

THROMBOPROPHYLAXIS USING LOW MOLECULAR WEIGHT HEPARINE AFTER ANKLE FRACTURES

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Abstract

Enhanced interest for prophylaxis and multidisciplinary approach of pathology, two main characteristics of modern medicine, radically changed the classical bone-solely-addressed approach of skeletal trauma. Studies demonstrated the incidence of Thrombo-Embolic Disease (TED), composed by Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE) after orthopaedic pathology, with a significant impact upon morbidity and mortality, thus making thrombo-prophylaxis (TP) an essential component of trauma treatment. Although there is no clear recommendation for TP following ankle fractures (as in hip fractures, for example), thrombo-embolic (TE) complications of these injuries have been detailed lately. In this retrospective study there are evaluated the effectiveness of TP using Enoxaparin sodium, a Low Molecular Weight Heparin (LMWH), in patients with operated ankle fractures in order to conclude whether prolonged TP after discharge is beneficial or not. The results of the study demonstrate that TE complications were more frequent when there was no long-term TP, thus endorsing the recommendations of establishing the TP regimen related to the TE factors, not only to the injury itself.

Rezumat

Interesul crescut pentru profilaxie și abordarea multidisciplinară a patologiei, două caracteristici esențiale ale medicinei moderne, au schimbat radical abordarea traumatismelor scheletului, adresată clasic doar leziunii osoase. Studiile au demonstrat incidența Bolii Trombo-Embolice (BTE), reprezentată de Tromboza Venoasă Profundă (TVP) și Embolia Pulmonară (EP) în patologia ortopedică, cu impact semnificativ asupra morbidității și mortalității, ceea ce a făcut ca Trombo-Profilaxia (TP) să devină o componentă esențială a tratamentului în traumă. Deși nu există recomandări clare privind TP după fracturile de gleznă (așa cum există pentru fracturile de șold, spre exemplu), complicațiile trombo-embolice (TE) ale acestora au fost descrise detaliat în ultimii ani. În acest studiu retrospectiv sunt evaluate eficiența TP utilizând Enoxaparina sodică, o Heparină cu Masa Moleculară Mică, la pacienții cu fracturi de gleznă operate pentru a hotărî dacă TP prelungită are sau nu beneficii. Rezultatele acestui studiu demonstrează frecvența crescută a BTE în absența TP prelungite, susținând astfel recomandarea de a stabili protocolul de TP al fiecărui pacient în conformitate nu numai cu leziunea traumatică, ci și cu factorii de risc TE ai pacientului.

Keywords: thrombo-embolic disease (TED), thrombo-prophylaxis (TP), ankle fractures, enoxaparine, thrombo-embolic risk

Introduction

Although the problem of incidence of Thrombo-Embolic Disease (TED) after pelvic, hip or femoral shaft fractures has been clearly described in literature, significantly less has been written about thrombo-embolic complications following ankle fractures [1, 6, 9]. Few studies evaluated thrombo-embolic events after these fractures, but as few as they are the idea of a real and challenging possibility for malleolar fractures to complicate with Deep Venous Thrombosis (DVT) or Pulmonary Embolism (PE) became increasingly debated. A study published by Pelet in 2012 found a global incidence of 2.99% of TED with a 2.66%

incidence of DVT and 0.32% incidence of PE after evaluating 1544 patients operated for ankle fractures during 8 years (1997-2005) [11].

The same idea was enhanced by a study published by Kavanaugh et al. who, after evaluating 3334 patients, discovered an incidence of 0.29% with symptomatic DVT and 0.36% with PE, with a global incidence of TED of 0.54%, thus underlining the necessity of changing the perspective of TED after ankle fractures and that of performing prospective randomized studies to properly identify the groups of patients with significant thrombotic risk [7].

Although Thrombo-Embolic Risk (TER) and protocols for thrombo-prophylaxis (TP) are clearly

stated for the so called “above the knee” injuries (pelvic and femoral fractures), no clear rules for TP in patients with fractures or dislocations distal to the knee have been established, despite the fact that increasingly frequent TE complications are reported in the literature after tibia or ankle fractures, even after foot fractures [1, 8, 10].

Different types of treatment have been described, both mechanical and pharmacological, and the interest of health care practitioners (physicians and pharmacists) was to find the most suitable methods to improve the outcome of the patients, according to the legislation in respect to patients’ rights [5].

An important point was the acceptance of the idea that there are fundamental differences between obstruction in chronic arterial disease and TE, thus requiring different treatments [2]. That is how, step by step, LMWH proved to have the maximum efficacy in TED, thus being used and studied in TE events after ankle fractures, where they demonstrated to be necessary and useful [12, 14].

Materials and Methods

In this retrospective study there were included 62 patients with ankle fractures operated in the Orthopaedics and Trauma Clinic of the Clinical Emergency Hospital Bucharest, between 01.06.2011 – 01.01.2013, evaluated for symptomatic DVT and PE. The study was performed according to the European Communities Council Directive of 24 November 1986 (86/609/EEC) and the treatment of the patients was approved and performed following the local Ethical Regulations.

