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EFFICACY OF PRP IN PRIMARY FLEXOR TENDON HEALING OF THE HAND

By

Ahmed Rami Majeed, Mohamed Ibrahim Zeidan, Mohamad Osama Ouf, Mohamed Salah El-Feshawy* and Ahmed Abd El-Moez Ali**

Departments of Plastic and Burn Surgery, Radiology* and Clinical Pathology**, Faculty of Medicine, Al-Azhar University

***Corresponding author:** Ahmed Rami Majeed, **E-mail:** ahmed.majeed@azhar.edu.eg

ABSTRACT

Background: Tendon injury represents a common cause of morbidity worldwide and is one of the commonest causes of disability especially among the worker group. Many theoretical and clinical studies support the efficacy of platelet rich plasma (PRP) in augmenting healing in different human body aspects.

Objective: Assessing the efficacy of PRP in primary flexor tendon repair.

Patients and methods: The study was prospective controlled clinical study included 40 patients visiting Al-Azhar University Hospital's emergency departments 20 of them treated with the conventional method the other 20 patients treated in the conventional method + PRP injection the cases treated and followed over period of December 2019 till October 2020.

Results: When comparing patient's characteristic in the two groups, there was no statistical difference between study groups regarding age, sex, affected side, zone of injury and tendon affected. However, there was a statistical difference between studied groups as regards 2nd and 3rd week pain scale follow up. There was no statistical difference between studied groups regarding 1st, 2nd & 3rd week TAROM%, and between studied groups regarding U/S assessment. There was a statistical difference between studied group regarding time of resuming activities with median of 4 SD 4-6 in group 1 (PRP Group) (p-value < 0.05), and median of 6 weeks SD 6-8 in group 2 (Non-PRP).

Conclusion: PRP injection is a simple, cost-effective procedure that shows significant promise in improving postoperative healing and pain.

Keywords: PRP, Flexor tendon repair, PRP in tendon repair.

INTRODUCTION

Different techniques for flexor tendon repair most of these techniques use flexor tendon core suture plus orientation sutures. The Modified Kessler repair is a modification of the original Kichmayr repair and considered one of the most popular and durable repair method *(Sebastin et al., 2016).*

The flexor tendons are important anatomical and physiological structures of the hand. They are the main element responsible for prehension movements: These are used in everyday life to grasp vigorously or delicately. They represent the livelihood of many workers, and their loss will cause disability and affect the patient even financially *(Kaddah et al., 2017).*

Platelet-rich plasma (PRP) injection is an endogenous easy cheap therapeutic technique that is gaining interest in

regenerative medicine due to its potential to stimulate and accelerate tissue healing. PRP is defined as an autologous biological product derived from the patient's blood, in which after a centrifugation process a plasma fraction is obtained with a platelet concentration higher than that in circulating blood. Platelets play a crucial role in the wound healing process thanks to their haemostatic function and presence of cytokines and growth factors. There are several growth factors which are known to be involved in the wound healing process, such as epidermal growth factor (EGF), platelet-derived growth factor (PDGF), insulin-like growth factor (IGFI, IGF2), fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), transforming growth factor (TGF-P); keratinocyte growth factor (KGF) *(Alcántara et al., 2018).*

Growth factors are a group of soluble and diffusible polypeptide substances that regulate growth, differentiation, proliferation, and cellular metabolism of numerous cell types. They promote endothelial and epithelial regeneration; stimulate angiogenesis, collagen synthesis, soft tissue healing, and haemostasis. The use of growth factors to promote tissue healing has existed since the 1940s, and they can be applied in a wide range of ways, either by traditional topical or intralesional administration or by using specific scaffolds or even gene therapy. Animal and human trials have reported successful PRP clinical applications for chronic skin ulcer, acute cutaneous wounds, burns, and plastic and cosmetic surgery *(Stone et al., 2020).*

Platelets, which are produced by megakaryocytes in the bone marrow, comprise up to 150 - 400 × 109 cells per litre of blood and circulate for about 10 days. To exert their healing function, platelets become activated at the site of tissue injury. Adhesion and Platelets in PRP release there intracellular stores predominantly a-granules (50- 80 a-granules per platelet), dense granules (3 - 5 granules per platelet) and lysosomes. To date, the effectors of the beneficial function of PRP therapies are growth factors such as PDGF, TGF, FGF, endothelial growth factor (EGF), hepatocyte growth factor (HGF), connective tissue growth factor (CTGF) and VEGF, among others all these factors theoretically will accelerate wound healing and provide excellent media for healing *(Andia et al., 2010).*

The present work aimed to assess the efficacy of PRP in primary flexor tendon repair.

