Thromboprophylaxis in Neurosurgical Patients at Jordan University Hospital: A Prospective Comparative Study**

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Abstract

Background and Objectives: Venous Thromboembolism (VTE) is potentially a life threatening complication in patients undergoing major neurosurgical procedures. There has been a general reluctance over the years to use anticoagulant prophylaxis for patients with head injury or in patients who need intracranial surgery. Intermittent Pneumatic Compression (IPC) and elastic stocking are widely used as prophylaxis against venous thrombo-embolism in these patients. The aim of the study is to assess and compare the value of VTE prophylaxis using a control group with Low Dose Unfractionated Heparin (LDUH) every eight hours alone with a study group using Intermittent Pneumatic Compression (IPC) and elastic stocking along with Single Dose Unfractionated Heparin (SDUH) at the time of anaesthesia induction on patients undergoing brain and spinal surgery.

Methods: A prospective case–control study was conducted at Jordan University Hospital, over 15 months during the period 2005-2006. A total of 223 patients were included. In the study group, 113 patients using single dose of unfractionated heparin at the time of anaesthesia induction along with Intermittent Pneumatic Compression (IPC) intraoperatively and compression Elastic Stockings (ES) post operatively were used until full ambulation.

In the control group, there were 110 patients in whom unfractionated heparin at a dose of 5000 units every 8 hours was used until full ambulation or for 7 days. All patients underwent either brain surgery or spinal surgery.

Results: The characteristics of the two groups were fully comparable except for the duration of surgery which was statistically longer in the study group (P= <0.001). Deep Vein Thrombosis (DVT) occurred in 3 patients in the study group, compared to 6 patients in the control group, of these 6 patients, 4 patients developed PE in addition to DVT and one of the four patients expired. The observed differences among these rates are statistically not significant (P=0.288).

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When pooled together, patients who developed VTE in both groups were older than those who did not have VTE. This difference was statistically significant (P=0.007).

Conclusion: The combination of elastic stocking, intermittent pneumatic compression along with single dose unfractionated heparin at the time of anaesthesia induction is comparable in effectiveness of reducing the incidence of VTE as the low dose unfractionated heparin alone in patients undergoing neurosurgical procedures of the brain or spine, despite the trend towards better results of the combined method.

Keywords: Deep Vein Thrombosis, Venous Thrombo-embolism, Neurosurgery, Pulmonary Embolism. Low Dose Unfractionated Heparin.

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Introduction

Venous Thromboembolism (VTE) is a major cause of morbidity and mortality in hospitalized patients and is the most frequent potentially life threatening complication in patients undergoing neurosurgical operations. Many neurosurgical patients are at a considerable risk for the formation of venous thrombosis, the incidence range is 18-50% for Deep Venous Thrombosis (DVT) and 0-25% for Pulmonary Embolism (PE), [9] Some studies found out that the rate of VTE in neurosurgical patients to be 25% [1, 2] with a mortality rate ranging from 9 -50%. [2]

The risk of DVT for combined cranial/spinal procedures performed without prophylaxis varied from 29% to 43%, [3] the incidence of DVT was greater for cranial than spinal procedures. [7] The rate of DVT and PE is thus quite significant and can lead to fatal outcomes. Evidence indicates that mechanical devices prevent Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) by limiting venous stasis and increasing fibrinolytic activity at both the local and systematic levels for venous thromboemoblism in neurosurgical patients. [1]

Large population-based studies have found that a variety of factors place the neurosurgical patients at increased risk for DVT. These include intracranial surgery, malignant tumors, lengthy operative procedures, prolonged immobilization, bed rest postoperatively, postoperative paralysis, older age, prone positioning on frames with flexion of the hips and knees, and distraction of the spine which compresses lower extremity venous return. [10]

The optimal strategy for prophylaxis against thrombo-embolism in elective neurosurgery is unclear. Physical methods, including intermittent pneumatic compression devices and compression stocking have been preferred to anticoagulant agents because of concern about intra-cranial bleeding. [5]

Neurosurgeons are concerned about bleeding complications and there have been limited data on the most efficient and safe prophylaxis in neurosurgery and spinal surgery patients.

The aim of the study is to assess a protocol of prophylaxis comparing Unfractionated Heparin (UFH) alone given perioperatively as at a dose of 5000 units subcutaneously every 8 hours for 7 days or until ambulation, which was the standard protocol used in our practice at Jordan University Hospital (JUH) (control group), and a second method using single dose of 5000 units unfractionated heparin given subcutaneously preoperatively at the induction of anesthesia along with mechanical prophylaxis with intermittent pneumatic compression device during operation followed by elastic stocking until ambulation (study group).

Patients and Methods

A prospective case-control study was conducted at Jordan University Hospital over 15 months during 2005-2006. A total of 223 patients who underwent neurosurgery (brain and spinal surgery) were included. All patients were Jordanians; the mean age of patients was 46.31 years (men = 45.37 years, women= 47.45 years; range 12-85 years).

