Original Article

Outcome of Autogenous Bone Marrow Injection in Tibial Fractures with Signs of Delayed Union

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ABSTRACT

Objective: To determine the outcome of autogenous bone marrow injection in tibial fractures with signs of delayed union in terms of clinical and radiological evidence of union.

Study Design: Descriptive randomized prospective study

Place and Duration of Study: This study was conducted at the Department of Orthopedic Surgery, LRH, Peshawar for a period of 6 months from January, 2020 to July, 2020.

Materials and Methods: Patients admitted with delayed union of tibial shaft fractures were included in the study. Under local anesthesia, bone marrow is aspirated from the anterior iliac crest using a special bone marrow aspiration needle into heparinized syringes to avoid clotting of the aspirate. The bone marrow is aspirated from multiple sites to minimize dilution of the aspirate with blood. Under fluoroscopy control, the aspirate is injected percutaneously into and around the fracture site.

Results: Total 38 patients include with delayed union of tibial fractures. 32 (84.2%) males & 06 (15.8%) females. In 22 (57.9%) patients mid-shaft of tibia was involved followed by distal tibia in 9(23.7%) patients and proximal tibia was involved in 7(18.4%) patients. 25(65.8%) patients were smokers while 13(34.21%) patients were nonsmokers. In 22 (57.5%) patients right side of limb was involved while in 16 (42.5%) left side of limb was involved. In 18 (47.5%) patients there is only 1 follow up followed by 2 follow ups in 11(28.9%) and 3 follow ups in 9(23.7%) patients. In 30 patients (78.94%), union was established after 3 months of follow-up and at the end of six months follow-up in 6(15.78%) patients. In delayed union of tibial fractures, the union rate was 94.73%.

Conclusion: Percutaneous autogenous bone marrow injection is a slightly invasive, safe, & inexpensive treatment option for tibial delayed unions and should be considered when the retained hardware seems to be intact & stable.

Key Words: Delayed union, Bone marrow, long bones, fracture healing, tibial shaft fractures

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INTRODUCTION

Delayed union is one of the most common complication in fracture healing which an orthopedic surgeon faces quite commonly. [(1)] Delayed union is defined as failure to reach bony union by 6 months or an un-united fracture that continues to show progress towards healing but taking time longer than expected. The delayed union is not always non-union but it can lead to one.[(2)]

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The most frequently involved bone is tibia. Both systemic & local factors are responsible for delayed union especially inadequate reduction, improper immobilization, distraction, loss of blood supply secondary to open fractures, infection and drugs intake etc.[(3)]

There are various methods available for the treatment of delayed union, each with a different level of invasiveness & outcome.[(4)] Low-intensity ultrasound or electromagnetic stimulation are two non-invasive approaches. Invasive method includes the use of bone morphogenic protein, stem cell therapy, open bone grafting, bone substitutes and finally Ilizarov, which is a versatile method of distraction osteogenesis. [(3)]

Open grafting of bone is related with risk of complications like infection, formation of hematoma & nerve injury etc.[(5)] The idea of percutaneous bone marrow injection was established to overcome the problems associated with traditional autogenous open bone grafting. [(6)]

Mesenchymal stem cells, also known as marrow stromal cells, are found in adult bone marrow. MSCs can differentiate into osteocytes, osteoblasts, adipocytes

& chondrocytes which are connective tissue cells. MSCs' ability to develop into bone-producing cells has sparked an interest in their clinical application in orthopaedic injuries to improve fracture repair & to treat bone abnormalities.[7] The marrow is taken from iliac crest by needle and then using a percutaneous approach, injected at the fracture site under the guidance of an image intensifier. [8]

Bone marrow is logically the transplant of choice since it is the only tissue that includes both inducible and determined osteoprogenitor cells.[9] Union has been achieved in 75% - 90% of reported tibial delayed union case series treated with bone marrow aspirate. [8]

Bone marrow injection promotes healing and it has many distinct advantages over the standard operative grafting. First, the complications at the donor and recipient sites are significantly diminished. Second, it can be performed in cases that are not fit for open bone grafting because of the poor condition of skin. Third, it can be repeated easily. Fourth, it utilizes the most osteogenic cells of a bone graft. Fifth, it can be performed under local anesthesia & avoids the risks of general and spinal anesthesia and can be used for patients with contraindication for general and spinal anesthesia. Sixth, it can be performed on an outpatient basis and decreases hospital stay. Seventh, it is cost effective.[9]

As our hospital is a very busy trauma Centre and receiving a large number of patients on daily basis, the procedure will be performed on patients as outpatient procedure. The procedure is suitable for high risk patients who are otherwise unfit for spinal and general anesthesia and for patients who are not willing for 2nd major procedure.

