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Prophylaxis of DVT with Enoxaparin in Patients Undergoing Total Knee Replacement

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Abstract

Objective: To evaluate the efficacy and safety of the low molecular weight heparin as prophylaxis against thromboembolism following total knee replacement surgery.

Methods: Post-operative bilateral lower extremity colour duplex scan was performed on 55 patients subjected to total knee arthroplasty. The scan was performed 7 days after surgery for detection of DVT. All patients were given Enoxaparin 40mg subcutaneous daily for 2 weeks as prophylaxis against DVT.

Results: Two patients were diagnosed as DVT by color duplex scanning and both were distal but only one was asymptomatic. Another patient developed pulmonary embolism and died subsequently. The major and minor wound problems were seen in two and six patients respectively; nearly all complications were seen in obese patients.

Conclusion: DVT is not a nonexistent entity in our population. Low molecular weight heparins are safe drugs but apparently the bleeding complications are more as compared to Western literature. Larger case control studies are required to determine the true efficacy and safety of LMWH (JPMA 56:72;2006).

Introduction

Deep venous thrombosis (DVT) is a common complication in patients who are hospitalized or bed ridden. Lower extremity orthopaedic surgery is recognized in Western countries as being associated with an exceptionally high risk of developing DVT and pulmonary embolism. Accordingly, prophylactic treatment of DVT has been established as the standard medical practice for lower extremity large joint replacement surgery in the Western countries. In contrast, DVT has received little medical attention in Asian countries because of a presumed low prevalence, conse-

quently the prophylaxis modalities are not conducted routinely.^{1,2}

Among all the drugs, Low Molecular Weight Heparins (LMWH) have received the most attention, but LMWH are not without side effects and are not 100% effective.^{2,3}

The efficacy and safety of these drugs have not been studied in our population. The study was done to evaluate the practice of giving LMWH in terms of efficacy and safety in patients undergoing total knee replacement surgery.

Patients and Methods

This observational cohort study was conducted at the Orthopaedic Division, Department of Surgery, of Aga Khan University Hospital, Karachi. All patients undergoing total knee arthroplasty constituted the target population. Patients having coagulation disorders or who were taking procoagulants or anticoagulants including anti-platelet drugs and Aspirin or who developed DVT in the past were excluded. Informed written consent was taken from every patient included in the study.

In all patients, prothrombin time (PT) and activated prothrombin time (APT) were done pre-operatively and those having abnormal values were excluded from study. All patients received 40mg Enoxaparin subcutaneously on anterior abdominal wall, night before surgery. Enoxaparin (40mg) was then repeated on first postoperative day and continued for a total duration of two weeks after surgery.

All surgeries were done under tourniquet control. All patients received two doses of prophylactic antibiotics. After surgery, all were managed according to the existing clinical pathways for total knee replacements at our institution, in the form of mobilization and range of motion of knee joints starting at 1st postoperative day. No other form of DVT prophylaxis was used like compression stockings.

The patients were monitored daily for symptoms and signs of DVT as well as major and minor haemorrhagic complications. All were subjected to mandatory bilateral Colour Duplex Scanning of both lower limbs by the same radiologist at postoperative day 7 or earlier if clinically indicated. All patients were assessed clinically at removal of stitches for the presence of DVT. Patients were also seen at 3 weeks after surgery and again assessed clinically for presence or absence of sign and symptoms of DVT.

Demographic and operative characteristics of patients were recorded. Type of surgery, diagnosis, side of surgery, age, body mass index, use of bone cement and operating time all are considered potential risk factors. The data thus obtained was analyzed using SPSS software version 10.

Results

Initially 63 patients were included in the study. Postoperatively, 8 were excluded because of improper follow-up after discharge, inability to undergo bilateral colour Doppler examination of both extremities. These patients were followed later for the presence of symptomatic DVT. None had any evidence of DVT. Finally 55 patients qualified for the study.

The mean age of the patients was 66 years with a

range of 35 to 77, with females being older, F:M::68:60 years. The male to female ratio was 1:2.5.

The mean hospital stay of the patients was 9.5 days with a range of 7 to 14. The mean body weight was 74kg (162.8lb), with a range of 55kg to 110kg. The body mass index was 28.9kg/m² (normal range 20.5-25 in females and 21-25.5 in the male). The upper limit for the morbid obesity is considered 35kg/m².⁴

Sixty-nine percent of surgeries were done in general anaesthesia using Sodium Pentothal and Isoflurane with the remaining being given spinal or epidural anaesthesia.

Postoperatively majority of the cases received intravenous opioid analgesics for pain management. Some cases received nonopioid analgesics due to hypersensitivity or associated medical conditions such as respiratory insufficiency.

Sixty-two percent patients had simultaneous surgery. Both knee joints were operated together by two operating teams, while in 25% of the cases the surgery was performed on one knee joint only. In 13% cases, patients underwent surgery in two stages in the same hospital admission with the second replacement done about 7 to 10 days after the first surgery.

The postoperative wound related complications were divided into two groups, major and minor wound problems. The major required surgical intervention in the form of wound exploration or drainage of haematoma. The minor wound problems were managed successfully by conservative methods. In the presented study, there were 6 minor and 2 major wound problems. The later included 2 cases of wound dehiscence who were subjected to reclosure of the wound. The minor wound problems comprised of swelling of the knee joint, erythema around the wound margins and wound discharge. All of them were managed successfully with conservative treatment. When the minor wound related problems were analyzed, five of six patients were having body mass index above 30kg/m² and there was only one patient with body mass index was less than 30kg/m² (p-value <0.001). In patients where major wound problems were identified, all patients were having a body mass index of more than 30kg/m² (p-value <0.001).

