EVALUATION OF RISK FACTORS FOR VENOUS THROMBO-EMBOLISM AND THROMBO-PROPHYLAXIS WITH UNFRACTIONATED HEPARIN IN POST OPERATIVE GYNAECOLOGICAL PATIENTS

FARRUKH NAHEED, KARIM KAMMERUDDIN, AMBER TUFAIL, PETER BAILLIE, ALI HUSSAIN

ABSTRACT

Objective — *To evaluate the risk factors responsible for venous thrombo-embolism (VTE) in post operative gynaecological patients and to observe the effect of thrombo-prophylaxis with unfractionated heparin in reducing postoperative morbidity and mortality.*

Study design — *Case control study*

Place & Duration of study — *The study was conducted in Obstetrics & Gynaecological Department at Fatima Hospital, Baqai Medical University Karachi, from March 2006 to February 2008.*

Patients and Methods — *One hundred and fifty post operative gynaecological patients were selected randomly, consecutively and alternatively. Risk factors i.e age > 45 years, high parity- more than 5, associated medical disorders (diabetes mellitus, hypertension and obesity-BMI >30 kg/m^2), prolong surgery, immobilization as well as past history of VTE, were recorded. All patients were divided into 2 groups. Group A included 75 patients who received thrombo-embolic prophylaxis with unfractionated heparin (5000 I.U.). subcutaneously, 8 or 12 hourly till they were discharged from the hospital, whereas equal number of patients taken in group B who did not receive any kind of thrombo-embolic prophylaxis. Detailed history, examination and investigations were done after consultation with medical department with regard to co-morbidities.*

Results — *Eight risk factors were evaluated in all post operative gynaecological patients. Among them age of patients > 45 years was considered to be significant in terms of post operative VTE events (p value= 0.058). Over all effect of thrombo-prophylaxis via subcutaneously unfractionated heparin (5000 I.U.) was found to be beneficial in reducing post operative morbidity.*

Conclusions — *Early recognition of possible risk factors for VTE especially females with age > 45 years is important for the prevention of post operative morbidity and mortality. Thrombo-prophylaxis by unfractionated heparin for most operable gynaecological patients was found to be beneficial and cost effective.*

Key words — *Thrombo-embolic prophylaxis, Unfractionated heparin, Venous thrombo-embolism.*

INTRODUCTION:

Deep venous thrombosis and pulmonary embolism are included in the definition of VTE,[1] and is an important cause of perioperative morbidity and mortality.[2] It is not clear how often fatal pulmonary embolism (PE) occurs after surgery, as risk varies with surgical procedures and associated co-morbidities i.e.; elderly age (> 45 years), obesity, metabolic disorders, immobility and prolong surgery. PE accounts for 10% of all post operative deaths and 3-4% of all symptomatic VTE events in the developed world.[3] The incidence of VTE increases with elderly female patients near menopause (age

Correspondence:
Dr. Farrukh Naheed
Department of Obstetrics & Gyanecology
Baqai Medical University
Karachi.

> 45 years) as compared to patients of reproductive age who often are not suspected preoperatively, resulting in significant diagnostic and therapeutic delay, thereby accounting for substantial morbidity and mortality.[4]

Various risk factors predispose to VTE. Knowledge of these provids the rationale for prophylaxis.[5] Prophylaxis has been shown to be more effective and safe than intensive surveillance, to overcome venous stasis, a hypercoagulable state and the presence of vascular injury during surgery. Low dose unfractionated heparin (5000 I.U) given subcutaneously either 8 or 12 hourly, is a useful thrombo-prophylaxis. It provides rapid therapeutic response for the prevention of VTE in surgical patients related to urogynaecology.[6, 7] The aim of this study was to evaluate certain risk factors responsible for VTE events in post operative patients and minimizing the morbidity and mortality by providing unfractionated heparin as a cost effective thrombo-prophylaxis.

PATIENTS AND METHODS:

This study was conducted at Fatima Hospital, Baqai Medical University Karachi, in the Department of Obstetrics & Gynaecology from March 2006 to February, 2008. All patients belonged to low socio economic community of Gadap Town. One hundred fifty post operative patients who underwent major gynaecological surgeries such as, laparotomy, vaginal / abdominal hysterectomy and laparoscopy were included. Risk factors for VTE studied were age > 45 years, parity > 5, diabetes mellitus, hypertension, obesity-BMI > 30 kg/m^2, past history of VTE, prolong surgery and immobility. Patients were equally divided randomly, consecutively and alternatively into 2 groups. Group A included all those cases who received thrombo-prophylaxis therapy (unfractionated heparin 5000 I.U) subcutaneously, 8 or 12 hourly post operatively, till they became fully mobilized and discharged from the hospital. Group B did not receive pharmacological thrombo-prophylaxis.

