Surgical fixation and grafting of traumatic distal tibia atrophic nonunion with or without platelet-rich plasma: A comparative study

Ghadeer H. Majeed, Mohammed Sh. Al-Edanni, Mokhalad Waleed Hatem, Sadeq A. Al-Mukhtar

Department of Orthopedic Surgery, Al-Kindy College of Medicine, University of Baghdad and Ministry of Health, Baghdad, Iraq

Objective: To compare distal tibia nonunion plating and grafting with and without platelet-rich plasma (PRP) regarding union rate, union time and complications

Methodology: In this prospective comparative study, 32 patients with nonunion tibia from July 2017 January 2019 were divided into two groups: group A (16 cases) were treated by plating and grafting with PRP and group B (16 cases) were treated by plating and grafting only.

Results: There was higher union rate in group A related to group B (81% vs. 69%) but statistically

not significant (p=0.256). Healing duration was significantly longer in group B (6.11 vs. 5.12) months(p=0.001). Regarding the postoperative pain, it was significantly less in groups A than group B.

Conclusion: Combining PRP with autologous bone graft results in a higher union rate, less healing duration, less post-operative pain, and more callus formation. (Rawal Med J 202;45:629-632).

Keywords: Tibial nonunion, bone graft, plateletrich plasma.

INTRODUCTION

Fractures of the tibia are seen in 4% of all fractures and relatively high rates of nonunion and malunion. The lower third of the tibial shaft is common site for fracture and about 25% are open type. The best management remains a matter of dispute, and in many states, there may be no solitary "best" management, depending on the "personality" of the fracture. Nonunion of the tibia are not unusual due to the subcutaneous location of the tibia and less soft-tissue coverage, leading to morbidity, need for frequent surgical procedures to treat, and permission the patient with functional debits. 3.4

The U.S. FDA defines a nonunion as a fracture that is at least 9 months old and has not shown any signs of healing for three consecutive months.⁵ Tibial nonunion occurs in about 2-10% of all tibial fractures.⁶ Fracture repair comprises cell recruitment, osteoinduction, and osteoconduction.⁷ Platelets have a chief role in cell recruitment in cooperation in the initial hemostatic phases and the additional phases of wound curing, discharging numerous growth factors and cytokines.⁸ Plateletrich plasma (PRP) is an autologous concentration of

human platelets in a small capacity of plasma. This preparation has a very high concentration of growth factors resultant from the granules released upon platelet activation and capable to motivate the migration and growth of bone-forming cells. ⁸⁻¹⁰ In this study, we compared distal tibia nonunion plating and grafting with and without PRP regarding union rate, union time and complications.

METHODOLOGY

This prospective study of 32 patients with distal tibia nonunion in the young age group was conducted in the Department of Orthopedics, Alkindy Teaching Hospital, Baghdad, Iraq, from July 2017 to January 2019 with follow up for at least nine months.

Inclusion criteria included both gender, unilateral limb, atrophic nonunion (aseptic), distal tibia fracture, age >20 years <55 years, bone defect <2 cm, and those treated conservatively by casting. Exclusion criteria were skeletally immature and >55 years old, hypertrophic nonunion, bone defect >2 cm, open or pathological fracture, patients treated with previous surgery, and patients unhealthy for an autologous gift (platelet count $<130 \times 10^9$).

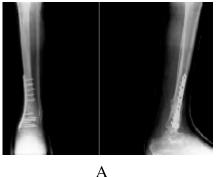
Patients were divided into two groups every other patient, all patients treated by open reduction and internal fixation by plating (locking plate) with an autologous bone graft from iliac crest. The first group (group A) with 16 patients (14 males and 2 females) we added PRP, and the second group (group B) with 16 patients (13 males and 3 females) without PRP.

All patients were assessed by full history and proper examination. Written consent after a full explanation was taken from all included patients. X-ray AP and lateral leg views were done for all patients, no CT-scan or bone scan were needed. All patients did preoperative anesthetic workup and preparation and ceftriaxone was given I.V to all

patients within one hour before surgery.

During surgical fixation, no tourniquet was used, for group A before skin incision blood was drawn from the patient 50cc from the cephalic or median cubital vein with 50 cc syringe with anticoagulant and then put it in PRP special tube, all done under aseptic technique and all preparation done in the operating theater. We fixed the fracture by 3.5 mm anatomical locking plate medial type. Then we apply the graft to fill the gap at the fracture site and we insert the prepared PRP only for group A by applying most of it at the graft and taking the gel layer to make a puffy coat surrounding the graft. The fibula was left without intervention. No drain was inserted and no back slab was used.

Figure. Post-operative X-Ray A. 3months, B. 6 months C. 9 months.