PATIENTS AND METHODS

The study was prospective controlled clinical study included 40 patients visiting Al-Azhar University Hospital's emergency departments 20 of them treated with the conventional method the other 20 patients treated in the conventional method + PRP injection the cases treated and followed over period of December 2019 till October 2020.

The patients divided into two equal groups: Group A: Patient got PRP injection to augment tendon repair, and **Group B:** Tendon repaired without PRP Augmentation.

Inclusion criteria: Primary tendon injury, Patient age ranged from 15-60 years' old, Males and females without selection,

Hand tendons injury flexure, zone 2 to zone 6 tendon injury, complete tendon cut.

Exclusion criteria: Younger than 15 years, older than 60 years, Partial tendon cut, Old cut, infected wound, associated skeletal injuries, Associated nerve or vascular injury related to the muscle (tendon) planned to be repaired.

Control Group: In which 20 patients with flexor tendon injury (complete cut) had been repaired by double modified Kessler + orientation continuous suture only.

PRP Group: In which 20 patients with flexor tendon injury (complete cut) had been repaired by double modified Kessler + orientation continuous suture augmented by autologous PRP injection in and around tendon repair site. **(Figure 1).**

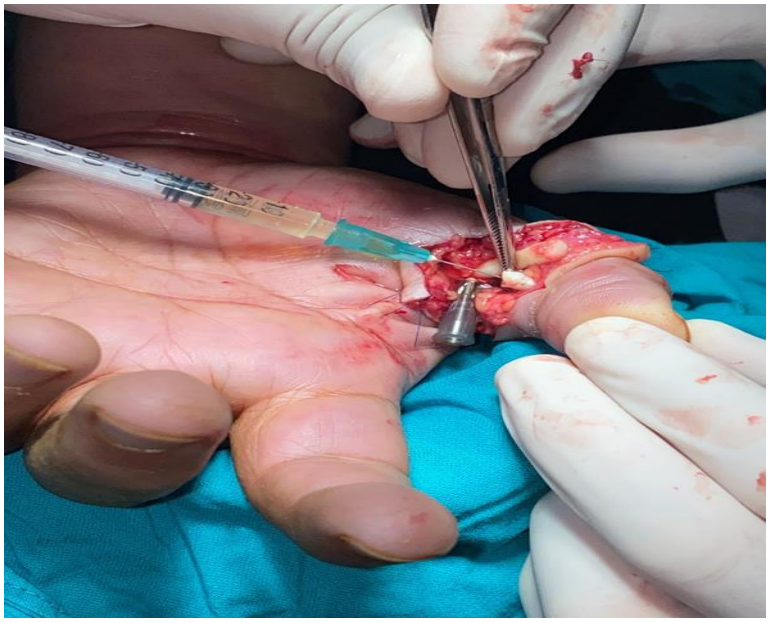

Figure (1): Delicate injection of PRP to the tendon of FPL of the Left hand of one of our patients at AL-HUSSIEN University hospital Cairo-Egypt.

Pre-operative investigation: CBC, PT, PTT, INR, Viral screen, and limb x-ray to exclude any associated fracture.

Patients assigned randomly to non-PRP or PRP group with considering the time from arrival of patient to the ER and the operation to be as short as possible to avoid any wound infection and the PRP preparation to be immediately before the operation, all patient were followed clinically 2,4,6 weeks post-operative by pain score (0-10), by Total Active Range Of Motion by The American Society for Surgery of the Hand (ASSH) and the degree of finger movement measured by Baseline Goniometer, Ultrasound assessment by radiologist at 2 weeks post-operative with pre-set Ultrasound criteria to evaluate tendon healing process.

Statistical analysis:

The collected data were coded, processed and analyzed using the SPSS

(Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Wilk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. Mann-Whitney U Test: is a test of significance used for comparison between two groups having quantitative variables without normal distribution (for non-parametric data). Quantitative data were expressed as mean ± SD (Standard deviation) median and inter quantile range (IQR). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

The mean age in the present work was 29.7 SD 9.6, where is in group 2 the mean age was 30.8+SD 9.2, There was no statistically significant difference between studied groups as regards age. There was no statistically significant difference between studied groups as regards sex, affected side, zone and tendon affected **(Table 1)**.

Table (1): Comparison between studied groups as regard age, sex, affected side, zone and tendon affected

Parameters \ Groups		Group I (N = 20)		Group II (N = 20)		P-value
Age (years)	**Mean±SD**	29.7±9.6		30.8±9.2		0.726
		No	**%**	**No**	**%**	
Sex	**Male**	12	60%	12	60%	1.0
	Female	8	40%	8	40%	
Affected side	**Dominant**	15	75%	16	80%	0.705
	Non-dominant	5	25%	4	20%	
Zone	**Zone II**	6	30%	8	40%	0.917
	Zone III	10	50%	8	50%	
	Zone IV	3	15%	3	15%	
	Zone V	1	5%	1	5%	
Tendon affected	**FDP**	12	60%	8	40%	0.2
	FDS	7	35%	9	45%	0.518
	FPL	4	20%	5	25%	0.705

No statistically significant difference between studied groups as regard 1st week pain scale regard 1st, 2nd & 3rd week TAROM%, but significant difference between studied groups as regard 2nd & 3rd week pain scales **(Table 2)**.

