

Research Article

Evaluating Effects of Autologous Bone Marrow Injection Obtained From Reaming of Intramedullary Interlocking Nailing in Closed Diaphyseal Fresh Tibia Fractures in Fracture Healing

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ABSTRACT: We performed a prospective, randomized controlled study on 60 patients with fresh closed diaphyseal tibial fractures to determine the effect of percutaneous autologous bone marrow injection on union rate. Sixty patients were randomized into a group of 30 patients each. 30 patients were treated with reamed intramedullary interlocking nail and 30 patients were treated with combination of reamed intramedullary interlocking nail and with 15-20 ml of autologous bone marrow injection at the fracture site percutaneously obtained at the time reaming. Fracture Union was defined clinically as ability to walk without any support and pain and radiologically as solid callus bridging the fracture fragments taking average mean time of 20.03 weeks in Interlocking nail group and 18.23 weeks in interlocking nailing with percutaneous autologous bone marrow injection (p value =0.03). Other possible determinants of union, complications and cost incurred in the treatment were similar in both the groups. The secondary procedures applied were more in the control group than in study[case] group.

Introduction:

Tibial diaphyseal fractures are the most common fractures encountered by orthopaedic surgeons with a frequency of 26 tibial diaphyseal fractures per 100,000 of population per year, males being more commonly affected than females with an incidence of 41 per 100,000 of population when compared to 12 of 100,000 population respectively.¹ Delayed and non-union of fractures, a common problem, is quite annoying. Several methods such as bone grafting have been used to counter this problem. Bones like tibia are notorious for delayed and non-union.²

In fracture shaft of tibia, union is delayed due to comparatively poor blood supply, and its compounding nature. Failure of implant due to infection retards osteogenesis at fracture site. Tibial fracture has been posing problems to the orthopaedists the world over.

Sir John Charnley (1961) said, 'We still have a long way to go before the best method for treating a fracture of the shaft of the tibia can be stated with finality.' Tibia, because of its very location is frequently exposed to injuries. It's one third surface being subcutaneous, it often suffers from open fractures. Furthermore, the blood supply to the tibia is already precarious and it is guarded by the presence of hinge joints at the knee and the ankle which do not allow for adjustment of the rotatory deformity.³

In this era of modern surgery various techniques like internal fixation by Dynamic compression plate and screws, interlocking nail, external fixator and Ilizarov technique have been tried to revolutionize the treatment of fractures with impending complications. Another technique of Osteogenesis

by Electromagnetic stimulation has also been useful. But bone grafting is still the standard orthopaedic procedure for complications like delayed and non- union of fractures.

A number of animal studies have demonstrated the osteogenic property of bone marrow stromal or stem cells in fresh fractures.^{4,5,6} Autologous bone marrow injection has also been used successfully in the treatment of delayed union and non-union of tibia fractures in human beings.^{6,7}

Various methods of osteoinduction in current practice are either extensive or expensive. Bone marrow as a natural source for osteoinduction was first described in the year 1869. Phemister described the autologous cancellous bone grafting to stimulate skeletal repair for non-union and delayed union.⁸ This concept is still unchanged. The osteogenic capacity of bone marrow was first demonstrated in rabbits as early as 1869 by Goujon⁹.

McGaw and Harbin (1934) were among the first to demonstrate the osteogenic activity of bone marrow.⁴ The concept of percutaneous bone marrow was introduced by Herzog in 1951.¹⁰ There have been many studies to demonstrate the osteoinduction properties and promote better healing and avoid delayed and non-unions. But few have combined these procedures with internal fixation like Govender et al.,(2002) in a prospective randomized controlled trial in 421 open tibial fractures, showed that application of recombinant human bone morphogenetic protein-2 (rhBMP2)-impregnated absorbable collagen sponge over the fracture along with intramedullary nail fixation was significantly superior to intramedullary nail fixation alone in reducing the

frequency of secondary intervention (because of delayed union) and accelerating fracture and wound healing.¹¹ Many have performed percutaneous autologous bone marrow injection in delayed and non-unions but Khanal et al (2004) performed a prospective, randomized study on 40 patients with fresh closed fractures of the tibial shaft to determine the effect of autologous bone marrow injection on the union rate. All fractures receiving bone marrow injections united in 3.65+/-0.49 months; 19/20 fractures treated conventionally united in 4.31+/-0.48 months (p=0.0004).¹²

