



E-ISSN: 2395-1958
P-ISSN: 2706-6630
IJOS 2022; 8(2): 306-310
© 2022 IJOS
www.orthopaper.com
Received: 25-01-2022
Accepted: 15-03-2022

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Role of coagulation profile in prevention of bleeding complications in primary total knee arthroplasty patients

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DOI: <https://doi.org/10.22271/ortho.2022.v8.i2e.3154>

Abstract

Introduction: Incidence of deep vein thrombosis (DVT) (1.9%-3%) and pulmonary embolism (PE) (0.01%) post total knee arthroplasty (TKA) in Asian population is less compared to western population (85% and 1.5%-10% respectively). Hence, routine chemoprophylaxis following Western protocols is debatable in Asia. Wound complications like bleeding, hematoma, blisters, skin necrosis are high with low molecular weight heparin (LMWH) as compared with Aspirin. Aspirin is associated with low rate of DVT and PE (0.008% - 0.35%). The aim is to study the coagulation profile and adverse events like DVT, PE and wound complications in postoperative TKA patients on pharmacological DVT prophylaxis and watch for correlation between coagulation parameters and bleeding complications, and accordingly administer thromboprophylactic agents.

Methods: Prospective observational study.

463 patients undergoing primary unilateral TKA were bifurcated into groups according to thromboprophylaxis given by two surgeons.

1. 271 patients received LMWH
2. 192 patients received Aspirin

Patients were evaluated with coagulation profile preoperatively and postoperatively and observed for wound complications, DVT and PE.

Results: The use of LMWH conferred a significantly higher incidence of wound soakage ($p < 0.001$) and drain volume ($p < 0.001$) than with aspirin. There was no significant difference in the incidence of DVT or PE between the two groups. There was a significant increase in the postoperative aPTT ($p < 0.001$) value over the preoperative value in correlation with drain volume in patients who received LMWH as compared with aspirin.

Conclusion: As wound complications are significant with LMWH, and there is no significant difference in the incidence of DVT/PE with LMWH and aspirin, a balanced view of risk-versus-benefit to be taken when prescribing thromboprophylaxis. Response of aPTT after 1-2 doses of LMWH is useful in identifying those who are likely to develop bleeding complications and LMWH to be switched to aspirin.

Keywords: Thromboprophylaxis, total knee arthroplasty, coagulation profile

Introduction

Deep vein thrombosis (DVT) post TKA is a relatively benign treatable condition, while pulmonary embolism (PE) is life-threatening and sometimes fatal^[1].

Most of the symptomatic venous thromboembolism (VTE) events occur up to 2 weeks after hospital discharge¹. Consequently, thromboprophylaxis after discharge should be considered owing to the risk period for VTE. However, evidence-based guideline recommendations for the prevention of VTE in these patients have not been fully implemented^[2].

Incidence of clinically significant DVT (1.9%-3%) and PE (0.01%) in Asian population² is less when compared to the Western population (85% and 1.5%-10%, respectively^[2, 3, 4]. Despite modernization of lifestyles and an aging population the incidence of symptomatic PE and DVT after TKA without prophylaxis is low in Asian countries and has not changed over time^[1]. Hence, the relevance of routine chemoprophylaxis after TKA adopted from the Western protocols has been questioned in Asian population^[1].

The ideal VTE prophylaxis and the risk benefit ratio of the chemoprophylactic agents following TKA remains controversial^[5, 6].

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There were no significant differences in the incidences of thromboembolism related events in Asian patients whether they received enoxaparin or not [6]. The risk of clinical DVT, and of fatal and nonfatal PE after TKA following a fast-track set-up with early mobilization, short hospitalization, and short duration of DVT prophylaxis compares favorably with published regimens with extended prophylaxis (up to 36 days) and hospitalization up to 11 days. This calls for a reconsideration of optimal duration of chemical thromboprophylaxis [7].

Intermittent calf compression using devices such as inflatable boots, worn either until the patient was discharged from hospital or for 17 days, during which all patients were fully ambulant, has been shown to significantly reduce the incidence of DVT in post TKA patients [8]. Multimodal thromboprophylaxis with calf compression devices and ankle pump exercises along with aspirin is highly effective in prevention of thrombotic complications as compared to individual prophylactic measures [8, 9, 10].

