THE ROLE OF TRACE ELEMENTS IN FRACTURE HEALING

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Gazi Medical Journal 5 : 67-69, 1994

SUMMARY : The effects of zinc, copper and magnesium on fracture healing have been investigated in an experimental rat model. Tibial fractures were created and the serum levels of these trace elements were determined at the end of 7^{th}, 14^{th} and 21^{st} post fracture days. Histopathological samples and radiograms were obtained on the same days for assessment of fracture healing. It has been concluded that especially zinc and copper have active roles in fracture healing and their deficiencies may be responsible for delayed fracture healing.

Key Words : *Fracture Healing, Zinc, Copper, Magnesium.*

INTRODUCTION

One of the may factors influencing bone fracture healing is the levels of serum trace elements. Zinc is a trace element which has positive effects on growth and wound healing (6, 9, 11). Zinc defiency causes skeletal anomalies and delayed fracture healing in rats (3, 13, 17, 20). It has been suggested that bone zinc content and bone strenght are correlated and zinc deficiency might cause osteoporosis (4).

Copper ise another trace element which has an important role in wound and tissue growth. In nutritional copper deficiency, anemia, neutropenia, nervous and cardio-vascular system defects and reproductive system abnormalities, fractures and collagen synthesis failure were observed (1, 7, 18).

Magnesium is an element which has a role in the calcium metabolism and 50 percent of its total content is found in bone (2).

MATERIALS AND METHODS

This experimental study was done at the Animal Laboratory of Medical Faculty of Gazi University and Atomic Absorbtion Spectrophotometry Laboratory of Gazi University Faculty of Science and Arts. Histopathological samples were assessed at Gazi University Medical Faculty, Department of Pathology.

In this study, 40 Swiss - Albino rats which were approximately 140-200 gr. were used. Ten of these rats formed the control group and the remaining 30 rats were divided into three group containing ten rats. In the experimental groups, tibial diaphyseal fractures were created by manipulation under ether inhalation anaesthesia. No external supports were used for fracture fixation.

At the end of the 7^{th} post fracture day 10 rats, 14^{th} post fracture day 9 rats and 21^{st} post fracture day 8 rats were sacrified. 2.5 cc blood samples were

obtained via intracardially. At the end of 12th post fracture day one rat and at the and of the 15th an 19th pos fracture days, two rats died.

RESULTS

There was a significant reduction in the plasma levels of zinc, copper and magnesium ($P<0.001$) at the end of the post fracture day.

The plasma levels of zinc and copper significantly increased ($P<0.001$) at the end of the 14th and the 21st post fracture days and reached normal serum levels at the 21st post fracture day.

Serum zinc, copper and magnesium levels are demonstrated in tables 1, 2, 3 and figures1, 2, 3.

Control	0.429 ± 0.038 mg/ml
7th day	0.283 ± 0.030 mg/ml
14th day	0.346 ± 0.027 mg/ml
21st day	0.425 ± 0.27 mg/ml

Table 1 : Serum zinc levels.

Control	1.865 ± 0.077 mg/ml
7th day	1.528 ± 0.068 mg/ml
14th day	1.667 ± 0.055 mg/ml
21st day	1.901 ± 0.070 mg/ml

Table 2 : Serum copper levels.

Control	122.6 ± 2.88 mg/ml
7th day	108.48 ± 1.63 mg/ml
14th day	122.1 ± 3.78 mg/ml
21st day	121.47 ± 2.07 mg/ml

Table 3 : Serum magnesium levels.

At the 7th post fracture day evidence of inflammation process of the bone healing was observed 14th post fracture day callus formation and 21stpost fracture day new bone formation and bone marrow tissue were observed histopathologically.

All fractures healed clinically and were radiographically confirmed.

