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Current Approach to Keloid Management

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ABSTRACT Keloids are benign skin tumors resulting from deregulated wound healing processes, characterized by fibroblast hyperactivity, increased collagen deposition, and resistance to apoptosis. These lesions extend beyond the original wound borders and often cause significant physical and psychological burdens, including pain, pruritus, and reduced self-esteem. Despite advancements in medical science, keloid management remains a challenge due to the lack of standardized treatment protocols and the high recurrence rates associated with many therapeutic options. This review examines the efficacy and limitations of existing treatment modalities, including silicone gel sheets, antifibrotic agents, intralesional injections, cryotherapy, radiotherapy, laser therapies, surgical excision, and combination therapies. Emerging approaches, such as botulinum toxin, antihypertensives, platelet-rich plasma, and others, are also discussed. This article underscores the need for large-scale, high-quality studies focusing exclusively on keloids to refine treatment algorithms and advance therapeutic strategies.

KEY WORDS: keloids, benign tumors, corticosteroids, cryotherapy, excision.

INTRODUCTION

Keloids are considered as benign fibroproliferative dermal tumors, unique to humans, triggered by trauma or irritation. Their clinical appearance is highly variable. Initially, keloids present as raised, hard papules with a tendency to grow into nodules. The surface is shiny, with or without telangiectasia. Early lesions are often erythematous, later turning purple or brown before gradually fading with age. One of the most significant features of keloids is their ability to extend beyond the original border of the wound. They tend to be aggressive, invading the surrounding healthy skin (1). Keloids may develop as a result of various cutaneous injuries and irritations, most commonly following trauma, surgical incisions, piercings, burns, acne, folliculitis, or varicella-zoster virus infections; however, in rare cases, they may occur spontaneously (2,3). The incidence is highest among young people, particularly between 10 and 30 years of age, where keloids significantly impair quality of life (1). Beyond aesthetic concerns, they can cause considerable pain, persistent itching, stiffness, and contractures. These physical symptoms can lead to psychological consequences, including reduced self-esteem and disruptions in daily life (4). Pedunculated keloids represent a specific subtype. These are most commonly observed on the earlobes, appearing as mushroom-like formations connected to the earlobe by a stalk. They are frequently the result of piercings, a popular trend among young people (5). The incidence of keloids varies greatly among ethnic groups. It is highest among African Americans and Hispanic populations of American origin and lowest among Caucasians (3).

Underlying the pathogenesis of keloid is the mechanism of skin healing. The mechanism itself is

a complex process involving several cells, molecules, and their interactions. Skin injury or irritation is an initial triggering event for formation, but it must involve the dermis (2). Fibroblasts are the main cells, and TGF-β is their main stimulator in skin healing processes. Their task is to create fibrotic tissue, primarily made of collagen, which closes the damage. Keloids form when key healing processes become deregulated and overstressed, leading to excessive accumulation of extracellular matrix (ECM) elements (6). Namely, keloid fibroblasts, which are more sensitive to TGF-β, have an increased density and proliferation rate, while their apoptotic rate is reduced. Additionally, TGF-β affects the work of metalloproteinases, whose main task is the degradation of ECM elements. All of this leads to the creation of hard tissue that grows excessively. Histopathologically, keloids most often consist of tissue filled with whorls and nodules of thick, hyalinized collagen bundles, a mucinous basic substance, and a few fibroblasts (7). Apart from TGF-β, many other effector molecules, such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), fibronectin containing additional domain A (Fn-EDA), IL-4, IL-5, IL-10, and IL-13, further promote collagen synthesis and tissue angiogenesis (6).

Several risk factors are empirically or statistically associated with the formation of keloids, including a personal or family history of keloids, belonging to skin-of-color ethnic groups, pregnancy, puberty, hypertension and skin injuries overlying osteogenic surfaces (3,8). The most significant risk factor is local mechanical forces. The underlying mechanism is mechanotransduction, the process by which cells translate mechanical forces into intracellular biochemical signals (9). Body regions frequently subjected to tension, such as the chest, shoulders, and back, are the most affected (1). There is substantial evidence suggesting that genetics plays a strong role in keloid formation. While keloids are more common in certain ethnic groups and families, no single gene has been identified that, according to Mendelian inheritance principles, directly causes keloid formation. However, a genome-wide association study identified four single-nucleotide polymorphisms (SNPs) associated with keloid pathogenesis (6). Additionally, various genetic elements, such as HLA polymorphisms and epigenetic changes and modifications, are associated with the development of keloids (10)

Despite advancements in modern medicine, the treatment of keloids remains challenging. Since no targeted therapy exists, various treatment modalities are used. These include non-invasive treatments such as silicone gel sheeting, antifibrotic creams, and compression therapy, as well as invasive treatments such as intralesional injections, radiotherapy, cryotherapy, and surgery. Each treatment modality has a specific response rate, which measures the extent to which the keloid decreases or resolves entirely. Additionally, the recurrence rate is monitored to determine how long it takes for the keloid to regrow.

