Role of Autologous Bone Marrow Injection in Treatment of Long Bones Delayed-Union

Arif Mahmood,¹ Sohail Razzaq,² Mehran Khan,³ Maqsood Akhtar,⁴ Muhammad Noman⁵

Abstract

Objective: To assess the frequency of success of percutaneous autologous bone marrow injections for management of delayed union of long bone.

Material and Methods: Study design- Descriptive case series Setting: Department of Orthopedic Surgery, Services Hospital, Lahore. Duration: One year 01-09-2023 to 30–08-2024 Data collection procedure: After approval from IRB, informed consent was taken. 65 patients fulfilling the inclusion criteria were admitted through OPD and received percutaneous bone marrow injection (40-80ml) at fracture site by a single surgical team under anesthesia with fluoroscope guidance. After discharge patients were followed in OPD for 6 months with radiographs. Success was labeled If complete callus was seen on radiographs within 6 months.

Results: Mean age was 40.03 ± 13.24 years with 33(50.8%) male and 32(49.2%) female. Mean duration of previous treatment was 5.20 ± 0.85 months. Success was seen in 54(83.1%) patients. Success rate was higher in the younger age group p-value=0.002. There was no effect of gender and duration of prior treatment in achieving union. Success rate of percutaneous autologous bone marrow injections was seen in 83.1%.

Conclusion: The autologous bone marrow injections at the fracture site is simple and effective method in delayed union of long bones to achieve union.

Keywords: Success, Percutaneous, Autologous, Bone marrow, Injections, Management, Delayed, Union, Long bone

How to cite: Mahmood A, Razzaq S, Khan M, Akhtar M, Noman M. Role of Autologous Bone Marrow Injection in Treatment of Long Bones Delayed-Union. Esculapio - JSIMS 2025;21(01): 36-40

DOI: https://doi.org/10.51273/esc25.2513217

Introduction

Bone fracture healing has largely been improved, even in complex fractures, with advances in fracture management protocols, hardware and surgical technique évolution. Non-union still has its existence in this world with incidence of 1 to 10%. It has three types depending upon the osteogenesis; including atrophic, oligotrophic and hypertrophic.

1,2. Department of Orthopaedic Surgery, SIMS/Services Hospital, Lahore 3-5. Department of Orthopaedic Surgery, Services Hospital, Lahore

Correspondence:

Dr. Arif Mahmood, Associate Professor, SIMS/ Services Hospital, Lahore. Email: drarifacs652@hotmail.com

Submission Date:	26-11-2024
1st Revision Date:	16-01-2025
Acceptance Date:	06-03-2025

Atrophic non-union is the type in which there is very little bone formation by the bone forming cells.¹ Bone healing is a physiological process in which proliferation of osteogenic cells result in bone formation which can be enhanced by various techniques, both surgical and non-surgical. One of the source of these precursor cells (osteoblasts) and stimulants of bone healing (bone morphogenic proteins), required for bone healing, is bone marrow. Other sources include periosteum, endosteum, fibroblasts and small blood vessels. These cell form bone by getting transformed into chondroblasts and osteoblasts.²

Bone healing can be either primary or secondary. In Primary healing bone heals without any callus formation. Pre-requisite for this healing are absolute stability, no movement at fracture site and no gap at fracture site. Bone heals without any callus formation. This process takes time of few months to complete.³ The other type is secondary healing (healing with callus formation). It involves enchondral and intra-membranous ossification⁴. Secondary healing is seen in fractures treated conservatively, by external fixation or internal fixation with intramedullary nails.³ When no callus is formed within 3 months or callus formation is very slow after surgical treatment, within 6 months of previous surgery, in fracture of long bones including tibia, ulna, radius, humerus and femur is defined as Delayed union.

