



PERCUTANEOUS AUTOLOGOUS BONE MARROW INJECTION IN THE TREATMENT OF DELAYED UNION AND NON-UNION OF LONG BONE FRACTURES AFTER DEFINITIVE FIXATION

Orthopaedics

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ABSTRACT

Introduction: Bone marrow is a source of osteoprogenitor cells that are key elements in the process of bone formation and fracture healing. The purpose of the study was to ascertain the osteogenic potential of autologous bone marrow grafting and its effectiveness in the management of delayed union and nonunion. **Materials and Methods:** This prospective study was conducted at the postgraduate department of orthopaedics SKIMS, Bemina Srinagar from August 2020 to January 2022. A total of 26 patients with nonunion or delayed union were treated with percutaneous bone marrow injection. The patients with delayed union and nonunion depending on the criteria that delayed union is lack of callus formation for more than 6 months, while non-union is lack of union after 9 months or no progression of healing for 3 months (6). In cases of delayed union bone marrow injections were given at a minimum of 3 months after the initial treatment with closed or open technique. **Results:** The results were found to be excellent in 15 (57.69 %) cases, good in 6 (23.08 %) patients and poor in 5 (19.23 %) patients. **Conclusion:** Bone marrow injection is a minimally invasive procedure done percutaneously. It is easy, safe procedure with no associated complications that may occur in bone grafting, thus reduced hospital stay and expenditure.

KEYWORDS

Long bone fractures, Delayed union, Non-union, Bone marrow injection

INTRODUCTION

Nonunion and delayed union is common problem seen in fracture healing and may be caused by several factors with or without any obvious cause. US FDA state non-union as when minimum 9 months has elapsed since injury and fracture shows no progressive signs of healing for 3 months [1]. One of the major complications in fracture treatment were delayed union and non-unions, because any fracture will end either by union or nonunion. Delayed union, by definition, is present when an adequate period of time has elapsed since the initial injury without achieving bone union. The fact that a bone is delayed in its union does not mean that it will become a nonunion. Nonunion is one end result of a delayed union, and the differentiation between the two is sometimes difficult to make. Classically the stated reasons for delayed union and nonunion are problems such as inadequate reduction, inadequate immobilization, distraction, loss of blood supply, and infection.

Numerous methods have been adopted to overcome this problem such as bone graft, electrical stimulation, ultrasound, bone transport and bone marrow injection. The non-operative methods include the use of low intensity ultrasound, electrical stimulation and electromagnetic stimulation but all these procedures are tedious, require sophisticated equipments, expertise and anaesthesia for surgery and are time consuming, hence a continuous search has been made to find out such an alternative method of treating delayed and nonunion which is safe, easy and economical. In recent times, percutaneous bone marrow injection has emerged as a successful alternative to traditional methods of treatment. Bone marrow injection has shown to have stimulated callus formation where autologous bone grafting has failed. Though all of these methods have shown varying degrees of excellent to good results but most of the techniques are tedious and require sophisticated equipments, expertise, anaesthesia and are time consuming, with added risk of infection (Garg et al., 1993) [2]. Osteogenic precursor cells which are capable of producing bone have been demonstrated among the stromal and endosteal cells of bone marrow, which are the key elements in the process of bone formation and fracture healing (Friedenstein, 1973). The determined and inducible marrow cells supplement periosteal and primitive mesenchymal cells to form cellular component of bone healing (Gray and Elves, 1979). It is a minimally invasive procedure with negligible complications.

The aim of this prospective study was to assess the results of percutaneous bone marrow injection in the treatment of fractures

presenting with delayed union and non-union following internal fixation.

MATERIALS AND METHODS

This prospective study was conducted at the postgraduate department of orthopaedics SKIMS, Bemina Srinagar from August 2020 to January 2022. A total of 26 patients with nonunion or delayed union were treated with percutaneous bone marrow injection. The patients with delayed union and nonunion depending on the criteria that delayed union is lack of callus formation for more than 6 months, while non-union is lack of union after 9 months or no progression of healing for 3 months [3]. In cases of delayed union bone marrow injections were given at a minimum of 3 months after the initial treatment with closed or open technique. Among 26 enrolled patients 18 (69.23 %) were males and 8 (30.77 %) were females (Table 1).