This article presents the outcomes of these treatment modalities through a systematic literature review. We searched the PubMed/MEDLINE database using the search terms "Keloid/therapy" and "keloid." By reviewing various meta-analyses and studies involving large sample sizes, we present the most favorable treatment algorithm. Only articles written in the English language were included in the evaluation.

THERAPY

Silicone gel sheeting

Silicone materials have been recommended as the "gold standard" for the prevention and treatment of keloids. Their effects are believed to be associated with the reduction of wound stretch, modulation of mechanotransduction, and improvements in occlusion and hydration (11). Silicone can be applied to the skin in the form of silicone gel sheets or topical silicone gel, typically for 12–24 hours per day, with twice-daily washing, for a minimum duration of 1 month (12). While early studies on silicone gel sheeting suggested high success rates in treating keloids, meta-analyses have concluded that silicone is not an effective treatment modality for keloid prevention (11). However, the meta-analysis conducted by O'Brien and Jones reported that silicone gel sheets alone can reduce keloid thickness and erythema (13).

Onion extract

The active ingredient in onion extract is Allium cepa, whose derivative, quercetin, is known for its anti-inflammatory, antibacterial, and collagen-suppressive properties. Onion extract is commonly used in scar prevention and as an initial therapy for pathological scars. Although studies have shown good results, including a decreased incidence of hypertrophic scars, it has proven ineffective as a therapy for keloids. Wananukul et al. reported no significant difference in keloid incidence between the treatment and placebo groups (14). However, onion extract contributes to the reduction of pain, pruritus, elevation, and redness when used in combination with other therapies (15).

Compression therapy

Compressive therapy involves applying localized pressure to the target area of the skin, i.e. the growth.

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The mechanisms of pressure therapy are believed to include mechanoreceptor-induced apoptosis of cells in ECM and pressure-induced ischemia, which alters fibroblast activity and promotes collagen degradation. Various materials can be used to apply pressure, including plaster casts, pressure earrings, and custom splints. At present, compressive therapy has proven effective as an adjunct to surgical excision in preventing ear keloid recurrence. Tahir et al. reported a recurrence rate of 10.66% for excision combined with compression earrings. The best results for compression therapy are achieved when the pressure device is worn for at least 12 hours per day, over a minimum period of six months, with a pressure of at least 24 mmHg (16).

Corticosteroids

Corticosteroids play a major role in keloid management, serving as a first-line treatment option as well as a preventive therapy. Corticosteroids impact multiple key pathways in keloid formation by reducing inflammation during the wound healing process. They also suppress collagen and glycosaminoglycan synthesis, inhibit fibroblast proliferation, and enhance collagen degradation. Several corticosteroids are available for treatment; however, triamcinolone acetonide (TAC) is the most widely used corticosteroid for keloid management (6). Intralesional TAC injections have been shown to reduce scar volume and height, improve scar pliability, and alleviate scar-associated pain and itching, as well as prevent recurrence. Morelli Coppola et al. reported that the response to corticosteroid injections alone is variable, with a regression rate of 70%–90%, but a recurrence rate of 33%–50% after 1 and 5 years, respectively (17). Typically, triamcinolone is injected at a concentration of 2.5 mg to 20 mg for facial keloids or 20 mg to 40 mg for non-facial keloids (12). This treatment can be used as monotherapy for mature keloids or as an adjuvant to surgical excision or laser therapy, achieving improved outcomes (18). However, local complications such as delayed wound healing, hypopigmentation, dermal atrophy, telangiectasias, scar widening, and systemic side effects, including Cushing's syndrome, may occur. Special caution is required when administering triamcinolone in children and in patients with multiple or very large lesions (17).

5-Fluorouracil

Primarily used as a chemotherapeutic agent, 5-fluorouracil (5-FU) is a pyrimidine analog that irreversibly inhibits thymidylate synthase, disrupting DNA replication and cellular proliferation (19). In vitro studies have demonstrated that 5-FU reduces fibroblast growth, induces fibroblast apoptosis, and decreases TGF-β-driven collagen synthesis (20,21). 5-FU can be used as monotherapy, in combination with triamcinolone acetonide (TAC), or as adjuvant therapy following surgical excision. The combination of TAC and 5-FU allows for lower doses of each agent, resulting in an improved side-effect profile. Bijlard et al. reported that intralesional 5-FU alone achieves good or excellent outcomes in 45–78% of patients, while combination therapy with intralesional 5-FU and TAC injections produced superior results. Regarding dosing, there is limited evidence on the efficacy and safety of TAC concentrations higher than 4 mg/ml. Therefore, it is recommended to use a ratio of 4:45 mg/ml for TAC and 5-FU (19). Intralesional 5-FU has also been studied as a post-excision treatment. Shin and Kim reported that keloid recurrence rates were significantly lower in patients treated with 5-FU following surgical excision (22). Possible side effects of intralesional 5-FU include skin erythema, pain, and ulceration (19).

