Basrah Journal Of Surgery

Bas J Surg, December, 22, 2016

THE ROLE OF AUTOLOGOUS PLATELET-RICH PLASMA IN THE TREATMENT OF SOME PAINFUL ORTHOPEDIC CONDITIONS: A BASRA EXPERIENCE STUDY

Midhat M Mahdi[*], Zuhair Al-Barazanchi[#]& Amer S AL-Saadi[@]

[*]MB,ChB, CABS, Consultant Orthopedic Surgeon, Orthopedic Department, Basrah General Hospital. [#]MSc, PhD, Consultant Hematologist, Basrah Children Specialty Hospital. [@]MB,ChB, DOS, Orthopedic Surgeon, Orthopedic Department, Basrah General Hospital, Basrah, IRAQ.

Abstract

The role of platelet-rich plasma in the pain relief and treatment of many orthopedic problems had gained lot of studies & practice. Yet, it hadn't been practiced in our locality. Thus, the study of its role in the treatment of certain enthsiopathies (plantar faciitis, achillis tendinitis and lateral epicondylitis) had been planned for.

A total of 63 cases of the three diseases were chosen for a case control study. They were divided into two groups: the case group who had been treated with local injection of autologous platelets rich plasma (prepared by the Trima accel cell separating machine) and the control group who were treated by local steroid injections. Pre and three post-treatment follow up of cases were done to assess the pain perception level using the simple visual analog scale (VAS).

Results had shown a statistically significant reduction in pain among cases compared to control. These results were comparable to many studies elsewhere in the world. This had led us to conclude the advice to encourage this type of therapy on a large scale of patients in the future with more detailed further studies about.

Introduction

Platelet-rich plasma (PRP), the plasma fraction of blood having a platelet concentration above baseline[1], had been used in orthopedics since the last few decades. Thousands of patients have gained benefits from this relatively safe therapeutic modality in many different problems like osteoarthritis, musculoskeletal soft tissue injuries (ligament, muscle and tendon tears) and tendinopathies. It is used either as the principal treatment or as an augmentation procedure (application after surgical repair or reconstruction[2-4]. The properties of PRP are based on the production, by the platelets, storage in both alpha and beta granules and release of multiple growth and differentiating factors that help in alleviating pain and modulating inflammatory reaction after activation, where, after the initial burst, more than 95% of the growth factors are secreted within one hour, and the continuum of their synthesis and secretion for the remaining several days of their life span[5]. These growth factors have a combined and complex interacting action on tissues to activate different sets of signaling pathways with the end result of ameliorating local inflammatory response[6,7].

Early success in using PRP to treat chronic refractory tendinopathy has led to consideration of its use in the management of recalcitrant cases of plantar fasciitis[8-12]. Local infiltration of PRP in Achilles tendinitis and lateral epicondylitis, had shown an improvement in pain relief and movement limitation, with all patients having at least moderate improvement and 96% of patients reporting mostly to complete improvement[13-17].

This study was designed to clarify the efficacy of autologous platelet-rich plasma local therapy in the selected tendinopathies (lateral epicondylitis, achillis tendinitis & plantar fasciitis compared to the local steroid therapy and which is more beneficial among each of them.

Patients and methods

A prospective case control study had been conducted in Orthopedic Department of Basra General Hospital between August 2013 and November 2014, where 66 patients with planter fasciitis, Achilles tendonitis and elbow lateral epicondylitis were selected. Diagnosis of each was established on clinical and radiological characteristics. Cases were subdivided to two groups: autologous (to avoid the possibility of sensitization or acute graft-versus host disease if allogeneic source was taken), platelet-rich plasma (PRP)-treated group (41 patients) and steroid-treated (control) group (25 patients). All patients were not diabetic, hypertensive or not on life-long medication for a systemic illness. Autologous platelet-rich plasma was prepared using the Trima Accel version 6 continuous-flow centrifugal system (Terumo BCT), using a disposable, closed, strictly sterile tubing set (figure 1).

