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Hypertrophic Scar Formation and Wound Healing Modulation Fatty Acids as Modulators of Severe Scars

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Abstract

Scar tissue usually generates severe discomfort in the short and long term. Common symptoms include anesthetics sequelae, pruritus, joint malfunction, new wounds on the scar surface, and pain. There are several treatments for scars, like compression, topical or intralesional steroid infiltration, 5-fluorouracil, dermabrasion, and surgeries with new scar tissue. For adult patients, it is easier to choose the treatment. However, compression is commonly applied in children to prevent treatments that have adverse effects. This study reports the outcomes of 15 patients submitted to abdominoplasty, traumatic wounds and post-burn scar treatments, which showed significant changes after the continuous use of an ointment composed of petrolatum, cod liver oil, BHT, *Chamomilla recutita* (chamomile) oil, *Helianthus annuus* (sunflower) oil, and *Prunus amygdalus dulcis* (sweet almond) oil. As components of the stratum corneum, unsaturated fatty acids influence the cutaneous structural and immune status and permeability. They also interfere with the maturation and differentiation of the stratum corneum and inhibit the production of proinflammatory eicosanoids, reactive species (ROS and RNS), and cytokines, thereby influencing the inflammatory response and possibly wound healing. This article aims to share our experience with the regular use of an ointment in adult and pediatric patients for three months. The increase in proinflammatory cytokine production at wound sites, resulting in a non-invasive, therapeutical, and effective cutaneous wound healing and scarring modulation, may provide a physiopathological explanation for the fast improvement of scars.

Keywords

Scarring, Burn Scar, Inflammatory Modulation, Cytokine, Sequelae, Fatty

Acids, Eicosanoids, Non-Adverse Effects, Aesthetics, Hypertrophic

1. Introduction

Burn surgeons observe daily that, immediately after the acute treatment, burn patients experience an undetermined evolution stage. That stage is challenging to manage, as it requires long rehabilitation times, particularly in flexion-extension areas, and surgical revisions.

In developing countries, scar treatment is usually challenging due to long distances to specialized centers, treatment costs, difficult access to medical technology, and insufficient recognition of these pathologies by the public health systems.

In Latin America and our practice, phototypes IV to VI of the Fitzpatrick scale are prevalent as brown skin tends to scar pigmentation and has a greater risk of forming hypertrophic or keloid scars [1] [2].

In cosmetic surgery, hypertrophic scars and keloids pose an aesthetic and functional problem. One study found that 60% of the patients were unsatisfied with the cosmetic results of their scars after dermatologic and cosmetic surgery procedures, and up to 90% wanted to improve their appearance [3].

Curefini was initially, and it is currently used as a topical treatment for epidermolysis bullosa and chronic wound healing. No adverse effects and good wound-healing outcomes have been reported. Our team has a long experience in surgical treatments, and we started using the product to treat small, ulcerated lesions that remain in the final stage of burn healing. We observed that healed areas improved faster, showing more elasticity, better texture, less itching, and reduced post-inflammatory vascularity and pigmentation.

Therefore, planning scars is just as important as planning flaps. An efficient topical medication, combined with usual therapies, may aid the modulation of healing stages.

2. Objectives

This article aims to demonstrate that the use of Curefini®, associated with traditional scar modulation therapies, is more efficient in producing better scar cosmetic and functional outcomes than only moisturizing creams associated with those treatments.

The evaluated treatment complied with the specifications for the clinical use of the drugs. In this regard, all clinical research should safeguard the dignity of participating subjects, ensuring their rights, particularly their autonomy and physical, mental, and oral integrity. [4]

3. Material and Methods

This study included 15 patients under acute stage resolution, treated or not with

grafts, presenting hypertrophic scars with erythema or pigmented scars up to six months from the start of healing.

Patients with scars older than two years and stable were excluded because they presented no measurable differences suitable for this study, keloid scars that could not be partially resected or submitted to z-plasty, or keloids requiring immunomodulatory treatment.

Both adult patients and pediatric patient surrogates granted their consent to participate in this study, per the ethical-legal regulations.

The topical medication used was Curefini®, an ointment composed of sunflower oil, cod liver oil, beeswax, sweet almond oil, petroleum jelly (Vaseline®), and butylated hydroxytoluene (BHT). [5]

The protocol was applied for three months. Curefini® was applied to hypertrophic scars resulting from burns or cosmetic surgeries. Photographic records were made at 30, 60, and 90 days of treatment to evaluate scar evolution in terms of scar pigmentation, itching reduction, and elasticity improvement. The Vancouver Scar Scale [6] [7] [8] (**Table 1**) and photographic records of the parameters specified in the protocol were used as a reference for scar evolution.

