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# Does zinc supplementation affect the clinical healing process of stress fracture?

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**Abstract**

Monitoring levels of local pain and weight-bearing are important subjective data used for clinical follow-up of fracture healing, in the foot stress fractures (SFs). Medical treatment has been focused on vitamin D and calcium intake, hovewer there has been no study on the effect of zinc for this fractures. The purpose of this study was to investigate the effectiveness of zinc supplementation on the clinical healing process of SFs in foot. We retrospectively analysed patients with stress fracture in foot. Patients divided into two groups as those who used oral zinc supplementation (group 1) (n=43) and did not use (group 2) (n=52) during clinical healin process. The clinical healing process of the patients were monitored with the Visual Analogue Scale (VAS) scoring system and time to painless Weight Bearing (WB) on the fracture site. The data of the patients were recorded at intervals of three weeks for up to six months. There was a significant difference between the groups according to the mean VAS pain score in the first three months ($p<0.05$). Although mean VAS pain scores were similar after 18 weeks, patients who used zinc in the first three months of clinical healing process had significantly lower pain at the fracture site compared to patients who did not use zinc. There was a significant difference between the groups according to the mean time to painless WB ($p<0.05$). Patients who used zinc of clinical healing process had significantly earlier painless weight bearing at the stress fracture side compared to patients who did not use zinc. As a result, zinc supplementation positively affects the clinical healing process of stress fracture in foot by reducing pain and time to painless weight bearing.

**Keywords:** Zinc supplementation, stress fracture, clinical healing process, pain, weight bearing

## Introduction

Stress fractures (SFs) arise from excessive and repetitive mechanical stress in physically active populations without adequate periods of rest [1]. In this fractures, healing process of bone is delayed due to an increase in osteoclastic activity that causes bone resorption, and most commonly was shown in the lower extremity especially foot [2]. Initial treatment of SFs is activity modification until symptoms subside [1]. In most studies, it has been reported that SFs can give full weight-bearing without restriction and the time to return to sports is prolonged [1,3,4].

Zinc has been suggested to promote bone formation through the augmentation of bone growth factors and the enhancement of osteoblastic cell proliferation, differentiation, and mineralization. Therefore, zinc plays an important role on bone metabolism and daily intake of zinc with a minimum of 12-15 mg is recommended to increase bone density [5-7]. Because of positively effect of on bone metabolism, we recommended our patients with SFs in foot to take 15 mg zinc picolinate oral capsule daily during clinical healing precess. Although most of the studies focused on the intake along with vitamin D and calcium as medical therapy [1,2,4], there is no study on the effect of zinc on clinical healing process of SFs in foot.

In this study, based on the available experimental and clinical evidence [5,8,9], we hypothesized (figure 1) that supplementation of zinc in stress fractures might be beneficial in the clinical healing process of these fractures. Reduction of pain at the fracture site and painless loading are clinical criteria used to evaluate the clinical healing process of the fracture [10]. For this purpose, we aimed to investigate the effectiveness of zinc on clinical healing process in patients with SFs in foot.

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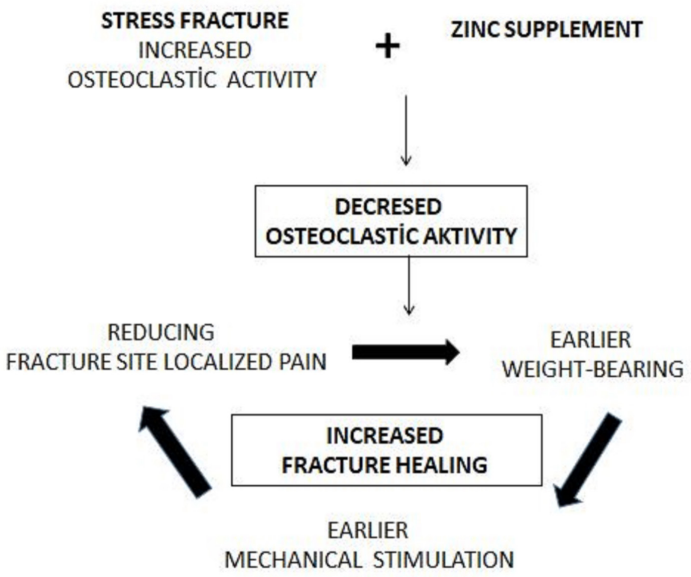


**Figure 1.** Schematic view of our hypothesis regarding the effectiveness of zinc supplementation on the clinical healing process in stress fractures

## Materials and Methods

After ethical approval was obtained from the Institutional Review Board (ethical board approval date: 29.11.2018 and number: E-18-2359), we retrospectively analysed ninty-five patients with SFs in foot between 2014 and 2018. All of the patients were candidate students who participated in the exams of our country's military or police academy schools. Participants were exposed to an extreme exercise program in order to be successful in the exams of these schools. They applied with complaints of localized pain in the foot, especially after long distance running. Our study, all stress fractures of the patients were localized in the foot. Demographic characteristics of the groups (fracture side, laboratory values, gender, body mass index, age) were listed in Table 1.