Table 1: Demography of patients

Parameters	No. of patients	Percentage
Sex	Male	18
	Female	8
Age group	18-35 Years	6
	36-55 Years	11
	> 55 Years	9
Mechanism of trauma	Road accident	16
	Fall	9
	Other	1
Fracture site	Tibia	5
	Femur	7
	Humerus	4
	Radius	6
	Ulna	4
Defect	Delayed union	14
	Non-union	12

All routine pre-procedure investigations including the radiological investigations were done to rule out any active infection. Proper clinical and biochemical evaluation done for all the patients who met the inclusion criteria to rule out any comorbidities affecting the progress of union. A written informed consent was taken from all the patients; they were fully explained about the whole procedure, cost of the procedure and complications of anaesthesia.

Inclusion Criteria

- Patients with delayed union or non-union
- Age ≥ 18 years.
- All these delayed union or non-unions having acceptable alignment, good bone apposition and stable fixation.
- Patients willing to give written consent and willing for follow-up.

Exclusion Criteria

- Patients with pathological fracture.
- Patients with multiple fractures.
- Patients with connective tissue disorder.
- Malnourished patients.
- Patients suffering from peripheral vascular disorder.
- Patients with compound fracture.
- Patients with tumor and metabolic bone disorder.

Procedure:

All the percutaneous bone marrow injections were given in the operation theatre. The patient was placed in supine position, the fracture site and the graft site were prepped and draped separately to avoid cross contamination. The entire procedure was done under local infiltration of 2% lignocaine injection. A 18-gauge I.V cannula was inserted under fluoroscopic guidance into the site of the delayed union. A 16-gauge Thomas bone marrow aspiration needle was inserted manually into the anterior iliac crest between the outer and inner table. The marrow was aspirated into a 10ml preheparinized plastic syringe with the needle always turned 45 degree for each aspiration. The marrow was aspirated in small fractions at a time (around 5ml) to reduce the degree of dilution by peripheral blood and to maximize the number of progenitors in the graft site. The aspirated bone marrow is then injected slowly (to limit cellular extravasation) into the previously marked site i.e. through the 18-gauge I.V cannula in the delayed union site. A compression dressing was given after the procedure and the patient was discharged on the same day. We injected 40-50 cc of bone marrows for femur and tibia, 20cc for humerus and 10cc for radius and ulna in all the cases [4].

Post-procedure Protocol And Follow-up:

The patients were followed up at an interval of 3-4 weeks to assess the union. Clinico-radiological evaluation of the union was carried out by painless total weight bearing without macromobility at the fracture site with radiographic evidence of healing on at least 3 of the 4 cortices at the original fracture site as described by Heckman [5, 6]. According to the criteria the results were graded as excellent when the fractures unites within 16 weeks of bone marrow injection, good when union occurs within 24 weeks and poor when union delay more than 24 weeks.

RESULTS

In this study a total of 26 patients were enrolled with the mean age of 48.9 (range 23-67) years. 18 (69.23%) patients were male and 8 (30.77%) patients were female. 16 (61.54%) had met with a road traffic accident, 9 (34.62%) had a history of fall and 1 (3.84%) had got injured from sports activity. In this study 5 (19.24%) had tibia fractures, 7 (26.92%) had femur fractures, 4 (15.38%) had humerus fractures, 6 (23.8%) had radius fractures and 4 (15.38%) had ulna fractures.

The average time from injury to percutaneous autologous bone marrow injection was 4.6 (range 3-6) months.

There were 14 (53.85%) patients of delayed union, among which 9 (64.29%) showed good union, 4 (28.57%) showed progressive healing and 1 (7.14%) ended with non-union. Among enrolled 26 patients, there were 12 (46.15%) of nonunion, out of which 8 (66.67%) patients showed good bony union.

The results were found to be excellent in 15 (57.69%) cases, good in 6 (23.08%) patients and poor in 5 (19.23%) patients (Table 2).

Table 2: Outcome of bone marrow injection

Result	Delayed union group (n=14)		Non-union group (n=12)		Total (n=26)	
	No. of patients	% age	No. of patients	%age	No. of patients	%age
Excellent	9	64.29	6	50.00	15	57.69
Good	4	28.57	2	16.67	6	23.08
Poor	1	7.14	4	33.33	5	19.23

