Original Research Article

Journal of College of Medical Sciences-Nepal, Vol-21, No.2, Apr-Jun 2025

ISSN: 2091-0657 (Print); 2091-0673 (Online) Open Access
DOI: 10.3126/jcmsn.v21i2.76222

Percutaneous Autologous Bone Marrow Injection for Delayed Union and Non-Union for Long Bone Fracture

Subash Chandra Jha[1], **Shreel Koirala**[2]

[1]Department of Orthopedics, Nepal Medical Colleg Teaching Hospital, Kathmandu, Nepal. [2]Department of Orthopedics, Sikkim Manipal Institute of Medical Sciences, Sikkim, India.

ABSTRACT

Background

Treating nonunion remains a significant challenge in orthopedic surgery. Approximately 5% to 10% of fractures result in delayed or nonunion, leading to impaired function and necessitating repeated hospitalizations and surgeries. The aim of this prospective study was to evaluate the effectiveness of percutaneous bone marrow injection for treating fractures with delayed union and nonunion following internal fixation.

Methods

Adult patient with closed long bone fracture treated surgically with internal fixation with acceptable alignment, good bone opposition and stable fixation who presented with delayed or non-union were included in the study. Desired amount of non-heparinized bone marrow was injected under image intensifier guidance immediately after aspiration. Second bone marrow injection was repeated at interval of 4-6 weeks of first injection. Serial X-rays were taken at each review until 9 month post procedure.

Results

The study included 27 patients with delayed union and 3 cases of nonunion of long bones, all of whom were treated with percutaneous autologous bone marrow injections. Our study demonstrated an 85.18% success rate in achieving union following bone marrow injection in case of delayed union while, 33.33% success in case of non-union. Our results were excellent in 53.33% (16/30) of cases, good in 23.33% (7/30), and poor in 23.33% (7/30).

Conclusions

The use of bone marrow to accelerate fracture healing is one of the promising methods of treating delayed union and non-union.

Keywords: bone marrow injection; delayed union; non-union.

Correspondence: Dr. Subash Chandra Jha, Department of Orthopedics, Nepal Medical College Teaching Hospital, Jorpati, Kathmandu, Nepal. Email: subash.jha@gmail.com, Phone: +977-9841805463. **Article received**: 2025-03-01. **Article accepted**: 2025-05-15. **Article published**: 2025-06-30.

INTRODUCTION

Nonunion and delayed union are common issues in fracture healing, often resulting from a variety of factors, both identifiable and obscure. Treating nonunion and delayed union remains a significant challenge in orthopedic surgery. Approximately 5% to 10% of fractures result in delayed or nonunion, leading to impaired function and necessitating repeated hospitalizations and surgeries.[1, 2] To address these challenges, several methods have been developed, including bone grafts, electrical stimulation, ultrasound, bone transport, and bone marrow injection. The current gold standard for treating atrophic nonunion involves surgical stabilization and open autologous bone grafting, with reported success rates ranging from 97% to 99%.[3] However, this approach is limited by the availability of grafting material and is associated with several complications, including persistent donor site pain, which affects up to 49% of patients, infection or devascularization of the fracture fragments, where healing is already compromised.[4] Bone marrow aspirates provides stimulus in animal experiment and in clinical evaluation of bone graft and bone substitutes.[5-7] However, the clinical use of marrow as an osteogenic source has remained limited. The aim of this prospective study was to evaluate the effectiveness of percutaneous bone marrow injection for treating fractures with delayed union and nonunion following internal fixation.

METHODS

This prospective study was conducted in the Department of Orthopedics, Birat Medical College and Teaching Hospital from Dec 2022 to Dec 2024, following approval from the institutional reviewcommittee. The study included 27 patients with delayed union and 3 cases of nonunion of long bones, all of whom were treated with percutaneous autologous bone marrow injections. Each patient provided written informed consent and the study adhered to the principles outlined in the Declaration of Helsinki. Adult patient with closed long bone fracture treated surgically with internal fixation with acceptable alignment, good bone opposition and stable fixation who presented with delayed or non-union were included in the study. Patients with pathological fractures, open fractures, infected fractures or fractures with neurovascular injuries were excluded from the study. Written informed consent was obtained from all participants, who were informed about the treatment plan. Patients were followed up post-surgery and assessed clinically and radiologically for fracture healing, joint movement, and implant failure. Delayed union was defined as the absence of radiographic progression of healing between three to six months, while nonunion was defined as no visible healing nine months post-injury, and no signs of healing for three months.[8] The procedures were conducted in the operating theatre (OT) with patients in a supine position. Separate draping for the fracture and graft sites was employed to prevent cross-contamination. A bone marrow aspiration needle was inserted in anterior or posterior iliac crest. The entire procedure was performed under local infiltration with 2% xylocaine and adrenaline. We also redirected the needle within the iliac crest to ensure the aspirate remained concentrated, following Muschler et al.'s recommendation to aspirate bone marrow from multiple sites to avoid dilution with peripheral blood.[9]