Bone healing is a process which is dependent on various physiological, biological and mechanical factors. Patient presenting with delayed/non-union should be thoroughly investigated to find out the etiological factors, which may be physiological and mechanical.^{5,6} Mechanical factors include implant loosening and failure which will need revision surgery in the form of redo fixation. The bone physiology can be improved by using various materials and substances and as a result there will be improved bone formation (genesis), induction (stimulation) and conduction. Autologous bone graft from iliac crest has all above mentioned properties and is considered the gold standard for the treatment of atrophic non-unions but it has associated donorsite morbidity⁷ Percutaneous bone marrow injections has the properties of osteogensis and osteoinduction. This is less invasive, day care procedure and without any associated donor site morbidity.^{8,9} Bone morphogenic proteins are also used to increase the osteoinduction and can be mixed with bone graft while doing bone grafting.¹⁰

Study by Muhammad Rehan et el achieved radiological union in 76.1% cases of delayed union after the injection of bone marrow aspirate taken from iliac crst.¹¹ One more study by Kaseem MS showed 95% success rate in non-unions and delayed union of the long bone after treating these cases using injections of autologous bone marrow.¹²

Study by Braly HL et el also showed success rate of 80% by using the aspirate of autologous bone marrow injections taken from the illac crest.¹³ Another study by Elsattar TA et el claimed 81.8% union treated with aspirate of autologous bone marrow injection.¹⁴

This study is being done to see the success rate of percutaneous autologous bone marrow injections in patients of delayed union especially in long bones. Through literature, it has been found that percutaneous autologous bone marrow injections can be >90% successful for management of delayed union in fractures of long bones. But, varied results have also been noticed in literature. Moreover, it is not in practice in routine due to lack of local evidence. So this study can bring us more evidence on the success or failure of bone marrow injection. We will be able to improve our practice by getting the local magnitude of delayed/ non-unions and the results of marrow injections in such cases.

Material and Methods

This descriptive case series was done in Orthopedic Department Unit 2 Services hospital, Lahore over the period of 1 year from 01-09-2023 to 30–08-2024. 65 patients of fractured long bones in which no callus was formed within 3 months or callus had very slow growth (detected on x-ray) after surgical treatment within 6 months of previous surgery were included in the study. This sample size was calculated with 95% confidence level, 10% margin of error and taking expected percentage of success i.e. 80% with percutaneous autologous bone marrow injections for management of delayed union of long bones.

Patients aged between 16-65 years of either gender, having diagnosis of delayed union of long bones were included in the study. These patients had fractures of tibia, femur, humerus, radius and ulna. Patients were excluded from the study if they had bilateral fractured limb, gap non-union, comminuted fractures (Ao type B2,C1,C2), septic non-union, osteroporosis, osteoarthritis, osteomalacia, positive RA factor (RA>14IU/ml), Alcoholism and addiction.

Patients were admitted through outdoor patient Department of Services Hospital, Lahore. An informed consent was taken. Demographic data including age, gender was obtained. Patient underwent percutaneous bone marrow injection by a single surgical team under anaesthesia. Aspiration of 40-80 mL of bone marrow was done from posterior iliac crest. This aspirated Bone Marrow was injected in and around the nonunion or delayed union site under C-ARM guidance. After procedure patients stayed in post-surgical ward for few hours and were discharged on same day. Follow up was done in outdoor patient department for 6 months. AP and Lateral radiographs of fracture site was done at each visit. Union (Success) was labeled if there was complete callus formation detected on radiograph within 6 months after bone marrow injection. Unsuccessful cases were treated further efficiently as per standard management protocols.

Data analysis was done with SPSS version 21. The quantitative variables which includes age, duration between previous and current treatment and BMI was presented as mean & Standard Deviation. The qualitative variable like gender, anatomical side and success was presented as frequency and percentage. After stratification of data for age, gender, BMI and duration of previous treatment we used chi-square test. p-value ≤ 0.05 was considered as significant.

