International Surgery Journal
El Ghazaly MA et al. Int Surg J. 2019 Nov;6(11):3932-3936
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20195098

Original Research Article

Topical platelets rich plasma implications in management of burn

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Received: 03 October 2019
Accepted: 19 October 2019

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ABSTRACT

Background: Burn injury is a major cause of trauma to the human body, causing death and disability with a long healing period and high health care costs. The mortality rate of burn injury is decreasing with new treatment modalities.
Methods: Fifty patients who underwent to use or not use the platelet rich plasma (PRP) technique in improving the process of healing in burn scars and graft either by physiological dressing or sub dermal injection between 2 groups. The study was conducted on patients presented to Plastic and Reconstructive Surgery Department of Abou Qir General Hospital and Menuofia University in the period from October 2017 to October 2018.
Results: On treating the burned area with PRP injection and conventional dressing, the minimal time taken for complete healing was 10 days, while the maximal time taken was 24 days with median 18 days while on treating the burned area with conventional dressing without PRP injection, the minimal time taken for complete healing was 14 days, while the maximum time taken was 32 days.
Conclusions: With application of PRP decreased the need of grafting through promoting the healing process of the wound of burned areas than areas not applied with PRP.

Keywords: Sub dermal injection, Topical application, PRP

INTRODUCTION

Burn injury is a major cause of trauma to the human body, causing death and disability with a long healing period and high health care costs. The mortality rate of burn injury is decreasing with new treatment modalities, although secondary infections and long healing periods still affect mortality rates. Early debridement and skin grafting are successful, but insufficient graft donor area and unsuitable patient circumstances for surgery hinder skin grafting. In these circumstances, using products that increase the wound-healing process often affect patient morbidity and mortality. For this purpose, different kinds of dressings and pharmacotherapies have been developed, but most of them are costly, and the mechanisms underlying these therapies have not been fully documented.[1]

Platelet-rich plasma (PRP) is a new adjunct that is increasingly used to treat soft tissue defects to accelerate soft tissue regeneration and in managing chronic non-healing wounds.[2]

Although much progress has been made in burn wound treatment, burns still often result in disfiguring and disabling scars, especially deeper burns that need surgical excision and skin transplantation. A deep dermal burn wound treated with a split skin graft, could benefit from the addition of PRP in several ways. PRP functions as fibrin glue with haemostatic qualities and with the release

of the growth factors provides a well-nourished site for the split thickness graft (SSG) and possibly increasing adherence as well as in growth of the SSG.[3]

Furthermore, the interstices of the SSG could heal faster and result in better scars due to the attributive effect of PRP as it promotes vascular in-growth and fibroblast proliferation, and possibly faster re-epithelialization, as has been shown in vitro models and chronic and acute wound.[4]

The objective of the study was to evaluate the role of the PRP and its effect in modifying and accelerating burn healing in different stages.

METHODS

A prospective study was carried on fifty patients in the plastic surgery Department at Menofiya University Hospital and Abo Quir general hospital. The study was done over one year from October 2017 to October 2018; we are going to use the PRP technique in improving the process of healing in burn scars and graft either by physiological dressing or sub dermal injection.

Patients were divided into 2 groups which are as follows:

Group A

Fifty patients were treated with physiological dressing or sub dermal injection with PRP.

Group B

Fifty patients were treated with conventional dressing without PRP application.

All cases included in this study will be subjected to the following as history and personal data, age, gender, date of admission and associated medical illness. Investigations was done like complete blood count, random blood sugar, bleeding profile (prothrombin time, platelet count, international normalized ratio), and liver and kidney function tests. In the post-operative visits, progression of graft intake, infections, healing of burn. The variables that were measured and compared amongst the two groups included healing of burn, graft intake and the hospitalization time. The age of patients ranged between 9 and 52 years with a mean of 32.5 years. 23 patients (46%) were below 30 years and 27 patients (54%) were above 30 years.

