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Effect of magnesium supplementation on diaphyseal tibia fractures: a pilot study

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ABSTRACT

Background: This study aimed to assess and compare the efficacy of magnesium supplementation in patients with long diaphyseal tibia fractures who have undergone surgical management with intramedullary interlocking nailing.
Methods: In a prospective, randomized trial, thirty patients were included, with half receiving magnesium (420 mg/day) along with calcium (500 mg/day) supplementation for 3 months alongside surgical treatment. Radiological outcomes were evaluated through postoperative X-rays using the radiographic union scale for tibia fractures (RUST) scoring system at 6 and 12 weeks.
Results: A significant difference was observed between the two groups. Patients receiving magnesium supplementation exhibited a notable improvement in RUST score, indicating an accelerated bone healing process.
Conclusions: This study demonstrates the efficacy of magnesium supplementation in achieving superior radiologic outcomes compared to patients who did not receive such supplementation. The findings suggest that adjuvant magnesium supplementation could be a viable therapeutic option to enhance bone healing outcomes in individuals with tibia diaphyseal fractures.

Keywords: Long bone, Magnesium, Tibia diaphyseal fractures, Operative

INTRODUCTION

A fracture is defined as any disruption in the continuity of bone. In recent years, the occurrence of long bone fractures has been on the rise, particularly due to the increasing frequency of road traffic injuries. Falls also pose a significant global public health concern, leading to potential re-injury. Studies indicate that falls have a prevalence ranging from 21.8% to 35.1%.[1] The impact of long bone fractures on society is considerable, involving losses in productivity, direct and indirect treatments costs, and an additional burden on morbidity and mortality. Given these challenges, effective management of long bone fractures becomes paramount. There is a pressing need for strategies that can expedite the healing process, facilitating a prompt return to daily activities.

Patients are commonly prescribed calcium postoperatively to support bone healing. Recently, several studies have suggested that magnesium supplementation may potentially enhance the process of bone healing. Magnesium has been found to influence cytokines, increase osteoblastic activity, and reduce osteoclastic activity. Furthermore, it serves as an essential cofactor for vitamin D synthesis and activation, creating a feed-forward loop that boosts intestinal magnesium absorption. This interplay contributes to the maintenance of magnesium homeostasis and overall calcium metabolism.

In clinical trials involving mice, the application of magnesium coated implants has demonstrated the potential to hasten callus formation, diminish the risk of non-union, and enhance the healing of fractures. The theoretical significance lies in magnesium's positive influence on early callus formation and fracture healing, aiming for a swift return to functional capabilities and the prevention of late complications. However, as of now, no study has been undertaken, and there is a scarcity of literature regarding supplementary therapies to expedite the fracture healing process, especially in long bone diaphyseal fractures where patients may face immobility or challenges in daily activities. Hence, the purpose of this study was to assess and compare the effectiveness of magnesium supplementation with calcium, specifically investigating whether it improves the RUST score more rapidly compared to the group receiving no magnesium supplementation and contributes to enhanced bone healing.

METHODS

This study, conducted at Dr. D.Y Pail medical college and hospital, Navi Mumbai, India, employed an open- label, prospective, randomized, and comparative approach. All procedures adhered strictly to ethical standards outlined by both the institutional and national committees on human experimentation, in alignment with the Helsinki declaration of 1975, with revisions in 2013. The institutional ethics committee (IEC) granted approval for this study, denoted by the reference number DYP/IECBH/2023/151.

Informed consent was duly obtained from every individual participant enrolled in the study. Over the period from September 2023 to January 2024, a cohort of 30 patients diagnosed with long bone diaphyseal fractures were enlisted and subsequently monitored for the ensuing 12 weeks. The study encompassed individuals with tibia diaphyseal fractures subjected to intramedullary nailing, aged 50 years or below, and of either gender. Through a computer-generated list of random numbers and employing a 4 block randomisation, half of the participants were randomly assigned to receive oral magnesium (420 mg/day) along with oral calcium (500 mg/day) tablets over the subsequent 12 weeks. Randomization was carried out with a 1:1 allocation for all participants. The statistical software used was SPSS.

Exclusion criteria for this study encompassed individuals aged 50 years or older, those with pre existing kidney or heart diseases, pregnant individuals, those with elevated serum calcium, elevated serum parathyroid hormone (PTH) levels, elevated serum vitamin D levels, abnormal liver function, an increased risk of osteosarcoma (including Paget's disease of bone), those with intestinal perforation, individuals undergoing lithium therapy, and those unwilling to provide informed consent.