Connolly et al. (1991), Verma and Kulshershta (1997) and Goel et al. (2005) injected bone marrow in non-union cases of tibia.^{13,14,15} Healey et al. (1990), R Bhargava et al. (2007) and Wani et al (2013) have injected bone marrow in delayed union.^{16,17,18} In the present study we attempted to combine percutaneous bone marrow procedure along with internal fixation to reduce the secondary procedures and improve bone healing in fresh tibia fractures. Bone grafting can be tried for improved bone healing without secondary procedures in case of fresh fractures.¹⁹

MATERIAL AND METHODS

Adult males and females age group presenting with tibial shaft fracture to orthopaedic department NIMS Medical College & Hospital, Shobha nagar, Jaipur were admitted and evaluated in the study from June 2015 to November 2016. Ethical clearance and informed consent were taken prior to study. Around 60 Patients fulfilling our inclusion criteria and those who were surgically fit, were included in the study.

Inclusion criteria:

1. Patients between 20 -65 years of age after epiphyseal closure.
2. Closed diaphyseal fractures.
3. Patients fit for surgery.
4. No systemic illness.

Exclusion criteria:

1. Patients age >65 years and <20 years without epiphyseal closure.
2. Patients with open fractures.
3. Patients unfit for surgery.
4. Patients not willing for surgery.

The patients were selected based on the history, clinical examination, radiography. The orthopaedics trauma association (OTA), AO classification of tibial diaphyseal fractures was followed for typing the tibial fracture. All the selected patients were treated with intramedullary interlocking nail and regular follow up for a period of six months was maintained at 4 weeks interval. The postoperative follow up and assessment was based on tenny and wiss clinical assessment criteria which is based on 100 point system by

grading as poor, fair, good or excellent.²⁰

RESULTS

In our study total 60 patients of closed diaphyseal fracture of tibia were treated with intramedullary interlocking nail (30 patients-controls) and combination of intramedullary interlocking nail and autologous bone marrow injection obtained while reaming at the fracture site. (30 patients-cases).

We included all patients between 21 to 65 years age. The mean age was 35.5years and 37 years for interlocking nailing with percutaneous autologous bone marrow injection and Interlocking nail, respectively. Males were predominantly affected in our study accounting for 90% as compared to females (10%). Commonest mode of injury was high velocity road traffic accidents that accounted for 60% in this study. The right side was more involved i.e. 68.3%, as compared to left side.

Most common fracture pattern seen was type 42-A (63.4%) and type 42- B(33.4%) and 42-C(3.3%). In our study we included distal 42 type A, 42 type B and 42 type C

Concomitant fibular fracture was present in 24 out of 30 cases (80%) and 22 out of 30 controls (73%).

Mean Operative time was 79 mins in Interlocking group ranging from 60-100 mins and was about 73.33 mins in interlocking nailing with percutaneous autologous bone marrow injection ranging from 55-95 mins .In our study patients in case group had a stay of 7.4days (mean) compared with 7.13 days (mean) of control group. The mean delay in surgery was 2 days in case group and 2.56 days.in control group.

Partial weight bearing was started in 6.16 weeks in interlocking nailing with percutaneous autologous bone marrow injection (range 3-10 weeks) which was significantly early than 6.7 weeks in Interlocking group (range 3-10 weeks) in this study.

Full weight bearing was started in 12.1 weeks in Interlocking group (range 8-18 weeks) which was 11.43 weeks in interlocking nailing with percutaneous autologous bone marrow injection (range 8-17 weeks). In the present study, the mean union time in the experimental group is 18.23weeks was significantly less than in the control group is 20.03 weeks.(table 1) (figure 1&2)

Table1: Descriptive data of **Radiological union**

	Mean(in weeks)	Std. Deviation	Mean difference	P value
Case	18.23	3.01	1.8	0.03 (S)
Control	20.03	3.38		

Test applied: unpaired t test

Table 2: Union time in different studies

Author	Group	Average time for union (weeks)
Lawrence B Bone ²¹ ,1986	IM nailing in closed tibia fractures	19weeks
Court brown et al ²² ,1996	Reaming im nailing	15.4 weeks
Khanal et al ¹² ,2004	Percutaneous bone marrow in closed fresh fractures	14.6+/-2
A Goel et al ¹⁵ ,2005	Percutaneous bone marrow injection in non-union tibia fractures	14 weeks
Shenoy et al ²³ ,2014	Autologous bone marrow in delayed union fracture tibia with external/internal fixator	12-18weeks
Chauhan, et al ²⁴ , 2015	Interlocking Nail in Diaphyseal Fracture of Tibia	20.13weeks
Present study	Case group	18.23 weeks
Present study	Control group	20.03 weeks



Figure 1: immediate postoperative xray of case with bonemarrow injection and intramedullary nailing



Figure 2: xray showing union after 12 weeks.