Dressing

The injected area was cleaned by saline then sterilized by ethyl alcohol cotton swab. The activated PRP was collected in 5 cm syringes (10 cm or 20 cm syringes are not preferred as its pump power will not be applicable with the insulin needle) and injected with insulin needle. Intradermal injection of PRP in one limb (upper and/or lower limb) was performed with one limb as treatment group and the other as control group. Patients were injected intradermally once every 2 days for about 3 weeks. PRP was prepared by a process known as differential centrifugation. In differential centrifugation, acceleration force is adjusted to sediment certain cellular constituents based on different specific gravity. The blood was centrifuged twice to separate PRP.

Technique

The first spin separate red blood cells at speed (1500 rpm at 15 min). The lower red blood cell layer was discarded. The upper plasma and middle layers contain platelets that were collected and further centrifuged again during the second spin. The second spin separate platelets from most of plasma volume (2300 rpm at 15 min) and precipitated lower third was collected with part of the plasma as PRP. PRP was prepared by drawing 10-30 cm of venous blood by venipuncture in acid citrate dextrose tubes, the amount of blood withdrawn was punctured according to the amount of the amount of PRP needed and the surface area injected. Every 15 cm of venous blood gave about 7-8 cm of PRP to be activated and injected. Each 20 cm^2 of the burned area is injected by 1 cm of PRP, so if the surface area injected is less than or equal 150 cm^2, only 15 cm of venous blood is needed. While if the surface area injected is more than 150 cm^2, so we need more venous blood in order to get more PRP to cover all this surface area. Before application of the PRP, it needs to be activated to release the growth factors contained in the α-granules of the thrombocytes. 10% calcium chloride was added to the resultant of platelets and plasma, inducing platelet activation.

Technique of application

The row area was cleaned by saline then sterilized by ethyl alcohol cotton swab. The activated PRP was collected in 5 cm syringes (10 cm or 20 cm syringes are not preferred as its pump power will not be applicable with the insulin needle) and injected with insulin needle. Application of PRP in row area in one patient performed as treatment group and the other row area in the same patient as control group. Patients were injected intradermally or spread as thin layer over the row area as physiological dressing once every 2 days for about 3 weeks.

Follow up

Parameters of follow up during hospital stay were duration of wound healing, Presence of infection, role of operations (grafting) and effect of PRP in process of grafting. Parameter of follow up after 3-6 months was the resultant scars.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM

Corp). Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level.

RESULTS

The present study was conducted in the Plastic and Reconstructive Surgery Department of Abou Qir General Hospital, Alexandria, Egypt and Menoufia University the findings are tabulated as below. 23 female (46%) and 27 male (54%), which agrees with other studies that stated that the incidence of burn is higher in males than females. The age of patients ranged between 9 and 52 years with a mean of 32.5 years. 23 patients (46%) were below 30 years and 27 patients (54%) were above 30 years.

Table 1: Distribution of the studied cases according to demographic data (n=50).

	No.	%
Sex		
Male	27	54.0
Female	23	46.0
Age (in years)		
≤30	23	46.0
>30	27	54.0
Minimum-Maximum	9.0-52.0	
Mean±SD	31.55±7.01	
Median	32.50	

In this study, the cause of burn was flame burn in 30 patients (60%) which is the most common cause of burn in adults, while chemical burn was the cause in 12 patients (24%) and only scald burn was the cause in only 8 patients (16%).

Table 2: Distribution of the studied cases according to burn site (n=50).

Burn site	No.	%
Both thighs and genetalia	7	14.0
Face	15	30.0
Both forearms and hands	18	36.0
Both chest and face	10	20.0

Our patients were suffering from deep dermal burns in different sites. Eighteen patients were complaining of deep dermal burn in both forearms and hands (36%). Hands were the common site we worked upon. Faces were the second common site as fifteen patients (30%) was suffering from burns of face, while 10 patients (20%) were suffering from burns of both chest and face and only we worked upon 7 patients (14%) whom were suffering from burns of both thighs and genetalia.

