

The effect of intraoperative subcutaneous heparin on prophylaxy of deep vein thrombosis (DVT) in surgical treatment of acetabular fractures

El efecto de la heparina subcutánea intraoperatoria en la profilaxis de la trombosis venosa profunda (TVP) en el tratamiento quirúrgico de las fracturas acetabulares

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Abstract

Introduction and objective: Thromboembolism after surgery is a significant problem in patients with acetabular fractures. This study aimed to evaluate the effect of intraoperative administration of subcutaneous heparin on prophylaxy of deep vein thrombosis and pulmonary thromboemboli during and after surgery.

Materials and methods: This study is a non-blinded trial in which 42 patients over 18 years old with acetabular fractures who required surgery were divided into two groups matched by age and sex. Patients were randomly assigned to one of two treatment groups: with and without heparin injection during surgery.

Inclusion criteria included patient with unstable posterior column or wall acetabular fractures that open reduction and internal fixation was the choice of treatment, patient more than 18 years old underwent this study. Exclusion criteria included a history of heparin-induced allergy and thrombocytopenia, a history of coagulopathy such as hemophilia.

Results: In this study 42 patients with acetabular fractures admitted to the orthopedic ward, 36 patients (85.7%) were male and 6 patients (14.3%) were female with a mean age of 49.2 ± 8.1 years. 20 patients (47.6%) received subcutaneous heparin during surgery and the other 22 patients (52.4%) did not receive heparin. In the group receiving subcutaneous heparin, proximal deep vein thrombosis was observed in one patient, while 5 patients (22.7%) in the group without heparin showed proximal deep vein thrombosis during surgery. There was no significant difference between the mean age of patients and the volume of intraoperative bleeding in the group receiving heparin (700 ± 50 ccs) and the group without heparin (600 ± 50 ccs).

Conclusion: Intraoperative subcutaneous injection of heparin can prevent deep vein thrombosis and pulmonary thromboembolism and reduce patient mortality. Intraoperative injection of subcutaneous heparin was not associated with a significant increase in intraoperative bleeding and had no considerable side effects.

Key words: Acetabular fractures, heparin, thromboembolism, Deep Vein Thrombosis, bleeding heparin.

Resumen

Introducción y objetivo: El tromboembolismo después de la cirugía es un problema importante en los pacientes con fracturas acetabulares. Este estudio tiene como objetivo evaluar el efecto de la administración intraoperatoria de heparina subcutánea en la profilaxis de la trombosis venosa profunda y la tromboembolia pulmonar durante y después de la cirugía.

Material y métodos: Este estudio es un ensayo no ciego en el que 42 pacientes mayores de 18 años con fracturas acetabulares que requerían cirugía fueron divididos en dos grupos emparejados por edad y sexo. Los pacientes fueron asignados aleatoriamente a uno de los dos grupos de tratamiento: con y sin inyección de heparina durante la cirugía. Los criterios de inclusión incluían a los pacientes con fracturas acetabulares inestables de la columna o la pared posterior cuyo tratamiento elegido era la reducción abierta y la fijación interna; los pacientes mayores de 18 años se sometieron a este estudio. Los criterios de exclusión incluían antecedentes de alergia a la heparina y trombocitopenia, y antecedentes de coagulopatía, como la hemofilia.

Resultados: En este estudio 42 pacientes con fracturas acetabulares ingresados en la sala de ortopedia, 36 pacientes (85,7%) eran hombres y 6 pacientes (14,3%) eran mujeres con una edad media de $49,2 \pm 8,1$ años. 20 pacientes (47,6%) recibieron heparina subcutánea durante la cirugía y los otros 22 pacientes (52,4%) no recibieron heparina. En el grupo que recibió heparina subcutánea, se observó trombosis venosa profunda proximal en un paciente, mientras que 5 pacientes (22,7%) del grupo sin heparina mostraron trombosis venosa profunda proximal durante la cirugía. No hubo diferencias significativas entre la edad media de los pacientes y el volumen de hemorragia intraoperatoria en el grupo que recibió heparina (700 ± 50 cc) y el grupo sin heparina (600 ± 50 cc).

Conclusiones: La inyección subcutánea intraoperatoria de heparina puede prevenir la trombosis venosa profunda y el tromboembolismo pulmonar y reducir la mortalidad de los pacientes. La inyección intraoperatoria de heparina subcutánea no se asoció a un aumento significativo de la hemorragia intraoperatoria y no tuvo efectos secundarios considerables.

Palabras clave: Fracturas acetabulares, heparina, tromboembolismo, trombosis venosa profunda, sangrado Heparina.

