Percutaneous Autologous Bone Marrow Injection In The Treatment Of Delayed And Non-Union Of Long Bones

Dr Shrivastav Rakesh*, Dr. Anurag Sapolia, Dr Ghugare Balaji W*** , Dr. Sagarsinh M Parmar******

*Prof & Head, Department of Orthopedic, GMERS Med College Gotri Vadodara-390021.,** ex- senior resident, govt. medical college & new civil Hospital Surat, *** Asst Prof , Department of Physiology, **** J/S (ORTHO) ,GMERS Med College, Gotri, Vadodara-390021

Abstract: Context: Bone marrow has been shown to contain osteo-progenitor cells. Percutaneous autologous bone marrow injection (PABMI) encourages early treatment of delayed union and non-union to expedite healing and minimize complications from prolong immobilization. Aims and objectives: To assess the outcome of PABMI treatment in delayed and non-union of long bones. Study design: Prospective study Participants and procedures: 24 cases (33 bones) of Delayed and non-union of long bones were selected. Percutaneous autologous bone marrow injection treatment was adopted for fracture healing. Change in pattern of union was followed after 12 weeks by clinical and radiological study. Results: 90% of tibial fractures, 66.66% of radial fractures and 50% of ulna fractures show clinical and radiological union. 100% of the fractures with no gap at the fracture site united, where the gap was less than 1 cm, 85% of bone united, in only 1 case the gap was more than 1 cm and it failed to unite. 7 out of 9 bones in hypertrophic non-union united, whereas 4 out of 6 bones in atrophic non-union united. Conclusion: Percutaneous autologous bone marrow grafting is an effective and safe method for the treatment of diaphyseal non union. We strongly believe that an injectable preparation that combines marrow with osteoinductive and osteoconductive agents should virtually eliminate the need for open harvesting and operative grafting of the problems associated with fracture healing. [Shrivastav R et al NJIRM 2013; 4(2) : 39-43]

Key Words: Bone marrow injection, Delayed union, Non union, Long bones

Author for correspondence: Dr R.K.Shrivastava, Dept of orthopaedics, GMERS Med College Gotri, Vadodara-Gujarat-390021, Email: shrivastava_rkumar@yahoo.com

Introduction: Sequel of the fracture like delayed union and non-union are major problems in all the hospitals everywhere. Bone grafting remain most common orthopaedic procedures till date. This technique, which involves operative removal of bone graft from a donor site, usually the iliac crest and operative implantation at the site of the delayed union or non union has been standard for decades. Bone graft is utilized frequently in conjunction with open reduction and internal fixation by any implant for treatment of non-union.[1,2]. The desirable approach is a simple method of providing cellular reinforcement at the fracture site, which enhances the rate of bone repair. Bone marrow contains many cell types of which Osteo-Progenitor or stem cell, determined Osteo-Progenitor Cell (DOPC) and Inducible Osteo-Progenitor Cells (IOPC) has been experimentally shown to have osteogenic properties. [3] The osteogenic potential of the implanted graft also has been shown to be due to these cell types. Bone marrow is taken from the iliac crest of the patient and injected at the site of delayed or non-union, which stimulates the process of healing. This method of percutaneous aspiration and injection of autologous bone marrow offers the advantage of fracture healing problems without operative exposure of either the donor or the recipient site. Thus it minimizes the complications associated with the bone grafting. The objective of this study is to present our experience on percutaneous autologous bone marrow injection for early union at the site of delayed or non union of long bones.

Material and Methods: In the present study, we have treated 33 cases of delayed and non-union of long bones in 24 adult patients at the Department of Orthopaedics, Government Medical College and New Civil Hospital, Surat from Jan 1999 to Jan 2001. Institutional Ethics committee approval was obtained to conduct the study. Written informed consent was taken from each participant and study was conducted according to World Medical Association declaration of Helsinki. The patients were selected randomly. All patients were treated as indoor patients. Patients under the age of 18 and patients with pathological fractures were not included in this study. Each patient was examined thoroughly and routine hemogram, urine examination and X-ray of the affected part and other investigations were done. Five patients had more than one bone affected while 19 patient had

only one bone affected, making a total of 33 long bones.

