

Original Research Article

Role of bone marrow infiltration in management of delayed union of long bones fracture

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ABSTRACT

Background: Usually delayed union of fracture long bones are managed by putting a bone graft at fracture site, but bone grafting have donor site complication like scar, infection, hernia, gait disturbance, cosmetic problem, as well as recipient site complication like soft tissue trauma, de-vascularisation of fracture fragment. Bone marrow infiltration is a minimally invasive method done percutaneously. It is easy, safe procedure with no associated complications that may occur in bone grafting.

Methods: This prospective study was conducted in the Department of orthopedics, Government Medical College, Kota from June 2011 to November 2013 to evaluate the efficacy of percutaneous bone marrow infiltration in cases of delayed union of long bones. 27 patients included in study with 28 bones, as one patient has given bone marrow injection in two bones (tibia & femur), so the cases included in study counted as 28 cases. The mean age of this study was 38.28 years, ranging from 18 years to 75 years. All cases were follow up after 4 to 6 weeks and thereafter one month interval. Final follow up was taken when fracture site shows clinical and radiological sign of union.

Results: Out of 23 united cases 19 had excellent results and 04 cases had good results. The five cases which fail to unite were taken as poor results.

Conclusions: Bone marrow infiltration is a minimally invasive, safe bone graft substitute for delayed union of long bones and have less complications.

Keywords: Bone marrow, Delayed Union in Tibia, Femur, Iliac crest, Jamshidi needle, Syringe

INTRODUCTION

Bone marrow contains a population of rare progenitor cells capable of differentiating into osteoblasts, chondrocytes, adipocytes, and muscle cells.¹ Hernigou et al. treated 20 non-united tibial fractures by injecting freshly harvested bone marrow into tibial defects and resulted in clinical and radiological union.²

The relationship between bony union and bone marrow is as follows: some of the cells of the callus originate in bone marrow and bone marrow cells are responsible for the formation of part of the bony callus.³

Bone marrow stem cells develop into hematopoietic and nonhematopoietic stem cells or marrow stromal cells, which are progenitors of skeletal tissue components such as bone and cartilage, as well as blood components.⁴

Most other tissues in the human body heals with scar, but bone has unique feature of repair by its own tissues, bone heals by forming new bone, so “Bone begets bone.”

However, in sizeable number of cases, it is either delayed or impaired. The period in which a bony fracture will unite cannot be arbitrarily stated as different bones heal in variable period of time depending upon many factors but generally, in delayed union there is clinical and radiographic findings that healing is taking place but it has not advanced at the expected rate for the location and type of bony fracture.

The risk of delayed union and nonunion increases with increasing energy of injury with the incidence approaching up to 20% in presence of open fracture and extensive soft tissue injury. The estimated prevalence for nonunion is 2.5%, even more for delayed union.⁵

Aims and objectives of this study were to evaluate the efficacy of percutaneous bone diaphysis. This study was carried out to evaluate the following- duration of bone union following bone marrow infiltration in delayed union of long bones. Complications and morbidity associated with bone marrow infiltration in delayed union of long bones.

METHODS

This prospective study was conducted in the Department of orthopaedics, Government Medical College, Kota from June 2011 to November 2013 to evaluate the efficacy of percutaneous bone marrow injection in cases of delayed union of long bones. Total 27 patients included in study with 28 bones, as one patient has given bone marrow injection in two bones (tibia and femur), so the cases included in study counted as 28 cases.

Inclusion criteria

Clinical: Skeletally mature patients, age of fracture more than 12 weeks, tenderness at the fracture site.

Pain on applying bending stresses. Radiological gap at the fracture site not more than 5 mm, no or minimum amount of callus.

Exclusion criteria

- Patients with infection and local malignancy will be excluded from the study.
- Skeletally immature patients will be excluded from the study, chronic smokers will be excluded from the study or they are motivated to stop smoking.

Preoperative assessment

Nicoll in his series of 705 tibial fractures, investigated the factors leading to delayed union and nonunion.⁶

According to him these factors were- initial displacement, comminution, soft tissue injury, infection distraction.

In 1958 Ellis also had similar observations in study of 507 tibial fractures.⁷ He classified tibial fractures into three groups of severity, as minor, moderate and major, on the basis of initial displacement, comminution and soft tissue injury.