Introduction

Treatment of pelvic and acetabular fractures remains a challenge¹⁻³. Venous thromboembolism (VTE) including deep vein thrombosis (DVT) and pulmonary embolism (PE) is a complication associated with these fractures^{4,5}. Studies have shown that in the absence of thromboprophylaxis, the incidence of DVT in patients with pelvic fractures is variable up to 61%⁶. Deep vein thrombosis is the most common cause of death of lower limb fractures (hip and pelvis) after the seventh day of admission.

In most of these patients, PE was difficult to diagnose before death, suggesting that PE may be the first manifestation of asymptomatic DVT⁷. Each year, about 10 million cases of venous thromboembolism are reported worldwide⁸. According to a Korean study in 1990 on the autopsy of patients undergoing spinal surgery, deep vein thrombosis accounted for 1.3% of deaths⁹. Patients can be classified according to their age, the presence or absence of other risk factors for VTE, and the type of surgery to be performed. Patients at lower risk of VTE require no special treatment but prophylaxis of DVT is needed as soon as possible, while patients at moderate or higher risk of DVT¹⁰.

Patients with pelvic trauma are at risk for thromboembolic complications, but effective guidelines have still to be adopted¹¹. A variety of thromboprophylaxis drugs are recommended in high-risk trauma patients. Low-dose heparin or intermittent pneumatic compression devices alone are not always effective in preventing DVT^{12,13}, whereas low molecular weight heparin (LMWH) has been shown to decrease DVT rates in patients with pelvis or lower limbs fractures¹¹. Anticoagulants, such as unfractionated heparin (UFH), low molecular weight heparin (LMWH), and warfarin, or antiplatelet agents, especially acetylsalicylic acid (aspirin), are pharmacological agents used for thromboprophylaxis. Prophylaxis of DVT is usually done with low-dose heparin (LDH). First, a subcutaneous dose of 5,000 units is injected 2 hours before surgery and repeated every 12 hours for up to 6 days. This method produces a good preventive effect in most patients¹⁴.

According to the literature and the predictable risk, anticoagulant therapy should be started as soon as possible. In a study by O'Donnell et al., low molecular weight heparin (LMWH) or warfarin was suggested as the treatment of choice for patients with spinal cord anesthesia and all patients with major trauma¹⁵. The results of a study by Wang et al showed that the risk of developing DVT is higher in patients older than 60 years, patients with trauma, patients with associated injuries, and surgery after 2 weeks in nonambulate multi trauma patients¹⁶. Steele et al.¹⁷ reported that LMWH if initiated without delay, is a safe and effective method

of thromboprophylaxis in high-risk patients with major pelvic or acetabular fractures. If remains unrecognized, DVT can lead to long-term complications from post-phlebotic (post-thrombotic) syndrome and predispose patients to recurrent VTE¹⁰. Because VTE in hospitalized patients is often asymptomatic, it is inappropriate to rely on early detection. In addition, non-invasive tests, such as ultrasound, have limited sensitivity for the diagnosis of asymptomatic DVT. Therefore, thromboprophylaxis is the most effective strategy to reduce morbidity and mortality from VTE in surgical patients. Despite this evidence, thromboprophylaxis is not used in clinical practice as surgeons believe that the risk of VTE is much lower to justify the potential hemorrhagic complications from the use of anticoagulants¹⁸. Despite the use of preoperative prophylaxis, patients are predisposed to DVT due to prolonged prone position, prolonged surgery time, and the use of blood transfusions. This study was the first to evaluate the effect of intraoperative administration of subcutaneous heparin on the surgical complications of acetabular fractures, including venous thrombosis, mortality, intraoperative bleeding, etc.

Materials and methods

This study aimed to evaluate the effect of intraoperative administration of subcutaneous heparin on the surgical complications of acetabular fractures. The study population included patients with acetabular fractures admitted to the orthopedic ward of Imam Khomeini Hospital affiliated with the Urmia University of Medical Sciences. The number of people in each group was determined to be 33 based on the following formula. Convenience sampling was used in this study.

