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Assessing the efficacy and safety of autologous bone marrow injections in treating delayed union of long bone fractures: A retrospective analysis

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ABSTRACT

Background: Delayed union in long bone fractures poses a significant clinical challenge, necessitating effective treatment solutions. The urgency for novel and effective treatment modalities is ever-increasing, especially considering the prevalence and complications associated with delayed union. **Aims and Objectives:** This retrospective analysis aims to assess the safety and efficacy of autologous bone marrow injections in treating delayed union in a diverse cohort of individuals with long bone fractures. **Materials and Methods:** The study includes 100 individuals aged 21–69 with varying fracture types. Fracture classifications comprised 40% closed fractures (n = 40) and 60% open fractures (n = 60). Notably, the femur had a higher prevalence of open fractures (n = 30) than closed fractures (n = 20). Tibia fractures demonstrated a similar propensity, with 25 open and 15 closed cases. Humerus fractures manifested an even distribution between open and closed categories (n = 5 each), indicating their relative resilience to open fractures. **Results:** Union was attained in 82 cases, with a mean union time of 7.4 weeks post-the-third bone marrow injection. The timeframe for the union varied widely, ranging from 4 to 17 weeks. In eight instances where bone marrow injections failed to achieve union, alternative treatment via bone grafting was necessary. No significant complications were reported; however, minor discomfort was experienced by 13% of the patients and was effectively managed with over-the-counter analgesics. **Conclusion:** This retrospective analysis demonstrates the high efficacy and safety of autologous bone marrow injections in treating delayed union in long bones, making them a promising alternative treatment strategy with minimal complications.

Key words: Delayed union; Long bone fractures; Bone marrow injection; Efficacy; Safety; Fracture union; Closed fractures

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INTRODUCTION

The delayed union of long bone fractures has long presented a persistent challenge in orthopedic practice, carrying substantial clinical and functional implications for affected individuals. The process of fracture healing is a complex interplay of various cellular and molecular factors. When fractures fail to unite within the expected timeframe, they result in delayed union, extending the patient's recovery period and sometimes necessitating additional interventions.[1] Given its profound impact on patient well-being and healthcare resources, there is a continuous quest for innovative treatment strategies to expedite fracture healing.

The management of delayed unions remains an area of ongoing research and clinical exploration. Conventional methods, such as immobilization, external fixation, and internal fixation techniques, have proven effective in many cases. However, a subset of fractures exhibit resistance

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to these traditional approaches.[2] This has led to the exploration of alternative strategies, including biological interventions aimed at stimulating and expediting the natural healing processes.

One particularly promising intervention is the use of bone marrow injections, which have garnered attention for their potential to enhance fracture healing. Bone marrow, known for its abundant source of mesenchymal stem cells, growth factors, and cytokines, plays a pivotal role in tissue repair and regeneration.[3] The rationale behind bone marrow injection is to harness these regenerative components to facilitate the formation of a robust callus and promote the timely union of the fractured bone. This approach presents an attractive proposition for managing delayed union, potentially reducing the need for more invasive surgical procedures and expediting the return to functional independence.

Delayed union in long bone fractures poses a critical clinical challenge, necessitating innovative treatment strategies. As bone marrow injections have shown promise in accelerating fracture healing in smaller cohorts, a broader understanding of their efficacy and safety in a retrospective analysis is warranted. This research seeks to expand the existing knowledge base by scrutinizing the impact of bone marrow injections in a significantly larger sample of 100 patients who have experienced delayed union of long bone fractures.

This retrospective analysis aims to provide a comprehensive examination of bone marrow injection's role in fracture healing by assessing both clinical and radiographic outcomes. Given the clinical significance of delayed union in orthopedics, the findings from this larger cohort could offer invaluable insights, particularly regarding treatment effectiveness and patient safety.

Aims and objectives

The aim of this retrospective analysis is to extend practical implications for the orthopedic community in managing delayed union conditions, with a specific focus on investigating the efficacy and safety of bone marrow injections within a substantial patient cohort. To achieve this aim, the research encompasses two primary objectives: To retrospectively evaluate the effectiveness of bone marrow injections in promoting fracture union, substantiated by both clinical and radiographic assessments. To conduct a thorough retrospective examination of the safety profile of this intervention, with a particular emphasis on assessing the incidence of adverse events and analyzing patient-reported outcomes.

