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Evaluation The Effect of Injecting Platelets Rich Plasma in Modulating Post Burn Scars

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ABSTRACT

Background: An innovative supplement known as platelet-rich plasma (PRP) is being utilised more often to cure soft tissue deficiencies, speed up the regeneration of new soft tissue, and treat chronic wounds that won't heal.
Objective: To evaluate the efficacy of injecting PRP in modulating the post burn scars at different stages.
Patients and Methods: This study is a prospective study, carried out on 48 patients as 3 groups each group had 16 patients in Al Menoufia University Hospital and Ras Al Teen Hospital. The first group was from day zero of burn till 4 weeks, the second group from 4 weeks till the 12th week and the third group from 12 weeks till the 6th month.
Results: Hyperpigmented scars in 7 (43.8%) of Groups I, II and III and they were improved with mean 2.00±0.816, 2.14±0.690 and 2.43±0.976 respectively. There were no statistically significant differences between the groups. Regarding depressed scars recorded in 2 (12.5%) of Group (I) and in 3 (18.8%) of group II, and in 1 (6.3%) of group III, they were improved with a mean of 4.00±0.000, 3.67±0.577 and 2.00±2.828 respectively. There were no statistically significant differences between the groups. While elevated scars were recorded in 8 (50.0%) of groups II and III, and 5 (31.1%) of Group (I). They were improved with a mean of 4.75±0.886 and 4.50±0.926, and 4.60±0.894 respectively, with no statistically significant differences between groups.
Conclusion: The current study showed that the treatment of post-burn scars with intralesional injection of PRP seems to be safe and effective as well as cost-effective. Our results showed that PRP effects were affected by duration of scars as treatment after short duration from burns gave better effect.
Keywords: Effect of injecting platelets, Modulating post burn scars, PRP.

INTRODUCTION

Burns have a high morbidity and fatality rate yet are underappreciated injuries. Burn injuries, especially severe burns, are complicated by an inflammatory and immunological response, metabolic abnormalities, and distributive shock that can cause multiple organ failure and be difficult to manage. It is crucial to note that the injury has an impact on the patient's quality of life and mental as well as physical health. As a result, burn injury patients cannot be deemed recovered once their wounds have healed since burn injury causes substantial long-term changes that must be treated in order to maximise quality of life. Therefore, burn care practitioners are faced with a variety of difficulties, such as managing acute and critical care, long-term care, and rehabilitation [1].

Platelet-rich plasma (PRP) is a plasma that has more platelets per unit of volume than regular blood. In animal trials, PRP has proven to be a successful agent for bone grafting, cartilage regeneration, neovascularization, and tissue deposition. These outcomes have raised interest in PRP and encouraged its usage in human surgical procedures [2]. PRP has reportedly been utilised in a wide range of procedures, primarily in spinal, maxillofacial, and difficult wound surgery. Only a small number of these trials contain controls to clearly show the function of the PRP, despite the fact that the results from these researches have offered good evidence supporting the therapeutic usage of PRP [3,4]. Another key factor that has not yet undergone a thorough analysis is the long-term impact of PRP on scar formation following burn damage. Numerous growth factors are generated from the platelets and leukocytes in PRP, and some of these growth factors are chemotactic in attracting inflammatory cells and a protracted inflammation that may result in hypertrophic scarring [5].

The role of individual growth factors in the complicated chain of events that make up scar development is still being studied. TGF- β 1, TGF- β2, and platelet-derived growth factor stand out among the growth factors because they are linked to keloid and hypertrophic scarring in burn wounds as well as regular skin wounds. On the other hand, it is yet unclear how PRP, a mixture of several growth factors, could affect scar formation. Up until now, there have only been a few articles on the emergence of hypertrophic scarring following the use of PRP for wound healing, and the majority of them have nothing to do with burn injuries [4]. Less discomfort and itching are experienced during the healing process thanks to PRP therapy. The cost-effectiveness of PRP in burn treatment is also among its most significant advantages. Compared to patients who did not undergo the PRP combo therapy, the cost of the hospital stay is reduced (by about 25%) [6].

