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Regular Article

The Effect of Various Types Low Molecular Weight Heparins on Fracture Healing ☆

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ABSTRACT

Introduction: Thromboembolic complications are the most common preventable cause of mortality and morbidity in trauma and arthroplasty patients. Therefore, this group of patients receive a prophylaxis for thromboemboli by mechanical or pharmacological methods. This study was designed to evaluate the effect of enoxaparin, nadroparin, dalteparin and fondaparinux on fracture healing in an experimental rat femur fracture model.

Materials and Methods: Thirty male, Wistar-Albino rats were divided randomly into five groups. A retrograde intramedullary kirschner wire was inserted under general anesthesia and then standard closed femoral shaft fractures were produced. After the production of fractures, treatment groups received enoxaparin, nadroparin, dalteparin and fondaparinux via subcutaneous injections and the control group received placebo injections for four weeks. The formation and healing of the bones were determined by clinical manual evaluation, radiographic and histopathological analyses.

Results: Histological callus formation scores were found to be significantly increased in the fondaparinux group when compared to the control group at the end of the fourth week. Other treatment groups' histological scores did not show any significant difference with the control group. The histological scores of all groups were compared and the fondaparinux group histological score was found to be significantly increased. The clinical and radiological scores between the groups did not show any significant difference.

Conclusions: A positive histological effect of fondaparinux on fracture healing was observed in this study. This enhancing effect of fondaparinux may be related to its synthetic and selective composition and non-inhibitory effects on osteoblasts and growth factors.

Introduction

Thromboembolic complications are the most common preventable cause of mortality and morbidity in trauma patients [1]. It has been shown that deep vein thrombosis (DVT) occurs in up to 65% of cases without perioperative anticoagulation [2]. Patients who have fractures in lower extremities, hip or vertebra cannot be mobilized in the perioperative period and mobilization may be delayed due to treatment protocols or complications. During this period, the reduced mobility increases the risk of thrombosis by up to 60% [3]. Therefore, trauma patients receive prophylaxis for thrombosis by mechanical or pharmacological methods.

The efficiency and reliability of low molecular weight heparins (LMWH), heparins and warfarins which are used for thromboprophylaxis in orthopaedic surgery have been compared in meta-analyses. In these studies it has been shown that LMWHs are superior to heparins and warfarins in preventing DVT and related pulmonary embolism [4,5].

Patients usually receive thromboprophylaxis during hospitalisation but recent reports have shown that this period must be extended due to postoperative thromboembolism risks. Symptomatic throboembolism risk increases at postoperative two weeks and can sometimes last for two or three months [6].

In clinical practice fracture patients receive LMWH for a prolonged time to prevent thromboembolic complications with DVT prophylaxis guides recommending five weeks use after hip fracture surgery or total hip arthroplasty [7]. LMWH can be used in the fracture healing period.

This study aimed to evaluate the effects of different types of LMWH; enoxaparin, nadroparin, dalteparin and fondaparinux on fracture

Abbreviations: DVT, Deep vein thrombosis; LMWH, Low molecular weight heparins; K, Kirschner; VEGF, Vascular endothelial growth factor; IGFs, Insulin-like growth factors.

☆ The research was carried out at "Gazi University Laboratory Animals Breeding and Experimental Research Center".

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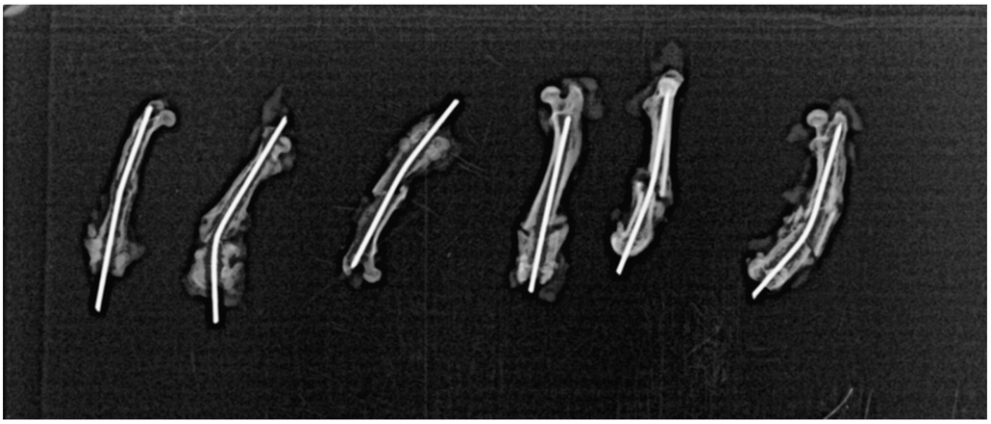

Fig. 1. Radiological appearance of the control group at week four.

healing in an experimental rat femur fracture model. We hypothesized that thromboprophylaxis using LMWH would delay fracture healing and fondaparinux would no effect on fracture healing.