Injection was accomplished in Orthopedic Wards, Basra General Hospital by mixing 0.5 mls of (2%) of lidocaine local anesthesia with 3, 2, 2 mls of PRP for planter fasciitis, Achilles tendinitis and lateral epicondylitis, respectively. The mixture was given intralesionally to the site of maximum tenderness. To generate thrombin which is important to activate platelets to secrete their growth factors, a peppering technique, by doing multiple short stabs in many directions to penetrate the periosteum with an audible and palpable gristly crunchy texture when touching it to make minor injuries using the injecting needle, was done before injecting PRP. Control cases were injected with a mixture of 0.5 mls (2%) of lidocaine local anesthesia and 1 ml (40 mg) of methyl prednisolone acetate intralesionally, too. After finishing injection, dressing with sterile gauze and bandaging was done and the patient was put on a prophylactic short course of antibiotics.

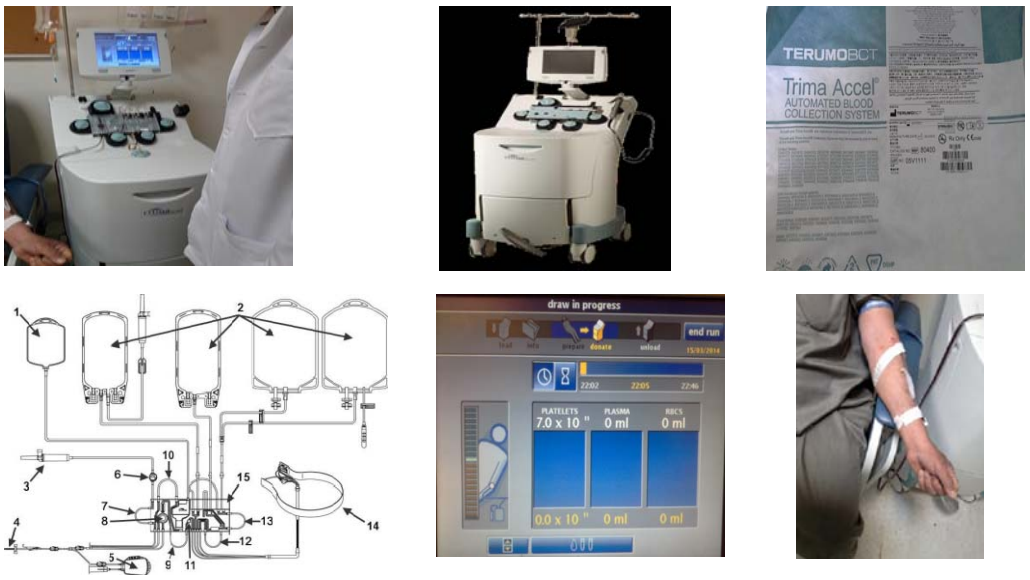

Figure 1: a. The Trima Accel system machine, overview, b. Trima Accel system during work, c. A diagram of the disposable set and tubing system, d. The disposable set before being opened for use, e. The Trima Accel display showing the progress of run, f. A patient being connected to the machine.

Pre- and three post-injection intervals (2, 8 & 16 weeks) pain assessment, was achieved using the visual analog scale (VAS) (Figure 2), a tool used frequently to assess pain. It is a rigid white plastic ruler, 100 mm in length, where the left extreme end indicates "no pain" and the right one the "worst imaginable pain" 18. Each patient was asked to move a vertical marker along the line to a position that best represents his current perception of pain between the labeled extremes. Though it is subjective, the VAS is a valid and reliable tool to measure of chronic pain intensity[19,20] and differences in pain perception over time[21,22]. Statistical analysis (both descriptive and analytical, using the ANOVA test, was done using the SPSS version 20[23].

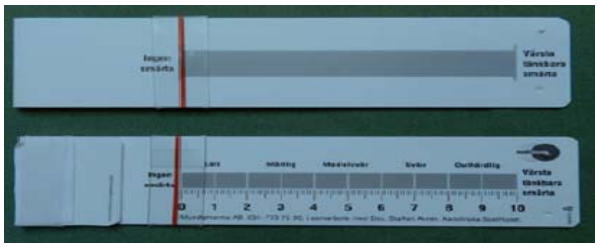

Figure 2: The visual analog scale used in the study

Results

Patients' age ranged between 20-80 years with a mean of (40.3±10.9) years. Table I demonstrates that 36 (54.5%) were males and 30 (45.5%) were females and 60% of them were in their productive age (20-60 years) with male predominance between 20-40 & 40-60 years(57.6% & 55.6%, respectively) while females predominate between 60-80 years(66.7%).