Mitomycin

The antibiotic mitomycin C (MMC), isolated from Streptomyces cespitosus, has traditionally been used as a chemotherapeutic agent and more recently as an anti-scarring agent. By inhibiting DNA, RNA, and protein synthesis, MMC prevents cell division and fibroblast proliferation. Attempts to use intralesional MMC (1 mg/mL) have been associated with worsening of the condition and the appearance of ulcerations. Therefore, topical MMC is currently applied at a concentration of 1 mg/mL, placed on gauze for three to five minutes, with repeated applications every three weeks. Shin et al. reported a recurrence rate of 16.5% for topical MMC. No adverse effects were noted at the 1 mg/mL dose (23).

Bleomycin

Bleomycin, a glycopeptide isolated from Streptomyces verticillus, acts as a cytotoxic agent with antineoplastic, antibacterial, and antiviral properties. Bleomycin suppresses collagen production, induces fibroblast apoptosis, and inhibits the synthesis of DNA and RNA. It is administered intralesionally at a dose of 1.5 IU/mL, with two to five treatments at monthly intervals required to achieve satisfactory regression (24). Two meta-analyses, conducted by You et al. and Kim et al., evaluated the efficacy of bleomycin. Both analyses, which included studies on hypertrophic scars, concluded that bleomycin may be a more effective option for treating keloids and hypertrophic

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scars compared to other treatments, including TAC, 5-FU, the combination of TAC and 5-FU, or TAC combined with cryotherapy. However, bleomycin should be used cautiously due to potential adverse effects, such as hyperpigmentation, pain, and ulceration (25,26). Huu et al. conducted a study on the Vietnamese population to evaluate the use of bleomycin for treating keloids. The study reported recurrence rates of 3.8%, 15.4%, 45.5%, and 50% after 6, 12, 15, and 18 months of follow-up, respectively. The high recurrence rates were attributed to the location of the keloids on the body (27).

Imiquimod

Imiquimod is an immunomodulator that reduces fibroblast collagen production by increasing local concentrations of interferon-alpha (IFN-α). IFN-α has been shown to decrease fibroblast activity in a dose-dependent manner, reduce glycosaminoglycan production, and increase collagenase levels (28). Imiquimod is used topically as a 5% cream. Shin et al. reported a keloid recurrence rate of 24.7% after six to eight weeks of using 5% imiquimod cream. Studies conducted on keloids located outside tension regions showed better results and lower recurrence rates (23). Common side effects of imiquimod include hyperpigmentation, erythema, irritation, and secondary infections, which typically resolve after discontinuing therapy (28).

Interferons

Interferon therapy is an emerging treatment with potential therapeutic effects against keloids due to its immunomodulatory, antiangiogenic, antiproliferative, and antineoplastic activities. Among the three isoforms of interferons, IFN-α and IFN-γ have been found to be particularly effective for keloid treatment, Specifically, IFN-α2b is used in keloid treatment by enhancing collagenase levels and inhibiting the secretion of collagenase inhibitors, such as metalloproteinases. IFN-γ also plays an important role in reducing fibrosis by inhibiting TGF-β. A review of available databases reveals that no meta-analyses currently exist on the efficacy or recurrence rates of keloids treated with this form of therapy. Every study or case report conducted so far demonstrates the efficacy of interferon therapy, either as monotherapy or in combination with other forms of treatment. Although interferon therapy has shown success, it is associated with adverse effects, including fever, headache, arthralgia, fatigue, chills, and confusion. Additionally, the treatment is expensive, which limits its accessibility (29).

Cryotherapy

Cryotherapy, in combination with the intralesional application of corticosteroids, is one of the most popular forms of keloid therapy. Cryotherapy involves freezing tissue below zero degrees Celsius, which induces tissue necrosis through damage to blood vessels and osmotic injury to cell membranes. Histologic studies following cryotherapy have identified several significant changes in scar tissue structure, including the reorganization of collagen fibers into a more compact, parallel arrangement, similar to that of a classic scar (30). Additionally, keloid tissue exposed to cryotherapy has been reported to exhibit reduced numbers of myofibroblasts and mast cells, as well as decreased production of TGF-β by dermal fibroblasts (31). Currently, cryotherapy options include spray, contact, and intralesional methods. Intralesional cryotherapy is considered the most effective form, as it allows for more precise and intense freezing of abnormal tissue, often requiring fewer treatment sessions to achieve satisfactory results. Van Leeuwen et al. reported an average scar volume reduction of 51% to 63%, although complete eradication of keloids was not consistently achieved. Keloid recurrence rates ranged from 0% to 24%. Common side effects of intralesional cryotherapy include temporary blistering of the lesion, postoperative pain, and temporary hypopigmentation. Patients with Fitzpatrick skin types IV to VI are at higher risk of developing persistent hypopigmentation (32).

