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Incidence of Deep Vein Thrombosis in Patients Undergoing Degenerative Spine Surgery on Prophylactic Dalteparin; A Single Center Report

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ABSTRACT

Objective: To determine the incidence of deep vein thrombosis (DVT) in patients undergoing spinal surgeries receiving prophylactic doses of Deltaparin in a single center in central Iran.
Methods: This cross-sectional study was conducted in Shariatee hospital of Isfahan during a 12-month period. We included all the patients undergoing elective spinal surgeries in our center during the study period who received prophylactic dosages of subcutaneous Dalteparin (5000 unit daily) the first postoperative day. Those with absolute contraindications of anticoagulation therapy were not included in the study. Patients were followed for 3 months clinically and the incidence of DVT was recorded. DVT was suspected clinically and was confirmed by color Doppler sonography.
Results: Overall we included 120 patients with mean age of 44.8±12.6 years among whom there were 54 (45%) men and 66 (55%) women. Lumbar discectomy (32.9%) and laminectomy (20.2%) were the most common performed procedures. DVT was detected in 1 (0.83%) patient in postoperative period. None of the patients developed pulmonary embolism and none hemorrhagic adverse event was recorded. The patient was treated with therapeutic unfractionated heparin and was discharged with warfarin.
Conclusion: Our results shows the efficacy of LMWH (Dalteparin) in reducing the incidence of DVT to 0.83%. These results also show the safety of Dalteparin in spine surgery because of lack of bleeding complication.

Keywords: Deep vein thrombosis; Spinal surgery; Dalteparin; Low molecular weight heparin (LMWH); Pulmonary thromboembolism (PTE).

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Introduction

The presence of thrombus within a superficial or deep vein and the accompanying inflammatory response in the vessel wall is termed venous thrombosis. Initially, the thrombus is composed principally of platelets and fibrin. Red cells become interspersed with fibrin, and the thrombus tends

to propagate in the direction of blood flow. The most important consequences of this disorder are pulmonary embolism and the syndrome of chronic venous insufficiency [1]. The annual incidence of deep venous thrombosis (DVT) is 50-139 per 100,000 people in the general population [2] and in postoperative neurosurgical patients ranges from 29-43% [3]. In about 20% of patients, the initial clinical manifestation of venous thromboembolism (VTE) is sudden death due to pulmonary embolism (PE) [4]. Venous thromboembolism is a common life threatening complication in patients undergoing neurological surgeries. Despite multiple studies of DVT prevention have been conducted over the last 30 years as well as the development of low molecular weight heparins (LMWH) and mechanical prophylaxis (sequential calf compression devices, calf stimulators, and antithromboembolism stockings), DVT is the most frequent systemic complication in patients undergoing neurological surgeries and PE can still be fatal [5]. Patients who undergo neurosurgical procedures are at high risk of developing DVT postoperatively [6].

Physical methods of thromboprophylaxis have been successful in reducing the incidence of postoperative DVT up to 50% [7] but the residual incidence remains considerable [8]. Both unfractionated (UFH) and LMWH have been shown to reduce the incidence of DVT consistently by 40-50% [9]. Heparin (UFH and LMWH) is widely used in the prophylaxis of DVT in moderate and high risk clinical settings. However, it is scarcely used in neurosurgical patients because of the potential consequences of bleeding in the brain or spine [10]. The major advantages of LMWH are improved efficacy and safety, longer half-life and reduced need for laboratory monitoring and lower risk of heparin induced thrombocytopenia [4,11,12].

Dalteparin is an LMWH indicated for patients undergoing abdominal surgery. Dalteparin has a predictable dose response and can be administered as a standard single daily subcutaneous dose for all patients. In therapeutic doses, dalteparin does not alter coagulation tests and therefore does not require routine laboratory monitoring, in contrast with adjusted-dose UH. Dalteparin is the second LMWH to receive approval by the Food and Drug Administration [13]. In the current study we determined the incidence of DVT in patients undergoing elective spinal surgery with prophylactic use of Dalteparin. We also assessed the safety of Dalteparin in these patients.

Materials and Methods

Study Population

This prospective cross sectional study was conducted in Shariatee hospital of Isfahan, a tertiary healthcare center during a 12-month period from December 2004 to September 2005. We included all the patients who were scheduled for elective degenerative spine surgeries and received prophylactic dosages of deltaparin postoperatively. Patients with contraindications of anticoagulation therapy including intracranial bleeding, severe active bleeding, recent brain, eye, or spinal cord surgery, pregnancy, and malignant hypertension were excluded from the study. We also excluded those with recent major surgery, recent cerebrovascular accident, and severe thrombocytopenia. Decreased renal function (serum creatinine >2mg/dL) test was also among the exclusion criteria. The study protocol was approved by institutional review board (IRB) and medical ethics committee of Isfahan University of Medical Sciences. All the patients provided their informed written consents before inclusion in the study.