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 [P_1(1-P_1) + P_2(1-P_2)]}{(P_1 - P_2)^2}$$

$$Z_{1-\beta} = 0.84, Z_{1-\alpha/2} = 1.64$$

Method

This study is a non-blinded trial in which 42 patients over 18 years old with acetabular fractures who required surgery were divided into two groups matched by age and sex. Inclusion criteria included individuals with acetabular fractures with posterior involvement who required surgery, individuals over 18 years of age, and consent to participate in the study. Exclusion criteria included a history of heparin-induced allergy and thrombocytopenia, a history of coagulation disorders, and a history of hemophilia and thalassemia. Based on the codes provided by Random Allocation software, the patients were randomly assigned to one of two treatment groups: the group with heparin injection and the group without heparin injection. For

patients treated with subcutaneous heparin, 5,000 units of heparin were injected subcutaneously before the surgical incision and after placing the patients in the prone position, while no anticoagulants were injected into the other group. Depending on the surgical site and patient's condition, the patients underwent a certain form of general anesthesia. Patients with primary embolism thrombosis and preoperative venous thrombosis were excluded from the study. According to common treatment methods, all patients should receive anticoagulants, including subcutaneous enoxaparin and antithrombotic stockings, from the time of admission and after surgery. Patients undergoing surgery in the prone position (lying on the abdomen) were placed in a group undergoing intraoperative prophylaxis with 5,000 units of subcutaneous heparin. The two groups were compared for complications including venous thrombosis, mortality, morbidity, intraoperative cardiovascular findings, intraoperative hemorrhage -estimated based on the amount of blood collected in the suction tank and the number of blood-soaked gauzes- and postoperative hemorrhage - estimated based on the volume of the Hemovac reservoir. After surgery, patients were visited daily and were evaluated for clinical symptoms including swelling, erythema, and pain in the lower extremities. In the case of clinical evidence, the patients were further evaluated using color Doppler ultrasound. All patients underwent color Doppler ultrasound on day 14 after surgery for deep vein thrombosis of the lower extremities. Data collection tools in the present study included checklists and a review of patient records.

Statistical analysis

Descriptive statistical methods were used in this study. Frequency analysis test (chi-square) was used to compare qualitative data and statistical analytical methods (independent t-test) were used to compare quantitative data between the two groups. Statistical analysis was performed using SPSS17/win software and a P-value less than 0.05 was considered significant.

Results

This study included 42 patients with acetabular fractures admitted to the orthopedic ward of Imam Khomeini Hospital affiliated to the Urmia University of Medical Sciences, of which 20 patients (47.6%) received subcutaneous heparin and other 22 patients (52.4%) did not receive heparin during surgery. The results showed that 85.7% of patients with acetabular fractures were males and 14.3% were females. The mean age of the patients was 49.2 ± 8.1 years. The results of the Fisher test showed that there was no significant difference between the sexes of patients with acetabular fractures admitted to the orthopedic ward in different study

groups (the group receiving subcutaneous heparin and the group without heparin during surgery) ($P < 0.05$). Therefore, male and female participants were matched between the two groups. The comparison results for the frequency of mortality, the frequency of proximal deep vein thrombosis (iliac and femoral), and drug side effects in patients with acetabular fractures between the two groups are presented in **table I**.

The results of the t-test showed that there was a significant difference in patients' mean age between the two groups (subcutaneous heparin receiving group and non-receiving group during surgery) ($P < 0.05$). Also, there was a significant difference in the mean intraoperative bleeding volume estimated in the group receiving heparin (700 ± 50 ccs) and the group without heparin (600 ± 50 ccs) during surgery ($P < 0.05$). However, no significant difference in the mean bleeding volume estimated in Hemovac was found between the two groups (300 ccs vs. 250cc, respectively) ($P < 0.05$). Moreover, no significant difference was also observed in the other variables (hospitalization time/ post-operative bleeding in Hemovac, cc/ heartrate / systolic hypertension / diastolic hypertension) between the two groups of subcutaneous heparin receiver and non-receiver during surgery. (**Table II**).

Discussion

The present study evaluated the effect of intraoperative administration of subcutaneous heparin on the surgical complications of acetabular fractures in patients admitted to Imam Khomeini Hospital. In the study of Wang et al¹⁶ to investigate the incidence and risk factors of deep vein thrombosis (DVT) in patients with pelvic and acetabular fractures, thirty-two (29.09%) patients sustained DVT, twenty-one (19.09%) patients showed proximal thrombosis, and three patients developed pulmonary embolism. Steele et al¹⁸ evaluated the outcome of a prophylaxis protocol for deep vein thrombosis (DVT) in 103 patients who underwent open reduction and internal fixation of pelvic and acetabular fractures. Low molecular weight heparin (LMWH) was administered within 24 hours of injury or in hemodynamically stable patients. The incidence of proximal DVT and pulmonary embolism was 10% and 5%, respectively. Proximal DVT occurred in 2 of 64 patients (3%) who received LMWH within 24 hours of injury and also in 8 of 36 patients (22%) who received LMWH more than 24 hours after injury. In the present study, lower extremity color Doppler ultrasound was performed for patients with clinical evidence of deep vein thrombosis and for all patients on a postoperative day 14. According to the results of this study, there was no significant difference between the mean age of patients and the volume of intraoperative bleeding in the group receiving subcutaneous heparin and the group without heparin ($P < 0.05$). Although previous studies have reported that patients over 30 are

Table I: Comparison of the frequency of mortality, proximal deep vein thrombosis, and drug side effects between the two groups.