Operative technique

All cases were admitted in ward, proper investigations and preanaesthetic checkup done. The procedure was explained to the patients and written informed consent taken. The procedure was performed under spinal anesthesia. Under all aseptic techniques, patients were put in supine position and donor and recipient sites were prepared separately but simultaneously to prevent cross-contamination of needles. Fracture site located with C-arm fluoroscopy in AP & Lateral view. In cases of femur a 16 or 18 gauge spinal needle and in cases of tibia 16 or 18 gauge simple needle was placed up to the bone at the fracture site in muscular attachment area with care of neurovascular bundle. After taking stab skin incision 4-5 mm, entry site made over anterior iliac crest percutaneously about 4-5 cm behind anterior superior iliac spine with 2 mm drill bit. A bone marrow biopsy needle or Jamshidi needle then pushed by hand about 6 cm into cancellous bone, so that tip lies between inner and outer table of iliac crest. The bone marrow was aspirated from the donor iliac crest with a 20 cc syringe to obtain more negative pressure. Adequate amount of marrow was aspirated from one site and to obtain more, multiple aspirates done. The aspirated bone marrow was infiltrated percutaneously immediately at the delayed union site with the help of a 16-gauge spinal needle or 16-gauge simple needle under C arm fluoroscopy. Marrow was injected slowly at the rate of less than 20 cc per minute. According the amount needed, the needle tip reoriented in both directions to get more marrow. Aspiration was taken in small amounts of 4-5 cc to reduce dilution by venous blood. On an average we injected about 50-60 cc in tibia and 60-90 cc in femur. Donor site stitched and dressed properly under aseptic precautions. Series of X-rays were taken at duration of 4-6 weeks. No second injection repeated. We assessed fracture union on X-rays for disappearance of fracture line at least 3 out of 4 cortices in AP and lateral view and clinically absence of pain and tenderness.

Postoperative management

At recipient site a compression bandage or a POP slab was applied immediate postoperatively, which was removed within 48 to 72 hrs. According to preoperative union status patient was motivated to walk with support or walk in PTB cast. Rehabilitation protocol was same as preoperative. All patients discharged within 3-5 days of hospital admission.

Follow up and evaluation of results

This prospective study was conducted in the Department of orthopaedics, Government Medical College, Kota from June 2011 to November 2013 to evaluate the efficacy of percutaneous bone marrow injection in cases of delayed union of long bones. 27 patients included in study with 28 bones, as one patient has given bone marrow injection in two bones (tibia and femur), so the cases included in this study counted as 28 cases. The patients were followed up after every 4-6 weeks and union was assessed clinical and radiological by union grading. A score of eight or more was taken as sound union. It did not change the standard treatment protocol like external

or internal fixation or cast immobilization. This treatment was only to increase bone healing. In cases of tibia and femur operated with intramedullary nails having gap or distraction then static screw or a set of screws was removed for dynamization postoperative assessment.⁴

RESULTS

Total 27 patients included in study with 28 bones, as one patient has given bone marrow injection in two bones (tibia and femur), so the cases included in study counted as 28 cases. Out of these 28 cases 26 were males and 2 females. The mean age of this study was 38.28 years, ranging from 18 years to 75 years (Table 1).

Table 1: Age and sex distribution.

Age (yrs)	Cases	Percentage (%)	Male	Percentage (%)	Female	Percentage (%)
18-35	15	53.57	15	53.57	00	00
36-55	10	35.71	08	28.57	02	7.14
>55	03	10.71	03	10.71	00	00
Total	28		26	92.86	02	7.14

Table 2: Site of delayed union.

Bone involved	Cases	Site	Cases	Percentage (%)
Femur	15	Upper 1/3	02	7.14
		Middle 1/3	12	42.85
		Lower 1/3	01	3.57
Tibia	13	Upper 1/3	03	10.71
		Middle 1/3	06	21.42
		Lower 1/3	04	14.28
Total	28		28	

Table 3: Types of fracture (according to Gustilo's classification).

Type of fracture	Cases	Percentage (%)
Closed	13	46.43
Open Grade- I	05	17.86
Open Grade- II	06	21.42
Open Grade- III A	04	14.28
Open Grade- III B	00	00
Open Grade- III C	00	00
Total	28	

Table 4: Union potential grading.

Union potential grading	Cases	Percentage (%)
Excellent	13	46.43
Good	15	53.57
Poor	00	00
Total	28	

Table 5: Time elapsed before the injection of bone marrow.