Postoperatively, patients started mobilizations from bed day with supports and no weight-bearing for the first 6 weeks. They visited orthopedic clinic at 2 weeks, 6 weeks, 3 months, 6 months, and 9 months postoperatively and each visit infection and wound problems, ankle dorsal flexion and Plain X-ray AP and lateral view were checked (Figure). Pain at the fracture site after starting partial or complete weight-bearing by the m

Statistical Analysis: The data were loaded into IBM-SPSS V24 software for statistical analysis. p<0.05 was considered as a discriminated point of significance.

RESULTS

The mean age was 35.43 ± 9.85 years (range 20-52). No statistically significant difference in proportional distribution between genders in both groups in this study (p=0.677) (Table 1). The mean

of healing duration in the PRP group was 5.12 ± 0.85 months shorter than group B (6.11 ± 0.45 months) and it was significantly (p=0.001). Visual analog score postoperatively was significantly higher in group B than group A at day 45 visit (p=0.047) and the same thing was noticed at 2^{nd} and 3^{rd} visit with p=0.001, 0.007, respectively, while there was no significant difference in pain at 4^{th} visit (p=0.151).

Table 1. Distribution of studied cases according to gender and the use of PRP.

Gender	N	%	Group A (PRP)	Group B (without PRP)	P-value
Male	27	85%	14(87.5%)	13(81%)	0.677
Female	5	15%	2(12.5%)	3(19%)	0.077

Table 2. Functional outcome regarding pain and callus formation and healing duration.

Functional outcome		Group A (PRP)	Without PRP	P Value
Healing duration	Mean ±SD	5.12 ±0.85	6.11±0.45	0.001
VAS	Day 45	2.6 ± 0.94	3.15 ± 0.74	0.047
	Day 90	1.3 ± 0.57	2.6 ± 0.82	< 0.001
	Day 180	0.5 ± 0.13	1.4 ± 0.63	0.007
	Day 70	0.25 ± 0.09	0.65 ± 0.45	0.151
X ray	Day 45	0.65 ± 0.18	0.45 ± 0.11	0.257
	Day 90	2.85 ± 0.88	1.4 ± 0.32	0.052
	Day 180	2.91 ± 0.91	2.3 ± 0.89	0.1
	Day 70	3.4 ± 0.88	3 ± 1.02	0.194

Table 3. Union rate for both groups.

Study arm		Group B (without PRP)	P Value	
Complete	13(81%)	11(69%)	0.256	
Failure	3(19%)	5(31%)	0.230	

Although the means of radiological healing (callus formation) formed in the PRP group at days 45, 90, 180, 270 were showed to be higher than that in the group without PRP, the differences between means were not significant (p=0.257, 0.052, 0.1, 0.194, respectively (Table 2).

The union rate was 81% of patients (13 patients out of 16) with PRP added showed complete union while 69% showed complete union in group B and there was no significant difference (p=0.256) (Table 3).

DISCUSSION

For healing rate and duration, it was found that the use of PRP increased the healing rate and decreased the duration needed for healing significantly. In our study, the healing rate was 81% in PRP group while 69% in the group B, similar to Malhotra et al, ¹¹ Memeo et al, ¹² Bielecki et al, ¹³ Thor et al, ¹⁴ Lee et al ¹⁵ and Ghaffarpasand et al. ¹⁶

A study by Sanchez et al recommended repeat at least three times injection of PRP to obtain a complete union.¹⁷ Studies against were those of Maricond et al¹⁸ and Say et al who did not obtain satisfactory healing of lower extremity non-union fracture with PRP injection.¹⁹

Some animal researchers used PRP in management

of long bone nonunion defects like Hakimi et al and found that combining PRP and autologous cancellous bone graft resulted in significantly improved bone regeneration related to using cancellous bone graft only.²⁰

By comparing of all those results to our study, we found most of them agreed to our study and results that most of the effect appears in the early stages of healing regarding pain or the callus formation. It will be comparable in late stages and this is might be due to the concentration of growth factors in PRP which decreases with time causing in decreased effect on healing.

CONCLUSION

Using the PRP in management of long bone nonunion combined with autologous cancellous bone graft with plate fixation showed a non-significant higher rate of union with a significant decrease in union time. Healing parameters regarding postoperative pain and callus formation showed better results in the PRP group but in the early stage (first 4 months).