All patients were evaluated preoperatively for the risk factors for VTE. Routine laboratory tests like x ray, ECG and specific tests like TSH, echocardiography, were done according to patient's condition or as advised by physician and for the anesthesia fitness. Monitoring of unfractionated heparin for the side effects (if bleeding) was done by sampling APTT (activated partial prothombin time) 8 or 12 hourly till the therapy continued. Similarly withdrawl of therapy depended upon the derangement of APTT. All those post operative gynaecological cases that had day care surgery like hysteroscopy and D and C or any bleeding disorders, were excluded from this study. The data was analyzed by SPSS version 10. Frequency and percentages were computed for presentation of all categorical variables. Statistically relative risks (RR) were calculated and the chosen level of significance was 5%.

RESULTS:

One hundred fifty post operative cases were evaluated for the risk factors which were responsible for thromboembolic events in surgical patients. Table I shows that among all the eight risk factors, the most common was age > 45 years in post operative gynaecological cases of both groups A and B (p value = 0.035,) (CI= 0.97 – 6.51, RR= 2.49). Other risk factor for VTE in an individual post operative patient was not found to be significant. Table II shows 100% good results after thrombo-prophylaxis in reducing post operative morbidity (p value= 0.058). There was no withdrawal of therapy due to heparin induced bleeding in this study.

DISCUSSION:

Venous thrombo-embolism which includes PE or deep vein thrombosis (DVT), is a significant condition with great bearing on well being of patients, especially those undergoing surgical procedures. This study evaluated 150 post operative gynaecological cases for the risk factors responsible for VTE events. Among surgical characteristics of patients, diagnosing VTE always require detailed history, thorough clinical examination and certain laboratory tests for the confirmation of co morbidities like hypertension, diabetes, obesity related problems. Prolong pelvic surgery (duration > 3 hours) further enhance VTE events.[8] This study showed that VTE occurred in the setting of multiple underlying risk factors and all were associated with the elderly age of female. So if patient is more than 45 years of age with major gynaecological surgery, then there is always a risk for post operative morbidities. It is because of menopause that leads to decrease in estrogen levels and cause certain metabolic changes in the body.

High cholesterol and triglyceride levels in patients with obesity and diabetes mellitus, cause increased blood viscosity, with surgical trauma thrombus formation may be precipitated.[9] Timings of VTE in all surgical patients is based upon age and related co-morbidities.[10] Same statistical significance is shown in our study regarding the age of patients. Similarly prolong surgery with significant blood loss is associated with increased risk for VTE events especially deep venous thrombosis either in one or both legs. It is because of high inflammatory response during and after surgical trauma. If patients belong to low socio economic class and are malnourished, this add significantly to problems like prolonged bleeding during surgery and results in increase incidence of post operative VTE.[11]

In our study all those patients who had morbidity and mortality due to VTE were > 45 years of age. In group A there was no morbidity as compared to five patients of group B, who did not receive heparin for post operative thrombo- prophylaxis. They suffered from DVT and ultimately required anticoagulant therapy for 3 months and referred to medical unit. Mortality in group B was associated with prolonged surgical trauma followed by prolonged immobilization in two patients who were having advance bilateral serous cytadenocarcinoma at the age of 70 year. Only one mortality was reported out of all 75 patients of group A, who presented with advance ovarian malignancy at the age of >75 years. She had a prolonged surgery, was malnourished and immobilized.

Table-I: Factors and Thrombo-prophylaxis in Postoperative Gynaecological Cases

Variables	Case (n=75)	Control (n=75)	RR (95% CI)	P – Value
Age (in years) > 45 > 45	66 (88.0) 09 (12.0)	56 (74.7) 19 (25.3)	2.49 (0.97 – 6.51)	0.035
Parity > 5 > 5	45 (60.0) 30 (40.)	42 (56.0) 33 (44.0)	1.18 (0.57 – 2.44)	0.653
Diabetes mellitus Yes No	3 (4.0) 72 (96.0)	3 (4.0) 72 (96.0)	1.00 (0.10 – 5.95)	0.812
Hypertension Yes No	11 (14.7) 64 (85.3)	11 (14.7) 64 (85.3)	1.00 (0.32 – 2.28)	0.749
Obesity(BMI = 30) Yes No	19 (25.3) 56 (74.7)	20 (26.7) 55 (73.3)	0.66 (0.27 – 1.64)	0.371
Past History of VTE Yes No	2 (2.7) 73 (97.3)	2 (2.7) 73 (97.3)	1.00 (0.37 – 2.7)	0.675
Prolonged Surgery Yes No	9 (12.0) 66 (88.0)	8 (10.7) 67 (89.3)	2.72 (0.45 – 16.6)	0.278
Immobility Yes No	4 (5.3) 71 (94.7)	6.(8.0) 69 (92.0)	0.23 (0.02 – 2.38)	0.220