Table 1. Vancouver scar scale.

Scar characteristic	
Vascularity	*Score*
Normal	0
Pink	1
Red	2
Purple	3
Pigmentation	
Normal	0
Hypopigmentation	1
Hyperpigmentation	2
Pliability	
Normal	0
Supple	1
Yielding	2
Firm	3
Ropes	4
Contracture	5
Height (*mm*)	
Flat	0
<2	1
2 - 5	2
>5	3
Total score	13

Despite being a subjective clinical assessment tool designed to describe scars in general—not hypertrophic scars—we chose the Vancouver Scar Scale in this study because it is simple, easy to apply in low-technology settings, and possibly the most recognized burn scar assessment method. The VSS remains widely applicable to evaluate therapy and as a measure of outcome in burn studies. [9]

3.1. Pathophysiology of Healing and Role of Polyunsaturated Fatty Acids

Pathological scars are caused by an excessive response to the activity of TGF-β1. Connective tissue growth factors are overexpressed 100- to 150-fold in hypertrophic and keloid scars, respectively, in response to this cytokine compared with normal fibroblasts. [10] [11]

Our treatment was based on studies that showed that the concentration of polyunsaturated fatty acids (PUFA, EPA, DHA) influences the synthesis and activity of proinflammatory cytokines and inhibits the expression of the gene induced by TGF-β1, inhibiting pro-fibrogenesis. [12] [13]

Those fatty acids may partially inhibit some inflammation processes, such as leukocyte chemotaxis, adhesion expression molecules and leukocyte interactions with the endothelium, the production of eicosanoids, such as prostaglandins and leukotrienes, from arachidonic n-6 PUFA, and T-cell inflammatory cytokine production and reactivity. Eicosapentaenoic acid (EPA) stimulates the biological activity of arachidonic acid (AA) derivatives and the synthesis of active mediators of inflammation resolution, such as resolvins and protectins. [14]

Those mediators compete with cyclooxygenases and lipoxygenases and reduce the expression of COX-2 and 5-lipoxygenase, with a beneficial anti-inflammatory effect of n-3 PUFAs. [15] [16]

3.2. The Role of Vitamin D in Inflammation

Supplied by sunflower, sweet almond oil, and cod liver oil, vitamin D significantly reduces IL-6 and TNF-α levels. Using cholecalciferol receptors, it directly binds to leukocyte DNA, activating the MKP-1 gene and thereby interfering in the inflammatory cascade. [17] [18]

3.3. Virgin Beeswax

It contains long-chain polysaccharides, long-chain free fatty acids, palmitic acid, and exogenous compounds. It is associated with other components as a skin protector, as it is highly hydrophobic. Studies carried out in 2016 report that it has antibacterial activity against *S. aureus* and antifungal activity against *C. albicans*. [5]

3.4. Study Description

Our experience with Curefini® in the combined treatment for burn sequelae began in 2019.

Our "patient 0" was an adolescent female admitted on 08/20/2019 due to an extensive burn by direct fire. She remained hospitalized for a long time due to *Pseudomonas* A infection acquired in the hospital. She was submitted to grafting and discharged on 10/25/2019 (Figure 1). On 03/12/2020, she started elastic bandage compression and Curefini® treatment (Figure 2).

The patient discontinued compressive treatment three months after the start and revisited the hospital on 04/19/2021, showing an elastic, hypopigmented scar with some hypertrophic nuclei under regression (Figure 3).

The patient was maintained under the ointment treatment only.

We then decided to apply an evaluation protocol of the topical treatment without interrupting the usual therapies.

4. Results

Healing is an active process that lasts 12 - 18 months.

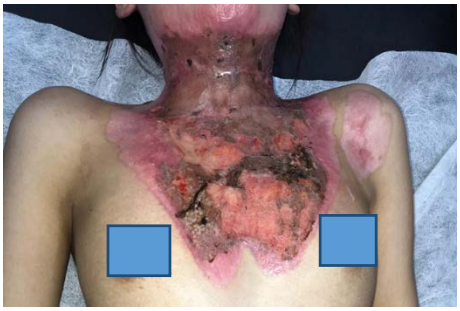

Figure 1. Thorax and neck burn.