Author contributions:

Conception and design: Mohammed Sh. Al- Edanni, Ghadeer H. Maieed

Collection and assembly of data: Ghadeer H. Majeed, Mohammed Sh. Al-Edanni, Mokhalad Waleed Hatem

Analysis and interpretation of the data: Sadeq A. Al-Mukhtar Drafting of the article: Ghadeer H. Majeed

Critical revision of the article for important intellectual content:

Mokhalad Waleed Hatem

Statistical expertise: Mohammed Sh. Al-Edanni, Sadeq A. Al-Mukhtar

Final approval and guarantor of the article: Mohammed Sh. Al-Edanni, Ghadeer H. Majeed

Corresponding author email: Mohammed Sh. Al-Edanni: mohammedaledanni@gmail.com

Conflict of Interest: None declared

Rec. Date: Feb 11, 2020 Revision Rec. Date: May 14, 2020 Accept Date: Jun 14, 2020

REFERENCES

- Boulton Ch, O'Toole RV. Tibia and fibula shaft fractures. In: Court-Brown CM, eds. Rockwood and Green's Fractures in Adults. 8th Ed. Philadelphia, PA: Wolters Kluwer; 2015: 2415-2427.
- Dimitriou Ro, Giannoudis PV. Tibial shaft fractures. In: George Bentley, eds. European Surgical Orthopaedics and Traumatology. New York: Springer; 2014: 2854-2856
- 3. Rodriguez-Buitrago AF, Jahangir A. Tibia Nonunion. Treasure Island, FL: StatPearls; 2018.
- 4. Dailey HL, Wu KA, Wu PS, McQueen MM, Court-

- Brown CM. Tibial Fracture Nonunion and Time to Healing After Reamed Intramedullary Nailing: Risk Factors Based on a Single-Center Review of 1003 Patients. J Orthop Trauma. 2018;32(7):e263-e269.
- 5. Calori GM, Mazza EL, Mazzola S. Non-unions. Clin Cases Miner Bone Metab. 2017;14(2):186–8.
- 6. Zura R, Watson JT, Einhorn T, Mehta S, Della Rocca GJ, Xiong Z, et al. An inception cohort analysis to predict nonunion in the tibia and 17 other fracture locations. Injury. 2017;48(6):1194-1203.
- 7. Rodriguez-Merchan EC, Forriol F. Nonunion: general principles and experimental data. Clin Orthop Relat Res 2004;419:4–12.
- 8. Dimitriou R, Tsiridis E, Giannoudis PV. Current concepts of molecular aspects of bone healing. Injury 2005;36:1392-404.
- 9. Latalski M, Elbatrawy YA, Thabet AM, Gregosiewicz A, Raganowicz T, Fatyga M. Enhancing bone healing during distraction osteogenesis with platelet-rich plasma. Injury 2011;42:821-4.
- Marx RE, Carlson ER, Eichstaedt RM. Platelet-rich plasma: growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod1998;85:638-46.
- 11. Malhotra R, Kumar V, Garg B, Singh R, Jain V, Coshic P, et al. Role of autologous platelet-rich plasma in the treatment of long-bone nonunions: a prospective study. Musculoskelet Surg. 2015;99(3):243–8.
- 12. Memeo A, Verdoni F, De Bartolomeo O, Albisetti W, Pedretti L. A new way to treat forearm post-traumatic non-union in young patients with intramedullary nailing and platelet-rich plasma. Injury. 2014;45(2):418–23.
- 13. Bielecki T, Gazdzik TS, Szczepanski T. Benefit of

- percutaneous injection of autologous platelet-leukocyterich gel in patients with delayed union and nonunion. Eur Surg Res. 2008;40:289–96.
- 14. Thor A, Franke -Stenport V, Johansson CB, Rasmusson L. Early bone formation in human bone grafts treated with platelet-rich plasma: preliminary histomorphometric results. Int J Oral Maxillofac Surg. 2007;36:1164–71.
- 15. Lee DH, Ryu KJ, Kim JW, Kang KC, Choi YR. Bone marrow aspirate concentrate and platelet-rich plasma enhanced bone healing in distraction osteogenesis of the tibia. Clin Orthop Relat Res. 2014;472(12):3789–97.
- 16. Ghaffarpasand F, Shahrezaei M, Dehghankhalili M. Effects of platelet-rich plasma on the healing rate of long bone non-union fractures: a randomized double-blind placebo-controlled clinical trial. Bull Emerg Trauma. 2016;4(3):134-8.
- 17. Sanchez M, Anitua E, Cugat R, Azofra J, Gua-Dilla J, Seijas R, et al. Nonunions treated with autologous preparation rich in growth factors. J Orthop Trauma. 2009;23:52–9.
- 18. Mariconda M, Cozzolino F, Cozzolino A, D'agostino E, Bove A, Milano C. Platelet gel supplementation in long bone nonunions treated by external fixation. J Orthop Trauma. 2008;22(5):342-5.
- 19. Say F, Turkeli E, Bulbul M. Is platelet-rich plasma injection an effective choice in cases of non-union? Acta Chir Orthop Traumatol Cech. 2014;81(5):340–5.
- 20. Hakimi M, Jungbluth P, Sager M, Betsch M, Herten M, Becker J, et al. Combined use of platelet-rich plasma and autologous bone grafts in the treatment of long bone defects in mini-pigs. Injury. 2010;41(7):717–23.