

Role of Percutaneous Bone Marrow Aspirate Injection in Delayed Union of Femur and Tibia Diaphyseal Fractures

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Abstract

Background: To compare the results of percutaneous bone marrow aspirate injection with autologous bone grafting in the treatment of delayed union of femur and tibia diaphyseal fractures using Union Scale Score.

Methods: In this randomized controlled trial 88 patients with delayed diaphyseal fracture union of either tibia or femur were divided into two groups of 44 patients each (Group A=bone marrow aspirate injections and Group B=autologous bone graft). The study outcome was assessed in terms of Union Scale Score after 6 weeks interval for 18 weeks time period. In Group A, the skin over iliac crest, about 2-4 cm from anterior superior iliac spine was infiltrated with about 3 ml of 2% plain lignocaine. A bone marrow aspiration needle with multiple distal holes was inserted between the two tables of iliac bone. Twenty ml bone marrow was aspirated. The needle was then replaced with a 16 gauge spinal needle and the BMA was injected in the vicinity of fracture site (non-union) under fluoroscope guidance. The recipient site was then sealed with band aid. In Group B, autogenous iliac bone graft taken by standard technique under general anaesthesia was harvested into the fracture site and immobilized by plaster of Paris cast where indicated. Fracture site mobility, tenderness and radiological features were assessed using the Union Scale Score in which union was considered with a score of 6 or more. In case of non-union, a secondary procedure was performed.

Results: At 18 weeks follow-up, 70.4% cases in percutaneous bone marrow group and 93.2% in autologous bone graft group had achieved union scale score of 6 or above, though this difference was significant (p-value, 0.01).

Conclusion: Percutaneous bone marrow aspirate injection is an effective alternative to autologous bone grafting for the treatment of delayed union of long bone fractures.

Key Words: Delayed union, Autologous bone grafting, Percutaneous bone marrow aspirate (BMA), Bone mesenchymal stem cells (BMSC)

Introduction

Fracture union is a complex and well-orchestrated physiological process and takes several years for bone to regain its original structure and function.^{1,2} An array of cytokines and signaling proteins control this complex physiological process.³ A complete union can be described as clinically having no pain, tenderness and radiographically, as solid cortical callus having bridged both fragments.⁴

Delayed bone union, accounting for 5-10% of all fractures,⁵ seriously affects physical and mental health of the patient and pose a major challenge for orthopaedic surgeons. In spite of all advances in treatment, results in additional financial burden on health care system and morbidity for the patient.⁶

The US Food and Drug Administration (FDA) described fracture non-union as "a non-union is established after minimum of nine months time period has passed since fracture and there is no progressive visible radiological evidence of healing for a period of approximately three months." Delayed union is defined as un-united fracture that continues to show progress towards healing or that have not been present for long enough to satisfy the definition of non-union.⁷ The non union of closed tibial shaft fracture is prevalent in 2.5% individuals and increases 5-7 fold in case of open fractures with considerable soft tissue damage.⁸

Autologous bone grafting possesses osteoconductive, osteoinductive and osteogenic cell components, thereby making it the "gold standard" treatment for fracture healing.⁹ Infection, painful scar, hematoma formation, anaemia and gait disturbance are some of the complications of this invasive procedure. Recent research has focused on the effectiveness of less invasive procedures so as to achieve similar results with fewer side effects.^{10,11}

Bone marrow aspirate is an effective source of mesenchymal stem cells and osteoprogenitor cells which in turn are the most important factors in process of bone formation and healing of delayed union. It also has the additional advantage of being minimal invasive, relatively safer, simpler, economical and short duration procedure.¹²

Herzog introduced percutaneous bone grafting for the first time in 1951 with the use of large bore needle and small cancellous chips to graft a non union.¹³ Connolly reported the results of autogenous bone marrow injections in treating 20 tibia fracture non-unions over a period of five years and achieved union of 18/20 cases (90%).¹⁴

Keeping in mind the considerable high influx of patients in emergency and outpatient departments of our tertiary care public hospitals like Pakistan Institute of Medical Sciences, Islamabad, sound case load management with limited resources and time constraints is always a challenge. Therefore, efficacy of this novel and simple technique was evaluated.