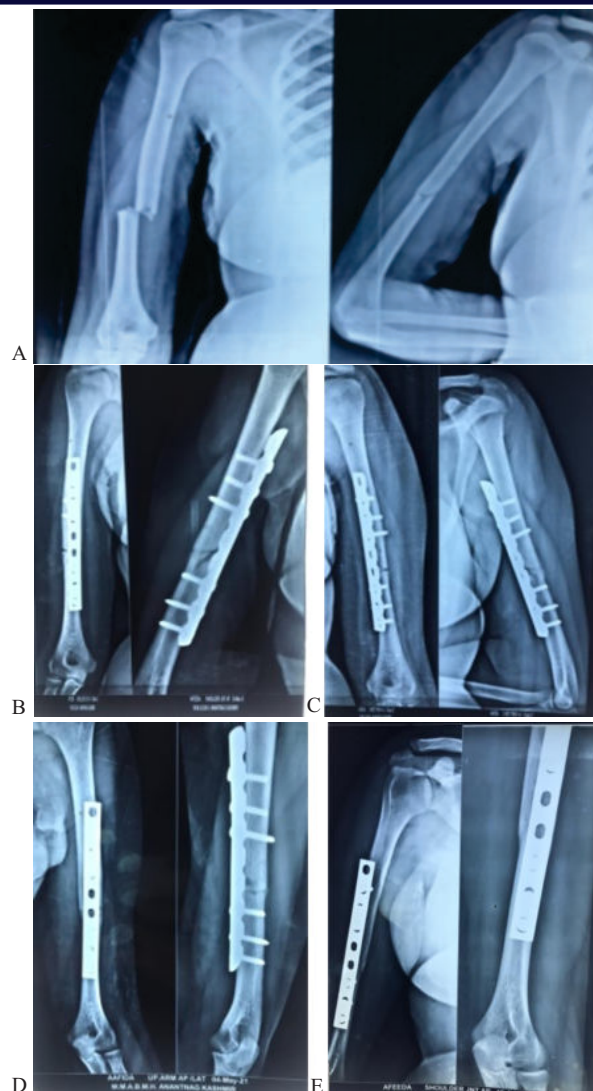


Figure 1: A (Radiograph showing fracture shaft of humerus), B (Immediate post-operative radiograph showing fracture fixation with LCDCP), C (Radiograph of 3 months follow-up), D (5 Month follow-up radiograph showing delayed union) and E (Radiograph at 6 weeks follow-up post bone marrow injection showing complete union)

DISCUSSION

Nonunion or delayed union of long bone fractures always has been a challenging problem. Various methods of treatment were sorted for delayed and nonunion from decades which includes exchange nailing, bone grating, stimulation by electric current and electromagnetic field, ilizarov fixation [7-10]. However the standard procedure of bone grafting was found to have associated complications as mentioned. Autogenous bone grafting has been the most commonly used procedure in the operative treatment. It involves morbidity at donor site such as hemorrhage, infection, the need for additional procedure, a painful and ugly scar, which adds to the disturbance of the vascularity of the fracture site when delivering the graft through an open method [11]. Few studies focused on less invasive methods such as ultrasound, bone growth factors (e.g. bone morphogenic protein), extracorporeal shock waves and bone marrow injection, aiming to achieve similar results but with fewer complications [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 of the fracture end of the proximal fragment. We recommend the early management of delayed union of fractures once diagnosed to achieve early union.

Skeletal healing is primarily a biological process, and depends upon cellular response. The most productive source of cells that influence

osteogenesis is considered to be autologous marrow. In the present study the effect of percutaneous autologous bone marrow injection in delayed union and nonunion of 26 long bones as a substitute for standard open grafting technique was studied. The osteogenic and osteoinductive property of bone marrow were first described by McGraw and Habin. Connolly and Healy have demonstrated that percutaneous bone marrow injection can successfully treat 78%-95% of nonunion cases. The work of Paley et al. showed experimentally that marrow produces optimal effect when used early in fracture healing process. Other similar recent studies have showed good union in their series of patients and concluded that percutaneous bone marrow injection is safe and easy procedure. The only complications noticed were infection and pain at the donor site which were subsided by analgesics and antibiotics. In this study which included 26 patients of delayed union and non-union, we observed union in 21 (80.79 %) patients which is comparable to other similar studies.

The selection of cases included in the study had high selection bias. The majority of the cases (14 out of 26) were of delayed union. The bone marrow was injected in the majority of the cases (19 out of 26) within 30 weeks since injury. The majority of the cases (21 out of 26) had good or excellent union potential score. The reason was obvious. Initially, there was reluctance to use the procedure in patients with established nonunion presenting more than a year after the injury, with sclerosed bone ends, occluded marrow cavity or with features of bone infection. Hence the patients who had good potential of healing according to the type of injury, but the fracture failed to unite in the expected time period were chosen for the study.