The injection site was marked prior to the procedure, and desired amount of non-heparinized bone marrow was injected under image intensifier guidance immediately after aspiration. Bone marrow injections of 40–50 cc were administered for femur and tibia fractures, 20 cc for humerus, and 10 cc for radius and ulna. Postoperative care included a compression dressing, and patients were discharged the same day, with follow-up reviews every 4-6 weeks. Second bone marrow injection was repeated at interval of 4-6 weeks of first injection. Serial X-rays were taken at each review until 9 month post procedure. Fracture site mobility, tenderness, and radiological features were assessed to confirm union, defined as the absence of local pain or instability and the ability to bear weight or use the limb normally. Radiological union was defined by the presence of callus bridging the fracture and partial obliteration of the fracture line in two perpendicular views. Results were graded

based on the criteria: excellent if the fracture united within 16 weeks without complications, good if union occurred within 24 weeks with treatable complications like superficial infection or joint stiffness, and poor if union took longer than 24 weeks or was associated with permanent complications such as osteomyelitis, implant failure, nonunion, limb shortening, or permanent joint stiffness.

RESULTS

The average age of participants was 46 years (ranging from 21 to 72 years), with male predominance (Table 1).

Table 1. Age and gender distribution. (n=30)	
Variables	**Frequency (%)**
Age group (year)	
< 25	8 (26.7)
25-50	12 (40)
> 50	10 (33.3)
Gender	
Male	22 (73.3)
Female	8 (26.7)

Out of 30 long bones, 6 femoral shaft fractures were treated with interlocking nails, 3 supracondylar fracture femur were treated with supracondylar nail and 2 intercondylar fracture femur were treated with distal femoral locking plate, 13 tibia shaft fractures were treated with tibia interlocking nail, out of 3 humeral shaft fractures 2 were treated with low-contact dynamic compression plates (LC-DCP) and one with humerus interlock nail, while 1 radius and ulna fracture and 2 radius fractures were managed with LC-DCP. Tibia fracture comprised 43.33% of cases in the study followed by shaft femur 20 % and supracondylar femur 10% (Table 2).

Table 2. Union rate according to different long bone.		
Long bone fracture	**Frequency**	**United**
Humerus	3	1
Forearm (Both Bone)	1	1
Radius	2	1
Femur Shaft	6	5
Supracondylar femur	3	3
Intercondylar Femur	2	1
Tibia	13	12
Total	30	24

Out of 30 patient included in the study 24 got united after bone marrow injection while 6 didn't unite (Figure 1). Our study demonstrated an 85.18% success rate in achieving union following bone marrow injection in case of delayed union while, 33.33% success in case of non-union (Table 3).

Table 3. Result according to the defect in union (delayed/ Non-union) of fracture.			
Defect in union	**Frequency**	**United (%)**	**Not united**
Delayed Union	27	23 (85)	4
Non Union	3	1 (33)	2
Total	30	24 (80)	6

Figure 1. 34 years male with: (A) delayed union tibia fracture received bone marrow injection, (B) Fracture united after 4 months.

Our results were excellent to good in almost 75% of cases (Table 4).