Patients and Methods

A randomized controlled trial was conducted at the Department of Orthopedic Surgery, Pakistan Institute of Medical Sciences, Islamabad for a period of eight months between May 2016 to January 2017. Sample size was calculated with the help of WHO calculator which turned out to be 88 patients with delayed diaphyseal fracture union of either tibia or femur and was divided into two groups of 44 patients each (Group A=bone marrow aspirate injection, Group B=autologous bone graft). Patient's inclusion criteria included age between 18 to 60 years, duration of fracture more than 12 weeks, abnormal mobility at the fracture site, tenderness at the fracture site and pain on applying bending stress. Patients were excluded if they were pregnant females (they can not be exposed to radiations of image intensifier), infected cases, pathological fractures or had established non union.

The study outcome was assessed in terms of Union Scale Score (Table 1) after 6 weeks interval for 18 weeks time period. In Group A, the skin over iliac crest, about 2-4 cm from anterior superior iliac spine was infiltrated with about 3 ml of 2% plain lignocaine. A bone marrow aspiration needle with multiple distal holes was inserted between the two tables of iliac bone. To minimize aspirating air into the syringe, it was ensured that all distal holes were well beyond

cortical wall. Twenty cc bone marrow was aspirated and site was sealed with a sterile tape. The needle was then replaced with a 16 gauge spinal needle and the BMA injected in the vicinity of fracture site (non-union) under fluoroscope guidance. The recipient site was then sealed with band aid. In Group B, autogenous iliac bone graft taken by standard technique under general anesthesia was harvested into the fracture site and immobilized by plaster of Paris cast where indicated. Patients of both groups were called at interval of six weeks for four months. Fracture site mobility, tenderness and radiological features were assessed using the Union Scale Score in which union was considered with a score of 6 or more. In case of non-union, a secondary procedure was performed. The final functional outcome as per Union Scale Score was compared among the study groups using chi-square test at 6, 12 and 18 weeks. A p-value of <0.05 was considered significant.

Table 1: Union Scale Score⁴ – Maximum Score 7.

Features	0	1	2	3
Mobility	Frank mobility in both planes	Restricted mobility in both planes	Minimum mobility in one plane	No mobility at all
Tenderness	Present	Absent		
Radiological features	No callus at all	Minimum ensheathing callus	Good ensheathing callus or internal callus with bridging of at least two cortex	Good internal callus with bridging of all four cortex

Results

Male cases were in majority in both study groups. The mean age was slightly younger in bone marrow group compared to bone graft group (31.2 vs 37.3 years respectively) (Table 2). At 18 weeks follow-up, the mean Union Scale Score was found slightly less in autologous bone marrow aspirate group than autologous bone graft group (5.9 vs 6.6) (Table 3). At 18 weeks follow-up, 31 (70.4%) cases in percutaneous bone marrow group and 41 (93.2%) in autologous bone graft group had achieved union scale score of 6 or above, though this difference was significant (p-value, 0.01) but overall the success rate of both procedures was quite high making a case for usage of percutaneous bone marrow grafting as a comparable alternative treatment modality (Table 4)

Table 2: Distribution of gender and age of patients in the two study groups

	Percutaneous bone marrow group (n=44)	Autologous bone graft group (n=44)
Gender		
Male	38 (86.4%)	36 (81.8%)
Female	6 (13.6%)	8 (18.2%)
Age (years)		
Mean ± SD	31.2 ± 10.5	37.3 ± 13.7