LASER therapy

LASER is an acronym for Light Amplification by Stimulated Emission of Radiation. Laser-based devices are classified into two categories: ablative and non-ablative. The most commonly used ablative lasers are erbium-doped yttrium aluminium garnet (Er:YAG) and carbon dioxide (CO_2) lasers. CO_2 and Er:YAG lasers target water molecules, resulting in local tissue changes, including collagen remodelling and reduced TGF-β levels (33). Non-ablative laser techniques have shown promising results, particularly when combined with the intralesional application of corticosteroids (34). Pulsed dye laser (PDL) induces hypoxia by destroying blood vessels, which disrupts disulfide bonds in collagen fibers and reorganizes them into new, healthy fibrils. PDL also promotes collagen remodelling by stimulating cytokine release and reducing TGF-β levels (35). Another laser commonly used in keloid treatment is the neodymium-doped yttrium aluminium garnet (Nd:YAG) laser. By reducing vascularization, Nd:YAG lasers decrease the accumulation of cytokines and vascular growth

factors, thereby minimizing abnormal collagen deposition (36). Forbat et al., in a systematic review of the literature, reported on the effectiveness and recurrence rates of laser therapy. To date, no randomized controlled trials (RCTs) have been published on the effectiveness of CO_2 or Er:YAG lasers for keloid treatment. For CO_2 laser treatments, keloid recurrence was observed between 2 weeks and 3 years post-treatment. Treatment with the Er:YAG laser resulted in a 22% recurrence rate 8 months after the procedure (37). Improved outcomes have been noted when CO_2 and Nd:YAG lasers are used in combination with triamcinolone acetonide (TAC) (17). Nd:YAG lasers showed variable recurrence rates 6 months after treatment, depending on the anatomical site of the keloid. One study reported recurrence rates of 52.9% for anterior chest keloids, 35.7% for upper arm keloids, and 25% for scapula keloids (37). PDL, when combined with TAC, may provide a synergistic effect, as corticosteroids reduce collagen synthesis and enhance collagen degradation (34). Possible side effects of laser therapy include hyperpigmentation, blistering, erosion, scabbing, and post-treatment purpura (33,35,36).

Radiation therapy

Radiotherapy, first described in 1906, is a widely applicable therapeutic option for keloids. It works by decreasing fibroblast proliferation, inducing cell senescence and apoptosis, and subsequently reducing collagen production and suppressing keloid formation (38). There are currently two forms of keloid radiation: external and internal. External radiation includes X-ray and electron beam radiotherapy (EBRT), while internal radiation is delivered via interstitial brachytherapy, which can be applied as either low-dose rate (LDR) or high-dose rate (HDR). Comparing the success and recurrence rates of different radiotherapy modalities is challenging, as most studies are retrospective and vary in terms of radiation doses, treatment intervals, recurrence definitions, and whether they include hypertrophic scars or keloids. Radiotherapy is less commonly used as monotherapy and is more often employed as an effective adjunct treatment following surgical excision. Mankowski et al. reported that post-excisional radiotherapy is more effective in preventing recurrence compared to radiotherapy alone. When comparing radiation modalities, postoperative brachytherapy demonstrated the lowest recurrence rate (15%), compared to recurrence rates of 23% for both X-ray and EBRT. This analysis utilized a biological effective dose calculator but did not provide a clear definition of recurrence and only included studies performed exclusively on keloids (39). Radiotherapy as monotherapy may be recommended for elderly patients in cases where surgical removal is not viable due to the keloid's location or size. Furthermore, radiotherapy applied to mature keloids has been reported to alleviate pain and pruritus (40). In a systematic literature review, Van Leeuwen et al. included only studies in which keloids were histopathologically confirmed after excision. They reported recurrence rates of 10.5% following HDR brachytherapy and 22.2% after external radiation (41). The maximal biologically effective dose for keloids is 30 Gy. Doses exceeding this threshold do not increase efficacy but do elevate the risk of secondary carcinogenesis. For high-risk anatomical regions, it is sufficient to deliver 18 Gy in three fractions over three days (approximately 30 Gy), 8 Gy in one fraction for earlobes, or 15 Gy in two fractions over two days for other body regions (40). Side effects of radiotherapy include various acute skin reactions that typically appear within the first ten days, such as erythema, pigmentation, epilation, and desquamation. Late reactions, occurring weeks after radiotherapy, include permanent pigmentation changes (hyperpigmentation or depigmentation), atrophy, telangiectasia, subcutaneous fibrosis, and, in severe cases, necrosis (41).