It was explained to the patients that zinc might have positively effect on bone metabolism, and those agreed to use it were recommended to use a daily oral capsule containing 15 mg of zinc picolinate during the clinical healing process of SFs. Patients were divided into 2 groups as those who used zinc group (group 1) and those who did not use zinc group (group 2).

The study eligibility criteria were as follows: located in foot, participants aged> 18 years, male and female patients, and at least six months follow-up. SFs without foot localization, surgically treated SFs and patients with metabolic bone disease [11,12] were excluded from this study.

As reported in the literature [1,2], activity modification was performed as initial therapy to the all patients. The fractured extremities of patients were fixed with a short leg plaster during 6 weeks and then plaster was removed. After the third week, the patients were asked to put as much weight-bearing on their extremities as they could tolerate the pain.

We used VAS pain score and time to painless weight bearing as clinical criteria [10] to evaluate the effectiveness of zinc use on the clinical healing process of stress fracture. The pain level at the fracture site of each patient was recorded according to the VAS pain scoring system [13]. For the level of pain, they were asked to give a score of 0 (minimum) to 10 (maximum). Mean VAS scores obtained at 3-week intervals for up to 6 months were compared between the two groups (Table 2). The duration of full weight bearing without pain [14,15] was recorded for each patient in the controls, and the mean time to painless WB was compared between the two groups (Table 3).

**Table 1.** Demographic characteristics of the groups.(BMI: Bady Mass Index)

| | Group1 (n=43) | Group2 (n=52) | P value |
|---|---|---|---|
| **Mean Age (range) (years)** | 24.56 (20-30) | 23.73 (19-29) | p>0.005 |
| **Gender (n, %)** | | | |
| **Male** | 24 (55.8 %) | 28 (53.8 %) | p>0.005 |
| **Female** | 19 (44.2 %) | 24 (46.2 %) | p>0.005 |
| **Daily smoking (Yes)** | 19 (44.18 %) | 23 (44.23 %) | p>0.005 |
| **Median(range) Concentration of 25(OH)D (nM)** | 13.84 | 14.96 | p>0.005 |
| **BMI (kg/m$^2$) (range)** | 23.2 (16.6–39.2) | 24.0 (15.4–37.4) | p>0.005 |
| **Location (n,%)** | | | |
| **Metatars** | 28 (65.11%) | 34 (65.38%) | p>0.005 |
| **Calcaneus** | 4 (9.3%) | 5 (9.6%) | p>0.005 |
| **Navicula** | 11(25.58%) | 13 (25%) | p>0.005 |
| **Affected site (n, %)** | | | |
| **Right** | 36 (83.72 %) | 43 (82.69 %) | p>0.005 |
| **Left** | 7 (16.27 %) | 9 (17.30 %) | p>0.005 |

**Table 2.** Comparison of the mean VAS pain scores between groups.(VAS: Visual Analogue Scale)

| | Group1 (n=43) | Group1 (n=52) | p value |
|---|---|---|---|
| **Mean VAS (3.week)** | 6.30 ± 1.14 | 8.75 ± 0.48 | 0.000 |
| **MeanVAS (6.week)** | 4.34 ± 1.04 | 7.25 ± 0.79 | 0.000 |
| **MeanVAS (9.week)** | 3.04 ± 0.99 | 5.63 ± 0.99 | 0.000 |
| **MeanVAS (12.week)** | 1.86 ± 1.12 | 2.94 ± 0.95 | 0.000 |
| **MeanVAS (18.week)** | 0.58 ± 0.62 | 0.44 ± 0.60 | p>0.05 |
| **MeanVAS (24.week)** | 0.32 ± 0.47 | 0.23 ± 0.42 | p>0.05 |

**Table 3.** Comparison of the mean time to weight bearing without pain between the groups

| | Group1 (n=52) | Group2 (n=43) | P value |
|---|---|---|---|
| **Mean time to return (weeks )** | 14.48 ± 1.95 | 12.18 ± 2.40 | p>0.05 |