In our study, Doppler ultrasonography was done in all patients and it was found that 2 patients had asymptomatic DVT and two independent radiologists confirmed the diagnosis. DVT was present in both cases on the operated side and in both distal veins were involved. One patient had been subjected to bilateral knee arthroplasty and one underwent unilateral knee arthroplasty.

One patient subjected to unilateral arthroplasty, developed pulmonary embolism as a consequence of DVT

and ultimately expired. The postoperative recovery was uneventful and patient was discharged on 9th postoperative day. He presented on 16th postoperative day with sudden onset of dyspnoea and chest discomfort. Electrocardiography, chest x-rays and cardiac enzymes excluded myocardial infarction. The diagnosis of pulmonary embolism was made by exclusion. The patient expired within 24 hours of presentation.

The mean requirement of blood in the form of packed cells was 1.4 pints with a range 0 to 5. Requirement was more in the cases of the bilateral knee replacement as compared to unilateral knee replacement surgery. There was no major difference observed between the simultaneous bilateral and staged bilateral procedure i.e. 1.7 and 1.5 respectively.

Among other complications, one patient developed myocardial infarction in the postoperative period while one patient developed heart failure; both of them were managed in the coronary care unit and survived.

The local tolerance at the site of the injection was good in majority of the patients, however, few patients complained of burning sensations on anterior abdominal wall for few weeks postoperatively. These abnormal sensations also resolved spontaneously.

Discussion

Venous thromboembolism is a potentially serious complication of arthroplastic surgery of lower extremity. Without prophylaxis, approximately 40% to 50% of total hip replacements and 50% to 70% of knee arthroplasty patients develop venographically verified DVT.⁵

A variety of mechanical and pharmacological approaches have been used to decrease this risk. However, pharmacological approaches, specifically warfarin sodium and low molecular weight heparin (LMWH) have received greatest amount of attention.

Main features of unfractionated heparin include its sub-optimal efficacy and risk of heparin-induced thrombocytopenia. Warfarin therapy needs regular dose adjustments and careful laboratory monitoring of PT levels. Advantages of low molecular weight heparins are enhanced efficacy and a decreased risk of heparin induced thrombocytopenia. The optimal duration for therapy is unknown.

There are two possible explanations for low prevalence of DVT in Asian countries.³ Firstly, the number of joint replacement procedures is much smaller than that in Western countries.³ Another possible reason is widespread use of clinical signs rather than venography as diagnostic criteria of DVT in Asian countries as clinical signs are shown to be insensitive and not specific enough in estimat-

ing the true incidence of DVT.¹ Accordingly, direct comparison of prevalence of DVT between patients from Asian and Western countries has been confounded because of the differences in diagnostic criteria.^{2,3} Another factor as a cause of low incidence of DVT in Asian population is Leiden mutation that involves point mutation of factor V gene which prevents the breakdown of factor V resulting in relative hyper-coagulability. The prevalence of this mutation was found to be significantly lower in Asian population as compared to Western population.⁶⁻⁸ This Prothrombin variant which also predisposes to clotting was found to be absent in Taiwanese and Japanese population.⁹

The incidence of asymptomatic DVT after major orthopaedic surgery in Japanese patients was only 15%.³ In the Korean population, the incidence of DVT in patients undergoing total hip replacement surgery was 20% in the control group not receiving any prophylaxis.¹⁰ In the Singapore population, a very low incidence of DVT was found in patients not receiving any prophylaxis¹¹. On the contrary, the incidence of DVT was quite comparable to the Western figures in Hong Kong¹² and Malaysian¹³ patients. In a recent venographically confirmed study from Japan³ done on patients undergoing total hip and knee replacement surgery without any form of prophylaxis, the incidence of DVT both proximal as well as distal, was found to be high. Incidence in the Indian patients undergoing various high-risk surgeries without prophylaxis, was found to be 28%.¹⁴ Hence the evidence regarding the prevalence of DVT without using any form of chemoprophylaxis after high-risk orthopaedic surgeries in Asian population is still equivocal.

Not much has been written about DVT in Pakistan. In a previous study¹⁵, on 750 operated patients in the orthopaedic service of a private hospital, twenty-five (3.3%) were identified as clinical DVT. These patients were categorized in two groups, group 1 (n=15) received no prophylaxis or some prophylaxis other than Warfarin and group 2 (n=10) received Warfarin. There were nine (1.6%) mortalities in this series. Mortality was 0.6% (p<0.06) in group 1 and 1.6% in group 2. It was concluded that incidence of DVT shown in this study is an understatement; it might have been much higher if those objective methods were used. In another study¹⁶ on 117 high risk patients undergoing surgery without prophylaxis, Technetium labeled venography showed 12.82% patients to have DVT. The study concluded that there is need to give prophylaxis to high risk patients undergoing surgery especially pelvic surgery.

In a randomized, parallel group, open labeled study¹⁷, the use of LMWH versus unfractionated heparin after elective TKR surgery in 453 patients showed the incidence of DVT by venography to be 24.6% in the LMWH group

and 34.2% in the unfractionated heparin patients.

In another study on 1942 patients subjected to total joint replacement surgery, DVT was encountered in 9.6% patients in the LMWH group, 16.1% in the unfractionated heparin group and 46% in the placebo group.¹⁸

In a recent Indian study¹⁹ where patients undergoing total hip replacement surgery were divided in 2 groups and Doppler scan postoperatively showed no evidence of DVT in these patients. In another study by same author²⁰ where DVT was assessed in patients undergoing THR and TKR surgery, 2 patients developed DVT all of them underwent THR surgery. The author concluded that the incidence of DVT in Indian patients is very low and is not comparable with American and European populations.

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