Surgical therapy

At first, logic dictates that keloid excision is an excellent way to deal with a benign growth. However, excision prolongs inflammation and provokes the regrowth of keloids. In fact, studies show that excision alone has a recurrence rate of over 50% (39). Small keloids, which result from skin tension, can be removed by excision, but adjuvant therapy is always necessary to reduce the possibility of recurrence. Excision is also a therapeutic option when keloids form on joints and cause contractures. For large and multiple keloids, partial and core excision are used to reduce the hard and thickened parts. To achieve better results, surgery should involve tension-reducing techniques, such as subcutaneous and deep fascial tensile-reduction sutures, Z-plasties, and local-flap transfer (43). Tensile-reduction sutures elevate the wound edges smoothly and relieve dermal tension. Ogawa et al. reported that these techniques help reduce recurrence rates (40). Regarding Z-plasty, case series studies of anterior chest wall keloids and upper-arm keloids showed that excision performed with Z-plasty and adjuvant radiotherapy resulted in recurrence rates of 10.6% and 5.3%, respectively, at 24 months. All recurrences were easily managed with steroid patches and injections (44,45). Flap choice depends on the affected region. Ogawa et al. reported that none of the 10 large anterior chest wall keloids recurred after par-

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tial or total resection and flap reconstruction. When using flaps, the donor site must undergo multimodal therapy to prevent the formation of new keloids (46).

Therapies under investigation

As described above, there is no therapeutic option that completely prevents keloid formation or, once a keloid has formed, removes it entirely without recurrence. Increasingly clarifying the pathogenesis of keloids and identifying risk factors opens possibilities for the design and development of new, targeted therapies.

As keloids are associated with hypertension, calcium channel blockers and angiotensin-converting enzyme (ACE) inhibitors have been explored. ACE inhibitors inhibit angiotensin II, which elevates the level of TGF-β and plays a prominent role in collagen biosynthesis and wound healing. Verapamil, on the other hand, triggers the synthesis of procollagenase in keloids and normal human cultured fibroblasts, leading to reduced production of fibrous tissue. Botulinum toxin-A has also been investigated, aiming to reduce muscle tension and, consequently, wound tension. Among various chemotherapeutics already in use, doxorubicin and tamoxifen have gained attention. Both exhibit antifibrotic properties, although they have the side effect of poor wound healing (47). As is well known, TGF-β isoforms play a key role in the pathogenesis of keloids. TGF-β3 has been shown to exert antifibrotic properties, resulting in a significant reduction in scarring. Avotermin, a recombinant human TGF-β3 polypeptide, has demonstrated significant scar reduction and improved appearance following intralesional injection (48,49). Platelet-rich plasma (PRP) is a concentrated autologous plasma that contains supra-physiologic levels of platelets and alpha granules rich in growth factors and cytokines. PRP has been popularized as an adjunctive treatment for various dermatologic conditions, and recent studies have focused on its role in keloid pathology. Increased levels of TGF-β in PRP have been proposed to activate a negative feedback mechanism in the TGF-β signaling pathway (50). Stem cells exhibit immunomodulatory and antifibrotic effects. Stem cells could potentially be used to prevent or attenuate the excessive inflammatory processes characteristic of keloids (47). Although these approaches bring optimism, more investigations and long-term studies are needed before they can be applied in clinical practice.

DISCUSSION

Currently, there are no standardized guidelines for the treatment of keloids endorsed by professional bodies. Several issues contribute to this lack of standardization. The pathogenesis of keloids is complex, with an underlying dysregulated mechanism of skin healing. Additionally, keloids are benign skin neoplasms, which further complicates our understanding. While significant progress has been made in understanding keloid pathogenesis, the key signaling pathway required to completely halt keloid growth remains unidentified. Today's treatment of keloids relies on case series, retrospective and prospective cohorts, and review articles. Comparing results is challenging due to the inclusion of hypertrophic scars, variations in treatment doses and intervals, differing follow-up periods, the heterogeneity of keloids, and other factors. Large, high-quality studies focusing exclusively on keloids are urgently needed. Furthermore, standardizing the measurement of therapeutic success is essential.

The treatment and prevention of keloids often begin with silicone sheets. Meta-analyses currently indicate that silicone sheets are effective in reducing redness and itching but should not be used as monotherapy. Instead, they are best employed as adjuncts to corticosteroid therapy. Intralesional corticosteroid therapy is considered the gold standard, offering variable but generally favorable results as monotherapy. However, a subset of patients does not respond, and recurrence rates exceed 30%. Contact or intralesional cryotherapy can complement treatment, particularly for auricular keloids, but further research is required.