The average time since injury to bone marrow injection was 4.6 months in our cases which is comparable with the average time of 4.1 months from injury to bone marrow injection as mentioned by John F. Connolly et al. [13] in their article.

In our study 7 (26.92 %) patients presented to us with femur fractures, out of which 100% union rate with average union time of 4.9 months was achieved after bone marrow injection. On the other hand Joao Antonio Matheus Guimaraes et al. [14] found 50% union rate with average union time of 5 months after bone marrow injection in their study of 16 cases with femoral shaft non unions after locked intramedullary nailing.

We observed that adequate quantity of bone marrow injection is necessary for individual bones to achieve an effective outcome which is in accordance with the results drawn by Ramji Lal Sahu et al. [4].

In our study with percutaneous autologous bone marrow injection we achieved excellent results in 60.86% cases, good in 17.39% cases and poor in 21.73% cases which can be compared with the results found by Ramji Lal Sahu et al. [4] in their study.

Autologous bone marrow injection is a relatively simple technique that can be performed in a minor OT with local anesthetic agents and hence it is very cost effective. It also avoids a number of serious donor or recipient site problems that may arise from the traditional bone grafting technique [13].

The bone marrow injection is safe, as the material injected is autogenous, so there is no risk of disease transmission or immune reaction [4]. The most significant role of autologous bone marrow injection is that it provides the early treatment of fractures whenever there is a query of future non-union at the fracture site, hence it can be used as a preventive method for future non-union in vulnerable cases [13].

The limitations of our study are the lack of comparison group with other methods of delayed union treatment, sample size was comparatively small and the duration of the study was less.

CONCLUSION

Bone marrow injection is a minimally invasive procedure done percutaneously. It is easy, safe procedure with no associated complications that may occur in bone grafting, thus reduced hospital stay and expenditure. It can be considered as an alternate method for bone grafting in delayed and nonunion of fractures.

REFERENCES

1. Terry Cinal S, James H. Beaty –campbell operative or orthopaedic 12th Edition chapter 59 vol.3 page 2982

2. Garg NK, Gaur S, Sharma S. Percutaneous autologous bone marrow grafting in 20 cases of ununited fracture Acta Orthop Scand 1993;64:671-2.
3. Henigou.2005 bi Tresslesr .2001 Bone Joint p.paignord ,A.malliom .G.Ronard H2005 b.the use of autologous bone marrow transplantation in non-union and a vascular necrosis of bone.
4. Sahu RL. Percutaneous autogenous bone marrow injection for delayed union or non-union of long bone fractures after internal fixation. Rev Bras Ortop. 2017;53(6):668–73.
5. Gross J, Diligent J, Bensoussan D, Galois L. Percutaneous autologous bone marrow injection for treatment of delayed and non-union of long bone: a retrospective study of 45 cases. Biomed Mater Eng. 2015;25(1 Suppl):187–97.
6. Heckman JD, Ryaby JP, McCabe J, Frey JJ, Kilcoyne RF. Acceleration of tibial fracture-healing by non-invasive, low-intensity pulsed ultrasound. J Bone Joint Surg Am. 1994;76(1):26–34.
7. Tylman D, Dziak A. Traumatologia narzadu ruchu. PZWL 1996.
8. Goreck A. Czynniki wzrostu tkanki kostna oficyna wydawnicza ASPRA JR; Warszawa 2004.
9. Russel AT, Taylor CJ, Lavelle D. Fracture of tibia and fibula. In: Fractures in Adults, Rockwood and Green 1991;3:1915-1982.
10. Saleh M. Nonunion surgery, Part 1. Basic principles of management. Int J Orthop Trauma 1992;2:4-18.
11. Ebraheim NA, Elgafy H, Xu R. Bone-graft harvesting from iliac and fibular donor sites: techniques and complications. J Am Acad Orthop Surg. 2001;9(3):210–8.
12. 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. Orthop Traumatol Surg Res. 2012;98(2):206–13.
13. Connolly FJ, Roy G, Tiedeman J, Dehne R. Autologous Marrow Injection for Delayed Unions of the Tibia: A Preliminary Report. J Orthop Trauma. 1989;3(4):276–82.
14. Antonio J, Guimarães M, Eugenia M, Duarte L, Cury MB, Isabel CC, et al. The effect of autologous concentrated bone-marrow grafting on the healing of femoral shaft non-unions after locked intramedullary nailing. Injury . 2014;45(Suppl 5):S7–S13.