%	8.3%	91.7%	

plasty (RR, 0.84; 95% CI: 0.41 to 1.75; p = 0.65). The studies that were included in the analysis all had a high risk of bias, poor to negligible evidence for the primary outcomes, and moderate to negligible evidence for the secondary outcomes, nevertheless. Another meta-analysis discovered that aspirin's risk of VTE did not significantly differ from rivaroxaban or low-molecular-weight heparin (RR, 1.52; 95% CI, 0.56-4.12).¹⁶ The investigation's evidentiary quality ranged from low to good⁹. According to a recent excellent study published by the Major Extremity Trauma Research Consortium, low occurrences of deep vein thrombosis, pulmonary embolism, and 90-day mortality were shown to be associated with aspirin-based thromboprophylaxis, which was found to be non-inferior to low-molecular-weight heparin in preventing death (METRC).¹⁷ The use of aspirin as the

only approach of VTE prophylaxis in hip and knee arthroplasty and hip fracture surgery is still under discussion, according to Flevas et al.¹⁸ Despite a lack of recent research in this patient population, Muscatelli et al. recommend low-molecular-weight heparin after hip fracture surgery. They claimed that randomized studies are currently being conducted in arthroplasty patients to help clinicians decide whether chemoprophylaxis is best, and that these studies should inform changes to current clinical practice guidelines.¹⁹ Our findings are consistent with previous research.

Deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE), the two most significant and curable causes of morbidity and mortality following surgery, are often referred to as venous thromboembolism (VTE). According to estimates, there are 2 million

new cases of DVT annually, 600,000 people develop PTE, and 10,000 people pass away.¹ The incidence of VTE among hospitalised patients is 960.5 per 10,000 person-years, which is 100 times higher than the incidence among community residents¹⁴, according to Heit JA et al. According to Wasim M. et al., routine chemoprophylaxis is not a common practise in Pakistan because it is widely assumed that VTE is not a problem in this country. The researchers discovered that DVT is common in Pakistan and strongly recommended prevention for patients undergoing high-risk surgery.¹⁵ We compared the efficacy of LMWH versus aspirin in preventing VTE.

The limited sample size, quasi-randomized study design, and lack of consideration of the comorbidities in this

study are its limitations, which may have an impact on the findings.

CONCLUSION

The difference in the incidence of VTE after hip arthroplasty with use of either Aspirin or Enoxaparin as prophylactic agents were statistically insignificant.