Table (2): Comparison between studied groups as regard pain scale and TAROM%

Parameters \ Groups			Group I (N = 20)	Group II (N = 20)	MW	P-value
Pain scale	1st week	Median	8	8	157	0.253
		IQR	7 - 8	7 – 8		
	2nd week	Median	7	5.5	**94.5**	**0.004**
		IQR	6 – 7	4 - 6		
	3rd week	Median	5.5	4	**76**	**0.001**
		IQR	5 – 6	2 - 5		
TAROM %	1st week	Median	50	55	134.5	0.076
		IQR	46.25 - 50	45 – 60		
	2nd week	Median	55	65	131.5	0.063
		IQR	51.25 – 58.75	50 - 65		
	3rd week	Median	60	70	138.5	0.096
		IQR	55 – 65	50 -75		

MW: Mann-Whitney U test, IQR: Interquartile range

There was no statistically significant difference between studied groups as regard Ultrasound (U/S) assessment **(Table 3)**.

Table (3): Comparison between studied groups as regard U/S assessment

U/S \ Groups	Group I (N = 20)		Group II (N = 20)		P-value
Poor	2	10%	1	5%	0.333
Fair	3	15%	3	15%	
Good	12	60%	8	40%	
Excellent	3	15%	8	40%	

There was highly statistically significant difference between studied groups as regard time of resuming activity **(Table 4)**.

Table (4): Comparison between studied groups as regard time of resuming activity

Time of resuming activity \ Groups	Group I (N = 20)	Group II (N = 20)	P-value
Median	6	4	**< 0.001**
IQR	6 - 8	4 - 6	

MW: Mann-Whitney U test, IQR: Interquartile range

DISCUSSION

The study included 40 patients divided into two equal groups Group I: Non-PRP group were 20 and Group II: PRP group Sixty percent of patients were males and 40% were females which reflected the higher incidence of tendon injuries in males more than females. The mean age

of patients reflected youth population who were more vulnerable to upper limb injury in comparison to other age groups.

Most authors believed that PRP enhance healing and provide the injured tissue with super amount of growth factors essential for the healing process *(Evrova and Buschmann, 2017).*

PRP is appealing for clinical application as a frugal source of growth factors. Because they are autologous, no concern for immunologic response. PRP is widely used in medicine as for treatment of musculoskeletal injuries. Clinical applications for PRP include rotator cuff repair, Achilles tendon repair, Achilles tendinopathy, and lateral epicondylitis; however, the efficacy of PRP is still controversial *(Kollitz et al., 2013).*

Biological therapies after tendon ruptures or lacerations are a new concepting target the Acceleration of the healing process with a true regeneration of the tendon tissue. All cues leading to a faster cell infiltration to the wound site, with increased cell proliferation and accompanied with proper ECM remodeling are desired effects *(Evrova and Buschmann, 2017).*

The positive effect of PRP in tendon healing was previously showed in vitro and in vivo. A cell culture study, tenocytes cultures were demonstrated that PRP stimulates cell proliferation and total collagen production, and endogenous growth factors *(De Mos et al., 2010).*

Nugraha et al. (2012) performed study about different protocols for PRP preparation found that PRP with PDGF BB 3401 pg/ml after processing through this protocol. This amount could still increase after activation which was not included and tested further in this study. The PRP for clinical treatment should be about 1,000,000 platelets per microliter. Given that whole blood contains approximately 200,000 ± 75 000 platelets per microliter, then the therapeutic PRP must have an average percentage of increase of about 400% in platelet count, Therefore, this experiment indicates that the optimum result from this experiment might be a standard for PRP making *(Nugraha et al., 2012).*

Kaddah et al. (2017) conducted a randomized controlled study on patients with affected fingers with no sex predilection ranging from 12-60 years with recent (within 3 days) sharp clean cut in zones 2, 3 & 5 and no associated skeletal or soft tissue injuries and any medical co-morbidity. At 12 weeks, the fingers full active flexion and extension is assessed using the Goniometer and the readings were plotted in the evaluation sheets and the results were calculated for the Strickland and TAM scores. The results in the two study groups were compared with no significant statistical difference between PRP and Non-PRP group at any time period during the evaluation.