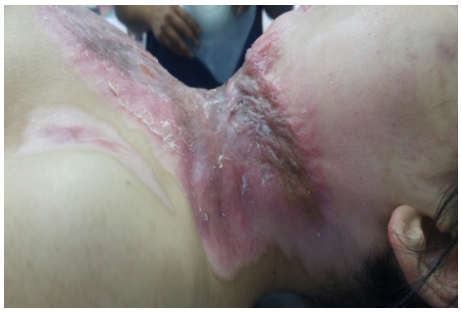

Figure 2. Neck graft.

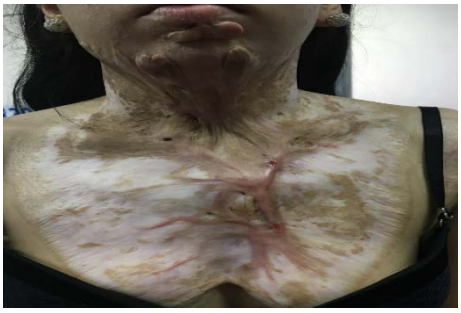

Figure 3. Thorax and neck burn 18 months later.

Although between the first 15 to 30 days the patients without compressive treatment showed an increase in purplish-red scar pigmentation, after 90 days the scars showed less erythema due to a decrease in the vascular scar component.

A notable decrease was observed in the Vancouver Scar Scale score in the treated patients during that period. (Table 2)

Although some scars initially showed severe pliability scores, the firmness, pigmentation, itching, and superficial lesions commonly observed in hypertrophic scars were reduced.

Patients who started topical treatment with Curefini® and required surgical treatment (surgical skin flaps, z-plasty, new grafts) showed better post-surgical healing of the new scars.

One of the adult patients presented wound dehiscence due to infection with *Staphylococcus* A (MRSA) and was submitted to surgical debridement and secondary intention wound healing, showing a rapid regression of the initial surgical wound.

It was not possible to evaluate one of the abdominoplasties at 60 days, but at 90 days post-surgery, the wound already had the characteristics of a mature scar.

Only one patient showed no changes between 60 to 90 days, but at 120 days, the wound remained stable.

No patient presented any irritation, pruritus, or allergy signs to the ointment used.

Photographic Record

Wound evolution between 30 and 90 days is shown below. Due to the vast number of records, only the most significant are shown. (Figures 4-18)

Table 2. Vancouver scar scale results.

Patient	*Age (yrs.)*	*Start treat.*	*30 D*	*60 D*	*90 D*	*Scar*	*Compression*	*Graft*
AL	46	**6**	**2**	**0**	**0**	Abdominoplasty	No	No
SS	43	**9**	**10**	**4**	**2**	Abdominoplasty	No	No
FA	49	**8**	**8**	**4**	**0**	Abdominoplasty	No	No
ID	2	**8**	**6**	**4**	**3**	Ant. Thorax burn	Yes	No
MM	10	**8**	**8**	**7**	**7**	Abdomen burn	Yes	No
CM	2	**12**	**8**	**6**	**6**	Neck burn	No	Yes
AL	18	**12**	**8**	**6**	**4**	Neck burn	No	Yes
FJ	6	**13**	**11**	**8**	**4**	Hand burn	Yes	Yes
CS	12	**7**	**4**	**4**	**4**	Hand burn	No	No
SV	5	**9**	**7**	**5**	**3**	Forearm burn	Yes	Yes
FA	4	**12**	**8**	**6**	**6**	Ankle burn	No	Yes
LB	16	**9**	**8**	**8**	**?**	Foot burn	No	Yes
MO	20	**5**	**1**	**0**	**0**	Ciliary burn	No	No
SM	45	**5**	**3**	**2**	**0**	Lower eyelid tumor	No	Yes
PS	82	**5**	**5**	**2**	**0**	Lower limb wound	No	No

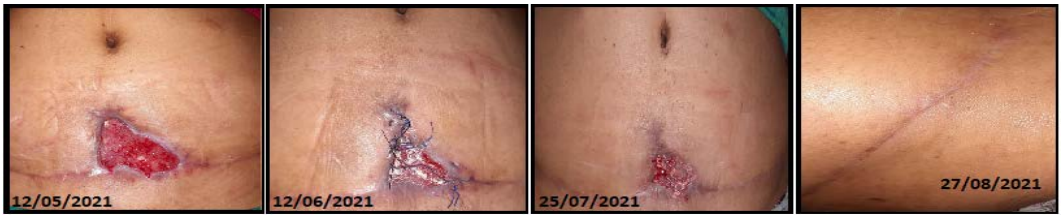

Figure 4. Abdominoplasty dehiscence by MRSA infection. Scar surface improvement.

