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Keloid Treatment Using Plasma Exeresis: A Pilot Trial Study

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Abstract

Introduction: Keloid scars and hypertrophic scars are more commonly seen after surgeries, suture placements, or other skin damages. Scars can be treated using a variety of methods, including topical compounds, surgery, and lasers. The aim of this study is to evaluate the effects of plasma exeresis on the treatment of keloid scars.

Methods: This experimental study was conducted on patients with keloid scars, defined as a treatment-resistant subtype of scars with extension beyond the primary skin defect and cauliflower appearance, in different parts of the body. The patients were treated with 2-to-3-session plasma exeresis. Scars were examined based on the Vancouver scar scale (VSS) before and 5 months after the treatment.

Results: A total number of 24 scars were enrolled in this study. The number of patients was 16. There was a decrease in the mean thickness of keloids from 2.20 to 0.54 ($P=0.000$). The mean pigmentation and pliability scores decreased from 1.54 and 2.16 to 0.375 and 0.541, respectively ($P=0.001$). There was a significant reduction in the keloid scar vascularity score from 1.666 to 0.541 ($P=0.000$). There was a decrease from 0.708 to 0.00 ($P=0.004$) in the mean itchiness score. After the intervention, the mean pain score was 0.000, compared to 0.7500 before the intervention ($P=0.003$). There was a decrease in the total score from 8.958 to 2.000 ($P=0.000$).

Conclusion: The plasma exeresis procedure is effective in destroying small keloid scars. Furthermore, results in less itching and pain, as well as no significant complications or recurrences.

Keywords: Keloid scar; Keloid treatment; Plasma exeresis; Plexr; Skin surgery.

Introduction

In the case of surgery, suture, or other skin damage, keloid and hypertrophic scars are more likely to occur as a result of an improper wound-healing process.[1] Environmental and genetic factors, as well as the location of the wound, determine the final shape and characteristics of the scars (e.g., pliability, color, thickness).[1-3] Patients may experience pain, itching, or paresthesia as a result of these unpredictable scars.[2]

Preventing keloid formation is the key way to reduce its subsequent problems, but sometimes even with the best efforts, scars still develop and intervention is required.[2] Various methods and procedures, such as topical compounds, surgery, and laser, are used today to treat scars.[2,4] The use of compounds such as silicones and vitamin E has shown promising results in preventing scar formation by reducing the proliferation of additional tissues. Additionally, injections of corticosteroids have shown positive effects in the treatment of keloid lesions by inhibiting inflammatory factors and causing apoptosis.[5,6] Direct tissue ablation is also achieved using lasers and surgical methods.

Plexr is a wireless and rechargeable device that ionizes the air between the device and the skin and turns it into plasma.[7] As a result, additional tissue can be transformed from solid to gas by the consequent energy. The device is available in 3 voltages: the lower one is a white handpiece (0.7w), the medium one is a green handpiece (1w), and the higher one is a red handpiece (2w). This device has made a significant impact on blepharoplasty procedures and is now being evaluated for several skin conditions, including acne and rejuvenation.[7-9]

To our knowledge, no trial has been conducted using Plexr to treat keloids. To evaluate how plasma exeresis affects keloid scars, we conducted this experimental study.

Materials and Methods

This study was a single-arm clinical trial that was conducted between April 2020 and February 2021 in teaching clinical centers of Tehran Islamic Azad University of Medical Sciences after it was approved by the ethics committee of Tehran Islamic Azad University of Medical Sciences.based on ethical standards and Declaration of Helsinki 1965 and its later amendments.

A non-random selection process was used to select patients with keloid scars (defined as a treatment-resistant subtype of scars with extension beyond primary

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skin defect and cauliflower appearance) in all parts of their bodies, who signed an informed consent form. Those patients who had the possibility of repeat visits and follow-ups were included in the study. Those patients who were unable to participate in the follow-up and those with severe complications (i.e., skin infection, post-inflammatory hyperpigmentation, or scar) or a history of other treatments within the last three months were excluded from this study.

In a predesigned checklist, demographic information, as well as the age, the duration of the keloid, and previous therapeutic methods were recorded. In addition to observing and palpating scars, we asked patients whether their scars were itchy or painful according to the Vancouver scar scale (VSS). The VSS is vastly used in both clinical practice and research to evaluate changes in scar appearance. It is a valid scale to assess treatment efficacy based on grading scars before and after treatment. The scoring of the VSS was conducted by an experienced dermatologist before and after the treatment.