Table 3: Comparison of Union Scale Score between the two groups

	Percutaneous bone marrow group (n=44)	Autologous bone graft group (n=44)	p-value
Initial			
1	0 (0.0%)	3 (6.8%)	0.01
2	3 (6.8%)	4 (22.7%)	
3	8 (18.2%)	14 (31.8%)	
4	15 (34.1%)	18 (40.9%)	
5	18 (40.9%)	5 (11.4%)	
At 6 weeks			
3	3 (6.8%)	0 (0.0%)	0.32
4	6 (13.6%)	9 (20.5%)	
5	19 (43.2%)	23 (52.3%)	
6	14 (31.8%)	11 (25.0%)	
7	2 (4.5%)	1 (2.3%)	
At 12 weeks			
3	3 (6.8%)	0 (0.0%)	0.10
4	0 (0.0%)	0 (0.0%)	
5	16 (36.4%)	10 (22.7%)	
6	13 (29.5%)	15 (34.1%)	
7	12 (27.3%)	19 (43.2%)	
At 18 weeks			
3	3 (6.8%)	0 (0.0%)	0.01
4	0 (0.0%)	0 (0.0%)	
5	10 (22.7%)	3 (6.8%)	
6	13 (29.5%)	11 (25.0%)	
7	18 (40.9%)	30 (68.2%)	

Discussion

Bone marrow, because of having great osteogenic properties, has already been widely used as bone graft substitute in basic research and clinical practice.⁵ Bone mesenchymal stem cells within the bone marrow play the pivotal role in the process of bone formation.^{15,16} Under the stimulation of bone induction signal, BMSCs proliferate and differentiate into osteoblasts, chondrocytes and adipose cells.¹⁷ According to multiple studies, better healing rate and lesser time needed for union could be achieved by concentrating the aspirated bone marrow with centrifuge machine.¹⁸⁻²¹

However, in our study, the bone marrow aspirate taken from the iliac crest was directly injected into the delayed union site. It was witnessed that more than 90% of the cases in the autologous bone grafting group achieved Union Scale Score of 6 or above at 18 weeks post treatment, whereas more than 70% in percutaneous bone marrow group achieved union after the same treatment period. The results were comparable with 88.3% reported in the study by Hernigou et al²² in 2006 and 76% reported in the study by Sugaya et al.¹⁸ Wani et al also reported that 75% of their non-union cases who were given percutaneous bone marrow, succeeded in achieving union after a mean period of 18.4 weeks.⁶

Elsattar et al witnessed 80% union achievement after autologous bone marrow injection.²³ Ahmed A and colleagues from Lahore reported that more than 80% of their cases achieved union after percutaneous bone marrow injection and they concluded that percutaneous bone marrow is an alternate option for patients with non-union of long bone fractures.²⁴ Lamture DR et al reported that autologous bone marrow graft is the choice of treatment in non-union fractures.²⁵ These findings are comparable to our study. Kassem et al assessed percutaneous bone grafting and found that it was able to achieve union in 95% cases.¹ There is scientific evidence^{7,12,13,24} suggesting the success of percutaneous bone marrow injection and its nearly similar effectiveness to autologous bone grafting makes it a perfect alternate.

On the other hand, autologous bone grafting technique is more costly, time consuming, requires general anaesthesia and has numerous donor and recipient site side effects like painful scar, infections, hematoma formation, anaemia and gait disturbance.²⁶ Acute and chronic donor site pain, affecting up to 60% of patients after iliac crest cancellous bone graft procedure has been reported.²⁷ Furthermore, the opening of recipient

site adds devascularisation risk which is damaging for an already impaired healing process.^{4,7}

There are other non-operative methods as well, which are performed by using low intensity ultrasound, electrical stimulation and electromagnetic stimulation. These procedures are sometimes tedious, time consuming, require sophisticated equipment and expertise. Search for a safe, economical and easy treatment technique for delayed union of fractures was always there and percutaneous bone marrow injection provides all these benefits. Additionally, aspirated bone marrow injection has also proven to jump start callus formation by increasing the regenerative potential where autologous bone grafting showed slow progress.²⁸

Excellent follow up and methodological rigor are key strengths of our study. Although the number of patients (n=88) evaluated in our study is greater than the limited count of local studies conducted on the outcome of percutaneous bone marrow injection technique in our population, continuation of data collection in multi-centric studies with long term functional outcome is need of the hour, so as to further delineate the utility of this technique.²⁹ Nevertheless, the proposed technique exhibited slightly inferior results than the current gold standard. The management of increased number of patients with limited resources, safety of procedure, lesser time in hospital and decreased complication rate surely outweigh the other aspects.

Conclusion

Percutaneous bone marrow aspirate injection is simple, economical and efficacious alternative to autologous bone grafting for the treatment of delayed union of long bone fractures.

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