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RESEARCH ARTICLE

Management of Keloid Scars: Surgical Versus Medical Therapy

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Abstract

Background: Keloids are benign fibroproliferative tumors that extend beyond the original wound. There are many different medical and surgical modalities to treat keloids.

Objective: This article provides a summary and review of the medical and the surgical options available in the literature for treating keloids. Furthermore, this paper organized the data into monotherapy versus combined therapy.

Methods: A literature review was conducted using PubMed and MIDLINE that included English publications trials and reviews from April 2005-June 2018.

Results: Monotherapy is unable to completely flattened keloids and a combination therapy is always needed. Monotherapy shows success with the intralesional steroid injection, but there is always a room for combination with surgical excision, or other therapies: 5-fluorouracil (5-FU), bleomycin and interferon, topical imiquimod, compression, cryotherapy, radiation, silicon sheeting and lasers or light-based therapies.

Conclusion: The treatment of keloid is tested by a big number of trials using different regimens proving the resistance nature of keloid.

Keywords

Keloids, Treatment, Management

Introduction

Keloids are benign fibroproliferative tumors that occur as a response to any kind of injury to the skin to susceptible individuals. Keloid tissue extends beyond the margins of the wound which distinguish it from hypertrophic lesions [1]. Keloids tend to grow symptomless, but still can often cause pain or itching. They have a functional, aesthetic, or psychosocial impact on patients, as highlighted by quality-of-life studies [2]. Individuals of African, Hispanic, or Asian descent appear at increased risk for the development of keloids [3]. Only a few locations have been known to become more prone to developing keloids. Keloids appear most often in the ear-lobe [4].

Treatments for keloids include surgical excision, intralesional or topical corticosteroids, other therapies: 5-fluorouracil (5-FU), bleomycin and interferon, topical imiquimod, compression, cryotherapy, radiation, silicon sheeting and laser or light-based therapies [1]. The treatment of keloids will always continue to be a little denouncing, as they frequently appear to come back. Monotherapy has a very high percentage of failure therefore, there are many tested combinations that can be used in order to achieve a more positive result, leading to a lower percentage in reappearance. In the literatures, there have been many therapeutic modalities and different combinations to reach an optimal treatment. However, there has not been solitary global therapy so far.

In our article, we provide a review of the medical and surgical treatment options for treating keloids.

Surgical

Excision alone

Excision of the keloid can be used as a monotherapy and has an effective role. However, the rate of reappearance after the excision performance alone ranges from 45% to 100% [5]. Thus, it is more commonly united with either a pre-operative or post-operative procedure, due to the high possibility of keloid to reappear, particularly right after a surgical excision. Surgical excision with a low-tension closure technique like zig-zag sutures including z-plasties are good for releasing the linear contractures and tension [6]. Surgical removal can still include a risk of reappearing, even though if there may have been different suturing styles and te-

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chniques used. In conclusion, there have been a lot of exhortations and post-operative procedures created to help slim down the chances of keloids to reappear. The following are the evidence of the modalities tried with excision.

Excision combined with medical

Mitomycin C: For approximately four minutes post-excision of an auricular keloid, it was documented to be 90% successful, with the dose of (0.4 mg/5 ml soaked cotton swabs). This procedure was performed on 10 patients, along with being observed for a course of 8 months [7].

Another application of mitomycin C was the use of 1 mg/ml on the wound for 3 minutes as in bailey study [8] and Gupta [9] or 5 minutes as in Chi [10] and repeat that after 3 weeks. The percentage in reappearance turned out to be around 0-10%. However, application of 0.4 mg/ml single application for 5 minutes in Sanders study [11] has a 40% recurrence rate.

Five-Fluorouracil was injected in 50 mg and 150 mg after keloid excision of earlobe. Recurrence was less than 4% and tissue necrosis seen in 3 out of 28 patients [12].

Imiquimod 5% cream applied to the resected keloid of earlobe after a course of 8 weeks had a recurrence rate of 25% [13] and 0% for 6 weeks in Stahower study [14]. The percentage of possible reappearance rate was high, 88.9% when applied on the trunk [15].