Results

Mean Age of patients in this study was 40.03 ± 13.24 years with a range of 18 to 65 years, of which 33(50.8%) were male and 32(49.2%) were female (Fig-1). Mean duration of previous treatment was 5.20±0.85 from Minimum of 4 to maximum of 6 months. As per operational definition success was seen in 54(83.1%) patient. Success rate was higher in the younger age group as compared to elderly patients; 18-30 years (33.3%), 31-40 years 29.6%, 41-50 years 20.4%, >50 years 16.7%, p-value=0.002 (Table-1). Success rate was equal for both male and female patients 50% in males & females, pvalue=0.783 (Table-2). Previous duration of treatment had no significant impact in success rate however it was seen that patients with longer previous duration of treatment had lower success rate (Table3).

Table 1: Success of Treatment in relation to Age of patients

-					
Success of treatment in different age groups	18-30 YRS (n=18)	31-40yrs (n=16)	41-50yrs (n=16_	More than 50 yrs n=15	Total n=65
Yes	18 (33.3%)	16 (29.6%)	11 (20.4%)	9 (16.7 %)	n=54(83.1%)
no	0 (0%)	0 (0%)	5 (45.5%)	6 (54.5%)	n=11(16.9%)
					P value=0.002



Table 2: Success of Treatment in relation to Gender of patients

C	male n=33	Female	Total success
Success		n=32	=65
Yes	n=27 (50%)	n=27 (50%)	n=54
No	6(54.5%)	n=5(45.5%)	n=11
			P value=0.783
			Chi-square 0.076

Table 3: Success of Treatment in relation to duration of previous treatment

-				
Success	Duration of treatment 4 months n=18	Duration of treatment 5 months n=16	Duration of treatment 6 months n=31	Total success
Yes	16	14	24	54
No	2	2	7	11
				P value =0.506
				Chi square=1.361

Discussion

In this study, percutaneous autologous bone marrow injection was successful in 54(83.1%) patients for management of delayed union of long bones. Success rate was higher in younger age patients as compared to older patients. (18-30 years: 33.3%, 31-40 years: 29.6%, 41-50 years: 20.4% & >50 years: 16.7%, p-value=0.002), No significant difference was seen for success in relation to gender of patients.

Studies have reported good success rate of

percutaneous autologous bone marrow injection. In literature success rate of 100% within 06-months have been claimed in past using percutaneous bone marrow aspirate injection. Kassem in his study showed that 95% of success rate of bone marrow injection in treatment of long bone nonunion.¹²

Braly showed that 81.8% patients attained bony union within 6 months of bone marrow injection.¹³ Elsattar in his study showed that 80% patients could attain complete union with percutaneous autologous bone marrow injections.¹⁴

Success rate of percutaneous autologous bone marrow injection reported in this study is lower as that of reported by Kassem et el¹² but comparable with Rehan,¹¹ Braly¹³ & Elsattar.¹⁴ However all the above discussed studies including this study showed success rate of percutaneous autologous bone marrow injection around 80%.

The injection of bone marrow produces good results in patients who are diagnosed with delayed unions in long bones, with otherwise mechanically stable fixation and absence of any infection. Even if bone union is not achieved after autologous bone marrow injection we have the option of traditional bone grafting with open technique and other procedures of reconstruction in our armamentarium.

Bone marrow injections are very rich in osteoprogenitor cells. These cells are directly involved in bone formation. Studies have shown that this technique is useful in enhancing the bone formation. When we take Bone marrow from anterior or posterior iliac crest with the help of trocar and cannula, this does not result in any morbidity at donor site. This procedure can be done as day care case which results in less financial burden on health care system

Matsuda Y et al have reported that Bone marrow aspirate injections has favorable results in non-union and delayed unions of long bone shaft fractures in both upper and lower extremity. In literature the use of bone marrow aspirate injections has also been reported for the treatment of delayed and non-unions of those patients who did not receive any prior surgical intervention.

The use of bone marrow is considered a simple and minimally invasive technique. The bone marrow injection is safe and risk free. When compared to iliac bone grafting there is no additional scar and no donor site morbidity. The bone marrow is injected percutaneously without disturbing the stability of fracture to accelerate fracture healing and this is one of the applications of the stem cell technology. It represents a promising method of application of tissue engineering in the orthopedic field, which avoids many of the complications of the traditional bone grafting method commonly used so far.