MATERIALS AND METHODS

Study design and participants

This study is a retrospective analysis designed to assess the efficacy and safety of autologous bone marrow injections for promoting fracture union in patients with delayed union of long bone fractures. The cohort comprised 100 patients aged between 21 and 69 years. Data for this study were sourced from the CSI Mission General Hospital, Trichy, Tamil Nadu, India. All participants had previously given informed consent as part of their original inclusion in the study.

Fracture classification and characteristics

Fractures were classified as either closed or open based on clinical and radiographic evaluations available in medical records. Of the 100 cases, 40% (n=40) were closed fractures, and 60% (n=60) were open fractures. Each fracture had been categorized by its location and severity, which guided the treatment strategy.

Intervention

All patients received bone marrow injections as their primary treatment. The bone marrow was aspirated from the iliac crest under aseptic conditions. This aspirate was then processed to isolate mesenchymal stem cells and growth factors. The bone marrow concentrate was introduced into the fracture site under fluoroscopic guidance. Each patient received a total of three bone marrow injections at 2-week intervals.

Assessment of fracture union

Fracture union was evaluated using both clinical and radiographic criteria. Clinical criteria included pain levels, range of motion, and weight-bearing ability. Radiographic criteria consisted of regular X-ray examinations to monitor callus formation and other signs of healing. Fracture union was considered achieved when evidence of cortical bridging and an absence of pain on weight-bearing were observed.

Outcome measures

The primary outcome measure was the achievement of fracture union, recorded as the number of cases that met the union criteria. Secondary outcome measures included time to union, assessed as the interval between the first bone marrow injection and confirmation of fracture union, and the occurrence of complications related to the procedure.

Data analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the participants. The mean and standard deviation were calculated for continuous variables like age and time to union. The

proportion of closed and open fractures was presented as percentages. Ranges for achieving union and the incidence of complications were also reported.

Ethical considerations

Institutional Ethics Committee approval had been obtained from CSI Mission General Hospital, Trichy, Tamil Nadu, India.

RESULTS

This retrospective analysis was conducted based on data from the Mission General Hospital, Trichy, Tamil Nadu. Its focus was to assess the safety and effectiveness of percutaneous autologous bone marrow injections as a remedy for delayed union in long bone fractures, providing insights into this innovative treatment strategy.

Demographic distribution

The study encompassed a cohort of 100 participants, spanning an age range from 21 to 69 years, resulting in a heterogeneous sample representative of a broad age spectrum (Table 1).

Fracture classification insights

Among the 100 cases assessed, 40% (n=40) were identified as closed fractures, while a notably higher proportion of 60% (n=60) were categorized as open fractures (Table 2; Figures 1 and 2).

Distribution by fracture type

Interestingly, the data revealed an unexpected pattern: open fractures were more prevalent than closed fractures, constituting 60% of the total cases, in contrast to the 40% that were closed.

Efficacy on bone union

Historically, a successful union was achieved in 82 cases, affirming the efficacy of the bone marrow injection approach. This significant rate of success underscores the potential of this treatment modality in facilitating fracture union (Table 3; Figures 3 and 4).

Table 1: Age distribution of participants in bone marrow injection study for delayed fracture union

Age range	Number of patients
21–69 years	100

Table 2: Classification of fractures in delayed union study

Type of fracture	Percentage	Number of cases
Closed fracture	40	40
Open fracture	60	60

Timing and treatment variability

On average, clinical and radiographic unions were achieved within 7.4 weeks after the third bone marrow injection. However, the data also highlighted substantial variability in the timeframes, ranging from 4 to 17 weeks, emphasizing individual variability in the healing process (Table 4).

Alternative treatments

In instances where bone marrow injections had not been effective (n=8), bone grafting had been utilized as an alternative treatment. This underscores the need for adaptable treatment strategies in managing delayed union.

Patient safety and experience

The study reported no severe complications related to the bone marrow injections. Minor discomfort had been reported by 13% of patients but had been effectively managed with over-the-counter medication, indicating the procedure's overall tolerability.