Table I: Age and gender distribution of the cases

Age in years		gender		Total
		Male	Female	
20-39	N	19	14	33
	%	57.6	42.4	100.0
40-59	N	15	12	27
	%	55.6	44.4	100.0
60-80	N	2	4	6
	%	33.3	66.7	100.0
Total	N	36	30	66
	%	54.5	45.5	100.0

Table II shows that those injected with PRP were 41 patients (62.12%) while those injected with local steroids were 25 (37.88%). Patients with Achilles tendinitis were 23 (34.8%), 16 (24.2%) were with tinnes elbow and 27 (41%) were with planter fasciitis.

Table II: Frequency of three pathologies studied among both treatment modalities

Type of treatment	Pathology	Frequency	%
PRP (41)	Achillis tendinitis	15	22.7
	Lateral epicondylitis	9	13.6
	Plantar fasciitis	17	25.8
Steroids (25)	Achillis tendinitis	8	12.1
	Plantar fasciitis	10	15.2
	Lateral epicondylitis	7	10.6
	Total	66	100.0

Table III shows that (21) (31.8%) were unilaterally and (45) (68.2%) were bilaterally affected. All of those who were bilaterally affected were complaining from either planter fasciitis or Achilles tendinitis and no one was complaining from lateral epicondylitis. Minority, (15.2%) of patients was athletics (still playing football or other sports for at least two hours weekly), 18.2% were smokers and 16.6 % had history of trauma (single major or minor repetitive). Half of patients were complaining of pain interfering with their daily activities. There was no statistically significant relationship between those factors and any of the enthesiopathies studied.

Table III: The frequency of certain clinical factors among cases

Clinical factor		Frequency	%
Involvement site	Unilateral	21	31.8
	Bilateral	45	68.2
Athletic history	Athletic	10	15.2*
	Non-athletic	56	84.8
Smoking	Non-smoker	54	81.8
	Smoker	12	18.2**
History of trauma	Minor repetitive	3	4.5***
	Major	8	12.1
Interference with activity	Interfering	33	50.0
	Not	33	50.0

* P. value 0.179. ** P. value 0.133. *** P. value 0.873.

Table IV shows that housewives and casual workers were the most affected than others (28.8 % and 24.2 %, respectively), followed by officers and teachers (19.7 % and 13.6 %).

Table IV: Occupation of the patients, frequency & percent

Occupation	Frequency	%
Officer	9	13.6
Casual worker	16	24.2
Teacher	13	19.7
Housewife	19	28.8
Engineer	2	3.0
Employer	5	7.6
Retired	2	3.0
Total	66	100.0

The results of PRP and steroid injection to patients on visual analog score

Table V shows that pretreatment pain score ranged between 6 to 9 and half of the total patients had a pretreatment VAS level 7, followed by that of 8 (36.4 %). However, on post-treatment follow up, there was a reduction of VAS among both treatment modalities, being more and stepwise and statistically significant among the PRP group than with steroid group (Table VI).

Table V: Pretreatment pain level (VAS) among total patients.

Pre-treatment VAS level	Frequency	%
6	4	6.1
7	33	50.0
8	24	36.4
9	5	7.6
Total	66	100.0

Table VI: Follow up of post-treatment VAS level among PRP and steroid group at the 2nd, 8th, 16th week's intervals.

Week	VAS of PRP± SD	VAS of steroid± SD	P.value
2nd	5.35± 0.98*	4.69± 1.01*	0.01*
8th	3.651± 0.89**	4.58± 0.64	0.001**
16th	2.631± 0.21***	5.04± 1.03	0.0001***

Table VI shows that the average pain score 2 weeks after injection was significantly reduced in both groups, being more after steroid treatment while after the 8th and 16th week, the reduction in VAS was significantly lower in PRP group with a return to increase slightly among the steroid group after the 16th week.