The aim of this study was to evaluate the efficacy of injecting PRP in modulating the post burn scars at different stages.

PATIENTS AND METHOD

This study was a prospective study that was carried out on 48 patients as 3 groups; each group

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contained 16 patients in Al Menoufia University Hospital and Ras Al Teen Hospital. The first group was from day zero of burn till 4 weeks, the second group from 4 weeks till the 12th week and the third group from 12 weeks till the 6th month.

Inclusion criteria:

Patients with raw area after burn, patients with post-burn scars, regardless of sex, age, or scar site, had scars that ranged in diameter from 2 cm to 15 cm and lasted from 1 month to 6 months. While exclusion criteria included non-co-operative patients, patients refusing the procedure, patients with bleeding issues, those using thrombocyte inhibitors fewer than 4 days before coming to hospital, and those taking more than 10 mg of corticosteroid daily, patients with uncontrolled systemic disease or autoimmune diseases, cardiac patients, patient with antiepileptic drugs, patient with liver or renal failure, positive hepatitis virus C and B patients and positive HIV patients.

The included patients were subjected to detailed history taking included: personal history such as age, sex, occupation, and marital state. Present history as duration, previous treatment, response to treatment, other medical disorders. Patients' socioeconomic status assessed using the socioeconomic scale (SES). Past history of chronic diseases included hypertension, diabetes mellitus, bleeding disorders and cardiac diseases. Family history of any disease. history of obesity, drug intake or smoking. History of comorbid diseases included renal, hepatic diseases or collagenic disorders…. etc. History of previous surgeries. They were subjected to examination of site, size, depth, and shape burn. Complete blood picture (CBC) included hemoglobin concentration (Hb%), red blood cells (RBCs), white blood cells (WBCs) and platelet count, renal function test included serum creatinine, blood urea and urine analysis, liver test profile included serum aspartate and alanine aminotransferases (AST and ALT), serum albumin, serum bilirubin, serum gamma-glutamyl transferase (GGT), prothrombin time and international normalized ratio (INR). Coagulation profile (INR, APTT, platelets and fibrinogen), Na, K, albumin ratio and serum protein level, random blood sugar (R.B.S), Hepatitis and AIDS markers.

Procedures:

A blood sample was aspirated and obtained using blood collection tubes from a peripheral vein using a butterfly 21G needle and a vacutainer kit (to prevent direct contact with blood samples) after the patients gave their informed permission. As an anticoagulant, sodium citrates are present in the blood sample tube. For 10 minutes, the tubes were centrifuged at 400 g. Following this stage, three layers were distinct: plasma, red blood cells, and a transitional layer.

Platelets and plasma are at the top, red blood cells are at the bottom due to their higher density, and the buffy coat, a thin, white intermediate zone made up of bigger platelets and leukocytes, is in the middle. The buffy coat was removed from the plasma using an 18G needle, and it was put into a another tube without any additions. Once more, the tubes were centrifuged for the same amount of time at 800 g (T = 10 min). The tubes held the platelet sedimentation and some red blood cells (erythrocyte-platelet clump) following this last centrifugation. At this point, the volume was decreased by eliminating two-thirds of the entire volume of plasma.

While this was going on, objective checks were made, pictures were taken, and a personal folder was filled up. The blood samples were separated by centrifugation to produce two parts of plasma: PPP in the top portion and PRP in the bottom. To prevent the PPP from contaminating the PRP, it was first gently aspirated. The remaining PRP was then aspirated out of the test tube and prepared for calcium gluconate activation in Figure 1 at a ratio of 0.1 mL per 0.9 mL of PRP. Within the following seven minutes, the PRP solution was ultimately administered.

Ethical consideration:

Patients' informed consent was obtained. The guardians' informed permission was obtained in cases where the patients were less than 18 years old. Records confidentiality was taken into account. The Faculty of Medicine, Menoufia University and the Egyptian Ministry of Health have both given their approval for every medicine utilised in the study. In accordance with the Declaration of Helsinki, the study was carried out.