Duration of injury	Cases	Percentage (%)
Below 16 weeks	22	78.57
Above 16 weeks	06	21.43
Total	28	

According to site of delayed union, 15 cases of delayed union femur and 13 cases of delayed union tibia, It mentioned in Table 2. According to gustilo's classification. There were 13 cases of closed fracture and 15 cases of open fracture in this study, with 05 cases of Open Grade- I, 06 cases of Open Grade- II and 05 cases of Open Grade- IIIA. No cases of Open Grade- III B and IIIC included in this study in Table 3. According to union potential grading, there were 13 cases of excellent and 15 cases of good union potential in this study. No cases with Poor union potential included in this study, It mentioned in Table 4. According to time elapsed before injection of bone marrow. There were 22 cases of duration of injury below 16 weeks and 06 cases of duration of injury above 16 weeks (Table 5).

Table 6: Results according to age and sex distribution.

Age	Cases	United	Avg. union time	Male	United	Female	United
18-35 yrs.	15	10	13.2	15	10	00	00
36-55 yrs	10	10	12.8	08	08	02	02
Above 55 yrs	03	03	16.33	03	03	00	00
Total	28	23		26	21	02	02

Table 7: Results according to site of delayed union.

Bone involved	Cases	Site	Cases	United	Avg. union time
Femur	15	Upper 1/3	02	01	11.0
		Middle 1/3	12	11	13.09
		Lower 1/3	01	01	12
Tibia	13	Upper 1/3	03	03	14
		Middle 1/3	06	04	14
		Lower 1/3	04	03	14.67
Total	28		28	23	

Table 8: Results according to types of fractures.

Type of fracture	Cases	United	Percentage (%)	Avg. time of union
Closed	13	12	92.3	12.75
Open Grade- I	05	05	100	13.8
Open Grade- II	06	04	66.67	12.75
Open Grade- III A	04	02	50	18
Open Grade- III B	00	00	00	00
Open Grade- III C	00	00	00	00
Total	28	23		

Results according to age and sex, patients in age group of 18-35 years, shows union in 10 cases with average union time of 13.2 weeks, as these are active years of life and person is more prone to severe trauma in this age group. Above 55 years union occurred in all 3 cases but average union time increased it is mentioned in Table 6. Results according to site of delayed union. Out of 15 cases of femur 13 cases united while out of 13 cases of tibia 10 cases united. Average union time was more for tibia, as tibia is more vulnerable to severe open fractures with concurrent soft tissue injury. It is mentioned in Table no 7. Results according to type of fracture, open Grade II and IIIA has low percentage of united cases as compared to closed & open Grade I fracture. All five cases of open Grade I fractures united but they had more Avg. Time of Union as compared to closed fractures. It is mentioned in Table 8.

Results according to past treatment, 1 case with GT cast takes in union 16 weeks, 1 case with debridement and ext fix shows no union. 14 cases with debridement & IM nailing in which 11 cases united in 14.18 weeks. 12 cases with IM nailing in which 11 cases united in 12.45 weeks, it is mentioned in Table 9.

Table 9: Results according to past treatment.

Past treatment	Cases	United	Avg. time of union
GT Cast	01	01	16
Debridement and ext. fix.	01	00	00
Debridement and IM nailing	14	11	14.18
IM nailing	12	11	12.45
Total	28		

Results according to union potential grading, all cases of excellent union potential grading had united. Upto 67% cases of good union potential grading united but at slower rate of union Table 10. Results according to time elapsed before the injection of bone marrow, 22 cases in duration of injury below 16 weeks 20 cases united in 13.25 weeks, 6 cases in duration of injury above 16 weeks 3 cases united 14.67 weeks, it mentioned in Table 11. Results according to union time after the injection of bone marrow, 19 cases united before 16 weeks of injection and 4 cases united after 16 weeks of injection and 5 cases shows no union, it is mentioned in Table 12.

Table 10: Results according to union potential grading.

Union Potential Grading	Cases	United	Percentage	Avg. Time of Union
Excellent	13	13	100	12.77
Good	15	10	66.67	14.3
Poor	00	00	00	
Total	28	23		

Table 11: Results according to time elapsed before the injection of bone marrow.

Duration of injury	Cases	United	Percentage	Avg. time of union
Below 16 weeks	22	20	90.9	13.25
Above 16 weeks	06	03	50.0	14.67
Total	28	23		

Table 12: Results according to union time after the injection of bone marrow.