To provide local analgesia, we applied topical Xyla-P (lidocaine 2.5% + prilocaine 2.5%) cream to the scars for 30 minutes. Only one patient received a lidocaine injection for analgesia, as the topical Xyla-P cream was ineffective. The scars were all treated with plasma using a red handpiece by a dermatologist. The plasma exeresis was performed by Plexr® (GMV, Italy) the spot-by-spot method. No skin contact was made between the tip and the skin. Scars with a diameter of less than two millimeters were treated in two sessions separated by one month. Scars thicker than two millimeters were treated in three sessions at one-month intervals. After each session, the carbon crust of sublimated scar tissue was dressed. It was recommended that patients not wash or manipulate the carbon crust. It was also requested that they cover the scar region for one month in order to protect it from sunlight. After the intervention, the patients used Avène's Cicalfate cream, which has a proprietary postbiotic formula that helps repair skin. Follow-up was conducted for five months to determine whether the disease recurred or if complications occurred. In order to evaluate the scars before and 5 months after the intervention, the VSS was used. In addition, the patients were asked to indicate their satisfaction with the treatment by selecting one of the following options: No significant change, good improvement, very good improvement, or excellent improvement.

IBM SPSS Statistics for Windows (version 21, IBM Corp, Armonk, NY) was used to analyze the data. The quantitative variables were reported as mean and standard deviation (SD). Qualitative variables were expressed as numbers and percentages. The Wilcoxon signed-rank test was applied to compare the scores before and after the treatment. A P value less than 0.05 was considered statistically significant.

Results

There were 24 scars analyzed in this study from 16 patients (12.5% men and 87.5% women), whose ages ranged from 19 to 55 (Table 1). The causes of keloid formation in most patients were post-surgical scars. Various areas of the body were affected, including the neck, leg, face, abdomen, axilla, breast, and chest (Table 1).

As shown in Table 2, the characteristics of the keloid scars prior to and five months after the intervention are summarized based on the VSS. The mean thickness of keloids decreased from 2.208 to 0.5417 five months after the intervention ($P=0.000$). Additionally, pigmentation and pliability scores decreased from 1.541 and 2.166 to 0.375 and 0.541, respectively ($P=0.003$, 0.000). In the 5th month of the follow-up, the keloid scar vascularity score declined from 1.666 to 0.5417 ($P=0.000$). By the end of the study, the average itchiness score had dropped from 0.708 to 0.000 ($P=0.004$). The mean pain score was 0.750 before the intervention, and it was 0.000 five months later ($P=0.003$). A mean total score of 8.958 was obtained before

Table 1. Demographic and clinical characteristics of patients and scars

Variable	Measurement
Age (y), mean (SD)	33.06 (9.11)
Gender (female), No. (%)	14 (87.5%)
Cause of scar, No. (%)	
Abdominoplasty	1 (4.2%)
Burn	1 (4.2%)
Chickenpox	6 (25%)
Mammoplasty	7 (29.2%)
Removal of the mole by RF	1 (4.2%)
Shoulder arthroplasty	2 (8.3%)
Skull fracture	1 (4.2%)
Surgery of the axilla breast	2 (8.3%)
Surgery of intestinal rupture	1 (4.2%)
Suture	1 (4.2%)
Unknown	1 (4.2%)
Scar duration (months), mean (SD)	57.25 (59.31)
Scar location, No. (%)	
Abdomen	5 (20.8%)
Areola	4 (16.7%)
Axilla	2 (8.3%)
Breast	3 (12.5%)
Chest	1 (4.2%)
Forehead	1 (4.2%)
Hand	1 (4.2%)
Leg	1 (4.2%)
Neck	1 (4.2%)
Shoulder	4 (16.7%)
Umbilical	1 (4.2%)