Out of 33 long bones, 4 humerus shaft fractures and 1 supracondylar humerus fracture were primarily treated with plating. Out of 3 radius fracture, 2 were treated with intramedullary nailing and 1 was treated primarily with plating. Out of 4 ulna fractures, 3 were treated with intramedullary nailing and 1 was primarily treated with plating. Out of 10 tibal fractures, 3 were treated with intramedullary nailing, 3 were with external fixator, 3 with plaster and 1 primarily treated with plating. Six fractures of the shaft of femur treated with intramedullary nailing. Two supracondylar fracture femur, 1 had intramedullary nailing and 1 had Angle blade plate. One subtrochantric fracture femur treated with Dynamic hip screw and side plate. Two fractures of neck of femur, 1 was treated conservatively and 1 had close reduction and internal fixation with cannulated cancellous screws. Patient was placed in the supine position under anaesthesia. A 16 number Bone marrow aspiration needle was used to harvest the bone marrow from the anterior iliac crest. [4] 20 c.c locking syringes were heparinised before starting the procedure. Large volume of the bone marrow was aspirated as far as possible. [(4)] Continued aspiration was avoided since this would draw off mainly venous blood. We had used around 100-200 ml of bone marrow for fracture of tibia and femur, 50-60 ml for humerus and 20-30 ml for radius/ulna.

A 16 or 18 no. aspiration needle was inserted into the site of delayed or non union under image intensifier and marrow was injected. The marrow graft was not the final treatment for the most of the fractures but was employed to supplement basic fracture immobilization techniques like plaster cast, functional brace etc. The fracture was considered united when bone crossed the fracture gap and the patient was able to weight bear or used the limb without local pain or instability. The end point of a case study was as arbitrarily considered as 12 weeks (3 months) after the procedure, after which the procedure was considered as a failure if no change in union pattern was seen.

Observation and Results: In the present series, 33 long bone fractures of delayed or non-union were treated with percutaneous autologous bone marrow injections and followed for a period of two years. Most of the patients were in the age group of second or third decade of life. Male preponderance with 22 males and 2 females in this study was observed. In which 18 patients sustained direct injury and 6 had indirect. Five patients in this study had more than one bone affected and the entire involved fracture site was in either delayed or non-union. In present study, 22 delayed and non union cases were initially closed fracture and 11 were compound fractures. In this study 18 cases were comminuted fractures, 14 were linear and 1 was segmental. None of the fracture with bone loss was included in present study. 60% of the long bones were initially treated by open reduction and internal fixation, 18% by closed reduction and internal fixation, 12% by closed reduction and plaster cast, 9% by open reduction and external fixation .Out of 33 long bone studied, 18 were in delayed union and 15 were in non union. Of these 15 long bones, 9 were hypertrophic non union and 6 were atrophic non union. Nine long bone fractures in our study were infected initially but none of the fractures had any sign of infection at the time of injection of bone marrow. The minimum time elapsed before the percutaneous autologous bone marrow injection was 4 months and maximum 24 months with an average of 7.8 months in this study. Union is considered delayed when healing has not advanced at the average rate for location and type of fracture (usually 9 months). Non-union is considered established when a minimum of 9 months have elapsed since injury and the fracture shows no visible sign of healing for 3 months. Most of the patient had discomfort at the donor site for one or two days, none had problems of persistent pain.

In all the fractures included in this study, bone marrow was injected once except for one in which marrow was injected twice at monthly interval. All

the 5 fractures of humerus, 1 fracture radius, 1 fracture ulna, 5 fracture tibia, 10 fractures of femur united within 12 weeks. The 7 fractures, which showed sign of healing at the end of 12 weeks, ultimately united without any further surgical intervention. Four fractures did not shows any sign of healing at the end of 12 weeks and needed further surgical intervention. The minimum time for union was 2 months and maximum 7 months with an average of 3.34 months in this study. When the time elapsed before the injection of bone marrow was less than 12 months all the fractures united after the injection of bone marrow, whereas when the time elapsed was 12 months or more only 33.33% of fractures united after the injection of bone marrow.

Results according to individual bones showed in Table no. 1. All the fractures of humerus and femur included in this study are united. 90% of tibial fractures, 66.66% of radial fractures and 50% of ulna fractures show clinical and radiological union, remaining 4 fractures failed to show any signs of healing.

Table-1: Result according to individual bones.

Bone	Humerus	Radius	Ulna	Tibia	Femur
No.	5	3	4	10	11
United	5	2	2	9	11
%	100%	66.66%	50%	90%	100%

Results according to type of defect in union showed in table no. 2. All the bones that were in delayed union united after autologous bone marrow injection. 7 out of 9 bones in hypertrophic non-union united, whereas 4 out of 6 bones in atrophic non-union united.

Table-2: Result according to the type of defect in union.

Defect In Union	Delayed Union	Non Union Hypertrophic	Non Union Atrophic
Number Of Cases	18	9	6
United	18	7	4
%	100%	77.77%	68.66%

Results exploded according to amount of autologous bone marrow injection showed in Table no. 3.The amount of bone marrow injected at the site of defective fracture healing affects the results, with success rate increasing as the amount of marrow injected increases.

