SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Surgery

Clinical and Epidemiological Profile of Deep Second Degree Burn Patients Treated with Platelet Lysate

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DOI: https://doi.org/10.36347/sasjm.2024.v10i08.007 | **Received:** 27.02.2024 | **Accepted:** 02.04.2024 | **Published:** 09.08.2024

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Abstract **Original Research Article**

The wound healing process in burn victims is still a problem today despite the advances made in the management of these patients with the different resuscitation regimens, the advent of antibiotic therapy as well as the different local treatments used. The local application of a high concentration of growth factor through the use of halogenic platelet concentrates lyzed by freezing- thawing has been done in the past with the aim of accelerating the healing process of the various wounds. The aim of this work is to describe Clinical and epidemiological profile of deep second degree burn patients treated with platelet lysate. A longitudinal and prospective study was carried out in 30 adult patients with deep second-degree burns with boiling water with a burned body surface area ≤ 5%, treated locally with allogeneic platelet lysate in the Burn centre and Plastic Surgery Service of the General Hospital "Dr. Juan Bruno Zayas Alfonso" in Santiago de Cuba, during the period of February 2015 to February 2016.A total of 30 adult patients have been studied. The mean age was 33.93. Female sex predominated with a male/female ratio of 1/2. The most frequent location of burns was in the lower limbs accounting for 36.6% of patients, followed by the upper limbs and anterior trunk at 26.7% in both cases. For the study group, the epitelization time was less than 21 days and in the majority of cases (66.7%) this time was 7-13 days. Non-relevant side effects were observed in 80% of patients and included pruritus (50%), perilesional erythema (8.3%) and pain in 29.2% of patients. Apart from these side effects, no complications have been observed in our patients. The promising results reported in this study and in the literature warn that platelet lysate may become a potential therapeutic candidate for deep second- degree burns from boiling water.

Keywords: second degree Burns, platelet lysate, regenerative medicine.

INTRODUCTION

The wound healing process in burn victims is still a problem today despite the advances made in the management of these patients with the different resuscitation regimens, the advent of antibiotic therapy as well as the different local treatments used.

Burn wounds do not always heal quickly and can lead to the appearance of scars that are a source of biomechanical or psychosocial problems for the majority of patients [1].

Several methods of local treatment exist nowadays but few of them would give healing results in a very short time and a good aesthetic result at the same time.

For this reason, the main need in patients with lesions that cause loss of skin integrity is their recovery in the shortest time, an aspect that is guaranteed with treatments that promote or accelerate healing, to which special attention is paid nowadays [1].

The local application of a high concentration of growth factor through the use of halogenic platelet concentrates lyzed by freezing-thawing has been done in the past with the aim of accelerating the healing process of the various wounds [2, 3].

The use of high concentrations of growth factor by halogenic platelet lysate is relatively simple, safe, effective, less costly, induces minimal side effects, non-painful, easy access and with a good healing level. This contributes to the improvement and well-being of people who suffer from these aggressions, which is why this therapeutic modality has become a fundamental pillar of the local treatment of burns.

Today, faced with the global financial challenge and various adversities, all countries, especially developing countries with limited resources, should therefore look for alternatives for the treatment of burn patients that are simple, safe, effective, at a lower cost, that induce minimal adverse effects, that are painless, easily accessible and with a better level of cure for the improvement of the well-being of their populations.

MATERIAL & METHODS

A longitudinal and prospective study was carried out in 30 adult patients with deep second-degree burns with boiling water with a burned body surface area ≤ 5%, treated locally on an outpatient basis with ABO compatible allogeneic platelet lysate obtained at the "Renato Guitar" Blood Bank, which were negative for infection screening tests and that according to the rules and procedures established for the use of Blood components were no longer useful for use as a hemostatic agent in the Burn center and Plastic Surgery Service of the General Hospital "Dr. Juan Bruno Zayas Alfonso" in Santiago de Cuba, during the period of February 2015 to February 2016. Patients with baseline platelet values ≥ 150 x109/L, hemoglobin≥ 110 g/l and acceptance through informed consent were included; and patients with a history of chronic non-communicable diseases without medical treatment or decompensated, with diseases of the hemolymphopoietic system, local or systemic infections, collagen diseases and confirmed malignancies were excluded, as well as patients who consumed medications such as anticoagulants or anti-inflammatories non-steroidal; Pregnant; patients with cellular or humoral immune deficiency (referred or proven by patients lab test) and patients with non-recent burns.