RF, radio frequency

Table 2. Vancouver Scar Scale Findings in the Study Population

	Before Intervention	In 5-Month Follow-up	*P* Value
	No. (%)	No. (%)	
Height			0.000
Flat	0	14 (58.3)	
<1 mm	6 (25)	7 (29.2)	
1-2 mm	9 (37.5)	3 (12.5)	
2-4 mm	7 (29.2)	0	
>4 mm	2 (8.3)	0	
Pliability			0.000
Normal	2 (8.3)	15 (62.5)	
Supple	9 (37.5)	5 (20.8)	
Yielding	1 (4.2)	4 (16.7)	
Firm	7 (29.2)	0	
Banding	5 (20.8)	0	
Pigmentation			0.001
Normal	6 (25)	19 (79.2)	
Hypopigmentation	6 (25)	1 (4.2)	
Mixed pigmentation	5 (20.8)	4 (16.7)	
Hyperpigmentation	7 (29.2)	0	
Vascularity			0.000
Normal	9 (37.5)	11 (45.8)	
Pink	2 (8.3)	13 (54.2)	
Red	1 (4.2)	0	
Purple	12 (50.0)	0	
Itchiness			0.004
None	15 (62.5)	24 (100)	
Occasional	1 (4.2)	0	
Requires medication	8 (33.3)	0	
Pain			0.003
None	15 (62.5)	24 (100)	
Occasional	0	0	
Requires medication	9 (37.5)	0	

the intervention and 2.0 after the intervention ($P=0.000$).

Based on patient satisfaction with the treatment for each lesion, 12.5%, 41.7%, 20.8%, and 25% of the patients reported no change, good improvement, very good improvement, and excellent improvement, respectively (Figure 1) Finally, the treatment was safe and no adverse event (except for temporary erythema up to 3 months) was observed.

Figure 2 shows three sample cases treated with Plexr.

Discussion

In our trial, Plexr was shown to be successful in treating keloids. The VSS scores decreased significantly after two or three sessions of plasma exeresis. Furthermore, no side effects or recurrences were observed in any of the 24 scars treated during the five-month follow-up period, and more than 87% of the patients reported satisfactory outcomes. The use of plasma exeresis appears to be effective in the treatment of small keloid scars without causing any significant complications.

As well as causing pain, itchiness, and an undesirable appearance, keloid scars negatively affect a patient's quality of life, both physically and mentally.[10] Moreover, differences in the individual and genetic characteristics of patients have hindered the effectiveness of treatment options.[11] A significant reduction in the thickness of keloids was observed in our study. In this regard, our method showed a greater success rate than medical treatments such as Hyaluronic Acid, Triamcinolone, and Verapamil injections which showed lower success rates.[12,13]

The pigmentation changes in our study did not occur during the five-month follow-up period, whereas studies using other methods, such as pulse dye lasers, radiofrequency ablation, cryotherapy, and Bleomycin injections, reported hypo-, hyper-, or depigmentation in their patients.[12,14-18] Based on the results of this survey, there was an improvement in the pliability of lesions. This improvement is comparable with results obtained from using CO_2 lasers and pulse dye lasers.[19,20] Despite the significant reduction in pruritus by our method, only a few comparable studies have demonstrated a reduction in itching by other methods.[20-22]

In a 2021 study by Ting et al, the plasma method was combined with radiotherapy to treat keloid scars. Contrary to our investigation, participants in this study who had keloid scars of various diameters benefited from only one plasma treatment session. However, in our study, scars that were taller received more plasma therapy treatments. However, side effects after the treatment, including radiation dermatitis, hyper- and hypopigmentation, and scar recurrence were also noted.[23] For this reason, we figured out that multi-session therapies with omitting the radiotherapy were more successful.

Sotiris et al employed plasma to treat skin conditions such as scars, hemangiomas, benign papillomas, and venules. Plasma was successful in removing the extra tissue, repairing the scar, and disabling the blood vessels in hemangiomas, and it is consistent with the present research. In this investigation, multiple sessions, depending on the severity, were required to treat conditions. In accordance with our study, this study introduced plasma technology as a simple, efficient method without recurrence in skin problems.[24]

Plasma was utilized to treat traumatic scars in Kono and colleagues' study. Similar to our trial, this study used a maximum of three therapy sessions. Plasma was consequently developed as an efficient and simple scar therapy technique. Their research found that plasma therapy enhanced the color of hyperpigmented scars and that scar improvement was connected to the selective