Table 4. Result based on final outcome.	
Result	**Frequency (%)**
Poor	7 (23.33)
Good	7 (23.33)
Excellent	16 (53.33)
Total	30 (100)

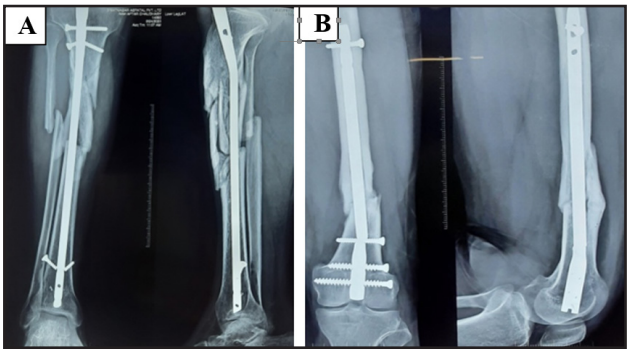

Figure 2. Both case receiving bone marrow injection: A. 60 years/ Male with delayed union tibia fracture received Bone marrow injection, fracture didn't unite with broken screws. B. 25 years/ Male with non-union distal femur fracture after receiving Bone marrow injection, fracture united with broken supracondylar nail.

Among patients with poor outcome 3 had non-union at final follow-up, 1 had non union with broken implant (Figure 2A), 1 had non-union with chronic infection with broken implant, 1 had chronic infection and 1 had broken implant with united fracture (Figure 2B). No patient suffered from local or systemic complications associated with the bone marrow transplantation procedure, such as infection, fat embolism, and compartment syndrome, and all patients were discharged within 24 hours after the surgical procedure.

DISCUSSION

Nonunion or delayed union of long bone fractures has consistently presented a significant challenge. Autogenous bone grafting has traditionally been the most commonly employed procedure in operative treatment. However, this method is associated with several complications at the donor site, including hemorrhage, infection, the need for additional procedures, and the development of painful and unsightly scars. Additionally, open grafting methods can disrupt the vascularity at the fracture site.[10] To mitigate these issues, alternative, less invasive methods have been explored, such as ultrasound, bone growth factors (bone morphogenic protein), extracorporeal shock waves, and bone marrow injections. These methods aim to achieve similar therapeutic outcomes with fewer complications.[11] In our study, we treated 30 cases of delayed and nonunion long bone fractures using bone marrow injections. This approach successfully avoided complications such as infection, hemorrhage, and unsightly scars. Tibial fractures comprised 43.33% of the cases in this study, reflecting the relatively high incidence of delayed and nonunion associated with tibial fractures. This is consistent with previous studies, which have attributed the higher incidence to the subcutaneous anatomical location and specific vascularization characteristics of the tibia.[12]

Our study demonstrated an 80% success rate in achieving union following bone marrow injection, highlighting the efficacy of autogenous bone marrow in accelerating fracture healing. Ma et al.[13] used bone marrow injections to promote healing in various fractures, including those of the tibia, femur, metatarsals, and humerus, even in cases with complications such as infection or pathological fractures, achieving similarly good results. Similar, study conducted by Bhargava et al.,[14] demonstrated union in 23 cases out of total 28 patients with delayed union and 3 with non-union of fractures of the long bones. The mean time of clinical and radiological union in their study was 12 week (range 7-18 weeks) after injection. In terms of complications, no infections or pain were reported at the donor or injection sites. Bone marrow injection is a simple, minimally invasive technique, with no risk of disease transmission or immune reaction since the material is autogenous. Compared to iliac bone grafting, it involves no additional surgical incisions or donor site morbidity and does not disturb the fracture site due to its percutaneous administration. Bone marrow injections represent a promising application of stem cell technology in orthopedics, avoiding many complications of traditional bone grafting methods. Hernigou et al.,[15] reported that hematopoietic stem cells are pluripotent and capable of differentiation; however, their number decreases in patients who smoke, consume alcohol, or use steroids. Concentrating the donor sample increases the number of pluripotent cells, crucial for successful outcomes. A potential limitation of our study was the absence of a control group treated with a different modality.

Comparison with other studies showed similar success rates. Sahu et al., attribute the high success rate (88.12% union) to careful case selection, focusing on biological rather than mechanical causes of delayed union or nonunion. There results were excellent in 68.81% (64/93) of cases, good in 19.35% (18/93), and poor in 11.82% (11/93). In terms of overall patient satisfaction, 68.81% (64/93) were fully satisfied, and 19.35% (18/93) were satisfied with the treatment outcomes.[12]

Majority of the studies stated that in specific patient the failure may be related to the improper reduction of the fracture and the long-time interval since the index surgery, leading to incipient atrophy ofthe fracture end. Hence delayed union could be better case selection than non-union. However we had only 3 cases of non-

union in our study making it a limitation of the study.

CONCLUSIONS

The use of bone marrow to accelerate fracture healing is one of the promising method of treating delayed union and non-union. However early recognition of delayed/non union gives better outcome for patient.