In all cases, these procedures were performed on an outpatient basis, spreading the platelet lysate over the lesion. Applications were performed with an interval of 2 days until the lesion was completely healed.

The evolution of epithelialization was evaluated by means of the clinical method; Measurement of the area of the burned area. Evaluations of safety and adverse events were performed by the authors.

Skin characteristics (the quality of the final post-burn skin) were evaluated at 30 days post-treatment using the Vancouver Scar Assessment Scale (VSS) for its adequate correlation with objective parameters and ease of implementation [4, 5].

Treatment was considered satisfactory when the patient met all treatment evaluation criteria and; Unsatisfactory: When the patient met one or none of these criteria.

The research was carried out in accordance with the ethical principles set out in the Declaration of Helsinki [6]. It was approved by the hospital's Research and Ethics Committees.

Percentages and totals were calculated for qualitative variables. The mean (X) and standard deviation were computed, as well as central tendency and dispersion statistics for the quantitative variables. The results were ported in tables and graphs.

RESULTS

In this study, 30 adult patients with deep second-degree burns with boiling water with a burned body surface area ≤ 5%, treated locally on an outpatient basis with allogeneic platelet lysate.

The mean age was 33.93. Female sex predominated with a male/female ratio of 1/2. The most frequent location of burns was in the lower limbs accounting for 36.6% of patients, followed by the upper limbs and anterior trunk at 26.7% in both cases.

The surface measurement of the burns at the beginning had an average of 252.5 ±176.2.

Table 1 shows the distribution of patients by burn epitelization time interval.

Table 1: Patients according to burn epitelization time interval

Burn healing time interval in day	Patients	
	Number	%
7 – 13 (n = 24)	20	66,7
14 – 20 (n = 29)	10	33,3
≥ 21 (n = 7)	0	0,0
Total (n = 60)	30	100,0

For the study group, the epitelization time was less than 21 days and in the majority of cases (66.7%) this time was 7-13 days.

The mean day of epitelization was 12 days with a standard deviation of 2.9 for a 95% confidence interval and extremes of 7 to 20 days.

From a clinical point of view, the healing of burns was characterized by the appearance of firm, confluent epidermal islets. The first islets appear after the second application of platelet lysate and the firm, confluent islets appear after the third application on the ninth day of treatment.

Non-relevant side effects were observed in 80% of patients and included pruritus (50%), perilesional erythema (8.3%) and pain in 29.2% of patients. Apart from these side effects, no complications have been observed in our patients.

From the analysis of the quality of the skin resulting from the healing process, it was appreciated that the scores obtained were directly proportional to the appearance of the skin; that mean, with less punctuation, a better appearance of the skin.

All patients scored between 0 and 5 with an average score of 3 points. Patients presented with post-burn scars with normal pigmentation and vascularity, adequate flexibility, sensitivity, and with equally adequate thickness/height. In relation to this, the result obtained was satisfactory (Figure 1).

