

Review on various combination therapies for the treatment of Hypertrophic scars and keloids

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ABSTRACT

Keloids and hypertrophic scars are mild proliferative growth of dermal collagen that results in various physical, physiological and cosmetic concerns. Till the date the basis behind the formation of these scars has not been fully defined, it is assumed that keloids- and hypertrophic scar-derived fibroblasts produce increased amount of collagen per cell compared with normal fibroblast. Thus suppression of the fibroblast becomes the basic approach for therapeutic treatment of the wound responses.

There is no permanent treatment for ablation of keloids and hypertrophic scars. A large number of trials have been taken on different drugs and different drug delivery systems and all of them are having variable results. Trials such as laser treatment, surgical procedures, intralesional injections of steroids have been taken for ablation of these scars. But most of these treatments are not permanent (intralesional injection), time taking (surgical procedures) and have a large probability of recurrence.

This review article summarizes the information on various therapies for the treatment of keloids and hypertrophic scars as well as their pros and cons

Keywords: Keloids, Hypertrophic Scars, Intralesional Corticosteroid Injection, Laser therapy, Surgical excision, Radio therapy, Cryotherapy

INTRODUCTION

Keloids and hypertrophic scars are skin abnormalities that usually occur after severe injuries, intensive burns, surgical procedures etc. They remain for years and cause major physical (itching, redness, stiffness), psychological and cosmetic concerns. Keloids are common yet poorly understood complication of wound healing that adversely affects the quality of life. Keloid scars may develop after surgeries, acne vulgaris, burn injuries or without any trigger. The main mechanism behind keloids is that the production of relatively higher proliferation and excessive deposition of collagen by the hypertrophic scar fibroblasts than the normal fibroblast. Thus suppression of the fibroblast becomes the basis of keloids treatment.

CURRENT TREATMENT STRATEGIES

Intralesional Corticosteroid Injection

Since mid 1960s glucocorticoids especially Triamcinolone Acetonide is used as a long term therapy for keloids. Triamcinolone Acetonide is considered as best approach for treatment of hypertrophic scars besides the side effects of glucocorticoids such as tissue atrophy, pain and pigmentation of scars. Triamcinolone Acetonide works best with younger keloids. In matured keloids, it softens and flattens the scar only to some extent. Triamcinolone Acetonide has

clinical efficacy ranging from 50-100 % and rate of recurrence varies from 9 to 50 % as reported. Despite few randomized, perspective studies, Triamcinolone Acetonide remains first line approach for early keloids and second line therapy for early hypertrophic scars if other conventional methods are not efficacious.

Cryotherapy

Cryotherapy can be used as a monotherapy or in combination with other therapies for treating excessive scars. When administered before intralesional injection, it seems to show marked improvement against keloids and hypertrophic scars. It is generally administered before intralesional glucocorticoid to cause enema of the scar cell. Cryotherapy induces vascular damage that may lead to anoxia and ultimately tissue necrosis. The use of Cryotherapy is only limited to small scars. Gap between sessions are required for post operative healing. Cryotherapy causes permanent hypo- and hyper- pigmentation, mild to moderate skin atrophy, blistering, post-operative pain and major handicaps.

Surgical Manipulation

Before performing any surgical excision, it is necessary to differentiate between scar and keloid. In case of hypertrophic scars, timing of procedure must be taken into consideration. Scars mature during one year and can show decreased contractures along with pigmentation, flattening and softening without physical manipulation. Thus surgical excision is not performed with hypertrophic scars even if the recurrence rates are low.

On the other hand, recurrence rate of keloids after excision are between 45- 100 %. Thus post excisional treatment is required. Generally intralesional corticosteroid injection or laser is performed, with caution. Excision sometimes cause longer scars than keloids scar and cannot control recurrence of scars in new area of trauma.