Barber et al. (2011) comparative series of patients undergoing arthroscopic rotator cuff repair was studied to assess healing influenced by PRP, the patients matched into two group on receive PRP and one did not, each with a mean age of 57 years (range was 44 - 69 years). Postoperative MRI studies showed persistent full-thickness tendon defects in 60% of controls (12 of 20) and 30% of PRP augmented repairs, showing clear

statistical difference with enhanced result in PRP group. Of the control group tears measuring less than 3 cm in anteroposterior length, 50% (7 of 14) healed fully, whereas 86% of the PRPFM group, tears measuring less than 3 cm in anteroposterior length (12 of 14) healed fully.

de Jonge et al. (2011) performed Randomized controlled trial to study the effects of a platelet-rich plasma injection in patients with chronic midportion Achilles tendinopathy at 1-year follow-up, with chronic tendinopathy 2 to 7 cm proximal to the Achilles tendon insertion patients randomized to receive either a blinded injection containing platelet-rich plasma or saline (placebo group) in addition to an eccentric training program showed no clinical and ultrasonographic superiority of platelet-rich plasma injection over a placebo injection in chronic Achilles tendinopathy at 1 year follow up.

CONCLUSION

PRP injection in primary tendon repair significantly improved the time needed to resume activities after tendon injuries, with a median of 6 weeks (SD 6-8) in Control Group and a median of 4 weeks (SD 4-6) in PRP Group. Post-operative pain was significantly improved in the second and third week in the PRP Group.

PRP injection is a simple, cost-effective procedure that shows significant promise in improving postoperative healing and pain.

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تقييم فاعلية البلازما الغنية بالصفائح الدموية وتأثيرها على الالتئام الأولي لآوتار اليد القابضة

أحمد رامي مجيد، محمد إبراهيم زيدان، محمد أسامة عوف، محمد صلاح الفيشاوي*، أحمد عبد المعز**

أقسام جراحة التجميل والحروق, الأشعة التشخيصية*، الباثولوجيا الاكلينيكية، كلية الطب، جامعة الأزهر**

E-mail: ahmed.majeed@azhar.edu.eg

خلفية البحث: تمثل إصابة الأوتار سببًا شائعًا للمرضي في جميع أنحاء العالم, وهي واحدة من أكثر أسباب الإعاقة شيوعًا خاصة بين مجموعة العمال. وتدعم العديد من الدراسات النظرية والسريرية فعالية البلازما الغنية بالصفائح الدموية في زيادة الشفاء في جوانب مختلفة من جسم الإنسان.

الهدف من البحث: تقييم فعالية البلازما الغنية بالصفائح الدموية في إصلاح وتر العضلة المرنة الأولية.

المرضي وطرق البحث: كانت الدراسة دراسة سريرية مستقبلية خاضعة للرقابة شملت 40 مريضاً يزورون أقسام الطوارئ بمستشفى جامعة الأزهر، 20 منهم عولجوا بالطريقة التقليدية، و 20 مريضاً عولجوا بالطريقة التقليدية مع حقن البلازما الغنية بالصفائح الدموية للحالات التي تم علاجها ومتابعتها خلال فترة العلاج من ديسمبر 2019 حتى أكتوبر 2020.

نتائج البحث: عند مقارنة خصائص المريض في المجموعتين لم يكن هناك فرق إحصائي بين مجموعات الدراسة فيما يتعلق بالعمر والجنس والجانب المصاب ومنطقة الإصابة والأوتار المتأثرة. ومع ذلك كان هناك فرق إحصائي بين المجموعة المدروسة فيما يتعلق بمتابعة مقياس

الألم في الأسبوع الثاني والثالث، ولم يكن هناك فرق إحصائي بين المجموعة المدروسة فيما يتعلق بالأسبوع الأول والثاني والثالث من TAROM٪، ولم يكن هناك فرق إحصائي بين المجموعة المدروسة فيما يتعلق التقييم بالموجات فوق الصوتية. وكان هناك فرق إحصائي بين المجموعة المدروسة فيما يتعلق بوقت استئناف الأنشطة بمتوسط 4، والانحراف المعياري 4-6 في المجموعة 1 (مجموعة البلازما الغنية بالصفائح الدموية)، ومتوسط 6 أسابيع والانحراف المعياري 6-8 في المجموعة 2 (غير- البلازما الغنية بالصفائح الدموية).

الإستنتاج: حقن البلازما الغنية بالصفائح الدموية هو إجراء بسيط وفعال من حيث التكلفة ويظهر وعدًا كبيرًا في تحسين الشفاء والألم بعد الجراحة.

الكلمات الدالة: حقن البلازما الغنية بالصفائح الدموية، إصلاح الوتر المثني، حقن البلازما الغنية بالصفائح الدموية في ترميم الوتر.