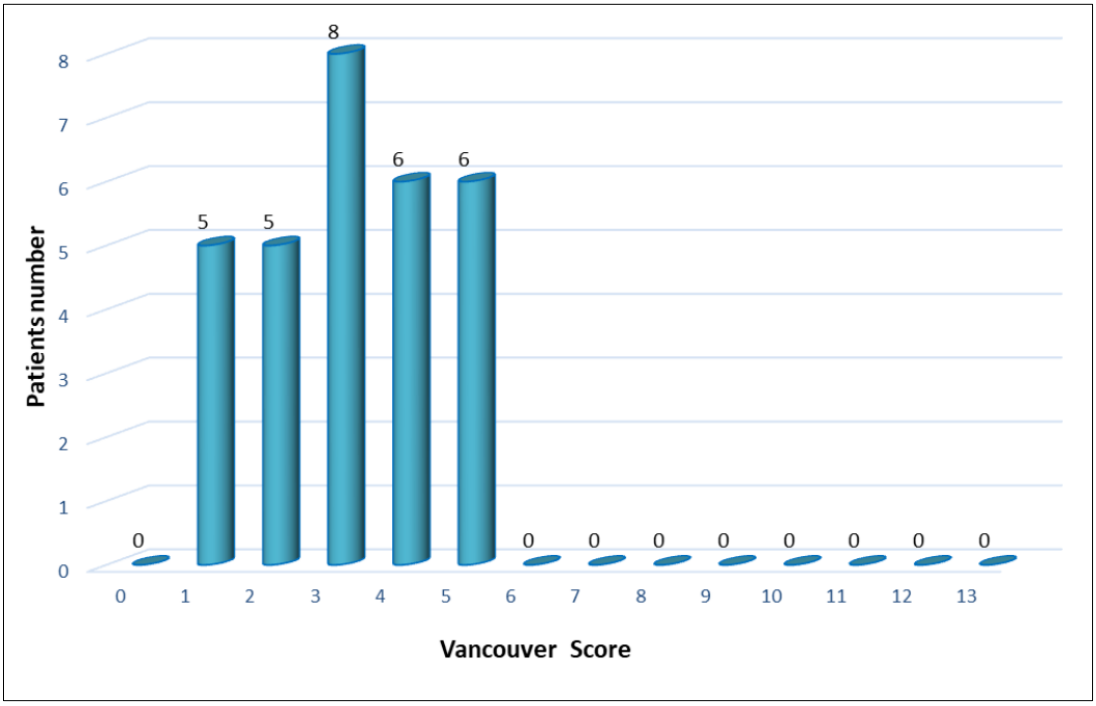

Figure 1: Patients according to the Vancouver score

All 30 patients achieved the outcomes for a satisfactory outcome as shown below in Table 2.

Table 2: Pacients according to the evaluation criteria of the treatment

Treatment Response Criteria and Therapeutic Evaluation		Patients	
		Number	%*
or more of the healed area before the 21 days	yes	30	100,0
	No	0	0,0
Complications	yes	0	0,0
	No	30	100,0
Vancouver Scale	0-5	30	100,0
	6-13	0	0,0
Therapeutic Assessment	Satisfactory	30	100,0
	Unsatisfactory	0	0,0

The outcome of the therapeutic evaluation was satisfactory and characterized by 0 complications in all patients in the study, a cure of 90% or more before 21 days from the start of treatment of the affected surfaces and a Vancouver assessment score between 0-5 points in all patients in the study.

DISCUSSION

Human platelet lysate has attracted much interest from many researchers as it is growth-factor rich for cell expansion, which is employed as a new therapeutic strategy. Due to the presence of a large number of growth factors, platelet lysates have potential

roles in wound healing, treatment of ocular graft-versus-host disease, osteoarthritis, Parkinson's disease, tendon regeneration, infertility, androgenetic alopecia, nerve repair and regenerative tissue, such as bone regeneration [7].

There is concrete evidence that out dated allogeneic platelet concentrates not used for transfusion are valuable sources of functional trophic factors, including growth factors, cytokines, chemokines, anti-inflammatory and antioxidant molecules [8].

In our study, it is evident that when platelet lysate is used locally, the average healing time of burns is reduced by 32.89% in accordance with the percentage reported in a previous study in second-degree burns of similar extent, depth and location [9]. In addition, platelet lysate reduces the healing time of these burns by 47.62% and 52.86% if it is assumed that they usually recover between 3 and 4 weeks, respectively.