Figure 1: Preoperative X-rays

Figure 2: Preoperative X-rays

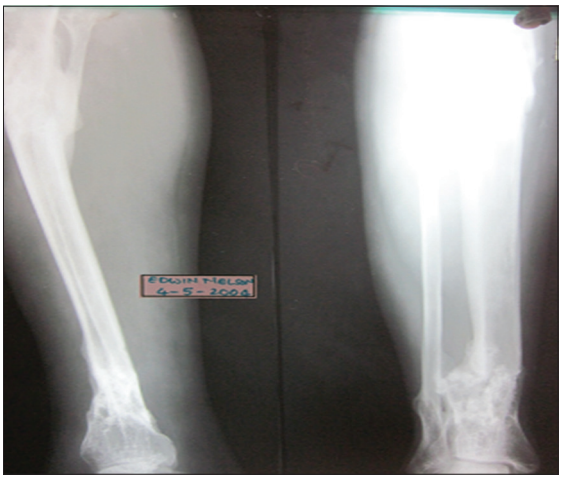

Figure 3: Two years postoperative

Figure 4: Ten years postoperative

Types of fractures by bone involved

Among the cases, out of 50 femur cases, 20 had been classified as closed fractures and 30 as open fractures. This observation suggests that the femur may be more susceptible to open fractures in this sample, potentially due to its location and the high-force injuries commonly associated with it, such as motor vehicle accidents.

For the tibia, 15 cases had been categorized as closed fractures, while 25 were open fractures. This trend parallels that of the femur, possibly attributed to the tibia's subcutaneous location, which makes it more prone to open fractures compared to other bones (Table 5).

In contrast, humerus fractures demonstrated an even distribution, with five cases each of closed and open fractures. This observation may be because the humerus is less exposed to high-impact injuries than lower-extremity bones and benefits from better soft-tissue coverage, reducing the risk of open fractures (Figures 5 and 6).

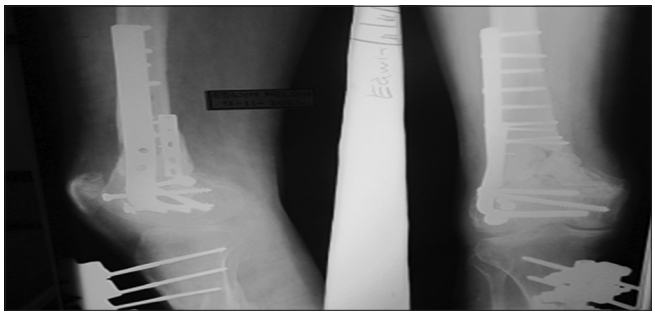

Figure 5: Immediate postoperative

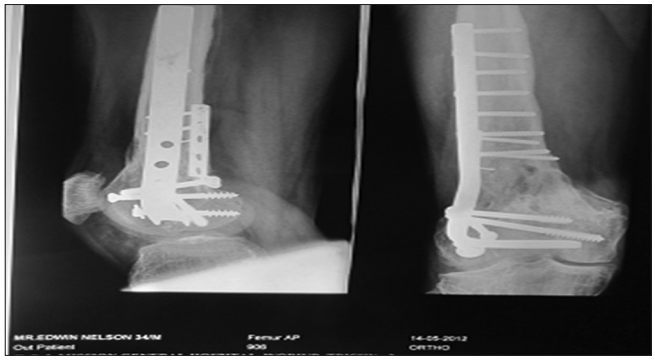

Figure 6: Ten year postoperative

Table 3: Types of bones involved and status of fracture union

Outcome type	Number of cases
Union achieved	82
Non-union (treated)	8

Table 4: Time to achieve fracture union in the study

Parameter	Time frame
Mean union time	7.4 weeks after 3rd injection
Range for union time	4 weeks to 17 weeks

Table 5: Types of fractures by bone involved

Bone involved	Closed fracture cases	Open fracture cases	Total cases
Femur	20	30	50
Tibia	15	25	40
Humerus	5	5	10

Average time to union

Reiterating, the mean time for achieving bone union had been 7.4 weeks post-the-third bone marrow injection, with a timeframe ranging from 4 to 17 weeks (Table 4).

DISCUSSION

Fracture healing is a complex and intricate biological process marked by a cascade of cellular responses and

interactions. Managing delayed and non-unions have been a focus of extensive research, resulting in various treatment methods, including grafting techniques and stimulation approaches. In this retrospective analysis, we evaluated the effectiveness of percutaneous autologous bone marrow injection in addressing cases of delayed union in long bone fractures.