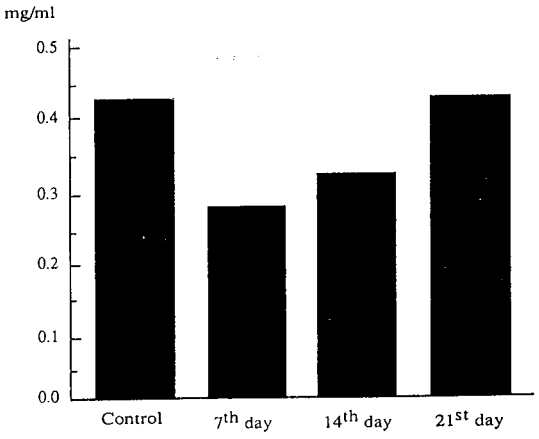

Fig - 1 : Serum zinc levels

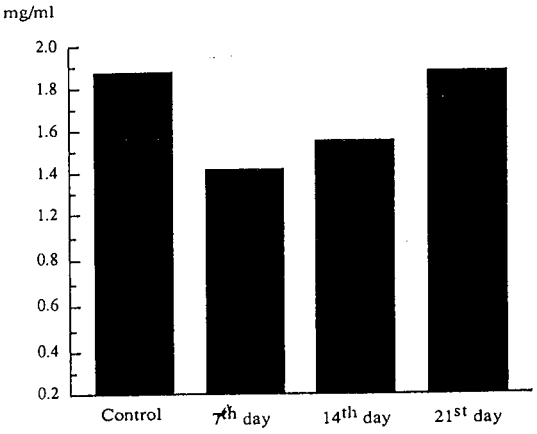

Fig - 2 : Serum copper levels

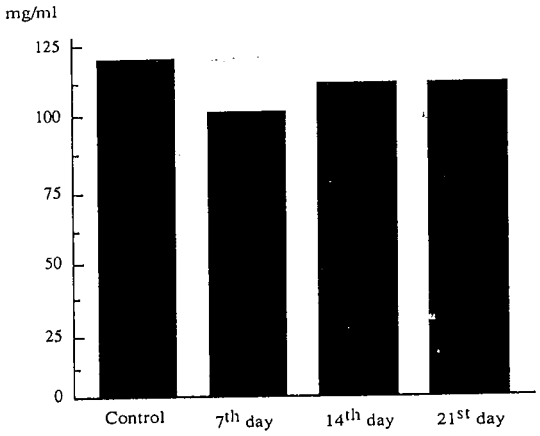

Fig - 3 : Serum magnesium levels.

DISCUSSION

Zinc is an element which has important roles in wound healing and osteogenesis (6, 9, 14, 15, 16). 95 percent of zinc is binded to proteins, especially

albumin in the plasma (10, 12, 19). The metal binding proteins are called metallothionins and these bind varying amounts of zinc (8). Metallothionins can be induced by stress such as starvation, infection, trauma and endotoxins (3, 5, 8). After lower extremity trauma in rats, it has been reported that serum zinc levels started to decrease after 24 hours and remained below normal levels for a week. This situation is considered to be the result of a decrease in plasma albumin levels and aminoaciduria, later on, because of catabolic reaction to trauma (3). This is tissues, primarily the liver (3). Also trauma might be a factor for secretion of cathecolamines to stimulate the parathyroides. This mechanism of adrenal activity might also cause hepatic zinc metallothionein production and reduction in serum zinc levels (3).

Two weeks after trauma catabolic reaction declines and urine albumin excreation decreases (2). It has been reported that zinc is deposited in fracture callus two weeks after fracture. Thus serum zinc levels increase gradually (2).

Copper migrates to the liver in the acute phase of trauma such as fracture (1, 10). Acute phase reactants are produced by stresses something like such as fractures, burns and infections. Because of these conditions, copper migration occurs in order to activate enzymes. As a results, plasma levels of copper decrease (1, 2).

Plasma copper levels increase in the healing phase of bone fractures because of the increase in seruloplasmin levels in the plasma (2). Plasma magnesium levels decrease in the early phase of bone healing because of its loss in urine and increase during bone healing (2). Our findings are correlated with the literature. We conclude that zinc and copper have an important role in bone healing and fractures may be more frequent in zinc and copper deficiency and in patients whose plasma zinc and copper levels are lower than normal. Therefore, in the early stage of bone healing, zinc and copper therapy might be beneficial.

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