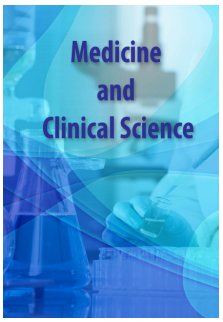
Medicine & Clinical Science

Case Report



Hydration and hypoxic-occlusion therapy (gel-wrap treatment) for hypertrophic scars and keloids

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Abstract

Keloids and hypertrophic scars are pathological fibroproliferative disorders characterized by excessive collagen deposition. The affected skin becomes raised and thickened, forming firm pink or red plaques. Common causes include trauma, burn, and surgery. Multiple studies on keloids and hypertrophic scars have been reported previously, leading to the development of various therapeutic approaches for them, most of which remain clinically unsatisfactory. In this study, three patients underwent the gel-wrap treatment: the gel (manufactured by ITO Co Ltd.) was applied to the lesion and the affected skin was wrapped with a polyvinylidene chloride film (Saran Wrap; Asahi Kasei Corporation). Satisfactory results were noted in all three cases. The gel-wrap treatment is more convenient and inexpensive than existing therapeutic approaches. Furthermore, reducing thymic stromal lymphopoietin seems crucial for the treatment of keloids and hypertrophic scars.

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Introduction

Keloids and hypertrophic scars are pathological, fibroproliferative disorders. Hypertrophic scars are confined within the boundaries of the initial wound, whereas keloids spread outside the original wound margins [1]. In histopathological findings, keloids contain collagen bundles, whereas hypertrophic scars are characterized by collagen nodules. Although there is continuous, intense inflammation at keloid margins, the central area has a much lower level of inflammatory cells, similar to those seen in hypertrophic scars. It has been hypothesized that keloids and hypertrophic scars may be successive stages of the same fibroproliferative skin disorder [2]. Conventional treatment with intralesional corticosteroid injection presents a few problems, including pain at the injection site and thinning or telangiectasia of the scar after multiple injections. Thymic stromal lymphopoietin (TSLP) has been shown to play a key role in keloid pathogenesis [3].

Trehalose, a disaccharide known for inducing a moisturizing effect, has been reported to reduce TSLP mRNA expression in the normal human cutaneous epithelial cells [4,5]. The molecular weight of Trehalose is 342 g/mol; hence, it can penetrate the epidermis. To aid its penetration into the epidermis, it is dissolved in the gel and applied to the keloidal skin surface, which is then covered with a wrap. Based on a controlled trial, the application of the gel without trehalose produced good results, similar to the application of the gel with trehalose.

In this study, three cases of fibroproliferative disorders were managed using gel-wrap treatment as first trial following up long time duration.

Methods

Written informed consent was obtained for the publication of photographs illustrating the clinical lesions of patients. All patients who consented to participate in the study were included. Patients who had a medical history of lesions were excluded. The gel used (ITO gel base; ITO Co., Ltd., Tokyo, Japan) was composed of water, glycerin, carboxyacrylic polymer, sodium polyacrylate, methylparaben, and propylparaben. The wrapping film (Saran Wrap; ASAHI KASEI CORPORATION, Tokyo, Japan) was composed of polyvinylidene chloride (PVDC), which is impermeable, ultra-lucent, and very thin (0.008–0.01 mm). In all three cases, a small amount of the gel was applied to the hypertrophic scar or keloid once daily, followed by wrapping with the PVDC film, which was then secured with surgical tape to make it adhere to the scar surface tightly (the gel-wrap treatment). No other treatment modalities, such as a pressure garment or intra-lesion steroid injection, were performed during the follow-up period.