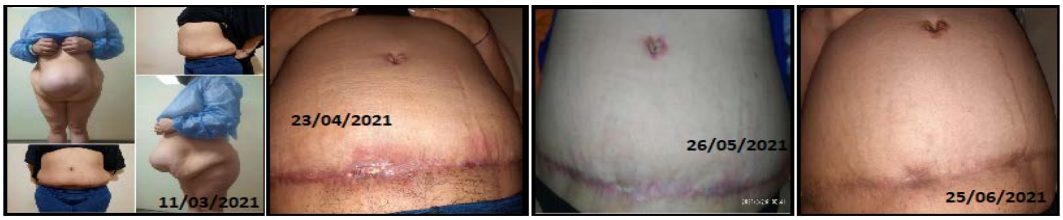

Figure 5. Abdominolplasty. Diabetic and hypothyroid patient.

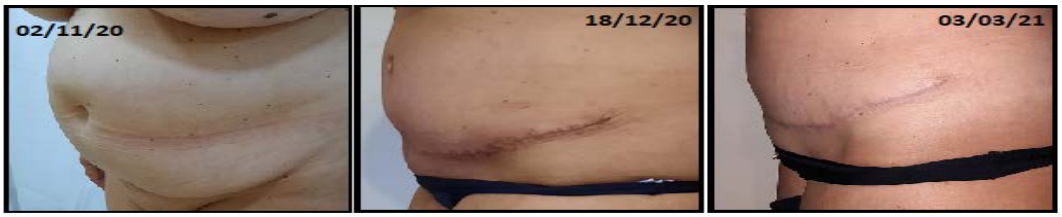

Figure 6. Abdominoplasty hypothyroid patient.

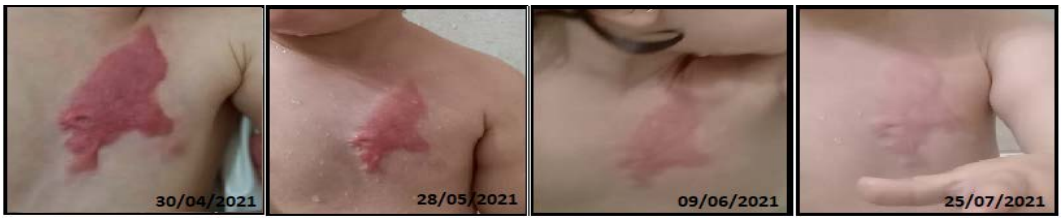

Figure 7. Thorax burn. Compressive treatment missed.

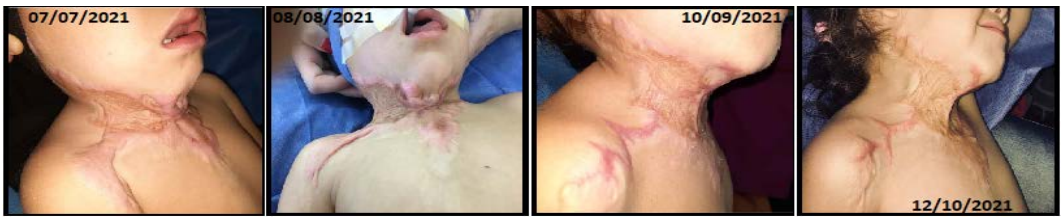

Figure 8. Neck and shoulder burn ropes. Z plasty and grafting.

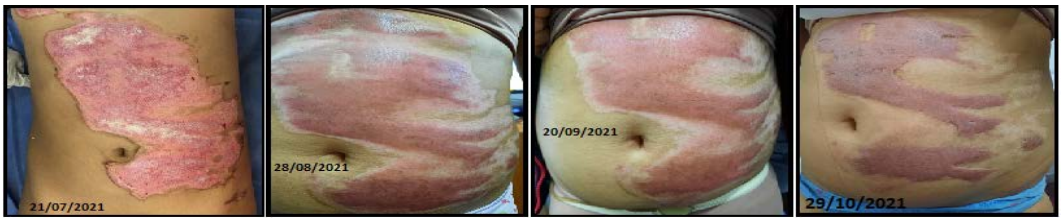

Figure 9. Abdominal 2nd degree burn without grafting. Scar surface improvement.