REFERENCES

1. Falck-Ytter Y, Francis CW, Johanson NA, Curley C, Dahl OE, Schulman S, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e278S-e325S. DOI:10.1378/chest.11-2404.
2. Berstock JR, Beswick AD, Lopez-Lopez JA, Whitehouse MR, Blom AW. Mortality After Total Knee Arthroplasty: A Systematic Review of Incidence, Temporal Trends, and Risk Factors. *J Bone Joint Surg Am*. 2018;100(12):1064-70. DOI:10.2106/JBJS.17.00249.
3. Hofstede SN, Gademan MG, Vliet Vlieland TP, Nelissen RG, Marang-van de Mheen PJ. Preoperative predictors for outcomes after total hip replacement in patients with osteoarthritis: a systematic review. *BMC Musculoskelet Disord*. 2016;17:212. DOI:10.1186/s12891-016-1070-3.
4. Douketis JD. The 2016 American College of Chest Physicians treatment guidelines for venous thromboembolism: a review and critical appraisal. *Intern Emerg Med*. 2016 ;11(8):1031-35. DOI:10.1007/s11739-016-1553-0.
5. Afshari A, Fenger-Eriksen C, Monreal M, Verhamme P; ESA VTE Guidelines Task Force. European guidelines on perioperative venous thromboembolism prophylaxis: Mechanical prophylaxis. *Eur J Anaesthesiol*. 2018 Feb;35(2):112-115. DOI:10.1097/EJA.0000000000000726.
6. Holden DN, Maceira E. Thromboembolism prophylaxis failure rates after hip and knee arthroplasty: comparison of aspirin and anticoagulants. *Curr Orthop Pract*. 2015;26(3):277 –80.
7. Parvizi J, Huang R, Restrepo C, Chen AF, Austin MS, Hozack WJ, et al. Low-Dose Aspirin Is Effective Chemoprophylaxis Against Clinically Important Venous Thromboembolism Following Total Joint Arthroplasty: A Preliminary Analysis. *J Bone Joint Surg Am*. 2017 Jan 18;99(2):91-8. DOI:10.2106/JBJS.16.00147.
8. Azboy I, Groff H, Goswami K, Vahedian M, Parvizi J. Low-Dose Aspirin Is Adequate for Venous Thromboembolism Prevention Following Total Joint Arthroplasty: A Systematic Review. *J Arthroplasty*. 2020 Mar;35(3):886-92. DOI:10.1016/j.arth.2019.09.043.
9. Matharu GS, Kunutsor SK, Judge A, Blom AW, Whitehouse MR. Clinical Effectiveness and Safety of Aspirin for Venous Thromboembolism Prophylaxis After Total Hip and Knee Replacement: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Intern Med*. 2020;180(3):376-84. DOI:10.1001/jamainternmed.2019.6108.
10. Anderson DR, Dunbar M, Murnaghan J, Kahn SR, Gross P, Forsythe M, et al. Aspirin or rivaroxaban for VTE prophylaxis after hip or knee arthroplasty. *N Engl J Med*. 2018;378(8):699–707. DOI:10.1056/NEJMoa1712746.
11. Ni Cheallaigh S, Fleming A, Dahly D, Kehoe E, O'Byrne JM, McGrath B, et al. Aspirin compared to enoxaparin or rivaroxaban for thromboprophylaxis following hip and knee replacement. *Int J Clin Pharm*. 2020;42(3):853-60. DOI:10.1007/s11096-020-01032-1.
12. Alamiri MA, Albsoul Younes AM, Aljouni JMS. Comparison between aspirin 325 mg and enoxaparin 40 mg as extended thromboprophylactic agents following major orthopedic surgery in Jordan University Hospital. *Drugs Ther Perspect*. 2019;35(1):36–42. DOI:10.1007/s40267-018-0563-6
13. Gelfer Y, Tavor H, Oron A, Peer A, Halperin N, Robinson D. Deep vein thrombosis prevention in joint arthroplasties: continuous enhanced circulation therapy vs low molecular weight heparin. *J Arthroplasty*. 2006;21(2):206–14. DOI:10.1016/j.arth.2005.04.031
14. Heit JA, Melton LJ 3rd, Lohse CM, Petterson TM, Silverstein MD, Mohr DN, et al. Incidence of venous thromboembolism in hospitalized patients vs community residents. *Mayo Clin Proc*. 2001;76(11):1102-10. DOI:10.4065/76.11.1102.
15. Wasim M, Samie A, Fawad A. Role of routine use of thromboprophylaxis in patients undergoing major surgery. *Pak J Med Res*. 2005;44(1):4-11.
16. Farey JE, An VVG, Sidhu V, Karunaratne S, Harris IA. Aspirin versus enoxaparin for the initial prevention of venous thromboembolism following elective arthroplasty of the hip or knee: A systematic review and meta-analysis. *Orthop Traumatol Surg Res*. 2021;107(1):102606. DOI:10.1016/j.otsr.2020.04.002.
17. Major Extremity Trauma Research Consortium (METRC); O'Toole RV, Stein DM, O'Hara NN, Frey KP, Taylor TJ, et al. Aspirin or Low-Molecular-Weight Heparin for Thromboprophylaxis after a Fracture. *N Engl J Med*. 2023;388(3):203-13. DOI:10.1056/NEJMoa2205973.
18. Flevas DA, Megaloikonomos PD, Dimopoulos L, Mitsiokapa E, Koulouvaris P, Mavrogenis AF. Thromboembolism prophylaxis in orthopaedics: an update. *EFORT Open Rev*. 2018;3(4):136-148. DOI:10.1302/2058-5241.3.170018.
19. Muscatelli SR, Charters MA, Hallstrom

BR. Time for an Update? A Look at Current Guidelines for Venous Throm-

boembolism Prophylaxis After Hip and Knee Arthroplasty and Hip Fracture.

Arthroplast Today. 2021;10:105-107. DOI:10.1016/j.artd.2021.06.015.

Author's Contribution

SIB conceived and designed the study, analyzed and interpreted the data, drafted and revised the manuscript, and gave final approval for publication. MBK, AZ, and FU contributed to data collection and revised the manuscript. SA conducted the statistical analysis, interpreted the data, and revised the manuscript. Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Authors declared no conflict of interest

Grant Support and Financial Disclosure

None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.