Complications encountered in control group were superficial infection in 2 patient (6.66%), delayed union in 3 patients (10%) and anterior knee pain in 5 patients (16.66%), Whereas in case groups were superficial infections in 3 patients (10%) and anterior knee pain in 6 patients (20%).

In our study, 7 out of 30 patients required secondary procedures in Interlocking group and 3 out of 30 patients in interlocking nailing with percutaneous autologous bone marrow injection. In our study, in control group the secondary procedures done were dynamisation in 4 patients (13.33% and bone graft in 3 patients (10%), whereas in case group dynamisation is done in 3 (10%) patients. In our study, excellent results were more common in Interlocking nail groups (53.33%), compared to interlocking nailing with autologous bone marrow injection (40%). The poor results according to tenny and wiss clinical assessment criteria were same in both groups. (Table 3)

Table 3: Qualitative data of Results

	Case	Control	Total	P value
Excellent	12 (40)	16 (53.3)	28 (46.7)	0.75
Fair	6 (20)	4 (13.3)	10 (16.7)	
Good	10 (33.3)	8 (26.7)	18 (30)	
Poor	2 (6.7)	2 (6.7)	4 (6.7)	

Test applied: Chi-square test

DISCUSSION

In our study, results are similar to other studies with bone marrow grafting along with internal fixation. Percutaneous bone marrow injection along with reaming intramedullary interlocking nailing fixation in acute tibial fractures is effective for bone union and for decreasing the rate surgical revision.

Results showed significant union rate compared to cases when only reaming intramedullary interlocking nailing is done, however these union rates were comparable but not significant

with other studies. In the study by Dai j et al, they concluded that BMP is more effective than controls in acute tibial fractures, for bone union and for decreasing the rate of surgical revision to achieve union. For the treatment of tibial fracture non-union, BMP leads to similar results to as autogenous bone grafting. Finally, well designed RCTs of BMP for tibial fracture treatment are also needed.²⁵

This is the first clinical randomized controlled trial that goes on to prove the experimentally demonstrable osteogenicity of bone marrow injection in fresh fractures of the human tibia when used along with intramedullary interlocking nailing. In the present study, the mean union time in the study group (18.23 weeks) was significantly less than in the control group (20.03 weeks) with a p value of 0.03, thus validating the high osteogenic potential of autologous bone marrow. In study of Govender et al., a prospective randomized controlled trial in 421 open tibial fractures, showed that application of recombinant human bone morphogenetic protein-2 (rhBMP2)-impregnated absorbable collagen sponge over the fracture along with intramedullary nail fixation was significantly superior to intramedullary nail fixation alone in reducing the frequency of secondary intervention (because of delayed union) and accelerating fracture and wound healing.²

The secondary procedures like bone grafting have been done among intramedullary interlocking nailing group but not in intramedullary interlocking nailing with bone marrow injection group. Thus it has similar results as that of BMP-2 application in acute tibial fractures, but this has to be done in a very large sample size to adequately assess the difference in non-union rates. Garrison KR, Shemilt I, et al. (2007), a meta-analysis on BMP role in fracture healing concluded that fracture healing without secondary procedures may occur more frequently when BMP is used at the time of surgery for acute tibial fractures.²⁶

Bone marrow injection used in our study has been obtained while reaming the medullary cavity. Reaming process of intramedullary interlocking nailing overcomes the disadvantage of donor site morbidity as compared to other studies where bone marrow is aspirated from anterior iliac crest and other sites. Thus we utilised the invaluable bone marrow that is going waste during the process of reaming in interlocking intramedullary nailing. This is a cost effective procedure as compared to application of bone morphogenic proteins used in other studies, which cannot be used in third world countries. The superficial infection rates were comparable in both groups however it has been overcome by effective antibiotic therapy and proper wound care.

In our study, the results were evaluated according to the Tenny and Wiss criteria. There were 93% good to excellent results in both the groups treated with Interlocking intramedullary nailing and Interlocking intramedullary nailing with autologous bone marrow injection.

Conclusion- We would like to highlight that bone marrow

obtained at the time of reaming, used as percutaneous bone marrow injection is a limited invasive technique, which could be applied for acute fractures along with intramedullary nailing, as a simple, safe, inexpensive and effective method useful for union, without requiring secondary procedures.

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