

Outcome of percutaneous bone marrow injection in delayed union and nonunion of long bone fracture

Pradeep Gandharva Guttalapalli^{1*}, Supradeeptha Challa²

¹Assistant Professor, ²Associate Professor, Department of Orthopaedics, GSL Medical College, Rajamahendravaram, Andhra Pradesh, INDIA.
Email: pradeepgandharva_85@yahoo.co.in, supradeep_challa@yahoo.co.in

Abstract

Background: Bone marrow is a good source of osteoprogenitor cells. Being a simple and minimally invasive technique with lesser complications, this study is intended to evaluate the effectiveness of percutaneous bone marrow injection in delayed union and non union and thus decrease the period of morbidity for the patients those are likely to go for non union. **Objective:** To present our experience in the effects of percutaneous bone marrow injection in delayed and non-union of long bone fractures. **Materials and Methods:** This prospective study was conducted in GSL Medical College, Lakshmipuram, Rajamahendravaram over a period of 2 years. We had 34 patients with fractures going for delayed union and non union treated by percutaneous bone marrow injection in our series of study. Cases with pathological fractures, infected non unions, malignancy and age under 15 years were excluded from our study. The collected data was analysed statistically. **Results and Conclusion:** We had 72.7% union achieved, another 18.2 % showed progression towards healing and 9.1% showed non progression for union. Union was better when bone marrow injection was given in a case of delayed union as compared to non union cases. This is a simple, easy and valuable technique to enhance bone healing and this reduce the period of morbidity due to delayed union and nonunion.

Key Words: Percutaneous bone marrow injection, delayed union, non-union.

*Address for Correspondence:

Dr. Pradeep Gandharva Guttalapalli, Assistant Professor, Department of Orthopaedics, GSL Medical College, NH-16, Lakshmipuram, Rajamahendravaram-533296, Andhra Pradesh, INDIA.

Email: pradeepgandharva_85@yahoo.co.in

Received Date: 15/06/2017 Revised Date: 09/07/2017 Accepted Date: 04/08/2017

DOI: <https://doi.org/10.26611/1020321>

Access this article online

Quick Response Code:



Website:

www.medpulse.in

Accessed Date:
06 August 2017

INTRODUCTION

Fracture healing is a specialized type of wound healing in which the regeneration of the bone leads to restoration of the skeletal integrity. There are five stages of healing in a fracture bone: Stage of hematoma, Stage of subperiosteal and endosteal cellular proliferation, Stage of callus formation, Stage of consolidation, Stage of remodeling. In most of the fractures healing occurs at a biologically optimum level. However in a small proportion of cases it is delayed or impaired. In delayed union there is clinical

and radiological evidence that healing is taking place but it has not advanced at the average rate for the location and type of fracture. Nonunion is said to exist only when actual evidence of cellular activity at the fracture site ceases and fracture is not uniting. The diagnosis of the nonunion is based on the presence of one or more of the following criteria like painless abnormal mobility, bony defect, sclerosis, surrounding the bone ends and obliteration of the medullary canal. FD A panel has defined non-union has established when a minimum of 9 months have elapsed since injury and the fracture shows no visible progressive signs of healing for last 3 months. There are various factors that is used to enhance union such as drugs, electro-magnetic fields, distraction and compression osteogenesis by Ilizarov, low intensity ultrasound therapy, autogenous bone graft^{1,2,3,4}. Autologous bone grafting has been the standard operative method for decades since the work of Phemister⁵ which involves operative removal of bone from the donor site usually pelvis and operative implantation at the site of delayed union or non-union. Autologous bone potentially contributes three vital components for