The most rapid epithelialization obtained with the platelet lysate found is consistent with that observed in the cornea and eye of 10 patients with ocular burns treated with platelet-rich plasma [10], traumatic wounds and friction burns treated with platelet-rich plasma in gel form [11], and venous ulcers [12]. For venous ulcers, the area of injury at baseline (67.8 ± 19.9 cm2) decreases by more than 95% at the end of treatment (12.3 ± 11.1 cm2) in less than 15 days when all patients are treated with platelet lysate. This result has been explained by the useful granulation of the tissue, epithelialization and contraction of the lesion edges and regeneration of hair follicles [12]. The tissue regeneration time is further shortened when platelet-rich plasma is combined with the ablative laser, because it accelerates angiogenesis and consequently skin rejuvenation [11].

The ideal treatment for the burn patient has not been established so far and consists of healing the lesion in the shortest time with minimal adverse events induced in the patient. The adverse events described are consistent with those documented in other studies [13]. The pruritus present in burns during treatment with platelet lysate can be explained by the intense inflammatory reaction caused by the release of growth factors by platelets and the release of histamine by the cells involved in this inflammatory process and which are activated by platelets as documented by Moya Rosa *et al*., [13]. Locally in burn injuries, the inflammatory process is much more intense and prolonged over time. Thus, macrophages and neutrophils produce a large number of chemical mediators, enzymes, free radicals, and reactive oxygen species, which may be responsible for the extent of tissue damage and the enlargement of the burned bed. This leads to a significant erythematous reaction with a prevalence of lesion surrounding oedema and consequently an increase of local pain [13].

It is possible that the anti-oedema effect of platelet lysate is due to early angiogenesis, in which the weak and permeable vascular bed is rapidly replaced by the appropriate vascular wall due to endothelial proliferation, as other authors warn [14].

The decrease in pain with platelet lysate, in general, has been explained by platelets having analgesic properties due to the release of protease-activated receptor 4 peptides and the large number of biomolecules and ligands, such as Platelet Factor 4 (PF4) and CD40L (CD40 ligand of helper T lymphocytes) [15]. In addition, platelet-rich plasma contains Mesenchymal Stem Cells (MSCs) multipotent that promote axonal regeneration and restore the normal biophysical properties of the axon, so these may be involved in the possible mechanism by which platelet-rich plasma leads to pain reduction [16].

The safety, the occurrence of minimal adverse events, high efficacy and the satisfaction of patients treated with platelet lysate are in agreement with those of Ávila Álvarez [17], who announces that the use of platelet-rich plasma is a simple, cost-effective, safe treatment option and the main adverse events described are pain, erythema and possible local infection.

The non-occurrence of infections in patients treated with platelet lysate, during the observation period, can be explained by the complete release of all growth factors, following lysis of platelets by the freeze/thaw method, and increases in the numbers of polymorphonuclear leukocytes and macrophages at the burn site which promotes increased defense against infection in the affected area. Platelets can interact directly with viruses, bacteria, fungi and protozoa through proteins with microbicidal properties that are involved in defence against pathogenic microorganisms. Among these proteins are peptides called thrombocidins that possess antibacterial and antifungal activity [18].

Our results show better skin quality resulting from the healing process of deep second-degree burns by boiling water with the application of platelet lysate, for the four variables analysed.

These results obtained with platelet lysate are characterized by the absence of hypopigmentation and hyperpigmentation of the skin with adequate vascularization. This post-burn scar is flexible, with adequate sensitivity and a normal height or thickness. In addition, patients treated with platelet lysate do not show the presence of hypertrophic scars or keloids. Despite this, superficial burns treated with platelet-rich plasma have been reported hypertrophic scars and keloids [19].