MATERIALS AND METHODS

This descriptive randomized prospective study was conducted from 16 Jan to 15 July 2020 in Orthopedic B Ward, Lady Reading Hospital Peshawar. It was done with the permission of the institutional review board. The minimum sample size was 651 calculated by WHO calculator, keeping the confidence interval 95%, standard deviation 1.96, the margin of error 0.012 and the expected prevalence/proportion of delayed union of tibia is 2.5%.[8] Due to rare cases of tibial delayed union previously operated with tibia plating, we can only include 38 patients in my study in the duration of 06 months.

All patients with delayed union of tibial fractures previously operated with tibial plating and also presented with 18-60 years with ASA1 and ASA2 status were included from the study. Patients with pathological fractures, malnourished patients (having lymphocyte count less than 10%) and infected fractures were excluded.

Patients history and examination were obtained. All surgeries conducted by single experienced orthopedic surgeon, CPSP fellow having minimum of five years of experience. Once the surgery is completed, standard post-operative protocols will be maintained. All patients were followed up for the next 4-6 weeks to detect clinical and radiological union.

Data was entered in SPSS 23. Age was presented as mean & standard deviation. Categorical data like gender, indication of surgery, smoking, post-surgery alignment and efficacy presented as frequency and percentages. Efficacy was compared by applying chi square test at $\leq$ 0.05 level. Test were applied on post stratification of age, gender, smoking and post-surgery alignment in which p Value less than 0.05 was considered as significant.

RESULTS

Total 38 patients were enrolled. There were 32 (84.2%) males & 06 (15.8%) female. The average age was 41.26 ± 10.87. The majority of the patients were between the ages of 31 and 40, 17 (44.73%) followed by 41-50 years 08 (21.05%). Table: 1. In 22 (57.9%) patients mid-shaft of tibia was involved followed by distal tibia in 9(23.7%) patients and proximal tibia was involved in 7(18.4%) patients. 25(65.8%) patients were smoker while 13(34.21%) patients were nonsmokers. Post-surgery alignment was good in 23(60.5%) while poor in 15(39.5) patient. Table: 2.

Table No. 1: Age & Parity Distribution

		Frequency (%)
Age	**Mean± SD**	41.26±10.87
	18-30 years	6(15.7%)
	31-40 years	17(44.73%)
	40-50 years	8(21.05%)
	51-60 years	7(18.42%)
Gender	**Male**	32(33%)
	Female	6(67%)

Table No.2: Frequency of Habits, fractures site, post-surgery alignment wise

		Frequency (%)
Habits	Smoker	25(65.8%)
	Non-smokers	13(34.21%)
Fracture site wise	Proximal	7(18.4%)
	Midshaft	22(57.9%)
	Distal	9(23.7%)
Alignment	Good alignment	23(60.5%)
	Poor alignment	15(39.5%)

Time to intervene after injury (duration in months) was 7 months in 15(39.5%) patients, 6 months in 13(34.2%) patients, 8 months in 9(23.7%) patients while 9 months in only 1(2.6%) patient. 27(71.1%) patients were given 2 injections while 11(28.9%) patients were given only 1 injection. In 18 (47.5%) patients there is only 1 follow up followed by 2 follow ups in 11(28.9%) and 3 follow ups in 9(23.7%) patient. Table:3

Table No.3: Distribution of duration of months, no of injection and follow ups

		Frequency(%)
Duration in months	**6**	13(34.2%)
	7	15(39.5%)
	8	9(23.7%)
	9	1(2.6%)
No. of injection	**One**	11(28.9%)
	Two	27(71.1%)
No. of follow ups	**One**	18(47.4%)
	Two	11(28.9%)
	Three	9(23.7%)

Table No.4: Frequency Attitude aboutThree IUCD as EC

		Frequency(%)
Limb Side	Right	22(57.9%)
	Left	16(42.1%)
Fracture union wise	Healed Fractures	36(94.7%)
	Non-union	2(5.27%)
Effectiveness (clinical/radiological/ both)	Clinical	3(7.9%)
	Radiological	7(18.4%)
	Both	28(73.7%)
Indication of surgery wise	Delayed union	36(94.7%)
	Non-union with implant failure	2(5.27%)

Table No.5: Stratification of effectiveness with respect to age, Gender, smoking status and indication of surgery

		Effectiveness		P value
		Yes	No	
Age	18-30 years	5	1	0.69
	31-40 years	15	2	
	40-50 years	7	1	
	51-60 years	5	2	
Gender	Male	29	3	0.78
	Female	5	1	
Smoking status	Smokers	17	8	0.57
	Non-smokers	11	2	
Indication of surgery	Delayed union	33	3	0.59
	Non-union with implant failure	2	0	

In 22 (57.5%) patients right side of limb was involved while in 16 (42.5%) left side of limb was involved. Post intervention effectiveness was clinically and radiologically in 28(73.7%) patients followed by only radiologically in 7(18.4%) patients while only clinically in 3(7.9%) patients. In 30 patients (78.94%), union was established after 3 months of follow-up and at the end of six months follow-up in 6(15.78%) patients, only two people (5.26%) were unable to form a union at the end of the six-month follow-up period. Other procedure, also open bones grafting or revisions surgery, was required for these patients. In delayed union of tibial fractures, the union rate was 94.73%. Table: 4.