If conservative therapy fails to yield improvement, 5-fluorouracil (5-FU) combined with intralesional corticosteroids, and ultimately laser therapy or surgical excision, may be considered. Although published clinical trials are limited, current findings suggest the use of PDL over other laser types for treating refractory keloids.

Surgical excision, although commonly utilized by plastic surgeons, should be viewed as the final step in the treatment algorithm. Excision alone has a recurrence rate exceeding 50%. For better outcomes, surgery should incorporate tension-reducing techniques, such as subcutaneous and deep fascial tensile-reduction sutures, Z-plasties, and local-flap transfer. While these methods yield promising results, further research is necessary.

To prevent postoperative keloid recurrence, adjunctive therapies are crucial. Intralesional corticosteroids, combined with silicone gels, represent one of the more conservative approaches to postoperative prophylaxis. 5-FU has demonstrated efficacy as post-excisional therapy, particularly when combined with corticosteroids, as this allows for lower doses and a

synergistic effect, thereby improving the safety profile. Compressive therapy has also proven effective as an adjunct to surgical excision, particularly for auricular keloids.

For carefully selected patients, radiotherapy following surgical excision is a viable treatment option. Although clinical trial data are lacking, current evidence suggests the superiority of high-dose-rate (HDR) radiotherapy over other forms. Additionally, chemotherapeutic agents such as bleomycin and mitomycin C, as well as 5% imiquimod cream, merit consideration as adjuncts to surgical excision for the treatment of refractory keloids.

CONCLUSION

Upon reviewing the available literature today, we would once again emphasize the need for large, well-designed studies specifically focused on keloids. This would allow for easier standardization of treatment algorithms and the measurement of therapy effectiveness. We believe that this approach could help focus on therapies that yield good results, leading to shorter treatment times and longer periods without recurrence. This would certainly result in greater patient satisfaction.

The conclusion of the literature review is that the treatment algorithm has not changed significantly in recent years. In the case of small and individual keloids, conventional therapy can be initiated. The gold standard is intralesional corticosteroid therapy, preferably in combination with silicone sheets. For refractory keloids, other intralesional therapies, cryotherapy, radiotherapy, or lasers should be considered. As a final step, or when keloids impair the function of the affected area, surgical methods combined with intralesional corticosteroids and radiotherapy remain an option. Thick, large, or multiple keloids should be treated aggressively and promptly, as they respond poorly to monotherapy.

References

1. tan S, Khumalo N, Bayat A. Understanding keloid pathobiology from a quasi-neoplastic perspective: Less of a scar and more of a chronic inflammatory disease with cancer-like tendencies. Front Immunol. 2019;10:1810.
2. Ogawa R. Keloid and hypertrophic scars are the result of chronic inflammation in the reticular dermis. Int J Mol Sci. 2017;18:606.
3. Shaheen AA. Risk Factors of Keloids: A Mini Review. Austin J Dermatolog. 2017;4:1074.
4. Bock O, Schmid-Ott G, Malewski P, Mrowietz U. Quality of life of patients with keloid and hypertrophic scarring. Arch Dermatol Res. 2006;297:433–38.
5. Har-Shai Y, Har-Shai L, Zouboulis VA, Zouboulis CC. Different Types of Auricular Keloids and Treatment by Intralesional Cryosurgery: Best Practice for Obtaining Long-Lasting Clinical Results. Dermatology. 2022;238:170-79.
6. Andrews JP, Marttala J, Macarak E, Rosenbloom J, Uitto J. Keloids: The paradigm of skin fibrosis — pathomechanisms and treatment. Matrix Biology. 2016;51:37–46.
7. Wang PH, Huang BS, Horng HC, *et al.* Wound healing. J Chin Med Assoc. 2018;81:94–101.
8. Adotama P, Rutherford A, Glass DA 2nd. Association of keloids with systemic medical conditions: a retrospective analysis. Int J Dermatol. 2016;55:38–40.
9. Kuehlmann B, Bonham CA, Zucal I, Prantl L, Gurtner GC. Mechanotransduction in wound healing and fibrosis. J Clin Med. 2020;9:1423.
10. Sadiq A, Khumalo NP, Bayat A. Genetics of Keloid Scarring. In: Téot L, Mustoe TA, Middelkoop E, Gauglitz GG, editors. Textbook on Scar Management. Cham: Springer; 2020. p. 61–67.
11. Hsu KC, Luan CW, Tsai YW. Review of silicone gel sheeting and silicone gel for the prevention of hypertrophic scars and keloids. Wounds. 2017;29:154–58.
12. Gold MH, McGuire M, Mustoe TA, *et al.* Updated international clinical recommendations on scar management: part 2–algorithms for scar prevention and treatment. Dermatol Surg. 2014;40:825–31.
13. O'Brien L, Jones DJ. Silicone gel sheeting for preventing and treating hypertrophic and keloid scars. Cochrane Database Syst Rev. 2013;9:CD003826
14. Wananukul S, Chatpreodprai S, Peongsujarit D, Lertsapcharoen P. A prospective placebo-controlled study on the efficacy of onion extract in silicone derivative gel for the prevention of hypertrophic scar and keloid in median sternotomy wound in pediatric patients. J Med Assoc Thai. 2013;96:1428–33.
15. Koc E, Arca E, Surucu B, Kurumlu Z. An open, randomized, controlled, comparative study of the combined effect of intralesional triamcinolone acetonide and onion extract gel and intralesional triamcinolone acetonide alone in the treatment of hypertrophic scars and keloids. Dermatol Surg.

