

Comparative Analysis of Low Molecular Weight Vs Unfractionated Heparin in Surgical Patients Receiving Deep Venous Thrombosis Prophylaxis

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ABSTRACT

Aim : To evaluate low molecular weight heparin and unfractionated heparin in prophylaxis of venous thromboembolism in terms of post operative haemorrhage in surgical patients.

Study design: Randomized control trail study

Place and duration of duty: Surgical Department, POF Hospital Wah Cantt and DHQ Teaching Hospital KDA Kohat from 7th September 2018 to 7th March 2020.

Methodology: Two hundred patients of moderate risk for venous thromboembolism were included in the study and divided into groups 1&2. Group 1 patients were receiving low molecular weight heparin and group 2 on unfractionated heparin. Patients in both groups were observed for post operative haemorrhage at 1st, 2nd and 3rd postoperative day.

Results: Post operative haemorrhage from surgical wound was noticed in a single patient of group 1 and 11 pts of group 2.

Conclusion: The chances of post operative haemorrhage are less in patient receiving Low molecular weight heparin in contrast to unfractionated heparin in prevention of venous thrombosis and embolism in surgical patients

Keywords: Venous thromboembolism, Heparin, Post-operative haemorrhage

INTRODUCTION

Venous thrombosis and pulmonary embolism is a common cause of morbidity and mortality in surgical patients.¹⁻⁴ Up to 6-7% of surgical patients develop deep venous thrombosis. Most of the cases are sub clinical hence remain undiagnosed.^{2,5} Even at the beginning this disease may presents as life threatening pulmonary embolism, so it is inappropriate to wait for clinical manifestations and then the treatment of established VTE. The unrecognized and untreated DVT may also leads to long-term morbidity and may predisposes patients to future episodes of recurrent VTE⁶⁻⁸.

Incidence of VTE in surgical patients depend on duration and type of surgery, period of postoperative immobilization, type and duration of anesthesia and some patient-related conditions like malignancy, old age, prior history of venous thrombosis, obesity, congenital and acquired thrombophilic disorders.^{9,10} For proper VTE risk stratification protocols that include patient-related and surgery-related risks should be adopted.¹¹ The Major surgery is defined as an operation that require general anesthesia for ≥ 30 minutes and such procedures carry high risk for VTE. There is comparatively high chances of deep venous thrombosis in patients undergoing surgery under general anesthesia than those being operated under regional anaesthesia¹².

Some clinically important risk factors for development of venous thromboembolisms are age more than 40, obesity, prolonged immobility (paralysis), major surgery, malignancy, pregnancy, and previous venous thromboembolism.^{2,13} Heparin and its fractionated derivatives, are the anticoagulants of choice when there is need for urgent anticoagulation³.

Heparin interferes with hemostatic function of platelets and endothelial cells that may lead to heparin induced thrombocytopenia and bleeding diathesis^{4,8}. Heparin in a fixed low dose results in 60-70% risk reduction for venous thrombosis and pulmonary embolism.^{5,9} The concept behind thromboprophylaxis is to halt the thrombin production that would otherwise occur during and after surgery when used in low dose.¹⁴ The incidence of hemorrhage with low molecular weight heparin is 0.39%⁷ and the incidence of hemorrhage with unfractionated heparin is 7%⁵. In literature there is scarcity of studies regarding the fact that low molecular weight heparin produces less micro vascular bleeding than unfractionated heparin in human beings^{1,13}.

The rationale of this research article was to provide an evidence based study of comparative analysis of unfractionated heparin versus low molecular weight heparin for its hemorrhagic complications.

MATERIALS AND METHODS

This study is randomized control trail study was conducted in the Department of Surgery, POF Hospital Wah Cantt and Divisional Headquarter Teaching Hospital KDA Kohat after IRB permission from 7th September 2018 to 7th March 2020. All the cases of major surgery in patients younger than 40 years and minor surgery cases in patients with age 40 years or above and in patients with risk factors were included. Uncomplicated minor surgery in patients younger than 40 years with no clinical risk factors, cases with fresh haemorrhage, coagulopathy or thrombocytopenia, gastrointestinal or genitourinary bleeding within the last two weeks were excluded. Patients were randomised into two groups. Group 1 received dalteparin sodium which is LMWH 2000 units subcutaneously in once daily dose and group 2 treated with unfractionated heparin, 5000 units subcutaneously three times a day. Patients were treated with these medicines 2 hours after surgery and continued up to post operative day 3. The patients were observed for surgical wound site haemorrhage at first 3 postoperative days. The data was analysis was performed through SPSS-20. The statistical test of significance (Chi-square test) was utilised for comparison of the two groups. P value <0.05 was considered significant.