Study Protocol

All the patients were examined by a neurosurgeon before the study and the positive findings were recorded in the data gathering form. We also recorded the demographic information including age, gender, body mass index, comorbidities, use of oral contraceptives and smoking were recorded. The surgery characteristics such as type and location of surgery, reason of operation, position during surgery, duration of surgery amount of blood loss and hemoglobin before and after surgery were recorded. Perioperative platelets, partial thromboplastin time (PTT), prothrombin time (PT) and fibrinogen were routinely monitored. Postoperative tests were performed either the same day (posterior transpedicular stabilization) or the day following surgery, depending on the type of surgery and the amount of blood loss. If major deficiencies were detected, fresh frozen plasma, prothrombin complex concentrate or fibrinogen was administered to maintain PT >60%, PTT <40 s, platelet >100,000 and fibrinogen >1.5 g/l. The surgical approaches included thoracolumbar discectomy, laminectomy and fixations. In cervical we performed cervical laminectomy or anterior cervical discectomy and fixation (ACDF). Posterior approaches were performed in prone position with both knees bended by a bolster placed under the heels. Lumbar discectomy was performed in knee chest position. Anterior approaches were performed in supine position with a bolster placed beneath the knees.

All the patients received daily subcutaneous injection of 5000 unit Dalteparin (FRAGMIN®, 5000IU 0.2ML SYRINGE, Behestan Pharmaceutical, Tehran, Iran) at the first postoperative day. The minimum duration of Dlteparin administration was 3 (range 3 to 5) days. Physical and pharmacological methods of antithrombotic prophylaxis other than Dalteparin and concomitant treatment with aspirin, other antiplatelets agents, or nonsteroidal anti-inflammatory drugs were not permitted during the trial.

Outcome Assessment

All the patients were assessed daily during

the hospital course to review their clinical status, including symptoms and signs of venous thromboembolism, bleeding side effects, and other adverse events. These include swelling, pain, rigidity, difference in calf diameter, homans sign, warmth, tenderness, and erythema. Patients with clinically suspected DVT, underwent color Doppler sonography and those with clinical features suggestive of PE underwent chest perfusion scan. The participating patients were followed by hospital visits, telephone calls or office visits until 90 days after surgery to document the occurrence of clinically overt venous thromboembolism, bleeding, other side effects or death. Patients with positive sonographic and perfusion scan results were treated with UFH and warfarin. Acute DVT, diagnosed in this study, were classified according to their anatomic location.

Statistical Analysis

According to the 4% incidence of DVT in postoperative period based on previous reports, 95% CI and alpha equal to 0.01, we required for the study. We included 120 patients to compensate for non-evaluable patients. All the statistical analysis were performed using statistical package for social sciences (SPSS Inc., Chicago, IL, USA) version 16.0. Data are presented as mean±SD and proportions as appropriate.

Results

Overall we included 120 patients undergoing elective degenerative spine surgeries who received postoperative dalteparin. The mean age of the patients was 44.8±12.6 (ranging from 21 to 79) years including 54 (45%) men and 66 (55%) women. There were 93 (77.5%) lumbar, 23 (19%) cervical and 4 (3.5%) thoracolumbar surgeries being performed in this study. Lumbar surgeries included 25.9% discectomy, 14.8% laminectomy, and 33.4% fixation. Cervical surgeries included 0.8% laminectomy and 18.3% ACDF. The characteristics of the patients and the operation data is presented in Table 1.

Only 1 (0.83%) patient developed DVT of lower extremity confirmed by color Doppler sonography. None of the patients developed PTE and no adverse events such as bleeding was recorded among the patients. The patient who had DVT was a woman aged 45 years with a body weight of 95kg. The patient had diabetes mellitus, hypertension, and dyslipidemia. She took oral contraceptive pill since 7 days before surgery. She was in complete bed rest for 20 days before hospitalization. She was diagnosed to have C4/C5 and C5/C6 for which ACDF was performed in the mentioned levels in supine position. She had 1.5 g/dL decrease in hemoglobin concentration. The operation duration was 150 minutes and anesthesia lasted for 190 min. Swelling, pain and redness were seen on the third postoperative day. Homans sign was positive. She received therapeutic dosages of heparin as DVT treatment and was discharged with warfarin.