The patients sustained the following inclusion criteria: skeletally mature patients over 18 years old, isolated closed uncomplicated ankle fractures (without ischaemia, compartment syndrome), compliance with the therapeutically protocol, with 12 months follow-up.

The exclusion criteria were: complicated or multiple fractures, polytrauma patients, uncompliant patients, pregnancy, loss of follow-up. The patients were given Enoxaparin sodium (Clexane®) for all the immobilization period (3 weeks) accompanied by non-pharmacological TP methods, and the study group was analysed regarding demographic criteria, as well as the duration of surgery, period of hospitalization, incidence of symptomatic DVT and PE.

Regarding the age and sex, there were 27 women and 35 men in the group, mean age 36 years old (19- 62 years old); as it is seen in Figure 1, most of the patients were 31-50 years old, there means active socially and professionally.

The mean time between trauma and the moment when TP started was 26 hours, since not all the

patients received TP in the first unit were they had been treated before coming to our hospital (Figure 2).

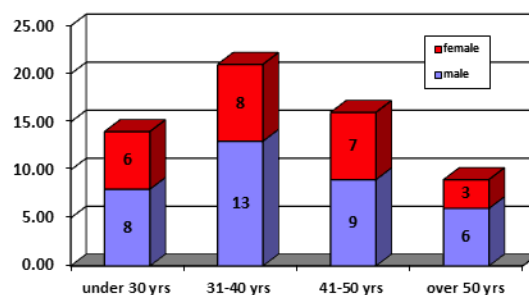


Figure 1.

Demographic data of the studied group

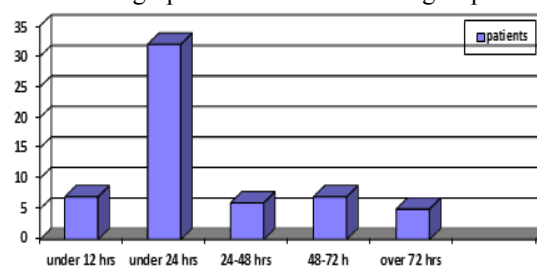


Figure 2.

Time between trauma and anti-thrombotic treatment initiation

Anti-thrombotic treatment was initiated depending on the moment of surgery, immediately after the risk factors became active; so, if surgery wasn't performed within the first 12 hours, TP started immediate after admission, until 12 hours before the estimated time of operation; if surgery was performed within the first 12 hours or after admission, TP started after surgery, 12 hours after induction of anaesthesia [12].

TP was performed with Enoxaparin Sodium (Clexane®), the dose being established after the TER was assessed according to Caprini scale [3]; dose adjustment was the following: 0.4 mL sc daily for the patients with low risk, 0.6 mL sc daily for the patients with medium risk, 0.8 mL sc daily for the patients with high risk and 0.6 mL sc twice daily (1.2 mL sc daily) for the patients with very high risk, Figure 3 representing the number of patients with each regimen [4].

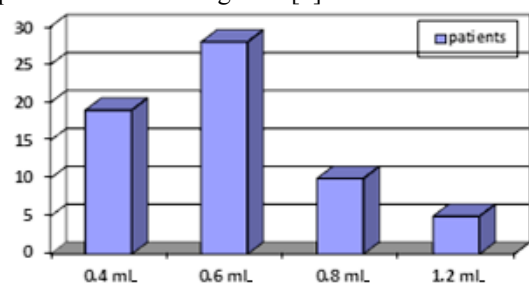


Figure 3.

Dose of Enoxaparin within the study group

The same protocol was used for all the patients: surgery (Open Reduction Internal Fixation) under tourniquet; antibiotic prophylaxis using 2nd generation Cephalosporins and Aminoglycosides; elastic bandage on the operated limb and elastic stocking on the other, 4 weeks after surgery; physio-therapy was started after 3 weeks. Pharmacological TP was performed with Enoxaparin sodium which was given for 3 weeks. Clinical follow up was performed after the same programme, and besides the scheduled visits, the patients were instructed to urgently come to the hospital whenever one the alarm signs for symptomatic DVT and PE would appear [13]. In patients with alarm signed for DVT and PE, positive diagnosis was established by evaluating the patients with alarm signs by Doppler ultrasound (for DVT) and contrast CT + D-dimers + Doppler ultrasound for PE.

Results and Discussion

There were 9 (1.4%) patients who came to the hospital (6 to unscheduled visits, 3 to scheduled visits) with alarm signs for DVT; Compression Doppler Ultrasound was performed and in 4 cases (0.6%) (2 males, 2 females), DVT was identified (3 cases- deep posterior tibia veins, 1 case- deep posterior tibia veins and peroneal veins). As for the other 5 cases, in 4 of them (0.6%), chronic venous insufficiency (CVI) was described, and post-thrombotic syndrome (PTS) was identified in the last case (0.16%), without any acute symptom of DVT described by the patient (Figure 4).

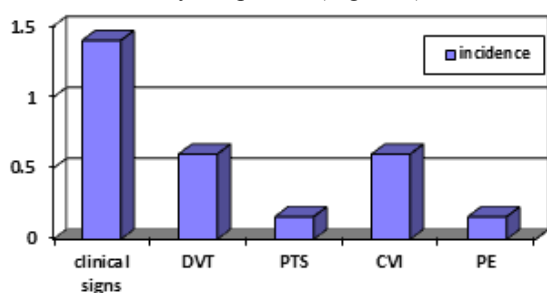


Figure 4.