Cases	Cases united	Percentage	Union grading
Cases united before 16 weeks of injection	19	67.86	Excellent
Cases united after 16 weeks of injection	04	14.28	Good
Cases not united	05	17.85	Poor
Total	28		

DISCUSSION

The osteogenic and osteoinductive property of bone marrow was first described by McGaw and Harbin.⁹ Conolly and Healy have demonstrated that percutaneous bone marrow injection can successfully treat 78%-95% of non union cases.¹⁰

The work of Paley et al showed experimentally that marrow gives optimal effect when used early in fracture healing process.¹²

Out of the 28 cases included in study, the youngest patient was of 18 years and oldest was of 75 years with the mean age of 38.28 years. More than half of patients were in age group of 18-35 years, this was similar to study done by Hernigou et al, Wilkins et al and Vikas et al.^{8,13,14} However the study by Bhargva R et al was not concerned about age and sex distribution.¹⁶ Clinical and radiological union was observed in 10 cases of 18-35 yr age group, 10 cases of 36-55 yr age group and 03 cases of above 55 yr age group with average union time 13.2 weeks, 12.8 weeks and 16.33 weeks respectively.

There were 26 males and 02 females in this study which was in contrast to most other studies. Union observed in 21 males and 2 females. There were 15 cases of femur and 13 cases of tibia in this study, with more prevalence of middle 1/3 fracture in both femur and tibia cases. This was in contrast to most other studies like Hernigou et al, Wilkins et al and Bhargva et al which includes most of tibial shaft fracture in their studies, because we had selected the cases on OPD basis randomly.^{13,14,16} Union

observed in 13 femur cases with average healing time of 12.84 weeks and 10 cases of tibia with average healing time of 14.2 weeks.

According to type of fracture 13 closed fractures and 15 open fractures included in this study. According to Gustilo Anderson Classification for open fractures 5 cases of type I, 6 cases of type II and 4 cases of type IIIA included in this study. That was somewhat similar to study by Wilkins RM et al. Union achieved in 12 cases (92.3%) of closed fracture. In open fractures union achieved in 5 cases (100%) of type I, 4 cases (66.67%) of type II and 2 cases (50%) of type IIIA fractures. All five cases of Open Grade I fractures united but they had more Avg. Time of Union as compared to closed fractures.

In this study 20 cases had no other associated injuries while 8 cases have other associated injuries like 3 cases with multiple injury, 2 cases with head injury, 2 cases with ipsilateral fracture femur along with tibia and 1 case of fracture forearm bones.

All cases of excellent union potential grading had united with average union time of 12.8 weeks. Upto 67% cases of good union potential grading united but at slower rate of union with average union time of 14.3 weeks.

In cases of duration of injury below 16 weeks 20 cases united and 2 cases had nonunion. Duration of injury above 16 weeks 03 cases united and 03 cases had nonunion. As the duration of injury increases, the time of bone healing also increases.

In this study which included 28 cases, we observed union in 23 cases (82.14%) with average union time of 13.4 weeks, which was comparable to other similar studies like Hernigou et al achieved union in 53 out of 60 patients (88.33%), Wilkins et al achieved union in 61 out of 69 patients (88.4%) and Bhargva et al shows union in 23 out of 28 patients (82.14%).^{13,8,16}

Out of five failed cases all gone into nonunion. Bone grafting was done for two cases and exchange nail with bone grafting done for three cases.

All the cases in our study were diagnosed to have delayed union. Cases were considered as delayed union if there was no sufficient callus formed in the first 3 months of follow up.

Bone marrow was injected in most of the cases at a minimum of 3 months following the initial treatment. The time period between initial treatment and bone marrow injection varied from 12 to 24 weeks with the mean time of 15.4 weeks.

The mean time since injury was 14.78 weeks for 23 united cases while it was 18 weeks for ununited or failed cases. Hence it is clear that percutaneous bone marrow injection is helpful in healing in early cases of delayed union.

Although there was high selection bias in favor of union, it cannot be said that union in these cases would have occurred even without the procedure as the mean time duration between the procedure and injury was about 15.4 weeks. The delayed union site which has no or minimal amount of callus, after bone marrow injection united in mean of 13.4 weeks. 18 cases showed formation of callus in first four weeks of injection.

The cases were followed upto 18 weeks post injection. The cases who did not have any improvement in callus formation upto 18 weeks regarded as failed cases.

In our study the amount of marrow varied 50-90 cc. It was not possible to comment on amount of bone marrow needed for fracture healing, as there were tight compartments in leg which not accommodate the desired level of bone marrow.

The average hospital stay was 4 days ranging from 2-5 days. There were no donor site or recipient site infection noticed in this study. Only one patient reported mild dull aching pain at donor site which relieved by mild analgesics.¹⁵

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. Learning

curve is short. It can be considered as an alternate method for bone grafting in delayed union of fractures. It can be given in cases in which delayed union is diagnosed or anticipated so as to prevent those fractures resulting in non-union and thus reducing the morbidity associated with non-union.

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Ethical approval: The study was approved by the institutional ethics committee

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