Radiotherapy

The use of radiotherapy as monotherapy does not show any success except in large doses. As radiations increase the risk of carcinogenesis, hence it is not given in large doses and with caution. Superficial X-rays, electron beam therapy and low to high dose rate bronchotherapy show good results in scar reduction when given in adjuvant to surgical excision. Radiations are assumed to inhibit neovascular buds and proliferating fibroblast which ultimately results in decreased collagen production. Radiation therapy usually starts within 24 to 48hours post operative to prevent side effects of surgical excision.

Laser Therapy

Since the introduction of laser therapy in dermatology for treating keloids, the therapeutic use of more and more lasers with different wavelength has been investigated and success rates are varied. The most prominent results are obtained from 585-nm pulsed-dye laser (PDL), which shows excellent results for treatment of younger hypertrophic scars and keloids. It works by causing local ischemia by destroying collagen. It induces neocollagenesis, collagen fiber heating with dissociation of disulphide bonds and subsequent collagen fiber realignment and decreased fibroblast proliferation. Side effects of laser therapy include hypo or hyper pigmentation and blistering.

EMERGING THERAPIES

IFN injections

The use of IFN injection in the treatment of keloids is based on the fact that IFN decrease the synthesis of collagen I and III. In vivo systemic administration of IFN- α 2b in systemic burned patients improves the clinical appearance of the scar and lower Van cower burn Scar Assessment score. Major side effects associated with IFN injections include pain and flu-like symptoms.

5-Fluorouracil

It is a cytostatic agent and considered among the most prominent antineoplastic agent for the treatment of malignancies of head and neck and colorectal cancers. It is widely used in treating large number of solid tumors. It was first introduced by Fitzpatrick in 1999 for the treatment of keloids. The fundamental behind using 5-Fluorouracil for keloids is that it suppresses the growth of fibroblast by inhibiting DNA synthesis. It has comparatively faster response in scar flattening and antiscarring application. Still it is not administered alone as it can cause leukopenia and thrombocytopenia.

Bleomycin

It is another neoplastic agent that was found to inhibit collagen synthesis by decreased stimulation of TGF- B_1 . It was introduced in mid 1990 for the treatment of keloids. Side effects of Bleomycin Sulphate are hyper pigmentation and dermal atrophy. It seems to be a promising option for treatment of keloids, however investigation and efficacy trials are needed for this agent.

POSSIBLE FUTURE THERAPEUTIC AGENTS

Some of the agents are still in experimental stage that are listed as-

Hydroquinone

A bleaching agent is used based on the fact that albino patients do not develop keloids and vitilgo often causes the underlying keloid to regress. It works best if used within 5 months of formation of formation of keloids.

Hyperbaric oxygen

As low oxygen tension stimulates fibroblast cell. Studies are being conducted to determine how fibroblast responds to low and high oxygen tensions.

COMPARISON BETWEEN VARIOUS THERAPIES

| S. No. | Treatment | Average recurrence rate | Primary results | Benefits |
|--------|------------------------------|-------------------------|--|--|
| 1 | Triamcinolone Acetonide | 33 % | 50-100% regression of scars after treatment but have high recurrence rates | Inexpensive, Easy to administer, Relatively safe |
| 2 | Surgical excision+ Radiation | 23 % | Significant reduction in recurrence as compared to | Low recurrence, fewer treatment sessions |

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| | | | individual monotherapy | required, quick relief |
| 3 | Surgical excision+Cryotherapy | 15 % | Excellent results with articular keloids | Ideal for articular keloids |
| 4 | TAC+ Laser therapy | 15 % | Superior results as compared to individual monotherapy | Ideal for large keloids |
| 5 | TAC+ 5-fluorouracil | 17.5 % | Significant reduction in recurrence as compared to individual monotherapy | Decreased side effects as compared to individual monotherapy |
| 6 | TAC+ Intralesional cryotherapy | 12% | Cryotherapy before TAC seems to show marked improvement against keloids and hypertrophic scars | Cost effective, widely available |

FUTURE RESEARCH

Although the keloids are affecting the whole world, there is no such animal trials on any of the therapies are available till date. As eagles and vultures show same effects against various therapies, still several trials are needed to be taken on various drugs and their delivery systems to find a therapy that show prominent effect with no or minimal side effects.

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