ORIGINAL ARTICLE

Role of injecting bone marrow aspiration injection in treating delayed union and non-union

Muhammad Akram, Muhammad Irshad, FaheemMubashir Farooqi, Ranjeet Kumar Sah, Muhammad Latif Shahzad, Ahmad Humayun Sarfraz, Syed Muhammad Awais

Abstract

Objective: To access the role of bone marrow injection in the management of delayed union and non-union.

Methods: The prospective study was conducted at the Department of Orthopaedic Surgery and Traumatology, Mayo Hospital, Lahore, from January 2012 to December 2013, and comprised patients who had long bone fractures that resulted in delayed or non-union and were treated with bone marrow injections. Aspiration of bone marrow was done from tibial tuberosity and was injected percutaneously at the fracture site. The whole procedure was carried out as a day case. Fracture site mobility, tenderness and radiological features were assessed using the Union Scale score.

Results: Of the 25 patients, 18(72%)were male and 7(28%) were female with an overall mean age of 38±12.96SD years (range: 17-61 years). There were 19(76%) tibial shaft fractures, 4(16%) had shaft of femur fracture, and 2(8%) had humeral shaft fracture. Mean time duration between the injury and the procedure was 34 ±3.46 SD weeks (range: 30-42 weeks). Overall, 23 (92%) patients showed union and the mean time of healing was 15 ±2.73SD weeks (range: 12-22 weeks) after the procedure.

Conclusion: Percutaneous bone marrow injection provided an alternative to open bone grafting, having least complications, especially for early intervention in the fracture-healing process.

Keywords: Bone marrow, K-wire, Non-union, Delayed union. (JPMA 64: S-154 (Suppl. 2); 2014)

Introduction

When a long bone such as femur, tibia or humerus is fractured in a normal person it requires a certain time for healing. However, this time varies according to age, species, bone involved, type and level of fracture, associated soft tissue injury and associated systemic illness. Delayed and non-union are major complications of the fracture treatment. The United States Food and Drug administration (FDA) defined non-union as being "established when a minimum of 9 months have elapsed since fracture with no visible progressive signs of healing for 3 months".[1] Delayed union is defined as un-united fractures that continue to show progress towards healing or that have not been present for long enough to satisfy the definition of non-union.[2] The delayed union is not always non-union, but it may end up in non-union and may occur due to inadequate reduction, improper immobilisation, loss of blood supply infection, and drugs intake. To achieve the union, multiple modalities are used such as distraction and compression osteogenesis by external fixators, autogenous bone graft, percutaneous autologous bone marrow injection and bone morphogenic protein injection at the fracture site.

Goujon in 1869 was the first one who demonstrated osteogenic capacity of bone marrow on rabbits.[3] Osteogenic activity of the bone marrow was demonstrated for the first time by McGaw and Habin.[4] Herzog in 1951 introduced the concept of percutaneous bone marrow injection. He used along bone needle and small cancellous chips to graft a non-union.[5] For the first time, Connolly and Shindell reported healing of un-united infected tibia by using percutaneous bone marrow injection.[6] Osteoblasts are known to be chief bone-forming cells, but now it has been shown that osteoblasts, fibroblasts and reticular cells etc. have common precursor cells; and these precursor cells are found in bone marrow and in certain areas of connective tissue framework.[7-10] The marrow which is taken from the proximal tibia and pelvic bone by needle in natural form without any separation of the contents and then injected at the fracture site under the guidance of image intensifier, by percutaneous technique, contains both types of cells i.e. induced-to-produce bone and the other is determined-to-produce bone. The induced-to-produce bone cells exist in all the connective tissues, while the determined-to-produce bone cells are found only in marrow.[11] As the bone marrow is the only tissue which contains both inducible and determined osteoprogenitor cell, therefore

Department of Orthopedic Surgery and Traumatology Unit-1, Mayo Hospital, Lahore.

Correspondence: Muhammad Akram. Email: akramaz@gmail.com

bone marrow is logically the graft of choice.[12] The method has the advantage of treating non-unions and delayed unions without surgical exposure of either the donor or recipient site.

The current study was planned to confirm the role and effectiveness of autologous bone marrow injection in the management of delayed unions and non-unions.

Patients and Methods

The prospective study was conducted at the Department of Orthopaedic Surgery and Traumatology, Mayo Hospital, Lahore, from January 2012 to December 2013, and comprised patients who had long bone fractures that resulted in delayed union or non-union and were treated with bone marrow injections.

Cases that did not show signs of union radiologically and infection were considered for injection. Infected and gap non-union cases were excluded. Infection was ruled out on the basis of normal erythrocyte sedimentation rate (ESR), total leukocyte count (TLC) and C-reactive protein (CRP) values. All fractures had acceptable alignment, good bone opposition and stable fixation. Injection was given with implant external fixator in situ. The bone marrow was injected at intervals of four to six weeks after radiological evaluation for union under fluoroscopy control.

The procedure was carried out in operation theatre (OT) as a day case. The patient was placed in supine position, proximal tibia and recipient area were draped separately to avoid cross-contamination. A two mm K-wire was used to drill the bone with T-handle and then a needle of gauge 16 was used for aspiration and a lumber puncture needle of gauge 16 was used for injection. The entire procedure was done under local infiltration with 2% xylocaine or ketamine or spinal anaesthesia. The recipient site was marked prior to the injection and immediately after aspiration, 40-50ml of the non-heparinised bone marrow was injected into the previously marked site under fluoroscopy guidance. A compression dressing was given postoperatively and the patient was discharged in the evening and reviewed after every 6 weeks. Serial X-rays were taken at review till the fracture got united.