Table VII: shows the VAS measurement & pain reduction, in patients according to their pathology separately in the intervals 2^{nd}, 8^{th} and 16^{th} week. It shows that for those with Achilles tendinitis, the mean of their pain score was significantly reduced from (6.00±1.00) to (2.67±1.01) in the PRP group compared to the steroid group who show an increment in the score from (4.67±1.00) to (5.00±1.22). Patients with lateral epicondylitis, also show a significant reduction of the pain score from (5.11±0.60) to (3.00±1.50) in PRP group compared to those with steroid group in whom pain score had increased from (4.50±1.51) to (4.77±1.03), while those with plantar fasciitis showed a reduction of pain score from 4.94±0.82 to 2.51±1.28 in the PRP group compared to those with steroid therapy (from 4.70±0.67 to 5.30 ± 0.94).

Table VII: Changes in the pain score in the three different pathologies treated by the two modalities in the form of mean and SD in intervales 2^{nd}, 8^{th}, 16^{th} weeks.

Pathology	Treatment modality	Mean of VAS pain assessment ± SD		
		2nd week	8th week	16th week
Achillis tendinitis	PRP	6.00 ± 1.00	4.00 ± 1.19	2.67 ± 1.01
	Steroids	4.67 ± 1.00	4.22 ± 0.66	5.00 ± 1.22
Lateral epicondylitis	PRP	5.11 ± 0.60	4.00 ± 0.86	3.00 ± 1.50
	Steroids	4.50 ± 1.51	4.67 ± 0.51	4.77 ± 1.03
Plantar fasciitis	PRP	4.94 ± 0.82	3.24 ± 1.25	2.51 ± 1.28
	Steroids	4.70 ± 0.67	4.80 ± 0.63	5.30 ± 0.94
P value		0.015	0.001	0.0001

Discussion

The significant pain reduction among Achillis tendinitis group who were treated with PRP, compared with the steroid therapy duting post injection follow up period was comparable to that found by Maffulli N et al 2004[24] who did a prospective study on different tendenopathies and found that the Achilles tendon group had the best response, with all patients having at least moderate improvement and 96% of patients reporting mostly to complete improvement with a reduction of VAS from (7.0±1.8) to (1.8±1.2) (P.=0.001). The increase in VAS in the steroid group was comparable to that reported by Fredberg U[25] et al who concluded that corticosteroid injection inside the tendon or near to tendon has a deleterious effect on the tendon tissue and may cause tendon rupture, thus should be unanimously condemned. It is also comparable to Dacruz D J et al[26]. Who reported that peri-tendonous injection of methyl prednisolone acetate is of no value in Achilles tendinopathy.

In planter fasciitis, the significant reduction of VAS among PRP-treated group was comparable to that reported by Martinelli N et al[27], who showed that VAS had decreased significantly among their patients from 7.1±1.1 before treatment to 1.9±1.5 at the last follow-up ($p<0.01$). However, though Akashin et al[28], in their prospective non-randomized comparison of PRP and corticosteroid injection for plantar fasciitis, had found that the mean (VAS) dropped from (6.2) to (3.2) in the steroid group and (7.33) to (3.93) in the PRP group at 6-month follow up, and both treatments appeared effective in reducing the VAS, yet, they had concluded that PRP injection appeared to be the safer of the two. In this study, no complication with steroid injection had been faced. However, Acevedo and Beskin[29] reported that in a group of 765 patients with a clinical diagnosis of plantar fasciitis, 51 were diagnosed as having a plantar fascia rupture. Of these 51 ruptures, 44 (86%) were associated with corticosteroid injection. Sellman JR[30] observed in a series of 37 patients with plantar fascial rupture and previous heel pain diagnosed as plantar fasciitis treated with corticosteroid injection into the calcaneal origin of the fascia, that one-third of these patients were reported to have rupture of the plantar fascia, described as a sudden tearing episode in the heel, and the remainder described mild-to-moderate pain reaching a conclusion was that although corticosteroid injections may be helpful in the treatment of "plantar fasciitis" but steroid may predispose to plantar fascial rupture.

