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Observation on role of bone marrow aspirate in the delayed union and non union of long bones

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Abstract

Background: Cells aspirated from bone marrow have been shown to provide stimulus for osteogenesis in animal experiments and in clinical evaluation of bone graft and bone substitutes. Despite this osteogenic characteristic, the clinical use of marrow as an osteogenic source has remained limited. The marrow is harvested by means of needle aspiration from the patient's pelvic bone and is then injected percutaneously at the nonunion site. This method offers the advantage of treating fracture-healing problems without operative exposure of either the donor or the recipient site.

Aim: The purpose of this study was to ascertain the osteogenic potential of autologous bone marrow injection and its effectiveness in the management of delayed union and nonunion.

Material and Methods: Autologous marrow injection was used to stimulate healing in 26 out of 34 patients were males. patients with delayed union and nonunion of fracture of the long bones This prospective study was done in Orthopaedic department of Darbhanga Medical College and Hospital in Laheriasarai, Darbhanga over a period of 2 years (2018 – 2020).

Surgical Technique: Bone marrow aspirated from the iliac crest was injected at the fracture site.

Results: Marrow stimulated callus formation sufficient to unite in delayed unions and nonunions immobilized with cast or intramedullary nails.

Conclusion: Bone marrow injection was as effective as open autogenous grafting but with considerably less complications. Thus, the technique provides a reliable source of osteogenic stem cells with numerous advantages compared with standard open grafting techniques.

Keywords: Bone marrow injection, delayed union and nonunion, long bone fractures

Introduction

Nonunion and delayed union are common problem seen in fracture healing and may be caused by several factors with or without any obvious cause. Autologous bone potentially contributes three vital components for healing which are osteoconduction, osteoinduction and osteogenic cells but operative harvesting is associated with numerous complications both at donor and recipient sites. In addition, the need to open the recipient site has added to the risk of devascularization of the fracture where healing is already impaired. 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) [15]. 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.

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Materials and methods

This prospective study was done in Orthopaedic department of Darbhanga Medical College and Hospital in Laheriasarai, Darbhanga over a period of 2 years (2018 – 2020). 34 patients with nonunion or delayed union were treated with percutaneous bone marrow injection. 26 out of 34 patients were males. One case was lost in follow up. Cases were considered as delayed union if there was no sufficient callus formed in the first 3 months of follow up. 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. Cases were considered as nonunion or anticipated to result in nonunion if there was no improvement in progression towards healing for consecutive 3 months. The average age of the patients were 40 years (15-65 years). This study included 11 femur, 13 tibia, 6 humerus, 4 radius. The time period from fracture treatment to bone marrow injection varied from 2 to 24 months. Study included 23 closed fractures. 9 cases of Gustilo Anderson Type 1 open fracture, and one each of type 2 and type 3. There were 28 cases of delayed union and 5 cases of non- union. Open procedures were done in 15 and closed in 17 fractures.

Inclusion criteria

1. Patients with delayed union
2. Patients with non-union.
3. Age criteria - 15 to 70 years.
4. All these delayed union or non-union having acceptable alignment good bone apposition and stable fixation.
5. Patients willing to give written consent and willing for follow-up.

Exclusion criteria

1. Patients with pathological fracture.
2. Patients with multiple fracture.
3. Patients with connective tissue disorder.
4. Malnourished patients.
5. Patients suffering from peripheral vascular disorder.
6. Patients with compound fracture.
7. Patients-with tumor and metabolic bone disorder.

Operative procedure

All patients were admitted and procedure was done in operation theatre after obtaining written informed consent. Patient was placed in supine position under Spinal anaesthesia. Iliac crest and draped along with the site of delayed or nonunion. About 25-40ml of bone marrow aspirated from these sites and injected into the recipient site using aspiration needle under radiological control. Post operatively dressing was applied and patients were discharged. Patients were followed up clinically and radiologically at an interval 4 weeks till an average of 8 months (3- 15 months). Clinically patients were checked for tenderness and abnormal mobility. Radiologically patients were evaluated for callus formation. Patients were also evaluated based on union scale score.

Results

This study included 34 patients, out of which one case was lost in follow up 24 out of 33 cases bone union was achieved (72.7%). Among the 33 patients 26 were males (78.8%).