In general, patients in the study experience closure of the lesion without scarring, which is safer and longer-lasting. This is supported by the knowledge that the fibroblast is the most important mesenchymal cell in

the wound healing process. It acts as a factory in the elaboration of the extracellular matrix, and as specialized machinery that allows, thanks to its contractile properties, the healing of the burn. In addition, in this healing process, the actions of the growth factor derived from platelets are highlighted (platelet Derived Growth Factor: PDGF) and platelet-derived growth factor-β (PDGF-β), provided by the lysate, which induce the formation of elastin (a common component of the normal dermis), but which does not occur during the healing process of the lesion. The absence of this component of the extracellular matrix of the normal dermis could explain the firmness and lack of elasticity of the scars, but when closure of the lesion is provided, it tends to be more effective [20].

Platelet lysate acts on the acute inflammatory response by modulating neutrophil activity and reducing edema and stimulates the chronic inflammatory response early so that it replaces the acute inflammatory response when it declines, as reported, so we can infer that platelet lysate can stimulate lymphocyte proliferation. This may be related to the release of growth factors, which have direct influences on the remodelling of the extracellular matrix and the release of vasoactive substances that help the subsequent phases of inflammation that modulate the inflammatory response, according to Utrillo Contreras [21]. The intense vascularization observed after treatment with platelet lysate demonstrates the acceleration of the angiogenesis process with the marked proliferation of newly formed vessels and fibroblasts. This finding may be related to the efficacy of the different growth factors released by platelets on soft tissue lesions and their action as a polymerized matrix of platelet-rich fibrin and cytokines that favor the proliferation of fibroblasts. The latter are responsible for maintaining the integrity of the tissues and participate in the composition of the granulation tissue. As a result, angiogenesis can be suggested to be the key link in the process of tissue revascularization and regeneration. Therefore, platelet lysate may be essential in promoting angiogenesis, a mode that is consistent with other studies [22]. With the use of platelet lysate, it is also evident that angiogenesis, neovascularization and consequently regeneration are stimulated with the rapid healing of burns; Thus, platelets act as a biological support on which the endothelial cells of the new blood vessels are deposited. In addition, they secrete various biochemical factors, including pro- and antiangiogenic growth factors that promote tissue reaction to inflammation and recruitment. Of connective tissue progenitor cells, a mode that agrees with other authors [22, 23].

It also reveals the early deposition of collagen fibers due to the abundance of fibroblasts, which also have an effect on the proliferation and differentiation of keratinocytes, essential in re-epithelialization. In addition, the presence of neoformed epithelium is due to the stratum corneum present in the samples. This, together with the intensity of fibroblast proliferation evidenced in histopathological findings, may support the hypothesis that platelet lysate is a biological material that acts through the polymerized matrix of platelet-rich fibrin and cytokines that favor fibroblast proliferation [23].

The transforming growth factor β1 it is a potent regulator of extracellular matrix synthesis as it increases the expression of the fibronectin gene and collagen, and inhibits collagen degradation. This leads to a reinforcement of the extracellular matrix, fibroblast proliferation, and collagen synthesis and accumulation, essential processes for wound healing [24]. Platelet lysate stimulates re-epithelialization with the growth and maturation of the new epithelium early, which is consistent with other studies [24, 25]. Aragón-Urrego *et al*., [24], demonstrate significant increase in collagen fibers in surgical skin wound repair in male rabbits Oryctolagus cuniculus, New Zealand when platelet concentrate is used. In addition, Ávila *et al*., [25], document the rapid re-epithelialization and deposition of collagen fibers due to the abundance of fibroblasts in the biopsy of the treated skin and the granulomatous reaction, demonstrating the regenerative effect of platelet-rich plasma on tissues in white adult rabbits New Zealand).

CONCLUSION

The promising results reported in this study and in the literature warn that platelet lysate may become a potential therapeutic candidate for deep second-degree burns from boiling water due to its safety, minimal adverse events, and high efficacy, low cost, high expectation and good degree of satisfaction of the patient for the final quality of the post-burn skin obtained and causes the regeneration and healing of these burns to be fast and with quality.

Conflict of Interest: None

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