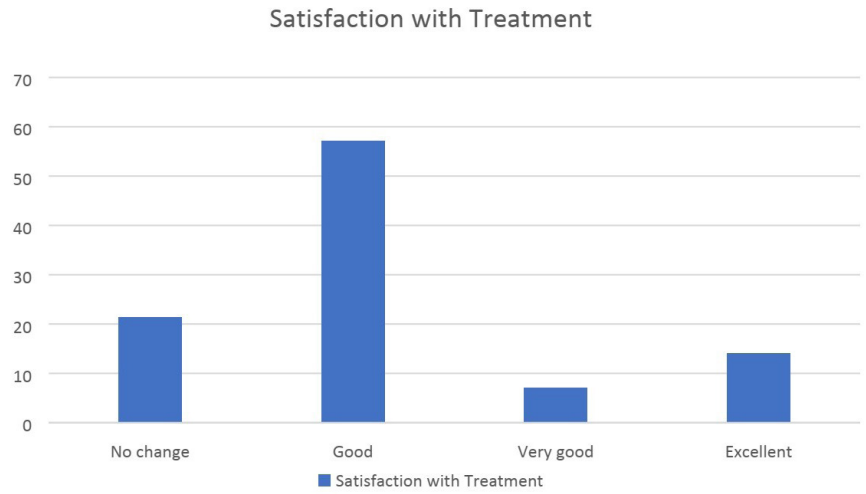

Figure 1. Patient satisfaction with treatment

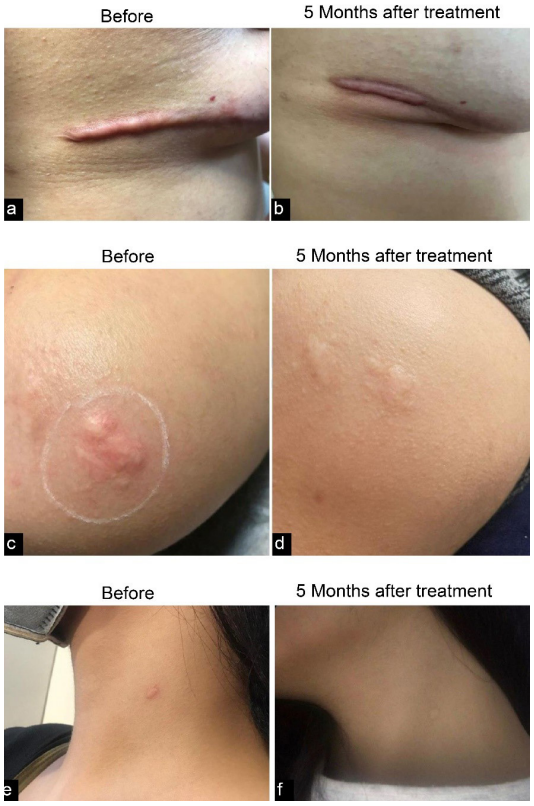

Figure 2. Three Sample Cases Treated With Plexr. (a) and (b) show the keloid scar before and 5 months after the treatment in a 44-year-old woman's right breast. (c) and (d) show the keloid scar before and 5 months after the treatment in a 19-year-old woman with a scar from an arthroscopy two years previously. (e) and (f) show the keloid scar before and 5 months after the treatment in a 29-year-old woman's neck, which had been the subject of a mole removal 3 months prior to the treatment

ruination of blood vessels, which is consistent with our findings. In addition, their research demonstrates that wide and deep scars do not respond well to plasma therapy.[25]

Keloids are considered challenging conditions for treatment in dermatology with no gold standard method. Previous surveys reported recurrence of the condition via methods like surgical excision or laser therapy .[26] Although recent studies have mentioned combination therapies for keloids like CO2 laser ablation followed by steroid injection,[27] platelet-rich plasma injection with surgical excision,[28] or plasma therapy with radiation therapy,[23] there is no consensus in this regard, and sometimes these combination therapies have led to unsuccessful outcomes or adverse effects. Choosing an effective monotherapy method can be beneficial in this regard. While we find more efficient monotherapy methods, the results of combination therapies can be more favorable.

The most distinguishing aspect of plasma therapy is that the injured epidermis remains intact for several days after treatment, resulting in a unique therapeutic environment in which the damaged epidermis works as a natural physiological dressing when the healing process occurs. Fibroblasts regenerate in large numbers. As a result, the qualitative effects of plasma may differ from those of other therapeutic approaches.[29,30] To the best of our knowledge, this is the first study to assess the effectiveness of plasma exeresis for keloid scars as a monotherapy.

In conclusion, plasma exeresis was found to be effective in destroying keloid scars. Additionally, it resulted in less itchiness and pain with no notable complications or recurrences during the 5-month follow-up period. Further studies with a control group and a larger sample size may shed better light on the efficacy of this method.

Competing Interests

None of the authors have any conflict of interest.

Ethical Approval

The study was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.IAU.TMU.REC.1399.369) and registered in the Iranian Registry of Clinical Trials (identifier: IRCT20220512054827N1; https://irct.ir/trial/63707).

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