DISCUSSION

There is no universally accepted definition of delayed union of a fracture. It is known that every given type of fracture tends to unite within a certain time period. Delayed union is defined as failure to reach bony union by 6 months or an un-united fracture that continues to show progress towards healing but taking time longer than expected.[10, 11] Bone marrow injection promotes healing more rapidly and effectively compared with standard operative grafting. It has many distinct advantages over the standard
operative grafting.

- First, the complications at the donor and recipient sites are significantly diminished.
- Second, it can be performed in cases that are not fit for open bone grafting because of the poor condition of the skin.
- Third, it can be repeated easily.
- Fourth, it utilizes the most osteogenic cells of a bone graft and does not introduce devitalized tissue (dead bone) and this could be used in children without damaging the growth plate.
- Sixth, it can be performed under local anesthesia and avoids the risks of general anesthesia or can be used for patients with contraindication for general anesthesia.
- Seventh, it can be used for certain clinical situations that would not be strong enough indications for open bone grafting, such as delayed union or fractures prone to delay union.
- Eighth, it is safe.
- Ninth, it is practical and time saving, as it can be performed on an outpatient basis and decreases hospital stay.
- Tenth, it is cost effective

However, bone marrow injection has some disadvantages; these include the lack of providing immediate mechanical stability as well as the risk of dilution with peripheral blood.[12]

In our study the mean age of the patients was 41.26 years. This was close to the studies by Nazar M et al[3]

and Akram M et al[7] 38 years while in Elsatter TA et al(9) the mean age was 37.66 years.

In our study we had 38 patients with male-to-female ratio was 5.4:1. This was close the study by Elsatter TA et al[9] which is 4:1 and by Nazar M et al[3] which was 1.5:1. In our study we have 25 smokers and 13 nonsmoker's patient which was close to the study Smoking was associated with an increased rate of non-union and delayed union as well as an increase in time to union in fractures of the tibial shaft.[13] Smoking is an important modifiable factor associated with delayed healing of fracture. Bones of smokers take longer to unite following tibia fractures or established delayed union.[13, 14]

In our study midshaft of tibia was in 22 cases while in the study by kaseem et al[15] the distal tibia was involved in maximum cases. Post-surgery alignment was good in 23 patients and poor in 15 patients who develop delayed union. It was close to the study by Nazar M et al[3] where post-surgery alignment was good in 30 patients and poor in 12 patients.

In our study two injections were given to 27 patients while one injection was given to 11 patients while in study by Elsatter TA et al[9, 16] three injection were given to 11 patients, four injection were given to 7 patients and two injection were given to 2 patients.

In this study there was one follow-up in 18 patients, two follow-ups in 11 patients and three follow-ups in 9 patients. While in the study by Elsatter TA et al and Akram M et al there were two follow ups in maximum patients. Right side of limb was involved in 22 patients and left side in 16 patients. It was close to the study by Akram M et al [7] and Nazar M et al [3]where the right to left ratio was 3:2.

Effectiveness (fracture healing) of Bone marrow injection was seen both clinically and radiologically while in study by kaseem et al [15] effectiveness was assessed only radiologically and in study by Elsatter TA et al [9] effectiveness was assessed only clinically. Union rate was 94.73% in delayed union of tibial fracture.it is close to the study by Nazar M et al [3] and Akram M et al [7] where the union rate was 92%.

CONCLUSION

Bone marrow aspirate is a big source of osteoinductive factors create by resident cells like endothelial cells, MSCs, osteoblasts, platelets & macrophages. It's essentially an auto-graft without bone matrix, and clinical evidence of its healing capacity is growing. In more nearly 90% of patients, cutaneous BMA injections for delayed unions resulting in lengthy bone bridging. At the end, we showed that protracted bone healing with autogenous BMA was equally effective as ABG therapy in achieving delayed union.

The conclusion of the study, percutaneous autologous bone marrow injection is slightly invasive, safe & cost-effective treatment option for tibial delayed unions & should be explored when the retained hardware appears to be intact & stable

Smoking is a significant modifiable factor linked to fracture healing delays. Smokers; bones take longer to fuse, after tibia fractures or established delayed union. [13,14].

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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