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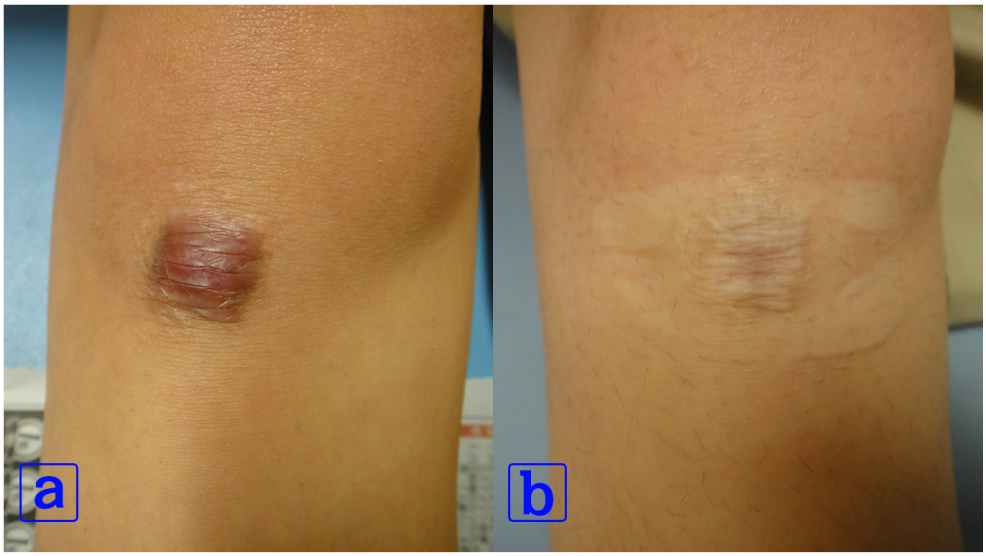

Figure 1. a: Case 1. A 22-year-old woman with a history of a hypertrophic scar on the right knee 5 months prior to presentation (pre-treatment).
b: Case 1. A 22-year-old woman with a hypertrophic scar on the right knee treated with the gel-wrap treatment (10 months post-treatment).

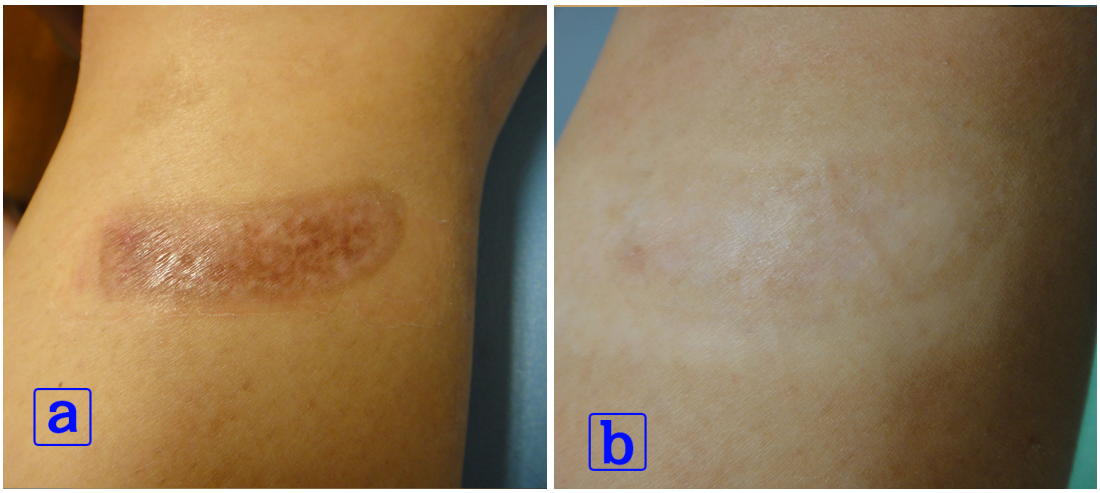

Figure 2 a: Case 2. A 16-year-old girl with a history of a pigmented hypertrophic scar on the left lower leg 2 months prior to presentation (pre-treatment)..
b: Case 2. A 16-year-old girl with pigmented hypertrophic scar on the left lower leg treated with the gel-wrap treatment (13 months post-treatment).