Fracture site mobility, tenderness and radiological features were assessed using the Union Scale score (Table) in which union is considered with a score of 6 or more.

Results

Of the 25 patients, 18(72%) were male and 7(28%) were female with an overall mean age of 38±12.96 SD years (range: 17-61 years). There were 19(76%) tibial shaft fractures, 4(16%) had shaft of femur fracture, and 2(8%) had humeral shaft fracture. Mean time duration between the injury and the procedure was 34±3.46 SD weeks (range: 30-42 weeks). The mean duration of injection procedure was 15 ±3.75 SD minutes (range: 10-25 minutes).

Eight (32%) patients had closed fracture, 7(28%) had Gustilo open fracture classification(13) grade I, 6(24%) had grade II, 3(12%) had grade IIIA and 1(4%) had grade IIIB. Three of the 4(75%) patients with shaft of femur fracture had been managed with closed interlocking nail, whereas 1(25%) case was managed by external fixators. One of the 2(50%) cases with fracture of the humeral shaft had been treated by Locking Compression Plate(LCP) while 1(50%) was managed by AO external fixator (Arbeitsgemeinschaftfür Osteosynthesefragen (German for "Association for the Study of Internal Fixation", or AO),. Of the 19 patients with shaft of tibia fracture, 11(58%) had been treated with close reduction and above-knee Plaster of Paris (POP), 2(10.5%) by closed reduction with interlocking nail and 2(10.5%) with open reduction and internal fixation with Dynamic Compression Plate (DCP), while 4(21%) were managed by external fixators.

Overall, 23 (92%) patients showed union and the mean time of healing was 15±2.73SD weeks (range: 12-22 weeks) after the procedure, while 2(8%) patients had to go for surgical treatment with cancellous bone graft.

The mean pre-injection Union Scale Score was 2 ±1 SD (range: 0-3) compared to 5.6±1.26 SD (range: 0-7) post-procedure. In united cases, it was 6.6±0.499 SD (range: 6-7). In 2(8%) cases of interlocking nails, pain was experienced after the procedure which was cured by giving analgesics during the hospital stay and oral paracetamol at the time of discharge. Pain was relieved after a day or two. There was no complication

Table: Union Scale Score - 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

from the procedure.

Discussion

Open fracture and soft tissue injury results in an increase in incidence of non-union from normal 2.5% to 13-16%. Recently, many methods have been introduced to achieve healing and manage delayed union in difficult orthopaedic situations. These include ways of bone grafting, use of bone graft supplements like amorphous hydroxyapatite as substitute of bone graft in cancellous and cortical bone. The bone graft acts as a scaffold with most of the cellular elements dying out and being replaced by creeping substitution.[14] Although these methods show good results and are acceptable, yet they have disadvantages of having all the risks of major surgery, including blood loss, infection and donor-site morbidity.[15]

The bone marrow was injected in all of cases at 34 weeks since injury. Of the 25 patients, 23 had good union potential score. Union was achieved at a mean time of 15 weeks after the procedure. So it is clear that fracture healing was accelerated by bone marrow aspiration injection.

Paley et al. in 1986 reported that when bone marrow is injected early in the fracture-healing process, it showed optimal results and had the poorest result when used in treatment of non-union.[16] Connolly et al. in 1991showed that early injection of autologous bone marrow in delayed union was a preventive treatment of non-union. They reported 6 to 12 weeks as the ideal time for bone marrow injection as it is the time when the initial inflammatory and osteoclasticresorption period of fracture repair has subsided.[17,18] Hence, when it is presumed that union is not going to be achieved as a routine, this procedure should be done as early as possible.

In this study we injected 40-50ml of marrow injection in all the cases of delayed and non-union fractures, yet we have no definitive conclusion regarding the amount of marrow injected. Hernigou P et al. in 2005 showed that efficacy of injected marrow was directly related to the number of progenitor cells.[19]

Healey JH et al. injected 50ml of aspirated marrow in 8 cases. Four of them were injected once, while the rest were given twice, but it did not significantly change the outcome.[20] Connolly et al. in a study of 20 cases used only one injection of 100-150 ml.[17] In another study, Garg et al injected 15-20ml of marrow aspirate twice with an interval of three weeks at the fracture site.[21] It has been observed that by increasing the concentration of marrow using centrifugation techniques results in increase in its osteogenic activity.[22,23] As the volume of injection mainly depends on the site of injection, so these techniques are very useful when injecting the marrow in a limited and small space.[22]

Stinchfield et al. reported that bone healing was impaired when bone marrow aspiration was used with heparin.[24] Thus, to avoid the potential impairment of bone healing, heparin was not used in our study.

Conclusion

Percutaneous autologous bone marrow injection in natural form proved to be very effective, simple, minimally invasive, safe and inexpensive method of treatment without the complications of tricortical/cancellous bone grafting and it can be carried out when the skin condition is poor. The results are gratifying and there is scope for further research into the healing process in different situations.

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