Materials and Methods

Thirty healthy adult male Wistar-Albino type rats were used in this study. The rats were similar in weight (425+/−25 g) and age (four months). All protocols regarding these animals were approved by national and institutional research ethics authorities.

The animals were randomly allocated into five groups of six rats, named A, B, C, D and E. Preoperative antibiotic prophylaxis was administered with Cefazolin Sodium 40 mg/kg. After the closed shaft fractures had been produced, the rats remained in cages and were allowed unrestricted weight bearing without any external support. Standardized food and water were given ad libitum.

Anesthesia was induced using intraperitoneal Ketamin 50 mg/kg and Xylazinne 10 mg/kg [10]. The animals were positioned supine on a surgical table and the surgical site was prepared. The arthrotomy was performed on the left knee and a threaded kirschner (K) wire of 0.8 mm diameter was inserted into the femoral intramedullary canal between the femoral intercondylar space. The K wire was cut, the patella was reduced and the joint capsule and skin were closed. After the K wire position had been confirmed by radiography, standard closed shaft fractures were produced with the use of a device defined by Bonnarens and Einhorn [9]. The fractures were confirmed by radiography.

Group A rats were named as the control group and received 1 ml normal saline, Group B received enoxaparin at a dosage of 1 mg/kg,

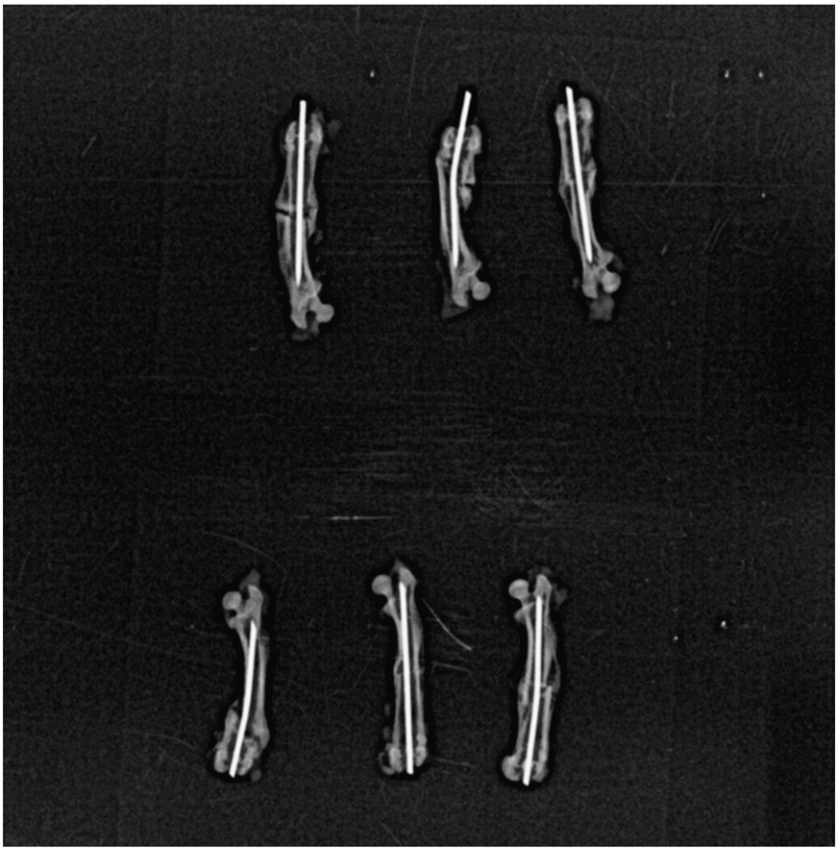

Fig. 2. Radiological appearance of the fondaparinux group at week four.