RESULTS

The mean age of the patients included in the study was 44±13 years in group 1 and 41±12 years in group 2. Sixty eight (68%) patients of group 1 were females and 32(32%) patients were male with female to male ratio 2.12:01 while in group 1, 61 (61%) patients were females and 39(39%) patients were male with female to male ratio of 1.5:1 (Table 1).

Bleeding was noted in 11 patients (11%) of group 1 receiving LDUH. Four patients (out of 11) developed surgery site haemorrhage on first postoperative day and in 5 patients on second postoperative day. However, bleeding in 2 patients was seen on third postoperative day. In group, prophylaxis provided with LMWH, only one patient (1%) had bleeding on first postoperative day. So there is statically significant (P=0.005) difference between group 1 and 2 in terms of post operative haemorrhage (Table 2).

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Table 1: Descriptive statistics of the patients (n=200)

Variable	Group 1	Group 2
Gender		
Male	32 (32%)	39 (39%)
Female	68 (68%)	61 (61%)
Age (years)	44±13	41±12

Table 2: Comparison of bleeding in both groups

Bleeding	Group 1	Group 2	Total	P value
Present	1	11	12	0.005
Absent	99	89	188	

DISCUSSION

Venous thromboembolism is the term currently used to refer both DVT that is deep venous thrombosis and pulmonary embolism which are preventable cause of morbidity and mortality it can happen as sequelae of surgery and trauma among indoor patients. The reported and estimated annual incidence of deep venous thrombosis is about 2 million, with 600,000 patients develop pulmonary embolism and is cause of deaths in 10,000 patients.¹

Eley et al¹⁵ have stated the incidence of VTE in hospitalized patients is more than 960 out of 10,000 patients per year which is very high figure as compared to incidence in community residents. Mirza et al¹⁶ suggested that routine chemo thromboprophylaxis is not a normal routine in Pakistan because it is assumed generally that VTE is not a problem of this region. Low dose unfractionated heparin (LDUH) and low molecular weight heparin have proven efficacy in decreasing the occurrence of venous thromboembolism^{5,13}. Literature shows that LDUH was the first studied blood thinner and was found very effective in reducing incidence of venous thromboembolism.¹⁶ Low molecular weight heparinis equivalent to or superior to low dose unfractionated heparin in thromboprophylaxis.^{17,18} Geerts et al¹⁹ have shown that subcutaneous use of unfractionated heparin decreases the overall incidence of deep venous thrombosis from 24 to 7%.

In group A, prophylaxis provided with LMWH, only one patient (1%) had bleeding on first postoperative day. There are no identical studies in our region comparing the Low molecular weight heparin and low dose unfractionated heparin in terms of bleeding from wound site. Bleeding was noted in 11 patients (11%) of group B receiving LDUH. Bleeding in 4 patients (out of 11) was noted on first postoperative day while bleeding in 5 patients occurred on second postoperative day. However, bleeding in 2 patients was seen on third postoperative day. This high incidence of bleeding in LDUH group is comparable with the incidence reported by Naz et al⁵ high incidence is also reported in western literature.

Chemoprophylaxis for VTE in patients with myocardial infarction also highlights the safety of LMWH over LDUH.^{20,21}

Geerts et al¹⁹ demonstrated that the efficacy of LMWH was comparatively more than LDUH in VTE prophylaxis in trauma patients. Their results showed that low-molecular-weight heparin should be considered for thromboprophylaxis of trauma patients, provided they do not have concomitant head injury to avoid the chances of intracranial haemorrhage.

But in contrast a study by Prandoni²² showed that the results of use of dose adjusted subcutaneous unfractionated heparin is comparable to fixed-dose nadroparin (LMWH) in terms of efficacy and safety..

Old age and male gender are the risk factors for venous thromboembolism and also for the recurrence of VTE.²³ This study also showed an increased risk of bleeding in the male gender as there were 1 male vs zero female of group A (LMWH group) in whom bleeding occurred and 7 males vs 4 females in group B (unfractionated heparin group) in whom bleeding occurred. The age could not be compared as most of the patients in our study were below 65 years of age. Use of low molecular weight heparin is questionable be used with caution in kidney failure patients²³.

Incidence of heparin induced thrombocytopenia is relatively low with LMWH. An estimated risk of 1-5% is reported with unfractionated heparin while a risk of less than 1% is reported with LMWH²⁴.

The benefits of low molecular weight heparin are single daily dose, easy to administer, decreased chances of post-operative haemorrhage and other complications associated with the use of unfractionated heparin and its more predictable anticoagulant effect.

CONCLUSION

In practice of general surgery venous thromboembolism is not uncommon, therefore there should be a protocol for stratification of patients regarding this post operative complication and there should be low threshold for starting thromboprophylaxis particularly with low molecular weight heparin which safe in terms of comparatively less chances of haemorrhage versus unfractionated heparin.

Conflict of interest: Nil

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