Before initiating the treatment, the investigators thoroughly assessed the clinical condition, conducted relevant investigations, and examined radiological scans to understand the fracture pattern and overall clinical profile of the patients. Following intramedullary fixation, 4 weekly serial X-rays were performed to evaluate the time required for callus formation. All patients underwent mobilization 2 days post-operatively and dynamization 8 weeks post-operatively, with uniform adherence to physiotherapy protocols for all participants.

Radiological assessment-The RUST scoring system assesses tibial fracture healing based on callus formation and fracture line visibility in AP and lateral radiographs. Scores range from 4 (no healing) to 12 (healed). Each of the four cortices is scored according to criteria in Figure 1, with total scores indicating the degree of healing.[17]

Overview of radiographic union scale in tibial fracture (RUST).

Score per cortex	Callus	Fracture Line
1	Absent	Visible
2	Present	Visible
3	Present	Invisible

Figure 1: Overview of RUST.[17]

RESULT

In this study a total of 30 patients with diaphyseal tibia fractures were enrolled (15 in each group). The baseline characteristics of the participants in both groups are included in Table 1. Mean age of the participants in the magnesium supplementation group was 35.2±7.9 years, whereas in other group was 36.3±9.8 years ($p>0.05$). 2 of these patients from the calcium only group, were lost to follow up. One patient from the magnesium supplemented group underwent delayed union, as opposed to 3 patients in calcium only group. No signs of osteomyelitis or impending infection was noted in any of groups.

Functional outcome-RUST score

Within the group: In the magnesium supplementation group at post op management 12 weeks, there was a significant improvement in the functional outcome (total RUST score) from the baseline ($p<0.001$). Similarly, in the non- supplementation group at post management 12 weeks, there was a significant improvement in functional outcome (total RUST score) from baseline ($p<0.001$)

Comparison between the two groups: The total RUST score was comparatively higher in the magnesium supplementation group at various time intervals (6 and 12 weeks) and this was statistically significant when independent t-test was applied ($p<0.001$) (Table 2).

Table 1: Demographic details of the patients.

Characteristics		Calcium (500 mg)		Calcium (500 mg) + magnesium (420 mg)		P value
		Value	%	Value	%	
Total patients of diaphyseal tibia fracture		15	100	15	100	
Mean age in years (±SD)		35.20±7.9		36.3±9.8		0.746
Median age in years (IQR)		35	13	42	19	0.744
Gender	Male	10	66.7	12	80	0.682
	Female	5	33.3	3	20	
Tibia shaft fracture	Left	11	73.3	5	73.3	0.0666
	Right	4	26.7	10	66.7	
Fracture type	Closed	9	60	9	60	1
	Compound	6	40	6	40	

Table 2: Comparisons of the RUST score in both the groups.

RUST score	Magnesium supplementation		P value
	Yes	No	
6 weeks	7.47±0.83	6.8±0.41	<0.001
12 weeks	10.33±0.98	9.6±0.63	<0.001