Chemoprophylaxis regimes are commonly employed in post TKA patients, however there are few studies in the literature examining wound related complications attributable to this therapy [6]. No significant differences were noted in incidence of DVT or PE in patients on low molecular weight heparin (LMWH) and aspirin [12]. Incidence of wound complications such as bleeding, blisters, wound hematoma, skin necrosis, infection is high with LMWH as compared to that with aspirin [6, 11, 12, 13]. Aspirin is inexpensive, easy to administer, and reasonably well tolerated, requires no blood monitoring, has an excellent safety profile, and continues to increase in popularity for VTE prevention after total joint arthroplasty [14, 15]. It is also a milder agent and unlikely to result in hematoma formation, which may increase both the risk of superficial wound infection and deep prosthetic joint infection and the need for further surgery which increases post TKA morbidity and prolonged hospital stay [14, 15]. Aspirin is also unlikely to result in persistent wound drainage, which has been shown to be associated with the use of agents such as LMWH and other more aggressive agents [14, 15].

The current study aims to compare the coagulation profiles in TKA patients receiving DVT prophylaxis with LMWH versus aspirin and compare the adverse events such as DVT, PE, bleeding from surgical wound, drain output, skin blisters in the above groups of patients and establish any correlation between the coagulation parameters and bleeding complications.

Materials and Methods

463 patients undergoing primary unilateral TKA at HOSMAT hospital, Bangalore from September 2016 to June 2018 were included in the study. Patients were divided into two groups operated by two different surgeons of comparable experience and expertise who adopted different methods of chemoprophylaxis. The postoperative protocols of the two surgeons were comparable in terms of physiotherapy, ambulation and duration of hospital stay.

1. Group 1 (271 patients) received LMWH
2. Group 2 (192 patients) received Aspirin

Inclusion criteria

1. All patients undergoing primary unilateral TKA
2. All patients undergoing bilateral staged TKA (interval of 3 to 6 months between the two knees)

Exclusion criteria

1. All patients undergoing primary bilateral staggered TKA.
2. All patients undergoing revision TKA
3. Patients with history of DVT in the past.

4. Patients on medication for coronary heart disease.

Methods

A total of 463 patients planned for primary TKA were assessed preoperatively with PT, aPTT and INR. Post TKA, patients were on epidural infusion for pain control up to second postoperative day and weaned off gradually on the third postoperative day. Post TKA, patients were put on pharmacological thromboprophylaxis on the day of surgery according to the preference of the surgical teams

1. Group 1 (271 patients): Injection LMWH 40 mg subcutaneous once a day till discharge. Post discharge, patients were continued on Injection LMWH 40 mg subcutaneous once a day for 2 weeks.
2. Group 2 (192 patients): Aspirin 75 mg oral once a day till discharge. Post discharge, patients were continued on aspirin 75 mg oral once a day for 2 weeks.

Patients were given physiotherapy from the day of surgery in the form of knee range of motion, ankle pumps, Mechanical calf pump devices and were mobilized on the first postoperative day in the form of full weight bearing walking with a walker aid. The surgical drain was removed after 24 hours of the surgery. Patients were assessed on postoperative day 1 with PT, aPTT, INR. Surgical wound examination was done on postoperative days 1, 3, 5 and on the day of discharge to look for bleeds, drain amount, blisters, skin necrosis and assessed for postoperative symptomatic DVT and PE. The range of duration of hospital stay was 5 to 7 days. Mean duration of hospital stay was 6 days.

Venous Doppler of the operated leg was done on 3rd postoperative day while the patient was still admitted in the hospital and on the 14th postoperative day when the patient came for suture removal on out-patient basis to assess for DVT.

All patients were followed up after 1 month and 3 months for evidence of wound complications and venous thromboembolic complications.

Various factors were subjected to statistical analysis to enable a comparison between the two groups, these included DVT, PE, wound complications, surgical wound soakage, drain volume, coagulation factors and correlation between coagulation factors and drain volume.

Method of statistical analysis

Data analysis was done with the help of a computer using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 22.0 for Windows).

Using this software, frequencies and percentages were calculated for qualitative variables. Means and standard deviations were calculated for quantitative variables. Student's unpaired 't' test and ANOVA test were used to test the significance of difference between quantitative variables and Yate's and Fisher's chi square tests for qualitative variables. A 'p' value less than 0.05 denotes significant relationship.