Our findings resonate with earlier investigations that underscore the osteogenic potential of bone marrow. The application of bone marrow injection, as observed in our data, yielded promising outcomes, consistent with the experimental work of Paley et al.[4] In their study involving rabbits, Paley et al.[4] demonstrated the positive impact of marrow injection on fracture healing, particularly when administered early in the healing process. This underscores the potential of bone marrow injection to facilitate timely and effective fracture union.

In addition, Connolly et al.[5] highlighted the preventive capabilities of autologous bone marrow injection in addressing non-unions. Our analysis contributes to the growing body of evidence supporting the efficacy of this intervention. The high success rate in achieving fracture union (82%) over a relatively short period (mean time of 7.4 weeks) underscores its potential clinical significance. The range for achieving union (4–17 weeks) underscores the individualized nature of healing trajectories, aligning with studies emphasizing the multifactorial nature of fracture healing.[11]

Goujon's early work[3] serves as a foundation for the exploration of the properties of bone marrow, emphasizing its significance in medical science. The relevance of his research highlights the longstanding intrigue surrounding bone marrow, forming a foundation for subsequent studies, including our own. Paley's experimental study[6] offers direct empirical evidence supporting the beneficial impacts of bone marrow injections, complementing our findings by demonstrating the functional advantages of using marrow to facilitate bone repair.

Our observations regarding the prevalence of open fractures in the femur and tibia, possibly due to their anatomical features and exposure to high-force incidents, align with trends in the literature. In contrast, the humerus demonstrates a more balanced distribution between open and closed fractures, suggesting it might be less prone to severe injuries resulting in open fractures.[15,16]

By examining our results, medical practitioners can focus on targeted preventative measures or treatment plans for fractures based on the type of bone involved. For high-risk bones like the femur and tibia, more aggressive treatment protocols for open fractures may be warranted.[15]

Studies conducted by Connolly[7] and Moon MS[8] into the preventive aspects and therapeutic applications of autologous bone marrow injections, accentuating the versatile uses of this treatment strategy, align with the objectives and outcomes of our study. Recent clinical observations by Lin et al.,[9] and Khanal et al.'s prospective trial[10] provide additional empirical support for the efficacy of autologous bone marrow injections in different settings and populations.

Galois et al.'s technical observations[12] offer in-depth insights into the intricacies of bone marrow injection procedures, complementing the clinical focus of our research and providing a comprehensive understanding of the intervention. Hernigou et al.'s exploration[13] of the concentration of progenitor cells in bone marrow enriches our understanding of the physiological mechanisms at play in the success rates observed in our data. Stinchfield's et al.'s work serves as a linchpin,[14] emphasizing the broader relevance of effective bone repair strategies and reinforcing the gravity and applicability of our findings within the larger context of orthopedic treatments.

Moreover, our results align with investigations that have highlighted the correlation between osteogenic activity and the concentration of progenitor cells. The safety profile of the procedure is a significant advantage, with minimal donor and recipient site morbidity, the absence of major complications, and manageable discomfort reported by a small percentage of patients. These findings echo studies emphasizing the advantages of percutaneous procedures, including reduced morbidity and hospital stays, making them preferable to traditional open grafting techniques.

Limitations of the study

This study is retrospective in nature, inherently limiting its ability to establish causality. The sample size is relatively small, and there was no control group for comparison. The wide range of union time suggests potential variability in outcomes.

CONCLUSION

In this retrospective analysis, our data underscore the efficacy and safety of percutaneous autologous bone marrow injection for promoting fracture union in delayed long bone fractures. This technique stands out as a valuable alternative to traditional grafting methods, stimulating osteogenesis without graft-related complications. The percutaneous approach offers advantages such as reduced morbidity, lower costs, and shorter hospital stays, while maintaining comparable outcomes to open techniques.

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Author's Contribution:
SK- Concept and design of the study, results interpretation, review of literature and preparing first draft of manuscript. Statistical analysis and interpretation, revision of manuscript; **BN-** Concept and design of the study, results interpretation, review of literature and preparing first draft of manuscript, revision of manuscript; **SR-** Review of literature and preparing first draft of manuscript. Statistical analysis and interpretation; **SB-** Concept and design of the study, results interpretation, review of literature and preparing first draft of manuscript. Statistical analysis and interpretation, revision of manuscript.

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