Conclusion

Results of this study showed that percutaneous autologous bone marrow injection is simple and effective tool for the management of delayed union of long bones and this method should be used for the management of delayed union before using any conventional method of treatment.

Conflict of Interest:	None
Funding Source:	None

References

- Rupp M, Biehl C, Budak M, Thormann U, Heiss C, Alt V. Diaphyseal long bone nonunions -types, aetiology, economics, and treatment recommendations. Int Orthop. 2018 Feb;42(2):247-258. doi: 10.1007/s00264-017-3734-5.
- 2. The Bone-Forming Properties of Periosteum-Derived Cells. Front. Cell Dev. Biol., 25 November 2020 Volume 8. https://doi.org/10.3389/fcell.2020.554984.
- 3. Bell A, Templeman D, Weinlein JC. Nonunion of the Femur and Tibia: An Update. Orthop Clin North Am. 2016 Apr;47(2):365-75. doi: 10.1016/-j.ocl.2015.09.010.
- 4. Affshana MM, Priya J. Healing mechanism in bone fracture. Journal of Pharmaceutical Sciences and Research 2015;7(7):441.
- Nauth A, Lee M, Gardner MJ, Brinker MR, Warner SJ, Tornetta P, Leucht P. Principles of Nonunion Management: State of the Art. J Orthop Trauma. 2018 Mar;32 Suppl 1:S52-S57. doi: 10.1097/-BOT.000000000001122.
- 6. Le Thua TH, NGUYEN D-T, PHAM DN, Khanh-Linh L, LE QNB, NGUYEN PH, et al. Mini-invasive treatment for delayed or non-union: the use of percutaneous autologous bone marrow injection. Biomed Res Therap 2015;2(11):389-95. DOI:107603/s40730-015-0026-9.

- Nicholas J. Murphy et al. Acute minimally invasive bone grafting of long bone fractures to reduce the incidence of fracture non-union: Medical Hypotheses 178 (2023) 111-131. DOI:10.1016/j.mehy.2023.111131.
- Bell A, Templeman D, Weinlein JC. Nonunion of the femur and tibia: an update. Orthop Clin North Am. 2016;47(2):365-75. DOI:10.1016/-j.ocl.2015.09.010.
- 9. G. Marongiu, A. Dolci, M. Verona, A. Capone.The biology and treatment of acute long-bones diaphyseal fractures: Overview of the current options for bone healing enhancement: Bone Reports, 12 (2020), Article 100249. DOI: 10.1016/j.bonr.2020.100249.
- Barcak EA, Beebe MJ. Bone Morphogenetic Protein: Is There Still a Role in Orthopedic Trauma in 2017? Orthop Clin North Am. 2017 Jul;48(3):301-309. doi: 10.1016/j.ocl.2017.03.004.
- 11. Muhammad Rehan Saleem et el role of percutaneous bone marrow aspirtate in the management of femoral delayed union and non-union fractures vol 73 No. SUPPL-1(2023): August http://DOI.org/-10.51253/pafmj.v73iSUPPL-1.4749.

- 12. Kassem MS. Percutaneous autogenous bone marrow injection for delayed union or non union of fractures after internal fixation. Acta Orthop Belg 2013;79(6):711-7. PMID: 24563979.
- Braly HL, O'Connor DP, Brinker MR. Percutaneous autologous bone marrow injection in the treatment of distal meta-diaphyseal tibial nonunions and delayed unions. J Orthop Trauma 2013;27(9):527-33. DOI: 101097/BOT.0B013e31828bf077.
- Elsattar TA, Alseedy AI, Khalil AAE. Bone marrow injection in treatment of long bone nonunion. Menoufia Med J 2014; 27(4):632. DOI: 10.4103/-1110-2098.149627.

Authors Contribution

- **AM:** Conceptualization of Project
- AM: Writing of Manuscript
- SR: Data Collection
- MK: Literature Search
- MA: Statistical Analysis
- MN: Drafting, Revision