Verapamil (calcium antagonism): The local injection of 2.5 mg/ml (0.5 ml-2 ml) after 7-17 days of the removal of keloid surgically, followed by one more injection a month after, had a reappearance rate of 45% [16].

Radiation: Radiotherapy application in keloids were tested mostly on the earlobes. surgical excision of keloids followed by post-operative 10 Gy radiation therapy, delivered immediately in two fractions. (simple or wedge) (0-48 hours of surgery) [17]. Postoperative keloid radiotherapy requires moderately high doses and optimal technique to be effective [18]. A comparative trial showed that excision followed by postoperative irradiation is safer and more effective than cryotherapy combined with intralesional steroids [19]. Another recent study showed that brachytherapy was effective in treating cases of keloids that were resistant to external beam radiotherapy [20].

Medical

Steroid

Injection: Intralesional triamcinolone (ILT) injection has proven efficacy in treating keloids in multiple trials. In a review for Darzi, et al. showed that at a 10 year follow up, triamcinolone injection resulted in 71% of the keloids to be completely flattened [21]. One of the greatest first line of treatment options for eliminating keloids is intralesional triamcinolone. It has shown to be effective as a monotherapy to reduce the volume of the keloids with a response rate of more than 50% in multiple studies [22,23].

ILT injection in conjunction with silicone gel or sheeting showed greater efficacy than ILT injection alone, and has become a top considerable first line treatment for keloid patients [24,25].

Topical cream: clobetasol propionate (Dermovate) 0.05% cream was shown in a study that under the dressing of silicone, it is just as effective as intralesional triamcinolone injection. It also has less local side effects in comparison with intralesional triamcinolone injections [26].

Retinoid

Retinoid is vigorous inhibitor of matrix metalloproteinases (MMPs) that are usually elevated in keloid tissue and may subsidize to their high metabolic activity [27].

In one study, isotretinoin and tretinoin reduced collagen synthesis in keloid fibroblast cultures while maintaining normal levels of prolyl hydroxylase, reducing production of collagenase, and increasing activity of elastase like neutral protease. Therefore, the effects of retinoid on collagen synthesis may be through differential modulation of connective tissue metabolism [28].

In a clinical trial of 28 hypertrophic and keloid lesions, the use of retinoic acid 0.05% solution, reduced keloids size in 79% of subjects [29].

In another study by Panabiere-Castaings, 11 subjects were treated with 0.05% tretinoin nightly for 12 weeks, and then a momentous reduction in keloids volume and size was reported. However, two patients were dropped out of the study due to irritant contact dermatitis [30].

Immunomodulatory agents

Five-fluorouracil: Five-Fluorouracil (5-FU) inhibits keloids and hypertrophic lesions formation via its effects on anti-angiogenesis, collagen synthesis, cell proliferation inhibition and fibroblast apoptosis (anti-tumor activity, combatively constrain the synthesis of thymidylate synthase, causing suppression of synthesis of thymidine and thus DNA). The inhibitory mechanism of 5-FU on blood vessels, which accounts for the special ability of 5-FU to inhibit keloid formation [31]. In a study of 28 patients treated with intralesional 5-FU 50 mg/mL at weekly intervals for 12 weeks, 78.5% of them had overall improvement of more than 50% and no regrowth seen over a 24-week follow-up period [32].

Imiquimod: Imiquimod is an immunomodulatory that works as an agonist of toll-like receptor 7 (TLR7). The activation of TLR7 by imiquimod will lead to local production of proinflammatory cytokines like IFN-alpha, tumor necrosis factor (TNF), IL-6 and IL-12 [13]. Once these cytokine are produced, imiquimod prompts

expression of apoptotic genes in keloidal tissue, which usually are dysregulated in keloids [33]. Keloids were treated by excision followed by imiquimod 5% cream nightly for 8 weeks and at a follow-up of 24 weeks, the recurrence rate was 0% [34] and around 28.6% in another similar trial [35].