113 patients in whom we used single dose unfractionated heparin subcutaneously 5000 units preoperatively at the start of anesthesia along with intermittent pneumatic compression device during operation followed by elastic stockings until full ambulation (study group) were compared with 110 patients in whom we utilized unfractionated heparin alone every 8 hours starting at induction of anaesthesia and continued for 7 days or until the patient was ambulating (control group).

The following variables were studied: age, gender, weight of the patient, duration of surgery, site of surgery, position of patient during the surgery, time for start of ambulation post operatively.

Deep Vein Thrombosis (DVT) was diagnosed in the presence of relevant clinical criteria and confirmed by Duplex ultrasound. Pulmonary Embolism (PE) was diagnosed in the presence of the relevant clinical criteria and confirmed by spiral CT.

The study protocol was approved by the Institutional Review Board (IRB) of the hospital. All investigated subjects gave written informed signed consent for their participation in this study in accordance with the Helsinki declaration.

Statistical Analysis

We used a case-control design to allow quantitative comparison between groups. All statistical tests were independent t-test. Pearson Chi square was used to test for association in the distribution of categorical variable. P-values less than the level of 0.05 were considered statistically significant. Fisher exact test was considered when the value is less than five. The analyses were performed using the SPSS package version 16.0.

Results

Clinical Characteristics

Clinical characteristics of the 223 patients who underwent neurosurgical (brain or spinal surgery) are shown in table (1). There were 101(45.3 %) females and 122(54.7%) males. The mean age of the patients was 46.31 ± 14.06 years with a range of (12 - 85) years.

OF the 113 study group patients, in whom mechanical prophylaxis along with single dose unfractionated heparin was used; 61(54%) are males and 52(46%) are females. Of the 110 control group patients, in whom the unfractionated heparin every 8 hours alone was used; there were 61(55.5%) males and 49(44.5%) females.

The mean age, weight, duration of surgery, ambulation post-surgery are shown in table (1) There were no statistical differences between groups in regard to age, gender, weight, duration of surgery, site of surgery, position during surgery, ambulation and risk factors for venous thromboembolism. P-value respectively was 0.054, 0.825, 0.284, 0.001, 0.111 0.072, 0.262 and 0.288, respectively. There was a statistical different in the duration of surgery being longer in the study group (P-value 0.001).

VTE Findings

Deep Vein Thrombosis (DVT) occurred in 3 patients (2.7%) in the study group and in 6 patients (5.5 %) in the control group 2-7 days postoperatively. Of the 6 patients in the control group, 4 patients (66.7%) developed PE in addition to the DVT and one of the four patients expired. The observed differences among these rates are not statistically significant (P = 0.288). The difference between patients who developed VTE in comparison with patients who had no

VTE there is a statistically significant in age P=0.007 table (2).

Table (3) shows the patients characteristics among the patients with VTE for patients and for patients without VTE who had IPCD, ES and LDUH and LDUH alone.

Table (1): Demographic and clinical characteristics of patients.

Characteristics	***LDUH, IPCD and ES Study group (113patients)***	***LDUH Control Group (110 patients)***	***Total (223 Patients)***	***P- value***
Age *mean ± SD*	*44.52 ± 13.80*	*48.15 ± 14.15*	*46.31 ± 14.06*	*0.054*
Range	*12-68*	*13-85*	*12-85*	
Gender				
Female	*52 (46%)*	*49 (44.5%)*	*101 (45.3%)*	*0.825*
male	*61(54%)*	*61 (55.5%)*	*122 (54.7%)*	
Weight – kg *mean ± SD*	*74.79 ± 8.387*	*73.60 ± 8.11*	*74.20 ± 8.26*	*0.284*
Duration of surgery *Mean ± SD*	*4.377 ± 2.04*	*3.57 ± 1.55*	*3.98 ± 1.86*	*0.001*
Site of surgery				
Intracranial	*33 (29.2%)*	*22 (20%)*	*55 (24.7%)*	*0.111*
Spinal	*80 (70.8%)*	*88 (80%)*	*168 (75.3%)*	
Position during surgery				
Prone	*64 (56.6%)*	*77 (70%)*	*141 (63.2%)*	
Sitting	*17 (15%)*	*8 (7.3%)*	*25 (11.2%)*	*0.072*
Supine	*32 (28.3%)*	*25 (22.7%)*	*57 (25.6%)*	
Ambulation post-surgery *mean ± SD*	*16.75 ± 17.16*	*19.61 ± 20.623*	*18.16 ± 18.96*	*0.262*
VTE				
Normal	*110 (97.3%)*	*104 (94.5%)*	*214 (96%)*	*0.288*
VTE (DVT or PE or both)	*3 (2.7)%*	*6 (5.5%)*	*9 (4%)*	

Table (2): Post-operative venous thrombosis for case and control group.

