Ineffective Treatment of Low-Molecular-Weight Heparin in Obese Subject with Traumatic Fractures of the Leg

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Int J Angiol 2016;25:e16–e18.

Abstract

Keywords

- thromboprophylaxis
- deep vein thrombosis
- enoxaparin
- lower extremity
- low-molecular-weight heparin
- risk factors
- young

American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, 9th edition, 2012, suggest no prophylaxis rather than pharmacological thromboprophylaxis in management of venous thromboembolism (VTE) risk of isolated lower leg injuries distal to knee requiring leg immobilization. Low-molecular-weight heparin (LMWH) is a class of drugs commonly used as antithrombotics in surgery and in case of prolonged bed rest and hypomobility. A 35-year-old obese man with no history of health disease (height, 170 cm; weight, 95 kg; and body mass index, 32.9 kg/m²) was involved in a car accident, and as a result of the trauma he suffered the compound fracture of left tibia and fibula. Tibial intramedullary nailing was performed. The injury was near the knee, and the patient was advised long-term bed rest. For these reasons, he was treated with enoxaparin 40 mg once daily subcutaneously. On the 7th day of hospitalization, the leg became edematous and reddish. A Doppler ultrasonography evaluation was performed which showed a massive deep vein thrombosis of left leg and then a pulmonary angiotomography showed a massive pulmonary embolism. In this clinical case, there was a pharmacological treatment failure to prevent VTE after orthopedic surgery and related long-term rest using enoxaparin at prophylaxis dosage in a patient without history of health disease but at high risk of VTE for obesity, trauma, orthopedic surgery, and immobilization. Enoxaparin dosage to prevent VTE in patients with high risk should be reconsidered and especially in obese a weight-adjusted dosage can be better than a fixed dosage.

American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, 9th edition, 2012, suggest no prophylaxis rather than pharmacological thromboprophylaxis in management of venous thromboembolism (VTE) risk of isolated lower leg injuries distal to knee requiring leg immobilization, with a recommendation of class II and level of evidence III.¹ This assertion derived from the results of the Cochrane review and is based on the onset of pulmonary embolism in a placebo group versus low-molecular-weight heparin (LMWH)–treated group that was not statistically

different without a demonstrated beneficial effect of LMWH in these patients. Exclusion of patients with high risk of DVT is the most important limit of this study.² However, it is noted that the risk of deep vein thrombosis (DVT) increases with proximity of the fracture to the knee. In 2011 Testroote et al, using a questionnaire, demonstrated that in the Netherlands, there is a substantial variation and inconsistency in practice among surgical and orthopedic departments about the management of thromboprophylaxis for all patients with immobilization for lower extremity injuries

(below knee), recommending thromboprophylaxis for all patients with immobilization for lower extremity injuries, irrespective of age and other risk factors.³ Nokes and Keenan, in a 2009 review of current status, recommended that patients with lower limb immobilization should be risk assessed and those deemed high risk for VTE should receive prophylactic LMWH for at least the duration of cast immobilization.⁴

Case

A 35-year-old man without history of health disease except for obesity (height, 170 cm; weight, 95 kg; body mass index (BMI), 32.9 kg/m²) was involved in a car accident and as a result of the trauma he suffered the compound fracture of left tibia and fibula. Tibial intramedullary nailing was performed (► Fig. 1a). Perioperative period was free of complication. The injury was near the knee and the patient was advised long-term bed rest. For these reasons, he was treated with enoxaparin 40 mg once daily (OD) subcutaneously from the first day of hospitalization and was considered at high risk for VTE. On the 7th day of hospitalization, the leg became edematous and reddish. A doppler ultrasonography evaluation was performed which showed a massive DVT of left leg (► Fig. 1c). Patient was slightly dyspneic. Arterial blood gas noted only a mild reduction of P_O₂ (73 mm Hg), with

normal pH and P_{CO}₂. A pulmonary angiotomography was performed that showed a massive pulmonary embolism (► Fig. 1b).

Discussion

Enoxaparin is an LMWH that reduces the risk of VTE in both medically ill and surgical patients. Its dosage in prophylaxis of VTE is 40 mg OD for high risk independent of body weight. In patients with severe chronic renal failure, a creatinine clearance (< 30 mL/min) is recommended a reduction of dosage (both in VTE treatment and prophylaxis). Freeman and Horner in a recent work demonstrated that in patients with extreme obesity (with an average BMI of > 60 kg/m²) enoxaparin 0.5 mg/kg OD is superior to both Food and Drug Administration–approved fixed enoxaparin dosing (40 mg OD) and lower dose weight-adjusted enoxaparin (0.4 mg/kg OD) for the achievement of target peak antifactor Xa levels (between 0.2 and 0.5 IU/mL).⁵ Costantini et al hypothesized that many trauma patients would be subtherapeutic on the standard prophylactic dose of enoxaparin, and in a recent work published in January 2013, Costantini et al also demonstrated that in trauma patients 30 mg twice daily (TD) enoxaparin dosage was inadequate for VTE prophylaxis especially in patients having larger body surface area. They finally suggest need for routine use of a higher dose of prophylactic enoxaparin in

Fig. 1 (a) Tibial fracture after surgery. (b) Angiotomography signs of pulmonary embolism. (c) Deep vein thrombosis of common femoral vein seen with ultrasound.

trauma patients.⁶ A weight-based dosing with enoxaparin in morbidly obese (0.5 mg/kg TD) proved to be sufficient in achieving antifactor Xa levels within the appropriate prophylactic range (range, 0.20–0.59 IU/mL) without additional adverse effects.⁷ In critically ill trauma and surgical patients, enoxaparin standard prophylaxis dosage of 30 mg TD leads to low antifactor Xa levels in 50% of them and low levels are associated with a significant increase in the risk of DVT.⁸

Conclusions

In this clinical case, there was a pharmacological treatment failure to prevent VTE after orthopedic surgery and related long-term rest using enoxaparin at prophylaxis dosage. The case is as peculiar as in a single young patient that was only moderately obese and had no other additional diseases, we observe four very important risk factors of VTE (obesity, trauma, orthopedic surgery, and immobilization) and a fixed dose of enoxaparin approved for VTE prophylaxis of patient at high risk was inadequate to prevent a massive DVT. Enoxaparin dosage to prevent VTE in patients with high risk should be reconsidered and especially in obese a weight-adjusted dosage can be better than a fixed dosage.⁹

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