Conflict of interest: None

Funding: None

REFERENCES

1. Hierholzer C, Sama D, Toro JB, Peterson M, Helfet DL. Plate fixation of ununited humeral shaft fractures: effect of type of bone graft on healing. J Bone Joint Surg Am. 2006 Jul;88(7):1442-7. [DOI] [PMID]
2. Mollon B, da Silva V, Busse JW, Einhorn TA, Bhandari M. Electrical stimulation for long-bone fracture-healing: a meta-analysis of randomized controlled trials. J Bone Joint Surg Am. 2008 Nov;90(11):2322-30. [DOI] [PMID]
3. Wilkins RM, Kelly CM. The effect of allomatrix injectable putty on the outcome of long bone applications. Orthopedics. 2003 May;26(5 Suppl):s567-70. [DOI] [PMID]
4. Dahabreh Z, Calori GM, Kanakaris NK, Nikolaou VS, Giannoudis PV. A cost analysis of treatment of tibial fracture nonunion by bone grafting or bone morphogenetic protein-7. Int Orthop. 2009 Oct;33(5):1407-14. [DOI] [PMID] [PMCID]
5. Connolly J, Guse R, Lippiello L, Dehne R. Development of an osteogenic bone-marrow preparation. J Bone Joint Surg Am. 1989 Jun;71(5):684-91. [PMID]
6. Burwell RG. Studies in the transplantation of bone. vii. the fresh composite homograft-autograft of cancellous bone; an analysis of factors leading to osteogenesis in marrow transplants and in marrow-containing bone grafts. J Bone Joint Surg Br. 1964 Feb;46:110-40. [PMID]
7. Hernigou P, Poignard A, Beaujean F, Rouard H. Percutaneous autologous bone-marrow grafting for nonunions. Influence of the number and concentration of progenitor cells. J Bone Joint Surg Am. 2005 Jul;87(7):1430-7. [DOI] [PMID]
8. Rupp M, Kern S, El Khassawna T, Ismat A, Malhan D, Alt V et al. Do Systemic Factors Influence the Fate of Nonunions to Become Atrophic? A Retrospective Analysis of 162 Cases. Biomed Res Int. 2019 Feb 19;2019:6407098. [DOI] [PMID] [PMCID]
9. Muschler GF, Boehm C, Easley K. Aspiration to obtain osteoblast progenitor cells from human bone marrow: the influence of aspiration volume. J Bone Joint Surg Am. 1997 Nov;79(11):1699-709. [DOI] [PMID]
10. Ebraheim NA, Elgafy H, Xu R. Bone-graft harvesting from iliac and fibular donor sites: techniques and complications. J Am AcadOrthop Surg. 2001 May-Jun;9(3):210-8. [DOI] [PMID]
11. Roussignol X, Currey C, Duparc F, Dujardin F. Indications and results for the Exogen™ ultrasound system in the management of non-union: a 59-case pilot study. OrthopTraumatol Surg Res. 2012 Apr;98(2):206-13. [DOI] [PMID]
12. Sahu RL. Percutaneous autogenous bone marrow injection for delayed union or non-union of long bone fractures after internal fixation. Rev Bras Ortop. 2017 Dec 29;53(6):668-673 [DOI]. [PMID] [PMCID]
13. Ma JT, Yu M, Zhang MC, Zhu XJ, Xu HY, Liang GJ. Clinical observation on percutaneous autologous bone marrow grafting for treatment of fracture nonunion. Zhongguo Gu Shang. 2009 Nov;22(11):862-4. Chinese. [PMID]
14. Bhargava R, Sankhla S, Gupta A, Changani R, Gagal K. Percutaneous autologus bone marrow injection in the treatment of delayed or nonunion. Indian J Orthop. 2007 Jan;41(1):67-71. [DOI].
15. Hernigou P, Mathieu G, Poignard A, Manicom O, Beaujean F, Rouard H. Percutaneous autologous bone-marrow grafting for nonunions. Surgical technique. J Bone Joint Surg Am. 2006 Sep;88 Suppl 1 Pt 2:322-7. [DOI]

Citation: Jha SC, Koirala S. Percutaneous Autologous Bone Marrow Injection for Delayed Union and Non-Union for Long Bone Fracture. JCMS Nepal. 2025; 21(2): 182-186.