Characteristics	***Patients with VTE In both groups***	***Patients without VTE In both groups***	***P- value***
	No= 9 (4%)	*No=214 (96%)*	
Age *mean ± SD*	*58.56 ± 10.83*	*45.79 ± 13.97*	*0.007*
Range	*42-75*	*12-85*	
Gender			
Female	*5 (55.6%)*	*96 (44.9%)*	*0.383*
male	*4 (44.4%)*	*118 (55.1%)*	
Weight – kg *mean ± SD*	*74.67 ± 10.52*	*74.18 ± 8.18*	*0.864*
Duration of surgery *mean ± SD*	*4.1 ± 1.55*	*3.97 ± 1.87*	*0.842*
Site of surgery			
Intracranial	*1 (11.1%)*	*54 (25.2%)*	*0.458*
Spinal	*8 (88.9%)*	*160 (74.8%)*	
Position during surgery			
Prone	*8 (88.9%)*	*133 (62.1%)*	
Sitting	*0 (0%)*	*25 (11.7%)*	*0.247*
Supine	*1 (11.1%)*	*56 (26.2%)*	
Ambulation post-surgery *mean ± SD*	*27.11 ± 35.0*	*17.31 ± 16.65*	*0.149*

Table (3): Patients characteristics among the patients with VTE for patients and for patients without VTE who had IPCD, ES and LDUH and LDUH alone.

Characteristics	Patients with VTE		Patients without VTE	
	Study Group No. 3 (33.3%)	Control Group No. 6 (66.7%)	Study Group No. 110 (51.4%)	Control Group No. 104 (48.6%)
Age mean ± SD	51.67 ± 5.13	62.0 ± 11.593	44.33 ± 13.92	47.35 ± 13.91
Gender				
Female	3 (100%)	2 (33.3%)	47 (45.2%)	49 (44.5%)
male	0 (0%)	4 (66.7%)	57 (54.8%)	61 (55.5%)
Weight – kg mean ± SD	68.67 ± 4.04	77.67 ± 11.759	74.95 ± 8.42	73.37 ± 7.87
Duration of surgery mean ± SD	5.38 ± 1.61	3.46 ± 1.14	4.35 ± 2.05	3.58 ±1.57
Site of surgery				
Intracranial	1 (33.3%)	0 (0%)	32 (29.1%)	22 (21.2%)
Spinal	2 (66.7%)	6 (100%)	76 (70.9%)	82 (78.8%)
Position during surgery				
Prone	2 (66.7%)	6 (100%)	62 (56.4%)	71 (68.3%)
Sitting	0 (0%)	0 (0%)	17 (15.5%)	8 (7.7%)
Supine	1 (33.3%)	0 (0%)	31 (28.2%)	25 (24.0%)
Ambulation post-surgery mean ± SD	13.33 ± 4.04	34.0 ± 42.19	16.85 ±17.38	18.78 ± 18.73

Discussion

Post-operative Deep Vein Thrombosis (DVT) remains a major problem in neurosurgical patients, the 2001 and subsequent ACCP consensus on DVT prophylaxis acknowledged a high incidence of disorder in neurosurgical patients.

The methods of providing DVT prophylaxis to patients undergoing neurosurgery is a controversial issue. West Virginia Medical Institute had various VTE prophylactic regimens for neurosurgery are any of the following: IPC (Intermittent Pneumatic Compression), without Graduated Compression Stocking (GCS), Low Dose Unfractionated Heparin (LDUH), Low Molecular Weighted Heparin (LMWH), LDUH or LMWH combined with IPC or GCS.

The current guidelines recommended post-op LMWH for intracranial neurosurgery. [11] We aimed in this work at assessing a new protocol used in our department and compare it with our current practice protocol to find out what type of prophylaxis is effective. In the new protocol, we used single dose unfractionated heparin subcutaneously 5000 units at the time of induction of anesthesia along with mechanical prophylaxis, intermittent pneumatic compression device and elastic stockings until full ambulation on 113 patients. Those were compared with patients in whom we utilized the Low Dose Unfractionated Heparin (LDUH) 5000 units every 8 hours begun preoperatively and continued for 7 days or until the patient was fully ambulated.