Results according to gap at the fracture site showed in Table no. 4. 100% of the fractures with no gap at the fracture site united. Where the gap was < 1 cm, 85% of bone united. In only 1 case the gap was > 1 cm and it failed to unite.

Table no. 3: Results exploded according to amount of bone marrow injection given

Bone	**Humerus**		**Radius**		**Ulna**		**Tibia**		**Femur**	
Amount of Bone Marrow (C.C.)	<20	>20	<10	>10	<10	>10	<70	>70	<70	>70
No.	1	4	2	1	3	1	2	8	3	8
United	1	4	1	1	1	1	1	8	3	8
%	100	100	50	100	33.3	100	50	100	100	100

Table-4: Result according to the gap at the fracture site.

GAP	**None**	**<1 Cm**	**>1 Cm**
No.	12	20	1
United	12	17	None
%	100	85	0

Comparison of results with the studies, showed in **table no. 5**. The success rate of our study is similar to that of other studies. In the study of Husseini [5], there is lower percentage of success rates as compared to others, because in the first half of his study he injected small amount of marrow, increasing the volume in second half where he got better results.

Table-5: Comparison of results with other studies

Study and year	No. of bones studied	No. of bones united (%)
Present Study	33	87.87
Healy et al, 1990	8	62.5
Connolly et at, 1991	20	90.0
Garg et al, 1993	20	85.0
Bieniek et al, 1993	30	87.0
Husseini	71	72.0

Results at the end of 12 weeks showed in table no. 6. The criteria used for the results were those adopted by Healey JH et al. [6, 7]

Table No. 6: Result at the end of 12 weeks

Result	No.	Percentage (%)
Excellent	22	66.66
Good	7	21.21
Poor	4	12.12

In the present study, it was found that in all the 4 cases the duration of bone marrow injections was more than 1 year. Out of these 4 cases, 2 were hypertrophic non-union and 2 were atrophic non-union. The amount of marrow injected was less in all the 4 cases as compared to other studies. In 1 case gap at the fracture site was more than 1 cm and in 3 cases it was less than 1 cm.

Discussion: Autologous bone grafting remains the gold standard for the treatment of delayed and non-union for the decades ever since the work of Phemister and Chutro [8] and others. It is supported by long track record in clinical practice as well as sound histochemical role of serving as a source of osteogenic cells, a stimulator of mesenchymal cells (osteo-induction) and mechanical or space filling agent (osteo-conduction). Bone grafting remains the most common orthopaedic procedure. Bone graft is thought to give its biological osteogenic effect through the presence of two types of osteogenic precursor cells(stem cells) which are both inducible working under the effect of stimulating factor and determined working without exogenous stimulus ,red marrow contain both cell types.

We studied the effect of percutaneous autologous bone marrow injection in delayed and non-union of 33 long bones, as a substitute for standard open grafting technique. 29 long bones out of the 33 studied healed, the minimum time for healing of fractures after bone marrow injection being 2 months and the maximum 7 months with an average 3.34 months. So, 87.87% of the delayed and non-union in our study healed which is similar to the result of Connolly et al and Garg et al, 4 bones failed to heal or show any sign of healing at a minimum period of 3 months and needed further surgical intervention.

All the fractures included in this study, which were in delayed union healed ultimately. Bone marrow injection can be used whenever one suspects a delay in healing of a fracture, thus encouraging healing and minimizing fracture disease. According to Connolly [9, 10] autologous bone marrow has been most useful for the preventive treatment of non-union by early injection in delayed union.

In this study, the results were almost similar in both the hypertrophic and atrophic type of non-union. Husseini [5] has observed that atrophic type of non-union shows lower success rate to achieve union. In present study, the success rate decreased with increased in the duration before autologous bone marrow injection. Husseini [5] made the same observation in his study group. If gap at the fracture site is more, autologous bone marrow injection is not an effective tool for the enhancement of healing, as it has no osteoconductive properties. The amount of injected bone marrow at the site of delayed union and non-union affects the healing process and success rate. More the volume of bone marrow injected more will be the concentration of the stem cells and more will be the enhancement of the healing process. In all the 4 bones, which failed to heal in present study, the amount of marrow injected was less than desired.

Conclusion: Current study concludes that with adequate amount of autologous bone marrow injection, successful union in delayed union or non-union of fractures of long bones can be achieved. We strongly believe that as the research on this subject is continued, ultimately an injectable preparation that combines marrow with osteoinductive and osteoconductive agents may virtually eliminate the need for open harvesting and operative grafting in delayed and non-union bone healing.

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