

Pharmacology and therapeutics

Topical delivery of triamcinolone via skin pretreated with ablative radiofrequency: a new method in hypertrophic scar treatment

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Abstract

Background Epidermal permeability alterations induced by ablative fractional resurfacing and low-frequency ultrasound technology may offer drug delivery for the treatment of hypertrophic scars through transepidermal drug delivery (TED). This technology can improve treatment efficacy and minimize side effects.

Objective To evaluate clinical response and side effects of TED technology in hypertrophic scars in the body and on the face using ablative fractional radiofrequency (RF) associated with low-frequency acoustic pressure ultrasound (US).

Methods Four patients with hypertrophic scars were treated with triamcinolone using fractional ablative RF and US. The treatment procedure comprised three steps: (i) ablative fractional RF for skin perforation; (ii) topical application of triamcinolone acetone 20 mg/ml on the perforated skin; and (iii) acoustic pressure wave US applied to enhance triamcinolone penetration into the skin.

Results Complete resolution was seen after one session in patients with scars on the nose and mandibular area. The scar on the neck showed complete resolution after four sessions. The scar on the knee showed a marked improvement after four sessions. Mild and homogeneous atrophy was observed in hypertrophic scars on the neck.

Conclusion Ablative fractional RF associated with acoustic pressure US is a new technology aiming to increase drug delivery into skin. This new method can improve the efficacy of steroids in hypertrophic scar treatment, minimizing the risks of localized atrophy and irregular appearance of the treated lesion.

Introduction

Hypertrophic scars (HS) are dysfunctions of the healing process in response to different injuries. HS appear four weeks after a triggering event, limited to the original wound, grow intensely for a few months, and then regress.¹ Treatment remains a challenge for dermatologists. Intralesional steroids are the first-line therapy, and triamcinolone is the one most used.² Use of intralesional steroids is painful, and atrophy is a common side effect.

Innovative technologies, such as transepidermal drug delivery (TED), provide an attractive alternative to conventional methods.³ Use of fractional YAG laser⁴⁻⁶ and CO₂ laser⁷⁻⁹ to create micro-channels in the epidermis with the aim of increasing skin drug permeability was recently reported. Similarly, there are studies reporting the use of low-frequency ultrasound (US) to increase skin permeability.¹⁰⁻¹²

We reported four cases of HS treated with TED. We used ablative fractional radiofrequency (RF) to open micro-channels in the epidermis before applying triamcinolone. Acoustic pressure US was applied over the steroid to push molecules into the dermis through the micro-channels pre-formed by RF.

Methods

A prospective study was carried out to evaluate the clinical efficacy and side effects of applying steroid in four cases of HS using both fractional RF and acoustic pressure US technology. None of the patients have had any clinical intervention before.

Case 1 was a 23-year-old woman (Fitzpatrick phototype II) with HS for six weeks, after having her nose pierced. Case 2 was a 44-year-old woman (Fitzpatrick phototype III) with HS on the knee for four months after a car accident. Case 3 was a 22-year-old-man (Fitzpatrick phototype III) with HS on the neck

Table 1 Patients demographics and biometric profile

Patient	Age (years)	Gender	Phototype	Scar age	Treatment area	No. of treatments
1	23	Female	II	6 weeks	Nose	1
2	44	Female	III	4 months	Knee	4
3	22	Male	III	3 months	Neck	4
4	50	Female	IV	2 years	Mandibular area	1

for three months after a tracheostomy. Case 4 was a 50-year-old-woman (Fitzpatrick phototype IV) with HS on the face (mandibular area) for two years after surgery to remove a melanocytic nevus (Table 1).

Before each session, the skin was cleaned with chlorhexidine. First, the fractional RF applicator, with a round mushroom-shaped tip and 110 tiny stainless pins $\approx 200 \mu\text{m}$ in length \times thickness, was applied on to the skin using the following protocol: 45 watts \times 3 passes. Secondly, triamcinolone acetonide (20 mg/ml) was dropped (0.1 ml each lesion) on the perforated skin surface. Finally, the acoustic pressure wave US applicator was applied using the following settings: frequency of the sonotrode vibration rate = 50 Hz; US energy intensity = 80%, for 30–60 seconds each lesion (Fig. 1).

Ablative fractional radiofrequency module

The ablative fractional RF module is incorporated into a unipolar RF-based hand-piece. The hand-piece receives RF energy, which includes a stationary tip (12 mm in diameter). An array of protrusions (tiny metal pins) arranged ≈ 1 mm apart is configured to cause multiple electrical discharges to be generated in response to the RF electrical power in a space between the protrusions and the skin. The ablative micro-plasma RF energy stimulates micro-sparks between the skin surface and RF protrusions, producing holes of 100–150 μm in depth (evaporation + thermal) and 80–120 μm in diameter (width) on the skin surface.