The minimal surface area injected was 48cm^2 and the maximal surface area injected was 360 cm^2 with median of 82 cm^2. We injected our patients 3 times per week for 2 weeks starting from day 1 which is the first day of admission and following up our patients for 3-6 months after healing. During injection there was pain at the sites of injection due to the burning sensation of the anticoagulant (sodium citrate) used in the tubes of PRP separation, this pain was decreased by the injection of narcotics prior the injection. Our patients were instructed to put compression garments immediately after healing to guard against keloid formation.

Table 3: Descriptive analysis of the studied cases according to burn area injected (n=50).

	Minimum-Maximum	Mean±SD.	Median
Burn area injected (cm^2)	48.0-360.0	110.35±73.24	82.0

Table 4: Descriptive analysis of the studied cases according to presence of infection (n=50).

Presence of infection	CD (n= 50)		PRP (n=50)		^{McN}p
	No.	%	No.	%	
Low load	10	20.0	30	60.0	0.021*
High load	40	80.0	20	40.0	

P= p value for McNemar test for comparing between CD and PRP; *=Statistically significant at p≤0.05; PRP=Platelet rich plasma; CD=Conventional dressing.

Table 5: Descriptive analysis of the studied cases according to duration of healing.

Duration of healing	PRP (n=50)	CD (n=50)	Z	p
Minimum-Maximum	10.0-24.0	14.0-32.0		
Mean±SD.	16.90±4.88	22.25±6.10	3.936*	<0.001*
Median	18.0	22.50		

Z,p: Z and p values for Wilcoxon signed ranks test for comparing between CD and PRP; *: Statistically significant at p≤0.05; PRP: Platelet rich plasma; CD: Conventional dressing.

PRP has many potential advantages as boosting the healing process by applying autologous growth factors, supporting homeostasis, and having antimicrobial capacity. Weekly cultures were taken from both the injected sites with PRP and the sites treated with conventional dressing only, the cultures revealed that there was high bacterial load (>10^5) at the burn sites in 40 patients (80%) whom were treated only with conventional dressing without PRP injection where there was low bacterial load (<10^5) only in10 patients (20%). While at the injected sites with PRP, there was high bacterial load only in 20 patients (40%) where there was low load of bacterial infection in 30 patients (60%).

DISCUSSION

PRP is a fraction of blood plasma with a platelet concentration above baseline. After activation of the platelets, growth factors are released, which are involved in wound-healing process.[5]

Platelets are most commonly known for their primary function in the initial phase of wound healing: the homeostasis. However, they are also involved in all the consecutive phases of wound healing. Platelets become activated after aggregation at a disruption of a vessel wall and release many growth factors and other substances. This secretion begins within 10 minutes after activation, with more than 95% of the growth factors secreted within one hour. For the next 5 to 10 days, activated thrombocytes continue to release additional proteins.[6]

The most studied of these growth factors are platelet-derived growth factor, fibroblast growth factor, transforming growth factor β, epidermal growth factor, vascular endothelial growth factor, and insulin-like growth factor, all of which participate in wound healing in numerous ways, such as by promoting chemotaxis, cell adhesion, mitogenesis, proliferation, and angiogenesis. Furthermore, platelets have been attributed with antimicrobial effects, as well as pain-relieving qualities. All of these features make platelets of potential therapeutic use in the treatment of difficult-to-heal wounds in the form of PRP, plasma with an enriched amount of non-activated platelets. After the PRP is activated, it forms a clot, supporting hemostasis, and releases its growth factors, which boosts the healing process.[7]

Most PRP products contain leukocytes because they are derived from the "Buffy coat," the layer of blood plasma that, after centrifugation, contains both platelets and white blood cells. Little is known about the effect of leukocytes in PRP. It has been suggested that they have antimicrobial properties.[8]

