ORIGINAL ARTICLE

Safety of Low Molecular Weight Heparin and Unfractioned Heparin in Prevention of Venous Thromoboembolism (VTE)

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Aim: To compare the safety of low molecular weight heparin and unfractionated heparin in prevention of VTE in surgical patients
Study Design: Randomized Control Trial.
Place: Surgical Department, POF Hospital Wah Cantt, a tertiary care teaching hospital affiliated with Wah Medical College.
Duration of study: From 1st January 2013 to 1st July 2014.
Methodology: Two hundred cases of moderate risk surgical patients for VTE were selected by non-probability consecutive sampling and divided into two groups A & B.
Group A: received low molecular weight heparin.
Group B: received unfractionated heparin.
Patients in both the groups were monitored for bleeding from the surgical wound at 1st, 2nd and 3rd postoperative day and the data was analyzed with SPSS version 17.
Results: There were total 200 cases operated under general anesthesia of more than 30 minutes duration having their base line investigations hemoglobin, platelet count and APTT in optimum range. Bleeding from the surgical wound was observed in 2 patient of group A and 10 patients of group B.
Conclusion: Low molecular weight heparin is safer than Unfractioned heparin in prophylaxis of venous thromboembolism.
Keywords: Low molecular weight heparin, Unfractionated Heparin, Bleeding.

INTRODUCTION

Venous thromboembolism (VTE) is a common cause of morbidity and mortality in surgical patients. Deep vein thrombosis (DVT) and pulmonary embolism are the two most common manifestations of venous hromboembolism[1]. Mortality rate is 6.4% for all patients with VTE, 9.7% for those with pulmonary embolism, and 4.6% for those with DVT[2].

Postoperative proximal DVT is present in 6% to 7% of general surgery patients. DVT usually starts in the calf veins, from where it may extend to the proximal veins, and subsequently break free to cause PE[3,4]. Half the cases of DVTs resolves spontaneously within 72 hours, and only one sixth extend to involve the proximal veins[5,6]. Postoperative thromboembolism occurs in the first 20 days after surgery; prophylaxis is given until the patient is discharged, normally ranging from 5 to 14 days[7]. Pulmonary embolism less likely to occur in association with DVT when patients had received prophylaxis with an antithrombotic agent (8% versus 42%)[8]. 10% of symptomatic PE cause death within 1 hour of onset[9]. Hemorrhage is the most common and best-recognized complication of heparin treatment. The bleeding rate for LMWH and UH was 2.6% and 5.3% respectively[10]. In contrast, Geerts et al. demonstrated bleeding rates for LMWHs and UHs of 2.9% and 0.6% respectively[11]. LMWH has an efficacy that is at least equivalent to that of LDUH. However some studies have reported significantly fewer wound hematomas and bleeding .[12-13] Reason for failure to use prophylaxis, especially in surgical patients, is because of bleeding complications , increased risk of wound infection, dehiscence and infection of a prosthetic device placed at the time of operation. Hemorrhagic complications of DVT prophylaxis are varied. They range from a transient decrease in hemoglobin levels to clinical bleeding requiring intervention (angiography or surgery).

Present study is designed to evaluate the safety of LMWH vs LDUH in prevention of VTE in surgical patients. This study will help to recognize safe method of thromboprophylaxis to counter act these misconceptions and for better use of prophylaxis in surgical patients.

MATERIAL AND METHODS:

This randomized controlled trial was carried out at Surgical Department, POF Hospital Wah Cantt, a

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tertiary care teaching hospital affiliated with Wah Medical College, from 1st January 2013 to 1st July 2014. Study protocol was approved by the Institutional Review Board.

Patients younger than 40 years requiring surgery under general anesthesia longer than 30 minutes and patients with age 40 years or above requiring surgery under general anesthesia less than 30 minutes were included in the study. Patients with active bleeding, severe bleeding diathesis, platelet count less than 100,000/dl, duodenal, Gastrointestinal or Genitourinary bleeding within the past 14 days were excluded.

Informed consent was taken from each patient. Sample size of 200 cases was calculated. Non-probability Consecutive sampling technique was used to sample the patients. Sampled patients were divided into two groups. Group A received low molecular weight heparin (enoxprine sodium) 2000 units subcutaneously in OD dose and group B received unfractionated heparin, 5000 units subcutaneously 8 hourly. Both the drugs were started after surgery and continued for 5 days. The patients were monitored for bleeding from the wound which is visible soakage of dressing. Dressing was changed every day. Data entered in a Performa.

Data was analyzed using statistical Package for social sciences (SPSS) version 17. Descriptive statistics are used to calculate means ± standard deviation for age. Frequencies calculated for gender and safety. Chi-square test used to compare the efficacy between the two groups. P value $\leq$ 0.05 will be considered significant.