2008;34:1507–14.

16. Tahir SM, Ihebom D, Simman R. Compression Therapy for Keloid Scars: A Systematic Review and Meta-analysis. Plast Reconstr Surg Glob Open. 2024;12:5864
17. Morelli Coppola M, Salzillo R, Segreto F, *et al.* Triamcinolone acetonide intralesional injection for the treatment of keloid scars: patient selection and perspectives. Clin Cosmet Investig Dermatol. 2018;11:387–96
18. Yuan FL, Wang J, Sun ZL, *et al.* Comments on "Comparison of efficacy and safety of intralesional triamcinolone and combination of triamcinolone with 5- fluorouracil in the treatment of keloids and hypertrophic scars: Randomised control trial"Burns. 2020;46:490-91.
19. Bijlard E, Steltenpool S and Niessen FB. Intralesional 5-fluorouracil in keloid treatment: a systematic review. Acta Derm Venereol. 2015;95:778–82.
20. Huang L, Wong YP, Cai YJ, *et al.* Low-dose 5-fluorouracil induces cell cycle G2 arrest and apoptosis in keloid fibroblasts. Br J Dermatol. 2010;163:1181–95.
21. Wendling J, Marchand A, Mauviel A, Verrecchia F.5-fluorouracil blocks transforming growth factorbeta-induced alpha 2 type I collagen gene (COL1A2) expression in human fibroblasts via c-Jun NH2-terminal kinase/activator protein-1 activation. Mol Pharmacol. 2003;64:707–13.
22. Shin JY, Kim JS. Could 5-fluorouracil or triamcinolone be an effective treatment option for keloid after surgical excision? A meta-analysis. J Oral Maxillofac Surg. 2016;74:1055–60.
23. Shin JY, Yun SK, Roh SG, Lee NH, Yang KM. Efficacy of 2 representative topical agents to prevent keloid recurrence after surgical excision. J Oral Maxillofacial Surg. 2017; 75:401.e1–401.e6.
24. Lee HJ, Jang YJ. Recent Understandings of Biology, Prophylaxis and Treatment Strategies for Hypertrophic Scars and Keloids. Int J Mol Sci. 2018;19:711.
25. You SJ, Li S, Hu CM, Zhong FY, Gan SH, Cai Y, *et al.* Safety and efficacy of intralesional bleomycin for keloids and hypertrophic scars: A systematic review and meta-analysis. J Cosmet Dermatol. 2024;23:3444-55.
26. Kim WI, Kim S, Cho SW, Cho MK. The efficacy of bleomycin for treating keloid and hypertrophic scar: A systematic review and meta-analysis. J Cosmet Dermatol. 2020;19:3357-66.
27. Dinh Huu N, Nguyen Huu S, Le Thi X, Van TN,Thi Minh PP, Trinh Minh T, et al. Successful Treatment of Intralesional Bleomycin in Keloids of Vietnamese Population. Open Access Maced J Med Sci. 2019;7:298-99.
28. Berman B, Maderal A, Raphael B. Keloids and hypertrophic Scars: pathophysiology, classification, and treatment. Dermatol Surg. 2017;43:3–18.
29. Mary Loordhuswamy A, Elango S. Interferon Therapy for Hypertrophic Scars and Keloids [Internet]. Recent Advances in Wound Healing. IntechOpen; 2022.
30. Har-Shai Y, Mettanes I, Zilberstein Y, et al. Keloid histopathology after intralesional cryosurgery treatment. J Eur Acad Dermatol Venereol. 2011;25:1027–36.
31. Awad SM, Ismail SA, Sayed DS, et al. Suppression of transforming growth factor-beta1 expression in keloids after cryosurgery. Cryobiology. 2017;75:151–53.
32. van Leeuwen MC, Bulstra AE, Ket JC, Ritt MJ, van Leeuwen PA, Niessen FB. Intralesional Cryotherapy for the Treatment of Keloid Scars: Evaluating Effectiveness. Plast Reconstr Surg Glob Open. 2015;3:437.
33. Tretti Clementoni M, Azzopardi E. Minimally Invasive Technologies for Treatment of HTS and Keloids: Fractional Laser. In: Téot L, Mustoe TA, Middelkoop E, Gauglitz GG, editors. Textbook on Scar Management. Cham: Springer; 2020. p. 279-286.
34. Khansa I, Harrison B, Janis JE. Evidence-based scar management: how to improve results with technique and technology. Plast Reconstr Surg. 2016;138:165–78.
35. Nischwitz SP, Lumenta DB, Spendel S, Kamolz LP. Minimally Invasive Technologies for Treatment of HTS and Keloids: Pulsed-Dye Laser. In: Téot L, Mustoe TA, Middelkoop E, Gauglitz GG, editors. Textbook on Scar Management. Cham: Springer; 2020. p. 263-270
36. Ogawa R. Long-Pulsed 1064 nm Nd:YAG Laser Treatment for Keloids and Hypertrophic Scars. In: Téot L, Mustoe TA, Middelkoop E, Gauglitz GG, editors. Textbook on Scar Management. Cham: Springer; 2020. p. 271-278.
37. Forbat E, Ali FR, Al-Niaimi F. Treatment of keloid scars using light-, laser-and energy-based devices: a contemporary review of the literature. Lasers Med Sci. 2017;32:2145-54.
38. Ji J, Tian Y, Zhu YQ, *et al.* Ionizing irradiation inhibits keloid fibroblast cell proliferation and induces premature cellular senescence. J Dermatol. 2015;42:56–63.