Tacrolimus: Tacrolimus (FK-506) is an immunosuppressant that is frequently used in the transplant to prevent rejection. This medication is also used by dermatologists in treating atopic dermatitis. Tacrolimus has multiple potential therapeutic targets in keloids. Tacrolimus blocks TGF-b/Smad, signaling pathway in keloidal fibroblasts by down-regulating TGF-β receptors and that reduces keloidal fibroblast proliferation, migration, and collagen elongation [36]. The application of tacrolimus 0.1% ointment twice daily for 12 weeks did improve keloids symptoms like tenderness, erythema, and pruritus but was not statistically significant in treating keloids [37].

Silicone

Silicone dressing is a non-invasive therapy for keloids. It has been used frequently in order to prevent and treat keloids. The side effects can include pruritus or contact allergic dermatitis [38] Silicone is available in different forms such as gel, sheet or cream. When applied after a surgical excision, silicone showed success in keloid prevention especially in high risk individuals but when used on keloids, it has not shown much success [39,40]. The exact mechanism of action of silicone dressing remains unknown but the most accepted theory is through occlusion and hydration effect on keloids [40,41].

Cryotherapy

Cryotherapy gives rise to vascular damage and ischemic cell death, which leads to a documented decease in blood supply and tissue necrosis with accomplishment percentages ranging from 50 to 80% for keloids [42]. Intralesional cryotherapy using needle to destruct the tissue by freezing was initially described by Weshahy [43]. However, Cryotherapy can be painful and sometimes may cause infection. Hypopigmentation was a major concern particularly for darker skin colored patients [44].

Lasers

Ablative carbon dioxide: When studying the differences between intralesional steroid with CO_2 laser versus with cryotherapy, the reduction in keloids size turned out to be higher in the CO_2 laser compared to cryotherapy [45]. Furthermore, A combination of fractional CO_2 laser and Pulsed dye laser (PDL) after injecting the lesions by triamcinolone every session for a total of 7 done at monthly intervals has been shown to be effective in treating keloids that was initially refractory to ILT alone on the upper back of a patient [46]. A report of 11 patients treated by CO_2 fractional laser followed by Pulsed dye laser (PDL) and long pulse Nd:YAG laser every month with the application of topical steroid cream to reduce the post-procedure inflammation. The results varied from excellent to no improvement in 3 out of the 11 patients. However, generalization is limited by the small sample size [47].

Non-ablative Pulsed Dye Laser (PDL): Prompts a selective destruction of small cutaneous vessels, leading to a decrease in more vascular areas and, ultimately, to hypoxemia. The affects of PDL irradiation are changing the collagen metabolism and prompt formulation of matrix-degrading enzymes such as matrix metalloproteinases (MMPs) and collagenase [48]. Various experimental procedures on the 585-nm tested the efficacy of Pulsed Dye Laser (PDL) alone in the practice of curing keloids. Improvement was minimized after careful observation of its effect on keloids of 11 patients, however, a minimal improvement in the erythema of the keloids was noted [49]. In comparison of PDL to no treatment care or intralesional steroid injection, the PDL revealed to have consistently minimal to medium improvement success in various trials and studies [50,51].

Conclusion

There are several reports of different medical and surgical treatment options for keloids presently in the literature which prove that keloid is very difficult to treat, and it has a strong likelihood of reappearance. Prevention can be possible through the application of silicone dressing in high risk individuals. Monotherapy by itself has proven success especially with the intralesional steroid injection, but there is always a room for combination with surgical excision, or other therapies: 5-fluorouracil (5-FU), bleomycin and interferon, topical imiquimod, compression, cryotherapy, radiation, silicon sheeting and laser or light-based therapies. Since keloids reappearance and resistance to treatment vary from a patient to another, it is important to be aware of the alternative tested regimens.

Conflicts of Interest

The authors have no conflicts of interest that are relevant to the content of this review.

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