

# The Review of Most Current Therapy for Large Area of Hypertrophic Scar and Keloid

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**Abstract:** For the large area scar or keloid, the treatment is still posing a great challenge. Because the invasive therapy has an unbearable pain and increased risk of side effect, like the steroid injection and cryotherapy, so the non-invasive therapy is actually the optimal choice for large area scar and children patients. Here we introduce the major modalities for the treatment of large area scar, like pressure therapy, Silicone, Onion extract, and scar massage. In addition, three aspects are recommended for the scar therapy: early use, combination use and persistent use, which is essential for a successful scar treatment.

**Keywords:** Hypertrophic scar, Keloid, Scar treatment, Large area scar.

## 1. INTRODUCTION

The hypertrophic scar and keloid are often occurred after wound injury, the size of them ranges from linear to large area. The difference between them is that the development of hypertrophic scar is often limited in the original lesion and has a tendency to regress automatically, but the development of keloid has no limitation and often overpasses the margin of the original wound and has no automatic regression. Clinically, for the small and linear scar, it is relatively easy to treat, but for the large area scar or keloid like 1-4 limbs, it poses a great challenge.

So far, there are many modalities for the treatment of the hypertrophic scar and keloid including invasive therapy and non-invasive therapy. The invasive therapy includes intrasional injection of steroid or 5-FU or bleomycin, and cryotherapy, and laser, etc. The non-invasive therapy usually includes pressure therapy, silicone gel, and onion contract, and massage, etc. All these modalities are reported with varied effectiveness on hypertrophic scar and keloid. However, it should be point out that not all the kind of modalities is suitable for any kind of scars. For example, the injection treatment is practically not suitable for the large area of scar, because there is unbearable pain and increased risk of side effect, like the steroid injection and cryotherapy. Therefore, for the treatment of large area of hypertrophic scar and keloid, the non-invasive therapy is still the most current modality in the burn center. Here, we introduce the major modalities for the treatment of large area scar.

## 2. PRESSURE THERAPY

Since 1970s, pressure garment has been the mainstay of treatment for hypertrophic scars in burn injuries [1]. Pressure therapy is performed by wearing custom garment or elastic bandage which exerts force on the scar or keloid and then induce the scar regression. Currently, there is general consensus on the use of pressure garment therapy for the prevention and treatment of scarring. In many burn center, it is the routine practice for the prevention of the scars after burn injury, which was reported have effectiveness from 60% to 85% [2-6], and was regarded as the standard first-line therapy for the large scar formation [6,7].

In order to get a good effectiveness, it is recommended that the pressure of the garments should be maintained between 20 and 30 mm Hg, and the duration of each day should be kept about 23 hours, persisting for 6 to 12 months at least [8]. The side effect of pressure therapy is discomfort from heat and sweating, the swelling of limbs, rashes, eczema.

For the mechanism of the pressure therapy, it is widely believed that the pressure on the scar could control collagen synthesis and accelerate scar maturation by limiting blood supply, oxygen, and nutrients [9]. Wang *et al.* proved that the very low oxygen and nutrition was found in the regressive scar tissue which could inhibit the collagen production and inhibit VEGF and TGF- $\beta$ 1 expression, eventually triggered cell apoptosis [10].

## 3. SILICONE GEL OR SHEETING

Silicone gel sheets (SGS) was first used as scar treatment in 1983 [11], reportedly it could reduce the size, redness, pain, and itching of scars, as well as promote skin elasticity, softness and even prevent scar formation [12-16].

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In these years, SGS has remained the favored scar therapy because more and more studies have confirmed its effectiveness in reduction of size and pliability for hypertrophic scars and keloids [17-24], and also showed the benefits in improving scar color [25,26]. In addition, silicone possesses many good properties for scar treatment including biocompatibility, easy removal, and extended wear time [27]. The major limitation is skin irritation in hot climates [28]. So far, SGS was recommended as the first-line therapy by the International Advisory Panel on Scar Management [29], especially for the small scar and keloid.

Regarding the mechanism of SGS, many studies have revealed that SGS provide an occlusion and hydration for the scar tissue, which could imitate the normal skin, and inhibit the fibroblast activity and collagen production [30-32]. Recent study revealed that the silicone consisted of a low molecular weight fraction, fraction IV [33], which was active and could reduce the collagen production. Emily *et al.* found that, when human keratinocytes and fibroblasts were exposed to fraction IV, the cell viability and proliferation were significantly decreased, and cell apoptosis happened [34].