Statistical analysis

With the use of the IBM SPSS software package version 20.0, data were input into the computer and analysed. The normality of the distribution was examined using the Kolmogorov-Smirnov test. Utilising range (minimum and maximum), mean±standard deviation, quantitative data were reported. Qualitative data were reported as frequency and percentage. We utilised the Kruskal-Wallis H test, the ANOVA test, and the Chi-square test. At the 5% level, significance of the results was determined.

RESULTS

In this study, there was no significant difference among the groups regarding age and gender. There were highly statistically significant differences between groups regarding duration of scar **(Table 1).**

Table (1): Comparison between groups as regard to patient's age (years), duration of scar and gender

	Group (I) (n=16)		Group (II) (n=16)		Group (III) (n=16)		P value
Age/year							
Min.-Max.	2.5-48		5-48		9-43		0.411
Mean± SD	20.97±12.760		22.75±16.434		26.94±12.190		
Duration of scar							
Min.-Max.	0-3		5-11		15-26		**<0.001***
Mean± SD	1.38±1.147		8.00±1.966		20.06±3.214		
Gender	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Male	6	37.5	9	56.3	10	62.5	0.338
Female	10	62.5	7	43.8	6	37.5	
Total	16	100	16	100	16	100	

*: Statistically significant

There were no statistically significant differences between groups regarding type and site of burn and skin type **(Table 2).**

Table (2): Comparison between groups as regard to patient's type of burn, site of burn and skin type

	Group (I) (n=16)		Group (II) (n=16)		Group (III) (n=16)		P value
	No.	**%**	**No.**	**%**	**No.**	**%**	
Type of Burn							
Scald	12	75.0	10	62.5	11	68.8	0.930
Flame	3	18.8	4	25.0	4	25.0	
Chemical	1	6.3	2	12.5	1	6.3	
Total	16	100	16	100	16	100	
Site of Burn							
Arm	3	18.8	5	31.3	4	25.0	0.984
Chest	3	18.8	1	6.3	2	12.5	
Face	3	18.8	4	25.0	3	18.8	
Forearm	3	18.8	3	18.8	3	18.8	
Hand	4	25.0	3	18.8	4	25.0	
Total	16	100	16	100	16	100	
Skin Type							
II	5	31.3	5	31.3	0	0	0.165
III	8	50.0	7	43.8	11	68.8	
IV	3	18.8	4	25.0	5	31.3	
Total	16	100	16	100	16	100	

There were no statistically significant differences between groups regarding burn ratio, and area and duration of injection **(Table 3)**.

Table (3): Comparison between groups as regard to patient's burn ratio, area of injection and duration of injection

	Group (I) (n=16)	Group (II) (n=16)	Group (III) (n=16)	P value
Burn ratio (%)				
Min.-Max. Mean± SD	18-30 20.12±6.29	20-34 22.67±8.16	16-31 21.43±8.50	0.190
Area of injection				
Min.-Max.	1-4	1-3	1-5	0.602
Mean± SD	2.00±0.816	2.13±0.619	2.00±1.033	
Duration of injection				
1st injection				
Min.-Max.	12-17	12-18	12-17	0.696
Mean± SD	14.50±2.033	14.87±1.928	14.31±1.852	
2nd injection				
Min.-Max.	20-159	25-43	25-38	0.085
Mean± SD	41.38±31.883	33.87±6.531	29.88±4.455	

*: Statistically significant

Furthermore, there were no statistically significant differences between groups, regarding the percent and improvement scale of hyperpigmented, depressed, and elevated scars **(Table 4).**

Table (4): Comparison between groups as regard to patient's hyperpigmented scars, depressed scars, and elevated scars

