

**REDUCTION IN TIBIAL SHAFT FRACTURE  
HEALING TIME WITH ESSENTIAL  
NUTRIENT SUPPLEMENTATION  
CONTAINING ASCORBIC ACID, LYSINE,  
AND PROLINE**

Dear Editor:

Despite advances in orthopedic techniques, healing of bone fractures is a prolonged process, demanding immobilization of the affected parts and, in the case of lower limbs, often a severe restriction of movement for several weeks. Stability of bone has been shown to be dependent on the stability and strength of the underlying collagenous connective tissue (Knot and Bailey, 1998; Oxlund et al., 1996). Various nutrients have been shown to influence bone formation at various stages. Studies on fracture healing in rats have shown that ascorbic acid is necessary for the differentiation and proliferation of osteogenic and chondrogenic cells (Sugimoto et al., 1998) and that vitamin C-supplemented rats with experimental fractures progressed through

the various stages of fracture healing faster than the placebo group of rats (Yilmaz et al., 2001). The Third National Health and Nutrition Examination Survey (NHANES III; Simon and Hudes, 2001) demonstrated that ascorbic acid nutrition was positively associated with increased bone mineral density and decreased incidence of self-reported fractures in humans.

In addition, lysine and proline, constituents of collagen and other proteins in the bone, have been shown to exert a positive effect on healing of fractures. Studies on experimentally produced fractures in rats demonstrated accelerated fracture healing with lysine and arginine supplementation (Fini et al., 1996; 2001; Torricelli et al., 2001, 2003). Several other dietary components, such as: protein, calcium, magnesium, zinc, copper, iron, fluoride, and vitamins D, A, and K, are required for normal bone metabolism (Jasminka and Kerstetter, 2000). All of these nutrients impact fracture healing, some more directly than others.

These findings prompted us to investigate the effect of supplementation with these nutrients on clinical fracture healing time. A randomized double-blinded placebo-controlled study was undertaken to evaluate the effect of essential nutrient supplementation, specifically enriched with ascorbic acid, lysine, proline, and vitamin B<sub>6</sub> on the healing time of tibial shaft fractures. One hundred and thirteen (113) patients admitted to Dr. Jamdar Hospital, Jabalpur, India, with unilateral displaced closed or grade I open tibial fractures were randomized to receive either standard care with placebo or with daily supplementation with an essential nutrient complex containing ascorbic acid (1500 mg), lysine (1010 mg), proline (560 mg), and vitamin B<sub>6</sub> (10 mg). Qualifying patients, on admission to the study, were clinically examined, radiographs of the affected limbs taken, fractures reduced under anesthesia, and above knee plaster casts applied. Radiographs were taken at each follow-up visit to confirm reduced alignment of fracture and proper callus formation. The primary outcome measure was the number of weeks required for fracture to be healed. Healing was defined as absence of abnormal mobility at fracture site clinically, absence of pain elicited by stressing the fracture or by walking, and radiographic confirmation of callus formation. A healing period of longer than 20 weeks without surgical intervention was considered delayed healing. Only 28 patients from the supplemented group and 42 from the placebo group returned for regular follow-up until fractures were deemed healed.

Data analysis demonstrated reduced fracture-healing time associated with experimental supplementation. For the per protocol (PP) analysis group, the mean fracture healing time of the supplemented group of patients ( $n = 28$ ) was 14 weeks and 17 weeks for the placebo group patients ( $n = 36$ ; Table 1). The percentage of patients with fractures healing in 10 weeks or less was 25% for the supplemented group and 14% for the placebo group (Table 2). However, the difference in healing time between the two groups did not reach statistical significance.

TABLE 1. EFFECT OF SUPPLEMENTATION ON FRACTURE HEALING TIME

Criterion	Supplement	Placebo
Number of patients	28	42
Age range (years)	15–65	12–75
Mean age (years)	32	31
Healing time (weeks)	14.3 ± 1.1	16.6 ± 1.0

TABLE 2. DISTRIBUTION (PERCENTAGE) OF PATIENTS BY FRACTURE HEALING TIME

Healing time	Supplemented	Placebo
10 weeks or less	25%	14%
11 to 15 weeks	39%	50%
16 to 20 weeks	21%	17%
More than 20 weeks	14%	19%

The patient evaluation and treatment in this study was based on routine orthopedic practices in India. In outpatient clinical studies, it is not possible to control certain variables known to influence the healing time of fracture, such as diet, hormonal status, functional activity, drugs used, treatment/placebo intake. To control these variables and obtain statistically significant results, one would have to either conduct the study in an inpatient setting during the entire course of treatment, or significantly increase the number of patients studied. In light of the large drop out rate in this study, we plan on conducting a future study with at least 200 participants to increase probability of achieving statistical significance.

It appears to us that until this is done, the trend in the reduction in healing time due to increased doses of ascorbic acid, proline, lysine, and vitamin B<sub>6</sub>, as seen in the present study, provides strong enough evidence to routinely use these supplements to accelerate the process of fracture repair. Benefits from such nutrient supplementation could have a positive impact on a large number of patients, ultimately resulting in earlier functional recovery. In addition, patients in the supplemented group reported improved well-being.

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