#### 4. ONION EXTRACT AND HEPARIN GEL

Contractubex® gel consists of a mixture of onion extract, heparin and allantoin. Ho *et al.* found that contractubex® gel was effective, safe and simple when applied for the prevention of scarring in 120 Chinese patients after laser removal of tattoos, in which it reduced the risk of scarring from 23.5% to 11.5% [35]. Willital and Heine studied the effect of contractubex® gel on 45 young patients with fresh scars and found that the scars in the treated group were narrower than the untreated group [36]. In addition, it was revealed that Contractubex gel was more effective than heparin and allantoin alone [37].

However, Chanprapaph *et al.* found that, although the early use of onion extract gel could improve scar height and symptoms, there was no significant difference in the improvement of scars' redness, pliability or overall cosmetic appearance [38]. For this reason, it was suggested that onion extract therapy should be used in combination with silicon dressing, in order to achieve a satisfying decrease in scar height [39].

Concerning its mechanism, the studies revealed that onion extract possesses fibroblast-inhibiting property, which not only reduces fibroblast activity and collagen production, but also increases the expression of MMP-1 [40], contributing to scar regression. In addition, Heparin

could interact with collagen molecules, inducing the formation of the thicker fibrils and promote the collagen maturation [41].

#### 5. SCAR MASSAGE

Massage therapy is a technique that could soften scar tissue and improve the scar pliability. Morien *et al.* reported that 8 children who were treated with 20-25 minutes massage daily for 3-5 days, and the range of motion was improved in the knees, neck, and shoulders [42]. Roh *et al.* compared 18 patients who received massage therapy and 17 patients who received standard therapy, the results showed that the massage-therapy group showed greater improvements in pruritus, VSS score, and depression than control group [43]. Filed *et al.* reported that greater improvements in pruritus, pain, anxiety, and mood in the 10 subjects who received massage therapy for 5 weeks than the 10 subjects who only received standard therapy [44]. Recently, Yoon *et al.* also reported that burn rehabilitation massage therapy could improve pain, pruritus, and scar characteristics to a significantly greater degree than only standard therapy [45].

Generally, the massage should be applied for scar tissue after 2 weeks of wound closure, and it is often performed with whitening cream, anti-redness cream, and moisturizing oil, which not only facilitate the massage, but also improve the scar appearance. The possible side effect is epidermis injury, acute infection and bleeding.

Regarding the mechanism, it was believed that massage has double effects including mechanical action and tissue relaxation. The mechanical action could disrupt fiber bands and increases the tissue pliability. Previous studies revealed that mechanical force could induce changes in the expression of extracellular matrix proteins and proteases, and also alter the structural and signaling microenvironment [46, 47]. In addition, the massage could stimulate the peripheral nerves and produce muscle relaxation, decrease painful sensations, and an overall sense of well-being. A study revealed that tissue massage could produce a significant elevation of beta-endorphins in healthy volunteers [48], supporting a role in pain relief and a sense of well-being.

#### 6. DISCUSSION

Considering the side effect, the invasive therapy is usually used for the small scars and keloid, and the non-invasive therapy is the optimal choice for large

area scar and children patients. Except for the modalities introduced as above, there also have other local ointment for the scar treatment, like the Vitamin E and steroid [49,50], also reportedly had some improvement on the scar. In addition, the treatment for large area scar is more difficult than small scar. Therefore, to get a good result of the scar treatment, the authors recommend three aspects, which are essential for the scar therapy: early use, combination use and persistent use.

Early use is more effective than later use for the scar treatment. Once the scarring formed, it is difficult to get it down. The early treatment could be applied after 10-14 days of wound healing. At the beginning of treatment, short time is used and then prolongs it gradually, because the newly skin is crisp and easy to be broken.

In addition, combination use is necessary for the larger area scar. Although there are many modalities for scar treatment, there have not one modality could eradicate the large area scar radically. Monstrey *et al.* recommended that pressure therapy combined with silicone could be a basic guideline for the widespread scar and keloid, if necessary, added with injection of corticosteroid and 5-Fu [51]. In our experience, firstly the scar was applied with local ointment like Contractubex® gel, and massaged for 5-10 minutes to promote the drug absorption, then attached with the silicone, followed with pressure garment. Based on this, it could get a better result.

Furthermore, persistent use is a key role to get good effectiveness. Generally, the troublesome and high cost from the scar treatment could reduce the patient's compliance, and then discounts the effectiveness. So the long persistence and standard performance should be educated to the patient and family members. Ignoring this, it often causes the failure of scar treatment.

## 7. CONCLUSION

Therefore, for the large area of scar and keloid, 2-3 kinds of modalities combination were suggested for scar treatment, and the pressure therapy combined with silicone gel could be the first choice. In addition, the early use and persistent use for the scar therapy were strongly recommended to get better effectiveness.

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Received on 13-10-2015

Accepted on 20-10-2015

Published on 23-11-2015

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