Acoustic pressure ultrasound module

The acoustic pressure module is comprised of a transducer, sonotrode, and distal (hollow) horn. It is applied perpendicular to the surface of the skin and in continuous contact with the skin surface in a circular (concentric-eccentric) in-motion movement of the sonotrode. The distal surface of the horn creates vibrational cycles (“push–pull”) on the medication

(triamcinolone) and skin surface to enhance delivery of the triamcinolone. The mode of operation is based on mechanical (acoustic) pressure and torques by propagation of US wave via the sonotrode to the distal horn and the creation of a “hammering”-like effect (“push–pull”) in the thin layer between the medication, treated skin, and operative surface of sonotrode. This layer should contain a delivered medication, which is chosen according to the disease to be treated. The hammering effect by the sonotrode creates transport of the delivered drugs/material to the area of preliminary RF perforated skin and increasing penetration of the drug into the skin.

The combined treatment (RF + US) protocol was done every 3–4 weeks until clinical improvement. The number of treatments ranged from one (cases 1 and 4) to four (cases 2 and 3) (Table 1).

Patients were submitted to dermatologic exam every 21 days during treatment and after 30, 90, 180 days and one year after the last session. They were advised not to use any other treatment during the study.

The degree of clinical improvement was evaluated according to a quartile scale of improvement: no improvement; 1 = 1–25% minimal improvement; 2 = 26–50% moderate improvement; 3 = 51–75% marked improvement; 4 = 76–100% excellent improvement. Side effects such as erythema, edema, and atrophy as well as the pain during procedure were evaluated on a three-point scale: 0 = absent, 1 = mild, 2 = moderate, 3 = severe.¹³ Digital photographs (Sony DSC-H9 – Super Steady Short 8.1 MP, Japan) were taken at baseline and at each follow-up visit to document clinical response.

Results

Complete resolution was seen after one session in patients with scars on the nose and mandibular area. The scar on



Figure 1 Procedural steps: (1) ablative fractional RF; (2) topical medication; (3) acoustic pressure US

the neck (furcula area) presented marked involution after three sessions and complete involution after four sessions. The scar on the knee presented a marked improvement after four sessions (Figs. 2–5).

All patients reported a mild burning sensation during the procedure. They presented mild erythema and edema just after the procedure, which persisted for 24–48 hours. Fine scale could be observed 7–10 days after the procedure. In one patient (case 3), mild atrophy, homogeneously distributed in the lesion, could be observed two months after session 4.

Discussion

In the last years, ablative fractional lasers have been used with the aim of increasing drug delivery.^{7,8} Wang *et al.*⁶ described the use of Erbium:YAG laser as a pretreatment to accelerate the response of Bowen's disease treated by topical 5-fluorouracil and Haerdersdal *et al.*,⁸ in 2010, reported the use of CO₂ laser before methyl aminolevulin-



Figure 2 Hypertrophic scar on the nose before treatment and 1 week after one treatment



Figure 3 Hypertrophic scar on the knee before and 3 months after four treatments

Figure 4 Hypertrophic scar on the neck (furcula area) before treatment, after session 3 and 2 months after four treatments



Figure 5 Hypertrophic scar on the face (mandibular area) before treatment and 1 year after one treatment

ate. In a recent *in-vivo* rat model study,¹⁴ Evans blue (EB) was used as a marker together with fractional ablative RF and acoustic pressure US modules for detecting transepidermal delivery. In this benchmark study, frozen section biopsies (qualitative) and spectroscopy (quantitative) measurements were analyzed in four different conditions on a rat's skin: (i) topical EB; (ii) EB + US; (iii) EB + RF; (iv) EB + RF + US. Histopathological studies (hematoxylin and eosin frozen section) revealed significant EB penetration in the EB + RF + US condition, when compared with EB + US and EB + RF conditions.

Multiple studies have shown improvement of laser treated scars using both ablative and non-ablative modalities. However, scar treatment with bimodal energy delivery devices for the purpose of TED of medication has not been reported.^{15,16} To our knowledge, this is the first study using a combination of physical methods (i.e. fractional ablative method and acoustic pressure US) for the treatment of scars. The ablative fractional method used was RF, which created micro-channels on the skin surface, and the acoustic pressure US was applied with the aim of pushing triamcinolone through these channels into the skin. Despite initial reports of poor response and high recurrence rate of HS after laser treatment,^{15,16} our study used fractional ablative RF and acoustic pressure US to increase triamcinolone permeability, and we could observe marked to excellent results within a few sessions with a long follow-up. In one case where mild atrophy was observed, it was probably caused by triamcinolone, as it is a very common side effect of steroids. In this case, we should have stopped the treatment after the third session and waited for continuous regression of the lesion.

The atrophic aspect of this lesion looked even worse than it really was because the HS was located in the concave aspect of the furcula region.

Conclusion

The use of a laser as a monotherapy modality for the treatment of HS is reported as non-effective with a high recurrence rate of HS.^{15,16} In contrast, the use of a method such as ablative fractional RF with the aim of increasing skin permeability is a new treatment option. HS treatment with fractional RF and acoustic pressure US allowed triamcinolone penetration with a marked to excellent response in a few sessions with few side effects.

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