RESULTS

Two hundred cases were evaluated in this study, 100 were allocated in each group. Bleeding from the surgical wound was noted and different aspects were statistically analyzed. The results were obtained for both groups. The mean age was 46±12 years in group A and 44±12 years in group B. In group A, 55(55%) patients were females and 45(45%) patients were male while in group B, 58(58%) patients were females and 42(42%) patients were male. The case-mix under study is given in table 1.

Bleeding was observed from the surgical wound in 2 patients of group A and 10 patients of group B. Bleeding in group A was observed on the 1st postoperative and 4th postoperative day with visible soakage of the dressing. Bleeding in 4 patients of group B was noted on the 1st postoperative day while bleeding in 3 patients was noted on the 2nd post operative day 1 patient on 3rd day and in 2 patients on 4th postoperative.

Table 1: Diagnosis of Study Population

Diagnosis	Group A	Group B
Inguinal hernia	20	18
Cholelithasis	18	22
Incisional hernia	8	7
Paraumblicle hernia	8	8
Intestinal Obstruction	7	10
pritonitis	7	5
Goiter	6	6
CA Breast	5	6
choledocholithasis	5	5
Ileostomy reversal	5	6
Colostomy reversal	4	2
Below knee amputation	4	3
Sub mandibular gland tumor	0	1
Parotid tumour	1	0
Stomach carcinoma	0	1
Carcinoma head of pancreas	1	0
Carcinoma rectum	1	0

DISCUSSION

Worldwide annual incidence of DVT is estimated to be 2 million, with 600,000 developing PE and 10,000 deaths. The incidence of VTE is reported to vary; it ranges between 62 and 143 per 100,000 individuals annually. Some reports describe variations in incidence among different ethnicities[14]. Wasim mirza et al. suggests that DVT is not rare in Pakistan and strongly recommends prophylaxis in high risk surgical patients. Unfractionated heparin and low molecular weight heparin are the most commonly used antithrombotic and thromboprophylactic agents.

LDUH was the first antithrombotic agent tested in trials because it has a beneficial effect on reducing serious complications (DVT and PE). Low-molecular-weight heparin is as effective as standard heparin or warfarin and does not require monitoring Traditionally, treatment for DVT required patients to be hospitalized . With subcutaneous injections of low-molecular-weight heparin, treatment of DVT can be given in the outpatient department[15].

Heparine has rapid clearance rate, rangs from 30 minutes to 2.5 hours, which allows easy and frequent adjustments of level. Heparin dose can be measured by using the activated partial thromboplastin time (aPTT)[16] .LMWHs have largely supplanted UFH in the clinic because of their more predictable pharmacokinetics and essentially a safety profile comparable to that of UFH .After subcutaneous injection, LMWHs achieve a higher bioavailability and a longer half-life (roughly 4 hours), allowing for a sustained effect with once or twice daily fixed or weight-adjusted dosages and monitoring of anticoagulant levels is usually not required[17]. As we compare our study with other studies

Green et al. observed non-fatal bleeding rates for LMWH and UH of 0% and 9.5% respectively. They also reported 2 patients (9%) who died of massive PE in the UH group, versus 0 patients in the LMWH cohort[18].

In contrast, Geerts et al. demonstrated bleeding rates for LMWHs and UHs of 2.9% and 0.6% respectively[11].

In the Spinal Cord Injury Thromboprophylaxis Investigators study, the bleeding rate for LMWH and UH was 2.6% and 5.3% respectively[10].

An other study showing opposite result in this study rate of haematoma requiring surgical intervention was 0·4 per cent (six of 1452 wounds) in patients who had UFH, compared with 1·8 per cent (32 of 1780 wounds) for LMWH[19].

Eley KA et al. observed increasing the dose of LMWH (dalteparin) did not seem to increase the risk of bleeding or formation of a haematoma[20].

Hull RD et al. observed bleeding risk was low in patients receiving LMWH preoperatively[25]. For patients at high risk for bleeding, the initial LMWH dose should be delayed until 12–24 hours after surgery.

As we compare our study with above mention studies it is clear that no definite data is available to reach the definite result some studies have same result as our but on other hand some studies shows contradictory results. These contradictory results are might be due to patient's selection, and type of procedure involve so a larger study which contain well compare able groups is further required to prove our hypothesis.

CONCLUSION

An appropriate preventive strategy in general surgery for VTE should take into account, keeping in mind the effectiveness, expense and possible complications of their use.

In moderate-risk hospitalized patients who are more than 40 years of age or undergoing major operations should receive LMWH which is safe and prophylaxis can be continued at home safely without monitoring.

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