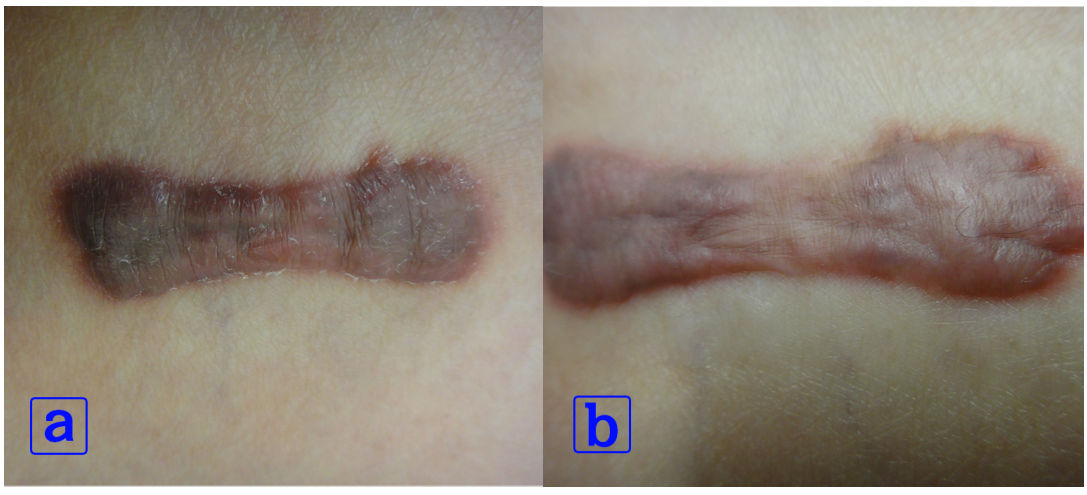

Figure 3 a: Case 3. A 58-year-old woman with a keloid on the right calf for 12–13 years before she visited the clinic (pre-treatment).
b: Case 3. A 58-year-old woman with a keloid on the right calf treated with the gel-wrap treatment (10 months post-treatment).

In my outpatient clinic, several patients with scars were treated using the gel-wrap treatment. Only a few patients developed mild contact dermatitis due to the gel or wrap. No significant side effects have occurred to date.

Results

The first case was that of a 22-year-old woman with a history of a hypertrophic scar resulting from a laceration on the right knee 5 months prior to presentation (Figure 1a). The scar was pruritic, dark red, firm, and raised. The gel-wrap treatment resulted in the reduction of pruritis, erythema, hardness, and height of the scar 1 month after treatment. The same scar 10 months after treatment (Figure 1b) showed visible improvement, with the properties of the scar surface (appearance and feel) being similar to those of normal skin.

The second case was that of a 16-year-old girl with a pigmented hypertrophic scar resulting from a burn injury on the upper portion of the left lower leg 2 months prior to presentation (Figure 2a). The scar was erythematous, pigmented, and slightly inflamed. It was treated using the gel-wrap treatment. After 2 months of treatment, the erythema, pigmentation, and thickness of the scar improved. After 13 months (Figure 2b), the properties of the surface of the scar were similar to those of normal skin.

The third case was that of a 58-year-old woman who had a keloid on the right calf for 12–13 years before she visited the clinic (Figure 3a). The keloid was dark red, firm, raised, and dumbbell-shaped. The patient experienced slight pruritis, spontaneous pain, and tingling. The keloid was treated with the gel-wrap treatment. The patient had no symptoms of tingling and pain at 1 and 2 months after treatment; however, she reported slight pruritus and pressure pain 6 months after treatment. Four months after treatment, the keloid was less firm—although its appearance was unchanged—and the patient's subjective symptoms had improved. Ten months after treatment (Figure 3b), the skin tone changed from dark to pale red. The firmness of the keloid improved, with its center being softer and paler than the margins, and a reduction in height was observed. Additionally, the patient reported a reduction in pressure pain.