	Group	Yes	No	Total
Mortality	Intraoperative heparin	0 (0%)	20 (100%)	20 (100%)
	No intraoperative heparin	2 (9.1%)	20 (90.9%)	22 (100%)
P-value		0.489		
Proximal deep vein thrombosis	Intraoperative heparin	1 (5%)	19 (95%)	20 (100%)
	No intraoperative heparin	5 (22.7%)	17 (77.3%)	22 (100%)
P-value		0.04		
Drug side effects	Intraoperative heparin	0 (0%)	20 (100%)	20 (100%)
	No intraoperative heparin	-	-	-

Table II: Research variables between the subcutaneous heparin receiving and non-receiving groups during surgery.

Variable	Group	N	Mean	SD	t-value	P-value
Age	intraoperative heparin	20	47.4	7.4	2.31	0.026
	No intraoperative heparin	22	52.4	6.5		
Time of hospitalization	intraoperative heparin	20	5.85	1.49	1.9	0.064
	No intraoperative heparin	22	6.63	1.17		
Intraoperative bleeding, cc	intraoperative heparin	20	3.2250E2	54.95213	2.31	0.026
	No intraoperative heparin	22	2.8091E2	61.01593		
Post-operative bleeding in Hemovac, cc	intraoperative heparin	20	91.2500	9.01388	1.18	0.244
	No intraoperative heparin	22	88.1818	7.7988		
Heart rate	intraoperative heparin	20	91.2	7.24460	0.39	0.698
	No intraoperative heparin	22	92	6.02376		
Systolic hypertension	intraoperative heparin	20	122.7	12.29	0.231	0.819
	No intraoperative heparin	22	123.6	12.55		
Diastolic hypertension	intraoperative heparin	20	87.5	6.78	0.281	0.78
	No intraoperative heparin	22	86.9	6.83		

at higher risk of developing DVT¹⁹, some studies have found no association between DVT and patient age²⁰. However, older age is often considered one of the factors associated with the higher risk for DVT²¹. Similarly, Kim et al²² reported a significant increase in DVT rates in patients with pelvic and acetabular fractures over 50 years of age. Therefore, elderly patients with pelvic acetabular fractures should be evaluated more precisely for DVT.

One of the reasons for the high prevalence of DVT in patients is the failure of effective anticoagulant therapy in the early periods after the injury due to the risk of bleeding¹⁹. For patients undergoing acetabular fracture surgery, ACCP guidelines recommended the use of LMWH, low-dose UFH, VKA, fondaparinux, aspirin (all grade 1B), or IPCD (grade 1C) for at least 10 to 14 days and up to 35 days²³. There is a limited number of studies comparing different pharmacologic agents and the results of these studies have not yet clarified which thromboprophylaxis agent is preferred^{24,25}. The incidence of DVT was 10% in the LMWH group versus 30% in the dextran 70 groups. The need for postoperative injection was higher in the Dextran 70 group, but there were no other differences in bleeding complications between the two groups. Gerhart et al²⁶ found lower DVT rates with the same LMWH (Org 10172) versus warfarin (7% and 21%, respectively) but there was no significant difference in PE or major bleeding complications. It is difficult to interpret the results of these comparative studies because of different medication doses, dosing regimens, population data, rehabilitation protocols, and methods for diagnosing

thromboembolic phenomena. Previous studies included both symptomatic and asymptomatic DVT since most of or all patients underwent postoperative imaging. These studies also included distal DVT, which has been found to have little clinical significance in the progression of PE compared with proximal DVT²⁷.

Conclusion

In acetabular fracture surgeries, prone positioning of the patients during surgery and prolonged surgical time make the patient more prone to DVT and eventually pulmonary thromboembolism. Therefore, intraoperative subcutaneous heparin, can prevent deep vein thrombosis and pulmonary thromboembolism and reduce patient mortality as well as not significantly increasing the patient's intraoperative bleeding and having no specific drug side effects.

Conflict of interest

The authors declare that they have no conflict of interest.

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