	Group (I) (n=16)		**Group (II) (n=16)**		**Group (III) (n=16)**		**P value**
Hyperpigmented scars	**No.**	**%**	**No.**	**%**	**No.**	**%**	
No	9	56.3	9	56.3	9	56.3	1.000
Yes	7	43.8	7	43.8	7	43.8	
Improvement Scale (0 – 10)							
Min.-Max.	1-3		1-3		1-4		0.862
Mean± SD	2.00±0.816		2.14±0.690		2.43±0.976		
Depressed Scars	**No.**	**%**	**No.**	**%**	**No.**	**%**	
No	14	87.5	13	81.3	15	93.8	0.565
Yes	2	12.5	3	18.8	1	6.3	
Improvement Scale (0 – 10)							
Min.-Max.	4		3-4		0-4		0.513
Mean± SD	4.00±0.000		3.67±0.577		2.00±2.828		
Elevated Scars	**No.**	**%**	**No.**	**%**	**No.**	**%**	
No	11	68.8	8	50.0	8	50.0	0.467
Yes	5	31.3	8	50.0	8	50.0	
Improvement Scale (0 – 10)							
Min.-Max.	4-6		4-6		3-6		0.894
Mean± SD	4.60±0.894		4.75±0.886		4.50±0.926		

*: Statistically significant at P <0.05

DISCUSSION

A product made from autologous blood called PRP has a high platelet concentration in the plasma. By centrifuging entire blood, it is created. Platelet-derived growth factor (PDGF), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), insulin-like growth factor-1 (IGF-1), transforming growth factor- β (TGF- β), and other growth factors and cytokines that support tissue repair and regeneration can all be released by activated platelets in PRP [7].

PRP has been widely employed in many surgical procedures and therapeutic therapies due to its straightforward preparation, high growth factor content, and low immunogenicity. PRP has demonstrated promising experimental and clinical outcomes in wound healing, especially in chronic wounds [8]. Numerous studies have supported the crucial function of PRP in tissue regeneration and wound healing. According to the results of several studies, PRP has a significant impact on vascularization. PRP can release more VEGF, which improves the prognosis of burn wounds by encouraging the vascularization of deep partial-thickness burns [9].

Bone marrow stromal cells (BMSCs) can thrive in an environment that is suitable for them, and PRP can work in tandem with BMSCs to speed up the healing of diabetic wounds by encouraging angiogenesis, cell proliferation, and the production of TGF- β1 [10]. PRP can also hasten local wound revascularization and encourage the growth of new capillaries in a skin flap transplant [11,12]. Additionally, PRP has reportedly been shown to produce a number of antimicrobial compounds, lessen local inflammation, and guard against wound infection. However, the theoretical support for these effects is not as strong as it is in the research of vascularization [13].

Additionally, PRP is successfully applied in a novel way in the therapeutic management of both acute and chronic wounds. PRP can speed up the healing of diabetic wounds, lessen the area injured by pressure ulcers, and enhance joint function in OA [14]. PRP aids in reducing the neuropathic pain, skin texture, and pigmentation of post-burn scars. The numerous GFs produced by PRP, which lead to neovascularization (NV) and nucleogenesis (NC), exacerbate the burn wounds' poor healing process [15]. Therefore, the primary goal of our study was to assess how well PRP injections worked to modify post-burn scars at various phases.

Additionally, **Klosová *et al.*** [16] assessed the impact of applying split thickness skin grafting (STSG) in conjunction with autologous platelet concentrate (APC) on scarring processes following surgery of severe burns as compared to STSG alone. 38 scars on 23 individuals were included in the study, and it was

discovered that applying STSG with APC together shortens the time it takes for the viscoelastic qualities of the scar to heal. In terms of R2 and Q1, two viscoelastic metrics, this was statistically significant.

Also, **Majani and Majani** [17] also sought to ascertain if PRP-induced angiogenesis may enhance the engraftment of the fat that was injected in scar regions. 11 patients in group 1 underwent lipografting without any prior PRP preparation, 11 patients in group 2 got PRP treatment seven to ten days prior, and 6 patients in group 3 with symmetrical scars underwent lipografting on the left side only and PRP and lipografting on the right side. In particular, when vascularization is more compromised and there is a more obvious loss of material, the study found that a sufficient preparation of the treated regions with PRP in conjunction with lipografting allows for more lasting repairs.