healing which are osteoconduction, osteoinduction and osteogenesis⁶. But operative harvesting and implantation at the fracture site has not been without complications both at the donor and recipient sites. Painful scar, hematoma, infection, muscle herniation, buttock anaesthesia fracture or subluxation and gait disturbances have been reported among the problems at the donor site thus prolonging the hospital stay and expenditure^{7,8,9}. The need to open the non union site has added the risk of infection or devascularisation of the fracture fragments where healing is already impaired. Hence a continuous search has been made to find out such an alternative method of treating delayed and non-union which is easy, economical and safe. Current search in basic science provides understanding of the factors needed for osteogenesis in bone substitutes. The osteoblast is very well known as chief bone forming cell, but now it has shown that osteoblast, fibroblasts and reticular cells etc have the common precursor cells and these common precursor cells are found in bone itself, in bone marrow and in certain areas of connective tissue framework^{10,11,12,13}. The cells aspirated from bone marrow are being shown to provide stimulus for osteogenesis in animal experiments¹⁴. The ability of marrow to form bone has been known for more than a century since the experimental work of Goujon¹⁵ in 1869. Burwell used the osteogenic potential of autologous red marrow to create osteogenesis in allogenic cancellous grafts^{16,17,18}. Bone marrow has also been used in combination with osteoinductive materials such as bonemorphogenic protein (BMP)¹⁹, demineralised bone matrix²⁰ and as a composite graft with bioceramics²¹. The concept of percutaneous bone marrow injection was introduced by Herzog²² in 1951. McGaw and Habin²³ were among the first to demonstrate the osteogenic activity of bone marrow. Percutaneous autologous bone marrow grafting offers advantage of decreased morbidity associated with classical open grafting techniques. Other advantages include decreased cost and hospital stay, as the procedures are performed in an outpatient setting.

MATERIALS AND METHODS

This prospective study was done in Orthopaedic department of GSL Medical College over a period of 2 years. 34 patients with non union 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 41.8 years (18-79 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 above 15 years.
2. Patients with clinical and radiological evidence of delayed union or nonunion.

Exclusion Criteria

1. Patients below 15 years
2. Patients who are not fit for surgery/anaesthesia
3. Infection, Malignancy
4. Patients who are not available for follow up.

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 or the tibial tuberosity was painted and draped along with the site of delayed or non union. 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 in 2-4 days. Patients were followed up clinically and radiologically at an interval of 6 weeks till an average of 8 months (3- 15 months). Clinically patients were checked for tenderness, abnormal mobility, pain on weight bearing. Radiologically patients were evaluated for callus formation.

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%). There were 28 cases of delayed union and 5 cases of non-union. 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%). Among the 22 closed fractures, 16 showed total union, 4 showed progression towards healing and 2 cases resulted in non union as compared to the 11 cases of open fractures which showed union in 8 cases (72.7%), progression towards healing in 2 cases and non union in 1 case. 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%). Out of 34 cases, callus was seen on the x ray in 1st month in 23 cases. Clinical union was seen in an average of 18 weeks (12-36 weeks) and radiological union in 22 weeks (11-36 weeks).

DISCUSSION

Various methods of treatment were sorted for delayed and non union from decades which includes exchange nailing, bone grafting, 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 Habin²³. Conolly²⁶ and Healy²⁷ have demonstrated that percutaneous bone marrow injection can successfully treat 78%-95% of non union cases. The work of Paley *et al*²⁸ showed experimentally that marrow produces optimal effect when used early in fracture healing process. Other similar recent studies²⁷ 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. 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. There were no donor site or recipient site infection noticed in this study.

SUMMARY

In this study 24 out of 34 patients showed good union (72.7%) which is consistent with the other similar studies. Out of 28 delayed union cases 22 showed good union (78.6%) compared to 40% union in 5 of the non union cases. The fractures those were treated by closed reduction methods initially showed better union. Patients below 45 years showed good union compared to older age groups. The effect of bone marrow on non union cases and communitied cases cannot be commented upon as the sample size is less. P value was found significant (<0.5) for the age, state of union at the time of bone marrow injection and quantity of bone marrow given.

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 non 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.