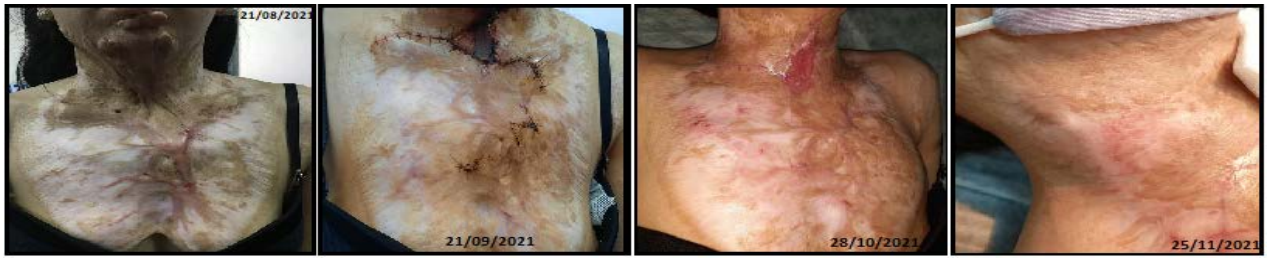

Figure 10. Fire 3er degree neck and thorax burn. Scar surface improvement. Jugular vein prominence.

Figure 11. Fire burn hand sequelae. Grafting without compressive treatment.

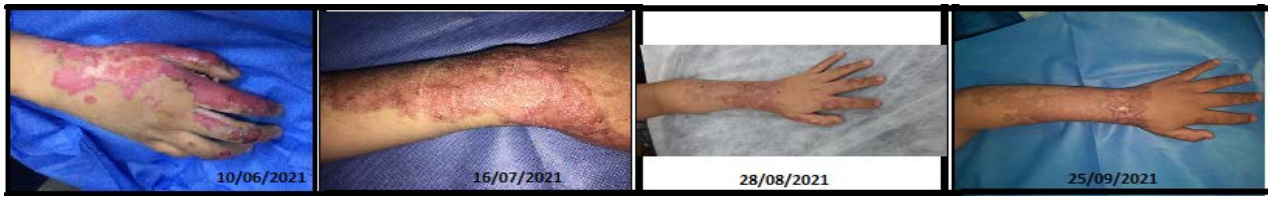

Figure 12. Fire acute 2nd degree burn wrist.

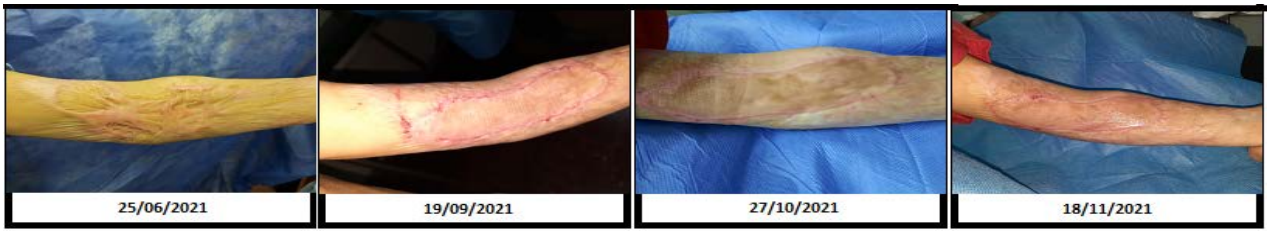

Figure 13. Arm sequelae. Grafting and compressive treatment.

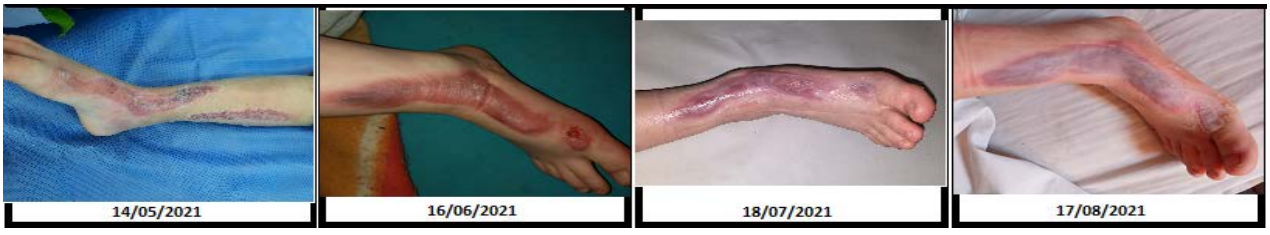

Figure 14. Acute 2nd degree foot burn. Grafting.