Results

463 patients with knee osteoarthritis, planned for primary unilateral total knee arthroplasty in HOSMAT Hospital, Bangalore, were eligible for the study from September 2016 to June 2018. The average age of patients was 61.58, 144 were males and 319 were females. Patients were divided into two groups based on the preferences of VTE prophylaxis of two operating surgeons. There were 192 patients in the Aspirin group (41%) and 271 patients in the LMWH group (59%). The demographics are represented in table 1.

Table 1: Demographics

Variable	LMWH	Aspirin
Average age	61.48	61.72
Males	88	57
Females	183	135
Number of patients	271	192

The use of LMWH was associated with a statistically

significant higher incidence of wound soakage than with aspirin ($p = 0.004$). The amount of drain volume was significantly high in LMWH group than in the aspirin group ($p < 0.001$). There were no statistically significant differences in the incidence of DVT or PE between the two groups. Also, there were no significant wound complications noted in both groups. The above data is represented in table 2.

Table 2: Incidence of soakage, drain volume, incidence of DVT/PE and wound complications

Variable	LMWH N, (%)	Aspirin N, (%)	P-value
Incidence of soakage	92, (33.9)	40, (20.8)	0.004
Drain volume (ml)	168.89	126.51	< 0.001
Incidence of DVT/PE	4, (1.5)	2, (1.0)	0.648
Incidence of wound complication	4, (1.5)	1, (0.5)	0.408

N= number of patients, % = percentage of patients

There was a statistically significant increase in the postoperative aPTT ($p < 0.001$) value over the preoperative

value in correlation with drain volume in patients belonging to the LMWH group than the aspirin group patients (Table 3).

Table 3: Correlation between increase in post op aPTT over preop aPTT and the drain volume over 200 ml or up to 200 ml (in the LMWH group and Aspirin group)

Group	Increase in post op aPTT over preop aPTT	
	LMWH group	Aspirin group
	Mean	Mean
Drain volume up to 200 ml	1.43	0.46
Drain volume above 200 ml	3.8	0.36
p-value	< 0.001	0.942

There was statistically significant ($p < 0.001$) association between increase in the postoperative aPTT over preoperative aPTT by more than 2 units or up to 2 units and drain volume

over 200 ml or less in the LMWH group but not in the aspirin group (Table 4).

Table 4: Correlation between increase in the post op aPTT over pre op aPTT by more than 2 or up to 2 units and drain over 200 ml or up to 200 ml in the LMWH group and Aspirin group

Group	Post op aPTT and pre op aPTT change in			
	LMWH group		Aspirin group	
	Up to 2 units	Above 2 units	Up to 2 units	Above 2 units
	%	%	%	%
Drain volume up to 200 ml	62.7	37.3	63.1	36.9
Drain volume above 200 ml	27.1	72.9	57.1	42.9
'p'	< 0.001		0.819	

% = percentage of patients

Discussion

The current study is a prospective, observational analytical study with the aim to compare the coagulation profiles in TKA patients receiving DVT prophylaxis with LMWH versus aspirin and compare the adverse events such as DVT, PE, bleeding from wound, drain output, wound complications in the above groups of patients and establish any correlation between the coagulation parameters and bleeding complications.

In our study the incidence of wound soakage was statistically significant in patients receiving LMWH as compared to those receiving aspirin. The drain volume was significantly high in LMWH group. Three patients developed DVT and one patient developed non-fatal PE out of 271 patients receiving LMWH. Two patients developed DVT on the second postoperative day and the third patient developed DVT on the third postoperative day. One patient developed non-fatal PE on fourth postoperative day. These three patients from LMWH group who developed DVT were not mobilized postoperatively due to severe pain. In the aspirin group, out of 192 patients, one patient developed DVT on the third

postoperative day and one patient developed non-fatal PE on fifth postoperative day. There were no episodes of DVT documented in patients who were mobilized immediately postoperatively.

There was a statistically significant increase in the postoperative aPTT values over the preoperative values in patients belonging to the LMWH group than the aspirin group patients. There was a statistically significant correlation between increase in post op aPTT over preop aPTT and the drain volume over 200 ml in the LMWH group. There was a statistically significant association between increase in the post op aPTT over preop aPTT by more than 2 units and drain volume over 200 ml in the LMWH group as compared to that in the aspirin group.