Table 1: State of Union

State of union	Frequency	Percentage
Delayed	28	84.8
Non union	5	15.2
Total	33	100.0

Fig 1: Among the 22 patients below 45 years, 18 showed good union (82%) compared to patients above 45 years. Out of 11 patients above 45 years only 6 patients showed good union (54.5%)

Fig 2: There were 28 cases of delayed union and 5 cases of nonunion. Out of 28 cases of delayed union, 22 cases showed good union (78.6%), 5 showed progressive healing. Only 2 cases out of 5 cases of non-union showed good bony union after bone marrow injection (40%).

Table 2: Callus formation

Callus	Outcome			Total
	United	Progressive Healing	Non-union	
1 st	23 74.2%	6, 19.4%	2 6.5%	31 100.0%
3 rd	1 100.0%	0.0%	0 .0%	1 100.0%
6 th	0 .0%	0.0%	1 100.0%	1 100.0%
Total	24 72.7%	6, 18.2%	3 9.1%	33 100.0%

Out of 34 cases, callus was seen on the x ray in 1st month in 23 cases.

Table 3: Radiological

Callus	Outcome			Total
	United	Progressive Healing	Non-union	
3	2, 66.7%	1, 33.3%	0.0%	3, 100.0%
6	18, 75.0%	5, 20.8%	1, 4.2%	24, 100.0%
9	4, 100.0%	0.0%	0.0%	4, 100.0%
Nil	0.0%	0.0%	2, 100.0%	2, 100.0%
Total	24, 72.7%	6, 18.2%	3, 9.1%	33, 100.0%

Radiological union was seen in an average 22 week.

Table 4: Site

Callus	Outcome			Total
	United	Progressive Healing	Non-union	
Ankle	1, 100.0%	0.0%	0.0%	1, 100.0%
Both bone forearm	1, 100.0%	0.0%	0.0%	1, 100.0%
Humerus	4, 80.0%	1, 20.0%	0.0%	5, 100.0%
Femur	8, 72.7%	0.0%	3, 27.3%	11, 100.0%
Radius	3, 100.0%	0.0%	0.0%	3, 100.0%
Tibia	8, 58.3%	5, 41.7%	0.0%	13, 100.0%
Total	24, 72.7%	6, 18.2%	3, 9.1%	33, 100.0%

Out of the 11 femur cases, 8 cases showed good union (72.7%). About 90% of the radius and humerus cases also showed bony union. Among the 13 cases of tibia, 8 showed union (61%). 5 showed progression towards healing.

Discussion

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 [1, 2, 3, 4] etc. However the standard procedure of bone grafting was found to have associated complications as mentioned. The osteogenic and osteoinductive property of bone marrow were first described by McGaw and Habin [23].

Conolly 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 Zuo has 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 34 patients, we observed union in 24 patients (72.7%) which is comparable to other similar studies.

Table 5: Comparison of results with other studies.

Year	No. of bones studied	No. of bones united (%)
Our study, 2020	34	72.7%
Rakesh Srivastav, 2013	33	87.87%
Healy <i>et al.</i> , 1990	8	62.5%
Connolly <i>et al.</i> , 1991 [16]	20	90%
Garg <i>et al.</i> , 1993 [15]	20	85%

Most of the cases in our study were diagnosed to have delayed union. Bone marrow was injected in most of the cases at a minimum of 3 months following the initial treatment. Fractures which failed to show expected progression towards healing were selected for the study. Only cases with minimal gap and displacement were selected for the study.

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 22 weeks (5.4 months). After bone marrow injection the fractures united in mean of 17 weeks. Hence it is clear that the percutaneous bone marrow injection had helped the fracture to unite, it had definitely accelerated the healing process.

The fractures treated previously by closed technique had union in 78.6% and those treated with open procedure the union was seen in 67%. Out of the 5 non-union cases, 2 cases showed union, 1 case showed progressive healing and 2 resulted in non-union. Out of the 28 delayed union cases 22 united (78.6%). The average hospital stay was 4 days ranging from 2-5 days.

Bone marrow injection was found to be more useful in cases of delayed union as compared to nonunion cases.

The effect of bone marrow injection in cases with nonunion of fractures cannot be commented upon as the sample size was less.

The age of the patient, state of union, type of fracture, quantity of bone marrow injected played a significant role with p value < 0.5 .

There were no donor site or recipient site infection noticed in this study.

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 and nonunion 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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