For those with lateral epicondylitis (LE), the significant VAS reduction of the PRP treated group in the post-treatment follow up [from (5.11±0.60) to (2.71±1.50) (P.=0.005)], was comparable to that reported by Allan Mishra et al[31] who did (at a time ranging between 12-38 months) follow up the PRP-treated patients and reported a 93% reduction in pain (range, 0-3), and 93% of these patients were completely satisfied with treatment, while 7% were partially satisfied. Those 93% were essentially pain-free (1 or less of 10 on VAS). Overall, the patients reported engaging in a mean of (99%) of the activities of daily living, (94%) of work or sporting activities. It is also comparable to Taco Gosens et al[32] who compared the effect of PRP and steroid therapy on lateral epicondylitis and reported that the PRP-treated group was more often successfully treated than the corticosteroid-treated group (P. =0001), and steriods failed to maintain the early pain relief in which the VAS re-elevated after a range of 8 weeks and patient became complaining again (where success was defined as a reduction of ≥25% on VAS).

Conclusion

The PRP seems to be superior to steroid injection in both the early and the remote

post-treatment follow up in all the three diseases studied above.

The PRP seems to be safer than the steoid local therapy as it is an auto-product of the body and has less chance to cause tendon rupture.

The preparation of PRP using the Trima Accel Machine is much more expensive than steroid therapy, besides, some of patients had experienced some phopia from the pheresis session itself, a thing that can be reduced by assurance and proper explanation.

Recommendations

More profound studies on the effects of PRP on each of the pathological conditions taken, separately with a larger scale of patients and for a longer time of follow up are needed to a certain their therapeutic effect in those diseases.

The encouragement of the supply of PRP-producing machines to make this pattern of treatment available to a larger number of patients in the future.

The establishment of cost-benefit types of studies on the effects of PRP compared to other modalities of treatment.