Table-II
Frequency of Morbidity and Mortality in Post Operative Cases

Factor	Group A Test (n=75)	Group B Control (n=75)	P Value
Morbidity (VTE)	Nil	5	0.058
Mortality	1	3	0.619

All these facts are comparable with international 10% incidence of post operative pulmonary embolism,[12, 13] and it was found to be low (2.6%) in our study. It was probably that our study was related with only gynaecological patients where as frequency of VTE after orthopedic surgeries is usually as high as 15-30% and rate of fatal PE is 0.2 – 0.9%.[15,16]

The incidence of VTE in deprived societies presumably because of low serum fibrinogen levels due to malnutrition. It is considered as a co-morbidity along with elderly age in our society. Hence the diagnosis of VTE events was made on the basis of clinical features of the post operative patients only. No confirmation was done via pulmonary angiogram due to its non availability in the hospital setup, neither autopsy was allowed. But doppler ultrasound was carried out in all suspected cases of DVT. In spite of all, the effect of thrombo-prophylaxis in each individual factor is not statistically significant except in elderly patients (age > 45 years). The use of unfractionated heparin as a prophylaxis in post operative gynaecological patients, can reduce the rate of venous thrombo-embolic events and found to be cost effective.

CONCLUSIONS:

Early recognition of possible risk factors for VTE especially females with age > 45 years is important for the prevention of post operative morbidity and mortality.Thrombo-prophylaxis by unfractionated heparin for most operable gynaecological patients was found to be beneficial and cost effective.

REFERENCES:

1. Ginsberg JS. Management of venous thrombo embolism. N Eng J Med. 1996;335:1816 – 28.
2. Weinimann EE, Salzman EW. Deep vein thrombosis. N Eng J Med 1994;331:1630 -41.
3. Sitzman BT. Prevention of preoperative deep venous thrombosis and pulmonary embolism. www.demsoline.org / Jax – Medicine / Dec 1998 Journal, thrombosis. htm.
4. Heit JA, Melton LJ, Lohse CM, Petterson JM, Steive S, Mohr DN et al. Incidence of venous thrombo embolism in hospitalized patients versus community residents. Mayo Clin Proc 2001;76:1102 – 10.
5. Nazeer A, Shabbir B, Kamal A, Qaisera S. An experience with venous thrombo embolism at Sir Ganga Ram Hospital, Lahore. Annals King Edward Med Coll 2004;10:103 –5.
6. Kearon C, Hirsch J. Starting prophylaxis for venous thrombo embolism post operatively. Arch Internal Med 1995;155:366 – 12.
7. Chorg BT. Heparin induced thrombocytopenia. Br J Haematol 1995; 89:431– 9.
8. Leizoroviz. A. Epidemiology of post operative venous thrombo embolism in Asian patients. Result of SMART venography study. Haematol J 2007;92:494 –9.
9. Aliya. A. Prevention of deep venous thrombosis and pulmonary embolism in preoperative period. J Pak Med Assoc 2005;18:343 –7.
10. Bjornana BT, Gudmumdsen TE. Frequency and timing of clinical venous thrombo embolism after major joint surgery. J Bone Joint Surg Br 2006;88:386 – 91.
11. Mumin MC, Rudy TE, Glynn NW, Cross LS, Rubash HE. Early in patient rehabilitation after elective hip and knee arthroplasty. JAMA 1998; 279:847–57.
12. Picciloi A, Prandoni P, Ewcsnstein BM, Goldhabez SZ. Cancer and venous thrombo embolism. Am Heart J 1996;132:850–5.
13. Olin JW. Pulmonary embolism. Rev. Cardiovascular Med. 2003;S:68 –75.
14. Kuroiwa M, Sco N, Furuya H. Incidence and characteristics of preoperative pulmonary embolism in Japan in 2004. 2006;55:1031- 8.
15. Clagett GP, Resich JS. Prevention of venous thrombo embolism in general surgery patients: Result of meta analysis. Ann Surg 1988;208:227– 40.
16. Pezzuloli G, Neri Serneri GG, Settembriane P. Prophylaxis of fetal pulmonary embolism in general surgery using low molecular weight heparin : a month centric, double blind, randomized control clinical trial verses placed (Step Study group). Int Surg 1989;74: 205 –10.
17. Mismethi P, Laporte S, Dermon JY. Analysis of low molecular with heparin in the prevention of venous thrombo embolism in general surgery. Br J Surg 2001;88:913 – 30.