Moreover, **Gentile *et al.*** [18] detailed the methods for making platelet-rich plasma (PRP) and stromal vascular fraction (SVF) as well as their therapeutic applications for treating facial scars. Ten individuals with burn sequelae (n = 6) and post-traumatic scars (n = 4) were recruited in the research. According to the study, there was a 63% maintenance of contour restoration in the patients treated with SVF-enhanced autologous fat grafts after a year, compared to just 39% in the control group (n = 10) treated with centrifuged fat transplant. After a year, there was a 69% preservation of contour restoration in the patients treated with fat grafting and PRP in comparison to the control group.

60 patients with traumatic scars were randomly assigned to one of three groups by **Cervelli *et al.*** [19], nonablative laser resurfacing, fat transplant paired with PRP, or all three treatments combined. They discovered that fat grafting with PRP and nonablative laser resurfacing was the scar therapy that worked the best. The three treatment modalities improved scar healing by 22% more than the fat graft and PRP group and by 11% more than nonablative laser resurfacing alone.

120 patients who had their venous access device removed within six months and either had PRP or no treatment for their port area scar were given a retrospective questionnaire by **Eichler *et al.*** [20] to gauge patient satisfaction with PRP-treated scars. The 20 patients who underwent PRP therapy demonstrated a substantial decline in their desire to lessen scarring in the port region, as well as a decrease in scar dissatisfaction (PRP: 10% vs. control: 40.2%). In a six-week study by **Nofal *et al.*** [21], 45 patients received intradermal PRP injections, skin needling, or a combination of the two therapies every two weeks. When compared to the control, all groups showed a statistically significant reduction in the number of acne scars, but no particular therapy stood out above the rest.

Additionally, **Gulanikar and Vidholkar *et al.*** [22] evaluated the effectiveness of platelet-rich plasma in treating acne scars and found that all scar types responded by shrinking in size. PRP worked better on rolling scars than on boxcar and ice pick scars. The study came to the conclusion that PRP is a safe, efficient, and well-tolerated office therapy for treating acne scars.

In order to research the outcomes of combining PRP with CO_2 fractional resurfacing for acne scars, **Lee *et al.*** [23] administered PRP to one half of a patient's face and saline injections to the other. With PRP therapy, erythema, edema, and post-treatment crusting all improved more quickly. Similar to this, after fractional CO_2 laser resurfacing, **Na *et al.*** [24] treated patients' bilateral inner arms with PRP or saline. In comparison to the control, they discovered that PRP therapy resulted in a thicker epidermis, better organised stratum corneum and collagen fibres, and greater collagen density.

PRP has also been used as a keloid treatment. **Jones *et al.*** [25] retrospective investigation included 49 patients who had ear keloid surgery and were subsequently given superficial radiation treatment (SRT) and PRP addition over the surgical site as postoperative care. In order to control keloids, they observed a 94% success rate, which supports the use of PRP in this combination therapy. Additionally, **Rezk *et al.*** [26] evaluated the viability of platelet rich plasma use in hair transplantation in the treatment of post burn scar alopecia and came to the conclusion that PRP in Follicular Unit Extraction is helpful in treating post burn alopecia. They also found that hair transplantation has fewer risks associated with anesthesia, fewer postoperative complications, and a quicker recovery time than other hair restoration procedures.

Additionally, **Yeung *et al.*** [27] investigation of the effects of LPRP on burn healing with a focus on fibroblast proliferation and treatment frequency in a clinical context was corroborated by our findings. There were 27 patients in the trial; 15 were in the PRP group and 12 were in the control group. In comparison to the control group, the healing rate of the PRP group was close to 80% and advanced to 90% in just three weeks.

CONCLUSIONS

In conclusion, the treatment of post-burn scars with intralesional injection of PRP seems to be safe and effective as well as cost-effective. Our results showed that PRP effects were affected by duration of scars as treatment after short duration from burns gave better effect. Additional research is needed to standardise the PRP preparation process, including parameters that impact the PRP yield, to optimise the platelet count in PRP for the best outcomes, and to determine the efficacy of PRP in treating all types of scars.

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