The results of our study showed the two groups to be comparable except for the duration of surgery which was longer in the study group. VTE and PE were seen less frequently in the study group but did not reach statistical significance because of the small sample size. Our results are similar to the results found by Epstein. In his study, Epstein found that pneumatic compression stocking prophylaxis effectively reduces the incidence of DVT (2.8%) and PE (0.7%). [6]

Many studies show the efficacy of different prophylaxis regimens against DVT/PE in a neurosurgical setting. ES alone reduce DVT rates by 79% and PE by 43% whereas LMWH reduced DVT by 90% and the PE by 67%. [10] The incidence of DVT in Neurosurgical patients was found to be 5.6% in one study. [7] In this study, ultrasound was used pre and post-operative to detect DVT. The incidence of DVT was higher in

patients who underwent craniotomy than those who had spinal surgery alone; 7.7% and 1.5%, respectively. [7]

In our study, we relied on clinical criteria alone for the suspicion of VTE which was subsequently confirmed by the appropriate radiological technique. This may account for the lower incidence of DVT in our patients who underwent intracranial surgery.

The higher incidence of PE in the control group is note-worthy since this is a serious complication. It shows that LDUH was given in our protocol is not enough. It may be possible to get better protection by using a combination of IPC and ES added to a single dose LDUH was given at the induction of anesthesia. The fact that figures did not reach statistical significance is explained by the small sample size and by the low incidence of PE in these situations.

Conclusions

Pneumatic compression device and elastic stocking provided effective prophylaxis against DVT and PE when combined with a Single Dose Unfractionated Heparin (SDUH) given at the time of anesthesia induction in Neurosurgical patients.

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الوقاية من الانصمام الختاري الوريدي في مرضى جراحة الاعصاب في مستشفى الجامعة الأردنية: دراسة استباقية مقارنة

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الملخص

الخلاصة والأهداف: الانصمام الختاري الوريدي من المضاعفات المهددة للحياة لدى مرضى الجراحات العصبية. كان هناك تردد على مدى السنوات الماضية لاستخدام مضادات الخثرات وقائيا لمرضى اصابات الرأس أو المرضى الذين يحتاجون جراحة داخل الدماغ. ان الضغط الهوائي المتقطع والجوارب المرنة هي مستخدمة بشكل واسع وقائي من الجلطات الخثرية الوريدية في هؤلاء المرضى. تهدف هذه الدراسة التي اجريت الى مقارنة قيمة التجلطات الوريدية الخثرية باستخدام مجموعة مراقبة على جرعات قليلة من الهيبارين (LDUH) كل ثماني ساعات وحدها مع مجموعة دراسة اخرى تستخدم الجوارب المرنة والضغط الهوائي المتقطع مع جرعة واحدة من الهيبارين (SDUH) عند المرضى الذين يخضعون لجراحة الدماغ والنخاع الشوكي ويتم اعطاؤها قبل العملية مباشرة عند التخدير .

الطريقة: دراسة استباقية للحالات والشواهد اجريت في مستشفى الجامعة الأردنية، على مدى 15 شهرا خلال الفترة 2005-2006 . واجريت على 223 مريضا .في مجموعة الدراسة 113 مريضا اعطوا الهيبارين لجرعة واحدة عند بداية التخدير مع الضغط الهوائي المتقطع خلال العملية والجوارب المرنة بعد الجراحة حتى يتحرك المريض كليا. في مجموعة المقارنة كان هناك 110 مرضى ممن اعطوا الهيبارين بجرعة مقدارها 5000 وحدة كل 8 ساعات حتى يتحرك المريض كليا أو لمدة 7 أيام. وخضع جميع المرضى إما لجراحة الدماغ أو جراحة في النخاع الشوكي.

النتائج: خصائص المجموعتين كانت متماثلة تماماً باستثناء مدة العملية الجراحية التي كانت ذات دلالة إحصائية P=0.001 التجلط الوريدي العميق حدث عند 3 مرضى من مجموعة الدراسة بالمقارنة ب 6 مرضى من مجموعة الشواهد حيث ان 4 من 6 اصيبوا بانصمام رئوي بالإضافة إلى الاصابة الانصمام في الاوردة العميقة وواحد من المرضى الأربعة قد توفي. الفروق الملاحظة بين هذه المعدلات ليست ذات دلالة إحصائية مهمة P =0.288 . عند دمج المجموعتين معا لوحظ ان المرضى الذين اصيبوا بتخثر الأوردة العميق اكبر عمرا من الذين لم يصابوا بالتخثر وكان هذا الفرق ذا دلالة إحصائية P=0.007.

الخاتمة: إن استخدام الجوارب المرنة والضغط الهوائي المتقطع مع حقنة واحدة من الهيبارين عند بداية التخدير تقلل حدوث تخثر الاوردة العميق بفعالية تقارن باستخدام جرعات قليلة متكررة من الهيبارين وحده لدى المرضى الذين يخضعون لجراحة الاعصاب في المخ أو النخاع الشوكي. على الرغم من المتعارف عليه بان النتائج افضل عند استخدام طريقة الجوارب المرنة والضغط الهوائي المتقطع مع الهيبارين.

الكلمات الدالة: تخثر الاوردة الميق (التجلط)، انصمام الاوردة الخثري، جراحة عصبية، انصمام رئوي، هيبارين.