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Case Report

Topical Clobetasol in Combination with Tretinoin for Prevention of Scar Formation After Superficial Skin Burn

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Abstract

Superficial second degree skin burns can heal with or without resulting scar. Scar formation occurs when inflammation remains in the dermis after re-epithelialization, contributing to changes in skin architecture. Suppression of inflammation and fibroblast activity using topical corticosteroids immediately after re-epithelialization may prevent scar formation. Additionally, tretinoin can increase trans-epidermal absorption and efficacy of topical corticosteroids. A superficial second degree burn on the upper back of a woman which was deeply erythematous, pruritic, and had become thickened and indurated after re-epithelialization was treated. Topical clobetasol propionate 0.05% ointment was applied twice daily with overnight occlusive dressing combined with topical tretinoin 0.05% cream, twice weekly. After three weeks of treatment, the area was flat with less pruritus and erythema. Drugs were tapered and discontinued after four months. Nine weeks after discontinuation of all treatments, the affected area was flat and showed no signs of scarring. Early therapy, immediately after re-epithelialization of inflamed healing superficial burns, can potentially suppress inflammation and prevent not only hypertrophic scarring but also architectural changes which lead to flat scars.

Introduction

In superficial second degree burns, the reticular dermis is intact. These wounds can heal with re-epithelialization without producing a scar. Any new collagen deposition and/or significant cellular or structural changes in the dermis may result in a change in normal architecture of the skin, and subsequently, the formation of a scar [1]. After re-epithelialization, inflammation in the dermis, characterized by deep erythema and pruritus, may take time to resolve. Inflammation in the dermis is associated with fibroblast over-activity and progression to proliferative phase of wound healing that is known to contribute to changes in skin architecture and scarring [2,3]. Suppression of inflammation and fibroblast activation immediately after re-epithelialization may prevent changes in dermal structure and scar formation.

Case Report

A 47-year-old Caucasian woman presented with a second degree thermal skin burn on her upper back. The burn was the result of hot water exposure that occurred a few hours prior to presentation. Her medical history and physical examination were otherwise unremarkable. There was no previous history of hypertrophic scar or keloid.

Initial treatment included debridement of ruptured blisters, while intact blisters were left undisturbed. Topical silver sulfadiazine cream under four layers of gauze was applied daily until complete re-epithelialization, which occurred in 14 days. After epithelialization, the healing lesion was flat, deeply erythematous, and pruritic. The patient was asked to wear an elastic compression garment. After

one week, the affected skin showed increased erythema and was thickened and indurated in some areas. Topical clobetasol propionate 0.05% ointment was then applied twice daily with overnight occlusive dressing to the affected area to reduce inflammation. After 10 days, erythema, thickening and induration was even more pronounced. Topical tretinoin 0.05% cream, twice weekly, was added to the therapy to reduce the thickness of stratum corneum and increase penetration of clobetasol. After three weeks, the area was flat and less pruritic and decreased erythema was observed in areas of the lesion. Treatment was continued for four months, during which time several attempts at reduction or discontinuation of tretinoin, occlusive dressing, or clobetasol were accompanied by recurrence of severe itching, skin thickness, and induration (Fig 1). None of the drugs alone were effective in control of inflammation and skin thickness. After four months, the skin was light pink. At this time, both drugs were tapered over two months and then discontinued. Nine weeks after discontinuation of all treatments, the affected area was flat and showed no signs of scarring. Some dyspigmentation and telangiectasias were present, but no erythema, skin atrophy, or scar was observed.

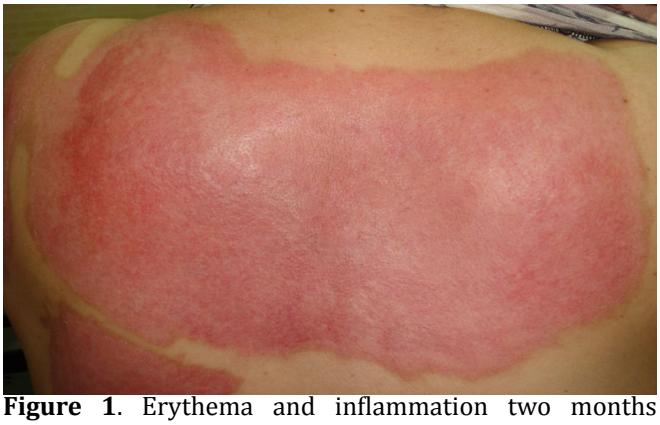

Figure 1. Erythema and inflammation two months after second degree burn of the upper back. Any attempt for reduction or discontinuation of tretinoin, occlusive dressing, or clobetasol was accompanied by recurrence of severe pruritus, erythema, skin thickness, and induration in some areas.

Discussion

The wound healing process is traditionally divided into three overlapping phases. In the initial inflammatory phase, macrophages enter the injury zone and phagocytize pathogens and tissue debris. In the second or proliferative phase, endothelial cells and fibroblasts proliferate. Macrophages induce fibroblasts to proliferate and lay down type III collagen via the secretion of platelet-derived growth factor and TGFβ1. In the final or remodeling phase, a portion of the newly formed cells undergo apoptosis. This process is critical because its aberration leads to hypertrophic scarring and keloids [1,4-6]. With maturation of the wound, type III collagen deposited in the proliferative phase is slowly degraded and replaced with type I collagen. However, this new collagen is oriented as small parallel bundles, differing from the basket-weave orientation of collagen present in normal dermis. The abnormal architecture of collagen, together with the absence of adnexal structures, produces a visible cutaneous scar. The extent to which these changes in skin structure arise after cutaneous injury depends on the severity and extent of inflammation and depth of injury; deeper cutaneous injuries give rise to more scar tissue [1,7].

Corticosteroids can potentially prevent the Intralesional injection of corticosteroids is the mainstay of treatment for keloids and hypertrophic scars [11]. formation of hypertrophic scars by a number of mechanisms: suppression of inflammation suppresion of transformning growth factor (TGF) β1, TGFβ2, and plateletderived growth factor; inhibition of fibroblast growth, proliferation, and collagen synthesis; and promotion of collagen degeneration [1,2,8-10]. Corticosteroids also have been used for the prevention of scar recurrence following keloid or hypertrophic scar surgery [9,12-14]. However, to our knowledge, there is no report of corticosteroid use for prevention of scars in any other setting including after burns.

Tretinoin reduces the thickness of stratum corneum, increasing trans-epidermal absorption of topically applied drugs including corticosteroids [15]. Retinoids also have complex effects on connective tissue metabolism [16]. They can reduce production of collagenase and collagen, and increase production of basic fibroblast growth factor and TGFβ1 by fibroblasts [17-19]. While systemic isotretinoin can result in increased susceptibility to keloid formation, tretinoin, on the other hand, has been used in the treatment of keloids [20,21]. In the presented case, we observed that a combination of clobetasol and tretinoin was more effective than clobetasol alone in controlling inflammation and prevention of hypertrophic scar formation. We propose that tretinoin enhanced the penetration and efficacy of clobetasol; however, we cannot be sure of the exact pharmacodynamics of tretinoin in the prevention of scar.

Conclusion

Depending on the extent of injury or subsequent inflammation, burns can result in scarring and disfigurement. Treatment with topical corticosteroids can potentially decrease the incidence of scar formation by suppressing inflammation and fibroblast activation. Combination of clobetasol and tretinoin was effective in control of erythema, thickening, and induration of the skin, which are early signs of hypertrophic scar formation, and prevented scar formation after a second degree thermal burn in one patient; however, more studies are needed to support this finding and evaluate the efficacy and safety of this treatment.

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