### Statistical analysis

The Shapiro-Wilk test was used to examine the conformity of continuous variables to normal distribution. Numerical variables were summarized by mean ± standard deviation, median (minimum; maximum), and categorical variables by frequency (percentage). After testing the necessary assumptions, the Kruskal Wallis test was used to compare numerical variables in the groups. If a significant difference was determined, Dunn's Bonferroni corrected pairwise comparison results were interpreted. In categorical variables, Pearson chi-square test was used for comparison between groups, and Monte Carlo (MC) Pearson Chi-square test result was given when the number of subjects in the cell was low. SPSS for Windows Version 21.0 program was used for statistical analysis and statistical significance level was accepted as $p < 0.05$.

### Results

Data of 104 patients with SFs in foot after overuse exercise in military and police academy schools election were retrospectively analysed. Nine patients with metabolic bone disease (hypoposphatasia in 2 patients, hyperparathyroidism in 3 patients and hyperthyroidism in 4 patients) were excluded from the study. There were 95 patients, 43 (45.3%) patients using zinc supplements in group 1, 52 (54.7%) patients not using zinc in group 2 included in this study. The mean age was 24.56 years (range, 20-30 years) in group 1 and 24,73 years (range, 19-29 years) in group 2. Demographic characteristics were similar in two groups (Table 1), and no statistically significant difference was found ($p > 0.05$) between groups.

According to the mean VAS pain scores of the groups, there were statistically significant differences between the groups in the first three months evaluated at $3^{th}$, $6^{th}$, $9^{th}$, and $12^{th}$ weeks ($p<0.05$). However, mean VAS pain scores at the$15^{th}$, $18^{th}$ and $24^{th}$ weeks did not show statistically significant difference between groups ($p> 0.05$). When was used zinc(group 1) in the first three months of clinical healing process , it was observed that fracture pain was lesser.

Mean time to painless WB were found to be 12.18 ± 2.40 weeks (range, 10-17 weeks) in group 1, 14.48 ± 1.95 weeks (range, 11-20 weeks) in group 2. There was a statistically significant difference between two groups ($p<0.05$). It was determined that the used zinc group was able to give WB to the fractured extremity earlier.

### Discussion

SFs of lower extremity are more common in the running population, and initial treatment is activity modification [1-3,14,15]. In our study, patients were candidate students of military/police academy schools, and we included SFs of this patients in the feet after long-distance running. We applied activity modification as initial therapy to all patients. Although medical therapy focuses on vitamin D, there is no study on the effect of zinc, which has an important role in bone metabolism, on the clinical healing process of stress fracture.

Zinc is an essential mineral that is required for bone homeostasis and [5,8], and the popularity of zinc ion studies in tissue engineering as in vivo / in vitro has recently increased significantly [9]. Based on these studies [5,8,9], we developed the hypothesis that zinc might be beneficial in SFs, and for this purpose we recommended zinc intake during the clinical healing process of SFs. The most important finding of this study was that it was the first study to report the effectiveness of zinc intake in the clinical healing process of SFs.

The most commonly used clinical criteria to evaluate clinical healing process of bone fracture were reduced pain at the fracture site and the ability to painless WB [18]. We used VAS pain score and time to painless WB as clinical criteria (10) to evaluate the effectiveness of zinc use on the clinical healing process of stress fracture.

The mean VAS pain scores of the zinc used group (group 1) were statistically significantly lower in the first three months ($p<0.005$), and we concluded that this might be due to the fact that zinc might reduce bone resorption and increase bone formation. We found mean pain-free weight-bearing times of 12.18 ± 2.40 weeks (range, 10-17 weeks) for the zinc used group and 14.48 ± 1.95 weeks (range, 11-20 weeks) for the zinc-free group. We determined

that the group using zinc could carry weight without pain in the statistically significant early period ($p<0.05$), and we concluded that the use of zinc was effective in shortening this period.

Our study has several limitations. Firstly, this study was a retrospective analysis with no control group of young patients without stress fractures. Second, the sample size in our study was relatively small compared to the large and prospective studies on stress fractures conducted on military recruits.

As a conclusion, zinc intake in the clinical healing process of stress fractures in foot shortened the time of fracture pain and early weight bearing. Further prospective studies with large case series are needed to demonstrate the effectiveness of zinc in the bone healing process in SFs.

**Conflict of interests**

*The authors declare that they have no competing interests.*

**Financial Disclosure**

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**Ethical approval**

*The ethic consent form was obtained from Ankara Numune Education and Research Hospital with a number of 2359.*

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