REFERENCES

1. Tylman D, Dziak A: Traumatologia Narządu Ruchu. PZWL 1996
2. Goreck A: Czynniki Wzrostu Tkanka Kostna Oficyna Wydawnicza ASPRA JR; Warszawa 2004.
3. Russel AT, Taylor CJ, Lavelle DG:- Fractures of tibia and fibulka. In: Fractures in Adults, Rockwood and Green. 1191,3,1915-1982
4. Saleh M: Non union surgery, Part 1. Basic principles of management. Int J Orthop Trauma 1992;2, 4-18.
5. Phemister DB. Treatment of ununited fractures by ionlay bone grafts without screws or tie fixation and without breaking down of fibrous union. J Bone Joint Surg 1947; 29:946-60
6. Glowacki J, Mullikan JB. Demineralised Bone Implants. Clin Plastic Surg 1985; 12:233-41
7. Gershuni DH, Pinsker R. Bone grafting for nonunion of fractures of tibia: A critical review J Trauma 1982;22:43-9
8. Cockin J. Autologous bone grafting: Complications at the donor site. J Bone Joint Surg 1972;53B:153.
9. Younger E M, Chapman MW. Morbidity at the bone graft donor site. J Orthop Trauma 1989;3:192-5

10. Urist MR, Burwell RG. Bone grafts, derivatives and substitutes. Butterworth-Heinemann:1994
11. Burwell RG: The function of the bone marrow in the incorporation of bone grafts. ClinOrthopRelat Res 1985; 200: 125-41
12. Beresford JN. Osteogenic stem cells and the stromal system of bone and marrow. ClinOrthopRelat Res 1989;240: 270-80
13. Ashton BA, Allen TD, Howlett CR, Eagleson CC, Hattori A, Owen M. Formation of bone and cartilage by marrow stromal cells in diffusion chambers *in vivo*. ClinOrthop Relat Res 1980; 151: 294-307.
14. Connolly J, Guse R, Lippilo L, Dehner R. Development of an osteogenic bone marrow preparation. J Bone Joint Surg 1989;71- A or B : 684-91
15. Goujon E. Recherches experimentales les proprietes physiologiques de la moelle des os. Journal de l'Anatomie et de Physiologie Normales et Pathologiques de l'Homme et des Animaux 1869; 6:399-412.
16. Burwell RG. Studies in transplantation of bone. VII: The fresh composite homograft-autograft of cancellous bone. An analysis of factors leading to osteogenesis in marrow transplants and in marrow containing grafts. J Bone Joint Surg 1964; 46B:110-40
17. Burwell RG. Studies in transplantation of bone. VIII: The treated composite homograft-autograft of cancellous bone. An analysis inductive mechanism in bone transplantation. J Bone Joint Surg 1966; 48B:532-66
18. Burwell RG. A study of homologous cancellous bone combined with autologous red marrow after transplantation to a muscular site J Anat 1961; 95:613.
19. Takagi K, Urist MR. The role of bone marrow in Bone Morphogenetic Protein- induced repair of femoral massive diaphyseal defects. ClinOrthop 1982; 171:224-31.
20. Tiedemann J, Connolly JF, Strater BS, Lippillo L. Treatment of nonunion by percutaneous injection of bone marrow and demineralised bone matrix. An experimental study in dogs, ClinOrthop 1991; 268:294-302.
21. Koualkowski A, Wallace WA, Prince HG. Clinical experience with a new artificial bone graft; Preliminary results of a prospective study. Injury 1990; 21: 142-4
22. Herzog K. Verlängerung osteotomischer Intervall durch percutane gezielte Verriegelung der Markkanäle, Unfallzeitschrift 1951; 42:226-30
23. McGraw WH, Habbins M. The role of bone marrow and endosteum in bone regeneration. An experimental study of bone marrow and endosteal transplant. J bone Joint Surg 1934, 14: 816-21
24. Slynarski K: Osteoindukcja nowo tworzących kości wielopiętrowych kości szkieletu Orthop Trauma Rehab 2000; 3, 8-10
25. Hammer R, Hammerby S, Lindholm B. Accuracy of radiologic assessment of tibial shaft fracture union in humerus. ClinOrthop 1985; 199, 233-238.
26. Connolly et al: Autologous Marrow Injection as a substitute for operative grafting of tibial nonunions. ClinOrthop 1991; 266, 259-270
27. Paley D, Young MC, Wiley AM. Percutaneous bone marrow grafting of fracture and bony defects. An experimental study in rabbits. ClinOrthop 1986; 208:300-12
28. Healy JH, Zimmermann PA, McDermott JM. Percutaneous bone marrow grafting of delayed and nonunion in cancer patients. ClinOrthop 1990; 256:281-5.

Source of Support: None Declared
Conflict of Interest: None Declared