Furthermore, leukocytes also produce growth factors involved in wound healing. Some authors do advocate a strictly platelet-pure PRP; however, so far there is no solid evidence that leukocytes in PRP have unwanted side effects, although theoretically they may have catabolic effects, which could influence wound healing negatively.[9]

Another aspect in which PRP products can differ is the fibrin content. The difference between PRP and platelet-rich fibrin (PRF) is that the latter has a more three-dimensional fibrin network, where PRP is more fluid. However, despite its apparent ease of preparation, a PRF clot might not be practical in certain applications such as injection, where a liquid or gel is more suitable.[9]

Platelet concentration factors have been reported to be between 2-fold and 8.5-fold. However, to analyze the platelet counts in PRP it is important to re-suspend the PRP completely before analysis, because platelets precipitate rapidly in this suspension.[10]

This is a critical procedure in the isolation process. It is unclear at present whether all studies that present data on platelet counts in PRP perform this resuspension, because this procedure is often not described.[11]

Quantification of growth factors in PRP has been performed in numerous studies and a substantial variation in growth-factor content was found. The level of growth factors in PRP depends on several factors:[12]

- First, it depends on growth-factor concentrations in the α-granules of the platelets, which is a patient variable.[11]
- Next, processing techniques vary, which results in different platelet concentration ratios and extent of platelet activation as well as fragmentation during preparation.[11]
- Furthermore, it depends on the leukocyte concentration in the PRP, because leukocytes also produce growth factors.[11]
- And finally, it depends on the completeness of platelet activation before measurement, because not all growth factors are released from the platelets during activation. No strict correlation was found between growth-factor amount and platelet count in the baseline blood or PRP; nor with donor age and sex. Despite this variability, growth-factor quantification still is the best kind of quality control of PRP because no suitable alternative exists.[13]

According to other papers in indications of PRP implications in treatment of lower limb ulcer as example of management of raw areas; clinical studies regarding the role of PRP in chronic wound healing are increasing in number comparing the effect of platelet-rich gel with 32 patients serving as controls. Healing rates were 96.15% in patients receiving platelet-rich gel against 59.37% in patients not receiving platelet-rich gel.[14]

In another paper, 19 patients with one wound/ulcer per patient were treated with a single dose of a combination of autologous PRP gel and subcutaneous injections of PRP in and around the wound periphery. All the patients showed healing of the wound with reduction in wound size, and the mean time to healing of the ulcers was 49.84±22.80 days. Reduction in pain was observed in all

the patients after treatment, and also, the quality of life of the patients significantly improved. The results demonstrated the safety and efficacy of autologous PRP in treating chronic non healing ulcers.[15]

In summary, a large heterogeneity exists in PRP products, originating from different preparation procedures, with different PRP content (leukocytes, fibrin-structure), different activation techniques, and an interpatient variability of baseline platelet values and growth-factor content. The only unambiguous factor is that PRP has an increased amount of platelets that are involved in wound healing by their growth factors and cytokines, which are released after activation.[12]

CONCLUSION

The injection of PRP at the burned sites with conventional dressing, decreases the duration of wound healing, decreases hospital stay, decreases the bacterial load of infection and decreases the need of grafting through promoting the healing process of the wound.

ACKNOWLEDGEMENTS

I would like to express my deepest gratitude and extreme appreciation Assistant Professor Dr. Hisham Shafik Abo Grida Professor of general surgery, Assistant Professor Dr. Yasser Mohammed El-Sheikh Professor of plastic surgery, Faculty of Medicine Menofia University for their kind supervision, kind advice constructive encouragement, generous help and guidance throughout the whole work which could not be a fact, without their guidance and kind help. I would like to express my great thanks to Dr. Medhat Samy Ali, lecturer of plastic surgery, Faculty of Medicine, Menofia University for his kind advice and help throughout the whole work.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: El Ghazaly MA, Grida HSA, El Sheikh YM, Aly MS. Topical platelets rich plasma implications in management of burn. Int Surg J 2019;6:3932-6.