TE events in the study group

Regarding the moment when these problems appeared, the cases of DVT (5 cases - 4 symptomatic and 1 PTS) became symptomatic after 2 weeks (3 patients), 4 weeks (1 patient) and 6 weeks (1 patient).

As for PE, 1 of the 62 patients (0.16%) was diagnosed with PE- male, 45 years old, smoker, 20 cigarettes daily, obese, with varicose veins and swollen legs, with familiar history of DVT, came to the hospital 2 weeks after surgery, 1 week after discharge, with acute thoracic pain solely.

The evaluation of TER in the study group according to Caprini scale proved that ALL the patients who developed TED were primarily evaluated as having at least a medium TER (Figure 5); more than that, if we consider that PE after an ankle fracture is exceptionally, the fact that the patient had very high TER makes the episode not be exceptionally any more, but predictable [3].

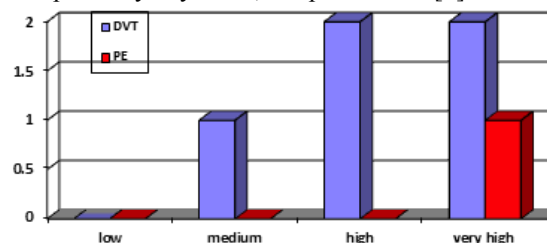


Figure 5.

Correlation between thrombo-embolic events and thrombo-embolic risk

So, although the number of patients within the study group is reduced, our analyses revealed that the only element which TED could be correlated with was the Thrombo-Embolic Risk, thus suggesting that this should be the coordinate which should guide the thrombo-prophylactic treatment.

The results of this study correspond to those published in literature and reflects the tendency to re-evaluate TER in “below the knee injuries”, as data published during the last 10 years showed an increasing incidence of TED, since the Virchow Triad, can be initiated by the fracture, as well as by surgery. More than that, it is to be underlined that TER is to be related not only to the injury, but also to the patient, since the same injuries in different types of patients generated significantly different incidences of VTE. This aspect led to the introduction of risk scales regarding TER, the one designed by Caprini assigning the patients with ankle fractures with at least 5 points because of: lower limb fracture AND surgery AND bed resting more than 72 hours, let alone if the patient has supplementary TE factors as obesity, swollen legs, varicose veins, or smoking, which are frequent conditions, which leads to “high TER” according to Caprini. Having said that, at least a medium-risk thrombo-prophylactic regimen should be given to these patients, despite the classical idea of ankle fractures not needing thrombo-prophylaxis, compared to hip fractures, for example.

Once concluded that TP is necessary, the method and the duration need to be Regarding the duration of TP, the onset of late TE events in the study group supports the idea of continuing TP not only for the duration of cast immobilization, but as long as the risk factor persist.

As for the method used for TP, once reconsidered the TER in patients with ankle fractures, the

situations when non-pharmacological means are solely used are exceptional. For most of the patients, specific drugs with anti-coagulant or, better than that, anti-thrombotic activity are the main TP methods. Despite its accessibility, Un-fractionated Heparine (UFH) has been replaced with LMWH due to their numerous advantages: they are effective and secure, they can be administered before and after surgery, there are little indications for adapted dosage, coagulation monitoring is not necessary. From the general class of LMWH, Enoxaparin has been widely used in trauma, as well as elective surgery, as it creates an adequate TE protection due to the antiXa: anti IIa report (over 4).

Conclusions

Although the incidence of TED following ankle fractures is not comparable to that implying pelvic or femoral fractures, the interest for this aspect of modern trauma is increasing due to the fact that TED affects especially young, active patients.

Limb trauma, especially those of the lower limbs, activates the Virchow Triad, which, added to patients pre-existing diseases and to surgery-related pro-thrombotic factors (such as reaming or tourniquet inflation and deflation), lead to the conclusion that TE events must be reconsidered as they are frequent and severe complications in orthopaedic surgery.

That is why TP should be established by assessing the TER of the patient, and not of the injury itself and it should be administered as long as the pro-thrombotic factors are active, and not for a fix period, as it is sometimes believed. Since surgery and post-operative treatment are different from one patient to another, the only unanimously applicable rule is that TP must reflect the TER (regarding the method, dose, duration).

Whenever possible, pharmacological TP is the method of choice, and, from several options, due to their pharmacological characteristics and clinical efficacy, LMWH are widely used. From them, Enoxaparin sodium has been intensively used because it's anti Xa: anti IIa fraction generates optimal anti-thrombotic activity and increased safety. This study suggests that it should not be discussed whether TP is indicated after ankle fractures, but to correctly identify the risk factors in patients with ankle fracture and supports the idea of personalized TP, adapted not to the disease, but to the patient, since even in allegedly "benign" ankle fractures, TE events are to be expected if risk factors exist. Further prospective randomized trials are necessary in order to validate guidelines for TP in "below the knee injuries".

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