Table 1. Characteristics of 120 patients undergoing elective degenerative spine surgeries receiving postoperative dalteparin as deep vein thrombosis prophylaxis.

Variable	Value
Age (years)	44.8±12.6
Gender	
Men (%)	54 (45%)
Women (%)	66 (55%)
BMI (kg/m^2)	24.6±6.8
Surgery Site	
Lumbar (%)	93 (77.5%)
Cervical (%)	23 (19%)
Thoracolumbar (%)	4 (3.5%)
Operation type	
Lumbar discectomy (%)	31 (25.9%)
Lumbar laminectomy (%)	19 (14.8%)
Lumbar fixation (%)	40 (33.4%)
ACDF (%)	22 (18.3%)
Cervical laminectomy (%)	1 (0.8%)
Instrument removal	6 (5%)
Vertebroplasty	1 (0.8%)
Operation duration (minutes)	206.5±49.6
Interval between operation and dalteparin (hours)	18.6±10.5
Anticoagulation therapy duration (days)	3.4±1.6
Blood loss (mL)	460.9±197.2
Hb change after surgery	1.6±0.8
Hospital stay (day)	6.9±2.7

Discussion

Incidence of deep vein thrombosis in the current study was 0.83% (1 of 120). The incidence of DVT in hospitalized patients is increasing [14]. Because patients with recent surgery have a 22 fold increased risk of postoperative VTE, a large research effort has been directed toward identifying the safest and most effective prophylaxis after surgery [15,16]. Major elective spine surgery is a recognized risk factor for venous thromboemboli (VTE), and PE is a significant cause of morbidity and mortality in this patient population despite the use of traditional prophylactic methods [14]. During spine surgery, there is pre-, peri- and post-operative activation of the coagulation cascade, which puts these patients at a similarly increased risk [17]. The risk for VTE in surgical patients is determined by the combination of individual predisposing factors and features of specific type of surgery. Advanced aged, prolonged procedure, and reduced preoperative and postoperative mobility are the risk factors for VTE in these patients.

In majority of the patients undergoing surgery, the risk for VTE has been adequately evaluated and the benefit of thromboprophylaxis established [18]. All neurosurgeons are concerned of hemorrhage in

postoperative period [19,20], but this is balanced by the contrasting fear of DVT and PE. Prophylaxis for DVT and PE is problematic for neurosurgeons [5]. For any kind of surgery, certain characteristics have been identified as risk factors for VTE. These include increasing age, prolonged immobility, stroke or paralysis, previous VTE, cancer and its treatment, trauma (especially fractures of the pelvis, hip or leg), obesity, varicose veins, cardiac dysfunction, pregnancy, and oral contraceptive use or estrogen replacement therapy [4]. Those with genetic hypercoagulopathic syndromes including factor V Leiden mutation, elevated antiphospholipid antibodies, deficiencies of antithrombin, protein C, and protein S are also uniquely susceptible to new onset and/or recurrent DVT and PE after neurosurgical procedures [21].

In neurosurgical studies review, the incidence of clinically DVT in elective spinal surgery has been reported up to 3.7% (range=0-11.2%) [22]. Spine surgery is a recognized risk factor for venous thromboembolism. There is no clear prophylactic protocol in spinal surgery. The low molecular weight heparin, nadroparin, added to graduated compression stockings results in a clinically significant decrease in VTE without inducing any significant increase of major bleeding [23]. Low dose heparin therapy is indicated for patients undergoing elective neurosurgical procedures, especially for patients over the age of 40 and for those under the age of 40 who are known to be at risk of developing thromboembolic complications [24]. Considering the low rate of DVT (2%) following posterior lumbar surgery and the potential complications of prophylactic anticoagulation, we continue to use intermittent pneumatic compression rather than elastic stockings for prophylaxis [25]. No prophylaxis is recommended after discectomy or limited laminectomy in patients without additional risk factors. Mechanical methods are recommended after spinal fusion or extended laminectomy [26] high risk LMWH or low-dose UFH plus mechanical methods [27], pneumatic compression stockings plus heparin [28].

In conclusion, our results shows the efficacy of LMWH (Dalteparin) in reducing the incidence of DVT to 0.83%. These results also show the safety of Dalteparin in spine surgery because of lack of bleeding complication. Further cohort studies are required to shed light on the issue.

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