References

1. Marx RE, Carlson ER, Eichstaedt RM, et al: Platelet rich plasma: growth factor enhancement for bone grafts. The journal of bone and joint surgery. 2009, 91-B: 987-96.
2. Ferrari M, Zia S, Valbonesi M, Henriquet F, Venere G, et al A new technique for hemodilution, preparation of autologous platelet-rich plasma and intraoperative blood salvage in cardiac surgery. Jan; 1987, Int J Artif Organs; 10(1):47-50.
3. Fernandes S, Romeu JC, da Silva JA. Platelet Rich Plasma: What should the rheumatologist expect?Acta Reumatol Port. 2015 Jul-Sep;40(3):214-22.
4. Moraes VY, Lenza M, Tamaoki MJ, Faloppa F, Belloti JC. Platelet-rich therapies for musculoskeletal soft tissue injuries. Cochrane Database Syst Rev. 2014 Apr 29;4:CD010071. doi: 10.1002/14651858.CD010071.pub3.
5. Marx RE: Platelet-rich plasma: evidence to support its use. J Oral Maxillofac Surg. 2004 Apr;62(4):489-96.
6. Bucholz RW, Einhorn TA, Marsh JL: Bone and joint healing. Rockwood & Green's fractures in adults. Sixth ed.,2004. Lippincott Williams & Wilkins.;300-11.
7. Sanchez AR, Sheridan PJ, Kupp LI: Is platelet-rich plasma the perfect enhancement factor ?: a current review. Int J Oral Maxillofac Implants;2003, 18:93-103.
8. Levy JC, Mizel MS, Clifford PD, et al. Value of radiographs in the initial evaluation of nontraumatic adult heel pain. Foot Ankle Int., 2006; 27:427–430.
9. Graham CE: Painful heel syndrome: rationale of diagnosis and treatment. Sports Med Arthrosc Rev,Dec. 2013; 21, 4:220-224.
10. Akfirat M, Sen C, Gunes T. Ultrasonographic appearance of plantar fasciitis. Clin Imaging.2003; 27:353–357.
11. Mischra A, Pavelko T: Treatment of chronic elbow tendinosis with buffered platelet rich plasma. Am J Sports Med.;2006; 34: 1774–1778.
12. Soomekh DJ: Current concepts for the use of platelet-rich plasma in the foot and ankle. Clin Podiatr Med Surg.;2001; 28: 155–170.
13. Hall M, Band P, Meislin R, Jazrawi L, Cardone D: Platelet-rich plasma: Current concepts and application in sports medicine. J Am Acad Orthop Surg.; 2009;17: 602-8.
14. Maffulli N, Sharma P, Luscombe KL: Achilles tendinopathy: Aetiology and management. J R Soc Med.;2004;97:472-476.
15. Gaweda K, Tarczynska M, Krzyzanowski W: Treatment of Achills tendinopathy with platelet-rich plasma. Int J Sports Med.; 2010; 31:577-583.
16. Pasternack I, Tuovinen EM, Lohman M, Vehmas T, Malmivaara A. MR findings in humeral epicondylitis. A systematic review. Acta Radiol.;2001; 42(5): 434-440.
17. Allan Mishra,Terri P:Treatment of Chronic Elbow Tendinosis With Buffered Platelet-Rich Plasma. The American Journal of Sports Medicine, Novemb.2006; Vol. 34. 1774-1778.
18. Choinière M, Amsel R: A visual analogue thermometer for measuring pain intensity. J Pain Symptom Manage.; May, 1996;11 (5):299-311.
19. Scott J, Huskisson EC: Vertical or horizontal visual analogue scales. Ann Rheum Dis.; 1979; 38:560.
20. Gaston-Johansson F: Measurement of pain: the psychometric properties of the Pain-O-Meter, a simple, inexpensive pain assessment tool that could change health care practices. J Pain Symptom Manage.; 1996; 12:172-81.
21. Williamson A, Hoggart B: Pain: a review of three commonly used pain rating scales. J Clin Nurs.; Aug, 2005; 14 (7):798-804.
22. Bijur PE, Silver W, Gallagher EJ: Reliability of the visual analog scale for measurement of acute pain. J Acad Emerg Med.; Dec, 2001; 8(12):1153-7
23. Rinaman WC. Exploring statistics with SPSS, 2005.Department of Mathmetics, Le Moyne College, Syracuse, NY 13214, PP:32-68.
24. Maffulli N, Sharma P, Luscombe KL. Achilles tendinopathy: Aetiology and management. J R Soc. Med.; 2004; 97:472-476.
25. Fredberg U. Local corticosteroid injection in sport: review of literature and guidelines for treatment. Scand J Med Sci Sports, 1997; 7 131-139.
26. Dacruz D. J. al. Achilles paratendonitis: an evaluation of steroid injection Brit.J.Sports Med, June, 1988;Vol. 22, No. 2, pp. 64-65.
27. Martinelli N, Marinozzi A, Carni S, et al: Platelet-rich plasma injections for chronic plantar fasciitis Sports Med Arthrosc Rev, Dec, 2013; 21, 4: 220-224.
28. Akashin E, Dogruyol D, Yuksel HY, et al: The comparison of the effect of corticosteroids and platelet-rich plasma (PRP) for the treatment of plantar fasciitis. Arch Orthop Trauma Surg.; 2012; 132:781–785.
29. Acevedo JI, Beskin JL: Complication of plantar fascia rupture associated with corticosteroid injection. Foot Ankle Int. 1998 Feb;19(2):91-7.
30. Sellman JR: Plantar fascia rupture associated with corticosteroid injections. Foot Ankle Int Foot Ankle Int. Jul. 1994;15(7):376-81.
31. Allan Mishra,Terri P:Treatment of Chronic Elbow Tendinosis With Buffered Platelet-Rich Plasma. The American Journal of Sports Medicine,Nov. 2006; Vol. 34; 1774-1778.
32. Taco Gosens et al: Ongoing Positive Effect of Platelet-Rich Plasma Versus Corticosteroid Injection in Lateral Epicondylitis. The American Journal of Sports Medicine, 2011; 39, 6:P1200-1208.