Discussion

Clinical knowledge and numerous studies have indicated that the formation of keloids and hypertrophic scars is associated with genetic, systemic, and local factors, including delayed wound healing, wound depth, and skin tension around the scars. Topical silicone gel sheeting has been a well-established treatment for the management of scars [6]. Current opinion suggests that hydration and occlusion are the likely mechanisms of therapeutic action of silicone gel sheeting. Hydration of the scar by occlusion causes downregulation of fibrogenic cytokines [7]. However, the detailed mechanism of therapeutic action of silicone gel sheeting is unclear.

The skin is divided into the outer epidermis, middle dermis, and inner subcutaneous layers, which are supplied with oxygen by the subcutaneous blood vessels [8]. Inflamed skin and scar tissues are different because their trans-epidermal water loss is higher than that of normal skin. No biological membrane allows for movement in only one direction. Hence, inflamed skin and scars may be supplied with little oxygen from the outer skin surface (room air) compared to normal skin. Epidermal hypoxia is necessary for maintaining skin homeostasis by the inactivation of prolyl hydroxylase (PHD), a sensor of oxygen concentration. In normoxia, PHD enhances hypoxia-inducible factor (HIF)-α degradation by hydroxylation of HIFs. However, this hydroxylation is inhibited in a hypoxic environment such as a PVDC film cover, which may be the case in this study.

The induction of TSLP expression is stimulated by TNF-α and inhibited under hypoxic conditions (1% O2) [9,10]. The oxygen concentration in normal adult human skin epithelial tissues is 0.5–5%. Therefore, TSLP expression is downregulated by HIF-2 in hypoxia [10].

TSLP plays a key role in allergic inflammation. It is produced mainly by the epithelial cells and promotes TH2-type immune responses by activating dendritic cells [11]. Expression of TSLP increases in the keloid tissue compared to normal tissue, and TSLP increases collagen I and collagen III expression in fibroblasts by transforming growth factor-β (TGF-β) regulation. Furthermore, after Shin et al. injected TSLP into the dermis of BALB/c mice, an overproduction of collagen was noted in the area [3]. Hence, TSLP is a potent inducer of collagen and TGF-β, thereby contributing to excessive extracellular matrix deposition.

In this study, patients were advised to apply the gel topically on the lesion and cover the affected skin with PVDC film every day. Contact dermatitis with a PVDC wrap has been reported [12]. Therefore, patients should be monitored for this side effect.

The gel-wrap treatment resulted in improved appearance and feel of the scar tissue surface, with most lesions attaining a normal skin color and tone after a long-term treatment period (6–12 months). The mechanism of the gel-wrap treatment can be summarized as follows: first, the hypoxic-occlusive condition induces HIF-2; second, the increased HIF-2 expression downregulates TSLP, which results in a reduction in TGF-β and collagen deposition. The similarity in mechanism between silicone gel sheeting and the gel-wrap treatment is not in the inherent anti-scarring property of and decompression by silicone gel sheeting, but in hypoxic-occlusive conditions resulting in a reduction of TSLP. Herein, collagen deposition of scars is reduced, as seen in Figures 1–3. The essential origin for keloid and hypertrophic scars may be TSLP. The duration of the gel-wrap treatment, like that of silicone gel sheeting, is long. However, gel-wrap treatment is more convenient and affordable than silicone gel sheeting. Thus, patients who have scars can achieve significant therapeutic efficacy with the gel-wrap treatment. This study is limited in that it does not clarify the detailed mechanism by which the hypoxic condition changes the biological activity of keloidal fibroblasts. It may be beneficial to analyze the genes of keloidal fibroblasts in a time series under hypoxic conditions.

Acknowledgments

I wish to acknowledge the late Mr. S. Tajima, a former professor in the dermatological section of the Defense Academy, for discussing the mechanism of trehalose.

Conflicts of interest

A patent application has been submitted by Haruyoshi Yamada for the use of the gel-wrap treatment (Japanese Patent Publication No. 2021-168897).

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