Multimodal thromboprophylactic approach which includes early postoperative mobilization along with aspirin given to the majority of patients at a low VTE risk is safe and effective in patients undergoing primary TKA [8, 9, 10].

An ideal agent would not only prevent DVT & PE occurrence but also minimize bleeding complications. LMWH, commonly used thromboprophylactic agent, is effective but

associated with bleeding risks and needs regular monitoring [11]. Aspirin, widely used antiplatelet drug, increases the bleeding time without affecting other coagulation parameters, has negligible bleeding risks [12, 14, 15], low rates of DVT & PE²¹, easy to administer, cardioprotective, cost effective, tolerated well and does not require monitoring [11, 12, 14, 15, 22].

NICE guidelines (2007) recommend extended VTE prophylaxis with LMWH in post TKA patients¹⁶ which is based on papers cited on 10-35 years old data when restricted ambulation and prolonged length of stay were common place. Now, patients are ambulatory within 24 hours of TKA hence results may lack relevance to modern orthopedic practice and lack evidence of absolute VTE risk in the modern era. The revised NICE guidelines (2018) recommend to balance the person's individual risk of VTE against their risk of bleeding when deciding whether to offer pharmacological thromboprophylaxis to surgical patients [17].

The American Academy of Orthopaedic Surgeons (AAOS) & The American College of Chest Physician (ACCP) evidence-based clinical practice guidelines (9th edition) in 2012, for the first time, acknowledged the use of aspirin as a means of DVT & PE chemoprophylaxis after total joint arthroplasty (TJA)^{18,19}. The adaptation of the recent ACCP guidelines by the Surgical Care Improvement Project (SCIP) has led to a resurgence in the use of aspirin as VTE prophylaxis following TJA¹⁸. Aspirin is associated with low rate of DVT & PE (0.008% - 0.35%) [18].

Beverland DE *et al.* in his study of 4253 primary hip and knee replacement patients stated that the fatal pulmonary embolism rate of 0.07% is a rare event after elective total joint replacement if aspirin is given. With modern surgical and anaesthetic practice, fatal pulmonary embolism is no longer common, but still continues to occur despite the use of anticoagulants. Data suggest that fatal PE is not common following elective primary TJA, and should no longer be considered high-risk procedures [21].

The Pulmonary Embolism Prevention (PEP) trial has shown a clear reduction in the incidence of fatal and symptomatic PE and DVT in patients with TKA who received low-dose aspirin²³. The beneficial effect of aspirin, on the venous circulation has also been demonstrated by the Warfarin and Aspirin (WARFASA) and the Aspirin to Prevent Recurrent Venous Thromboembolism (ASPIRE) trials [21, 24].

Increased rates of wound complications, noted with LMWH chemoprophylaxis, tend to increase the morbidity, hospital stay & may require further surgical intervention and increased need of blood transfusion. Hence there's a need to balance the risks and benefits of chemoprophylactic agents.

Based on the finding of statistically significant association between increases in the postoperative APTT over preoperative APTT by more than 2 units and drain volume over 200 ml or less in the enclax group in our study, the postoperative thromboprophylaxis can be altered. There being a wide variation in the aPTT values around the control value, baseline aPTT values may not be accurate.

Hence, an increase in the aPTT value after 1 dose of LMWH administration on first postoperative day is a better guideline. Rapid increase in aPTT by 2 or more units is significantly correlated with bleeding complications (*p<0.001) and hence in patients who are expected to have bleeding complications, LMWH can be changed to aspirin

The study had its own limitations being a non-randomized study and patients were operated by two different surgeons, but of comparable efficacy and expertise.

Conclusion

Results from this study show that there is a significant increase in the risk of surgical wound bleeding and drain volume when LMWH is used in post TKA patients as compared to aspirin. As potential complications of wound problems are significant, a more balanced view of risk versus benefit needs to be taken when prescribing thromboprophylaxis for this patient group. Incidence of deep vein thrombosis is nil in patients who were mobilized immediately postoperatively. Multimodal thromboprophylaxis with mechanical calf pump devices, early postoperative mobilization along with aspirin when administered to low-risk patients is safe and effective following primary total knee arthroplasty. Response of aPTT after 1-2 doses of LMWH is useful in identifying those who are likely to develop bleeding complications. In patients who are expected to have bleeding complications, LMWH can be switched over to aspirin to avoid any further surgical wound bleeding.

Acknowledgments

There was no funding provided for this study.

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