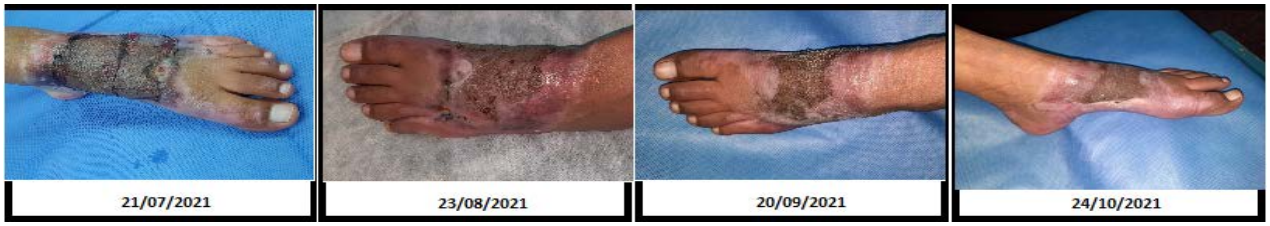

Figure 15. Acute 3rd degree foot burn.

Figure 16. Traumatic wound and friction burn. Scar surface improvement.

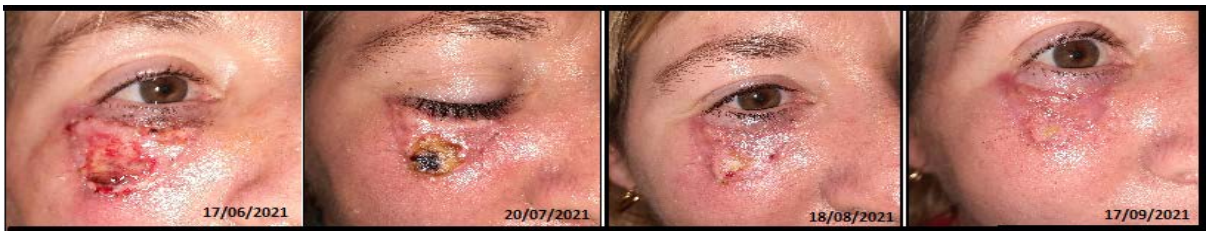

Figure 17. Lower lid Basal Cell Carcinoma. Epidermolysis on the full thickness graft.

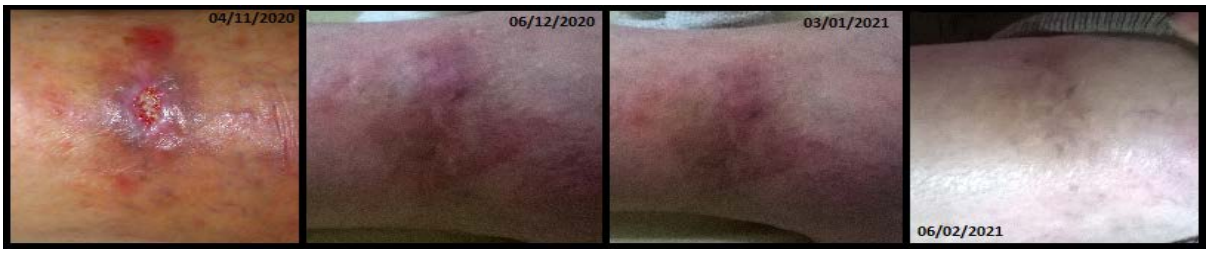

Figure 18. Traumatic wound in Chronic Venous Insufficiency.

5. Conclusions

Using a topical treatment with minimal risk of adverse effects as a complementary therapy to inhibit chronic inflammation significantly reduces the number and complexity of scar revision surgeries, provides better comfort for patients requiring compressive dressings, and produces more elastic and less visible scars in a shorter time.

Based on our experience, surgery planning may be now different, as the use of Curefini® before surgery allowed for obtaining more elastic scars and planning flaps with the same grafted skin as the new scars are easier to conceal.

In cosmetic surgery, the use of Curefini® immediately post-op shortens healing time and provides satisfying scar results.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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