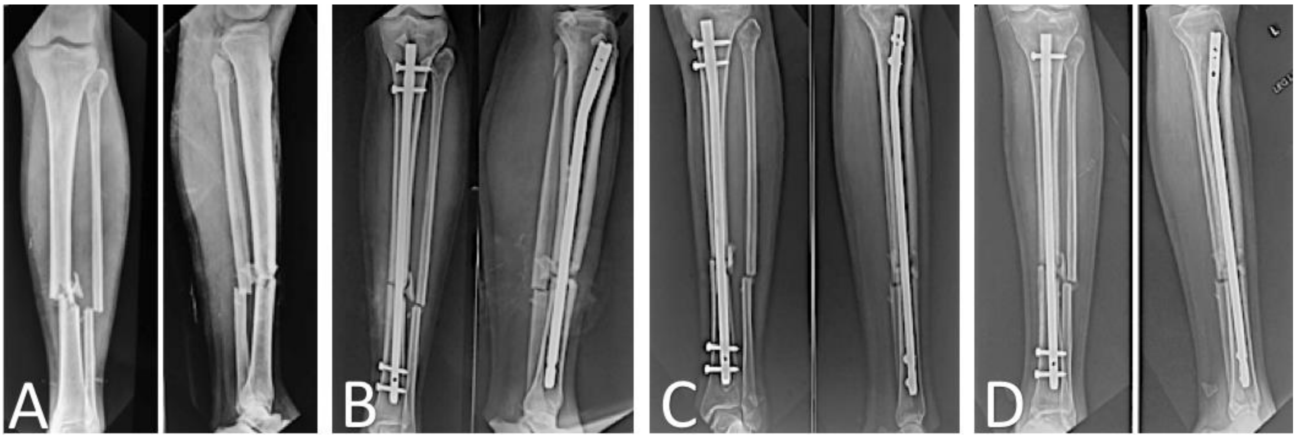

Figure 2 (A-D): Plain radiographs of a patient who was not given magnesium supplementation. (A) Preoperative x rays, (B) immediate post-operative X-rays (RUST 4), (C) 6 weeks post-operative X-rays (RUST-6) and (D) 12 weeks post-operative X-rays (RUST-8).

Figure 3 (A-D): Plain radiographs of a patient who was given magnesium supplementation. (A) Preoperative X-rays, (B) immediate post-operative X-rays (RUST-4), (C) 6 weeks post-operative X-rays (RUST-7) and (D) 12 weeks post-operative X-rays (RUST-10).

DISCUSSION

Bone fractures are frequent traumatic injuries that lead to a cascade of systemic and local physiological as well as biochemical changes.[2]

Inflammation is vital for pathogen clearance and tissue homeostasis. In bone injury, realised cytokines and growth factors attract inflammatory cells, crucial for fracture healing, emphasizing the significance of the initial fracture haematoma and subsequent inflammatory response.[3] Fracture repair relies on cellular and molecular processes. Supplements with trace elements (Fe, Zn, Cu) and vitamins mitigate inflammation, but disruptions in these elements heighten inflammatory responses. The mechanism of calcium (Ca) and magnesium (Mg) supplements in multiple fractures are unclear. Speeding up fracture healing via trace element supplementation to modify the inflammatory microenvironment is a key goal in treatment.[4] Insufficient serum magnesium is independently linked to a higher risk of fractures, as supported by evidence.[5] Combining magnesium with other nutritional compounds enhances bone formation for fracture healing, as indicated by research.[6]

Magnesium is a vital and essential element involved in nearly all metabolic processes in the human body.[7] It is also vital for muscle and bone function, offering strong skeletal protection and acting as a cofactor in calcium metabolism.[8] Oral magnesium supplementation can enhance bone mineral density and size, supporting fracture healing.[9]

The United States food and nutrition board (FDA) recommends a daily magnesium intake of 420 mg for men and 320 mg for women.[10]

The Indian council of medical research (ICMR) suggests a daily magnesium intake of 440 for men and 370 for women.[11]

According to Song et al calcium and magnesium levels are linked to the severity of multiple fractures. Supplementation may reduce inflammation, potentially benefiting bone recovery and the overall disease process.[12] In Razzaque study, elevated extracellular magnesium induces MAGT1-dependent and TRPM7-dependent magnesium entry, increasing intracellular ATP and accumulating synaptic vesicles in isolated rat DRG neurons.[13]

This aligns with previous findings where magnesium supplementation for 30 days or more increases serum concentrations and bone magnesium content. It indicates a crucial role of magnesium in the bone healing process for fracture patients through its influence on circulating magnesium balance.[5] Magnesium toxicity is less concerning as hypermagnesemia is rarely observed without renal insufficiency. Normal kidneys can effectively excrete large amounts (250 mmol/d) of magnesium.[14-16] In this study, all patients underwent dynamization at a mean time of 46 days. Typically, dynamization is carried out two to three months after nailing to ensure adequate callus formation, which serves to prevent excessive movement at the fracture site.[17]

This study revealed positive radiological outcomes with magnesium supplementation, indicating its potential as an osteoblastic agent for enhanced bone healing and a quicker return to work. This pioneering clinical study highlights functional benefits in tibia shaft fractures. However, further rigorous clinical trials are needed to validate and support these encouraging results.

This study has its limitations, including its single center setting, a small sample size as a pilot study, and limited short term follow ups. The inclusion of heterogenic treatment groups makes it challenging to generalise the positive outcomes of magnesium to a broader population. Moreover, the RUST scoring system may not be applicable in pseudoarthrosis. Future studies should address these limitations by incorporating a larger sample size, a more extended follow up period and a rigorous design to further validate the potential benefits of magnesium.

CONCLUSION

Magnesium supplementation proved effective, leading to superior radiological outcomes compared to calcium alone in patients. While adjuvant magnesium therapy shows promise for enhancing radiological outcomes, further comprehensive clinical studies are necessary to support its recommendation.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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