39. Mankowski P, Kanevsky J, Tomlinson J, Dyachenko A, Luc M. Optimizing radiotherapy for keloids: a meta-analysis systematic review comparing recurrence rates between different radiation modalities. Ann Plast Surg. 2017;78:403–11
40. Ogawa R, Tosa M, Dohi T, Akaishi S, Kuribayashi S. Surgical excision and postoperative radiotherapy for keloids. Scars Burn Heal. 2019;5:1-11.
41. van Leeuwen MC, Stokmans SC, Bulstra AE, Meijer OWM, Heymans WM, Ket JCF. Surgical excision with adjuvant irradiation for treatment of keloid scars: a systematic review. Plast Reconstr Surg Glob Open. 2015;3:440.
42. Huang C, Liu L, You Z, Du Y, Ogawa R. Managing keloid scars: From radiation therapy to actual and potential drug deliveries. Int Wound J. 2019;16:852–59.
43. Ogawa R. The Most Current Algorithms for the Treatment and Prevention of Hypertrophic Scars and Keloids: A 2020 Update of the Algorithms Published 10 Years Ago. Plast Reconstr Surg. 2022;149:79-94.
44. Arima J, Dohi T, Kuribayashi S, Akaishi S, Ogawa R. Z-plasty and postoperative radiotherapy for anterior chest wall keloids: An analysis of 141 patients. Plast Reconstr Surg Glob Open. 2019;7:2177.
45. Dohi T, Kuribayashi S, Tosa M, Aoki M, Akaishi S, Ogawa R. Z-plasty and postoperative radiotherapy for upper-arm keloids: An analysis of 38 patients. Plast Reconstr Surg Glob Open. 2019;7:2496.
46. Ogawa R, Ono S, Akaishi S, Dohi T, Iimura T, Nakao J. Reconstruction after anterior chest wall keloid resection using internal mammary artery perforator propeller flaps. Plast Reconstr Surg Glob Open. 2016;4:1049.
47. Memariani H, Memariani M, Moravvej H, Shahidi-Dadras M. Emerging and Novel Therapies for Keloids: A compendious review. Sultan Qaboos Univ Med J. 2021;21:22-33.
48. Ferguson MW, Duncan J, Bond J, Bush J, Durani P, So K, et al. Prophylactic administration of avotermin for improvement of skin scarring: three double-blind, placebo-controlled, phase I/II studies. Lancet. 2009;373:1264–74.
49. So K, McGrouther DA, Bush JA, Durani P, Taylor L, Skotny G, et al. Avotermin for scar improvement following scar revision surgery: a randomized, double-blind, within-patient, placebo-controlled, phase II clinical trial. Plast Reconstr Surg. 2011;128:163–72.
50. Jones ME, McLane J, Adenegan R, Lee JA, Ganzer CA. Advancing keloid treatment: a novel multimodal approach to ear keloids. Dermatol Surg. 2017;43:1164–69.