Drugs Ther Perspect (2016) 32:526–529
DOI 10.1007/s40267-016-0330-5

DISEASE MANAGEMENT

Treat keloids and hypertrophic scars with a combination of interventions to obtain the best results

Adis Medical Writers[1]

Published online: 28 July 2016

Abstract Despite the availability of a multitude of therapeutic modalities, the treatment of keloids and hypertrophic scars remains extremely challenging. There is no clinical consensus regarding the most appropriate treatment, although currently available data support the use of silicone gel sheeting and intralesional steroid injections as first-line options. In general, outcomes appear to be improved when combination therapy is used.

A clinical challenge

Keloids and hypertrophic scars result from perturbations in the wound healing process that lead to excess collagen synthesis and deposition [1]. Besides frequently being pruritic and painful, such pathological scarring can cause disfigurement, functional impairment, emotional distress and psychological damage [1, 2].

Specific areas of the body that are relatively more susceptible to developing keloids or hypertrophic scars include the sternal skin, earlobes (piercings), shoulders and upper arms (vaccinations) and cheeks (acne) [1, 2]. Keloids occur more commonly in Black, Hispanic and Asian individuals than in Caucasians, with darker pigmented skin carrying a 15-fold increased risk [1, 2]. There is some evidence for a genetic predisposition, although the precise mode of inheritance is not yet clear [1]. Although keloids can occur at any age, they are more common in individuals aged <30 years [2], with their incidence peaking at 15–24 years [1]. Individuals with elevated hormone levels (e.g. during puberty or pregnancy) may also have an increased risk of developing keloids [2].

This article provides a summary of the clinical challenges in the prevention and treatment of keloids and hypertrophic scars, as reviewed by Trace et al [1].

Prevention is best

Given the challenges in treating pathological scarring, efforts should be made to prevent the occurrence of keloids and hypertrophic scars whenever possible, although this may not always be practical to achieve [1]. Prior to any surgical procedure, physicians should establish if the patient has had any previous problems with scarring, and the potential for keloids or hypertrophic scars to develop should be discussed. Ear piercing and other elective procedures (such as elective mole removal) should be discouraged in patients with a known predisposition to pathological scarring [2]. The use of proper atraumatic surgical technique is critical to help minimize the risks of keloids or hypertrophic scars; wounds should be closed under minimal tension [1, 3]. For patients considered at high risk of developing pathological scarring, preventive measures, such as the prophylactic use of silicone-based products, is recommended [1].

Establish realistic expectations with the patient

The treatment of keloids and hypertrophic scars remains very challenging [1–3]. A wide variety of therapeutic modalities are available (Tables 1, 2, 3), with each

✉ Adis Medical Writers
dtp@adis.com

[1] Springer, Private Bag 65901, Mairangi Bay, 0754 Auckland, New Zealand

Table 1 Summary of pharmacological modalities for the prevention and treatment of pathological scarring, as reviewed by Trace et al. [1]
Intralesional steroid injections
Mechanism of action: acts as an anti-inflammatory; also suppresses fibroblast proliferation and inhibits α2-macroglobulin, leading to increased collagen degradation and scar regression [4, 5]
Intralesional triamcinolone can reduce lesion volume, with response rates of 50–100 %
Continue serial injections (3–4 weeks apart) until an acceptable outcome is achieved or until adverse effects become unacceptable
Results may be enhanced when steroid injections are used in conjunction with other therapies (e.g. intralesional 5-fluorouracil, topical or intralesional cryotherapy, laser treatment or surgical excision)
Small (focally raised) keloids: use intralesional steroid injections in combination with silicone gel or sheeting as a first-line option
Large (raised >0.5 cm) keloids: use monthly intralesional triamcinolone (± adjuvant cryotherapy) as a first-line option
Recalcitrant lesions: use post-operative intralesional triamcinolone to prevent keloids from recurring after their surgical excision [6]
Use lidocaine to attenuate common adverse effects, such as pain and bleeding [2]
Use of low steroid doses may help minimize other adverse effects, such as atrophy, telangiectasia, hypopigmentation and adrenal insufficiency (rare)
5-Flurouracil
Mechanism of action: inhibits DNA synthesis, thereby targeting rapidly proliferating cells
Effective as monotherapy in treating hypertrophic scars and small, more recently developed keloids
Effective in combination with surgical excision in treating keloids that are recalcitrant to intralesional triamcinolone injections [7]
Adverse effects, particularly pain and hyperpigmentation, are common
Do not use in pregnant women or immunosuppressed patients due to the risk of systemic adverse effects
Imiquimod 5 % cream
Safe and effective treatment with few adverse effects
Mechanism of action: not known precisely, but likely involves enhancing local production of cytokines and altering expression of apoptosis-associated genes [8, 9]
Optimally used as an adjunct to surgical excision of keloids in low tension areas (e.g. the auricle)
Bleomycin
Mechanism of action: inhibits DNA, RNA and protein synthesis
Routes of administration include intralesional injection, multiple puncture deposits, Dermojet® injection and tattooing
May be suited to the treatment of large, bulky lesions or to recalcitrant lesions [10, 11]
Generally well tolerated with cutaneous application at doses used in the treatment of keloids; common adverse effects are local hyperpigmentation and atrophy

Table 2 Summary of non-invasive modalities for the prevention and treatment of pathological scarring, as reviewed by Trace et al. [1]
Silicone gel therapy (silicone gel sheeting or cream)
Effective both for prevention and treatment of pathological scarring
Non-invasive treatment that is particularly suited to children and patients intolerant of other modalities
Mechanism of action: not fully understood, but is proposed to involve the processes of hydration and occlusion [12]
Adverse effects are minimal, and include local irritation
Pressure therapy
Non-invasive treatment that can be used for preventing and limiting pathological scarring following thermal injury
Also suitable as a non-invasive option for the treatment of earlobe keloids
Treatment of established scars:, pressure garment therapy may be considered a second-line option for use in combination with other treatments (e.g. surgery)
Mechanism of action: not fully understood, but is likely multifaceted and may involve both molecular and mechanical processes
Therapy is limited by the ability to provide consistent application of pressure and adequate anatomic fit, but a variety of materials and devices have been developed to address these challenges

treatment option having a varying degree of effectiveness [1–3]. Largely due to the limited amount of data available from well-designed randomized controlled trials, there is no clinical consensus regarding the most appropriate treatment for these lesions [1, 2]. The best evidence supports the use of intralesional steroid injections (Table 1)

Table 3 Summary of surgical, cryotherapy and laser treatment of pathological scarring, as reviewed by Trace et al. [1]
Surgery
A multitude of surgical techniques are available for the treatment of keloids or hypertrophic scars in various body locations
Recurrence rates are high (45–100 %) when excisional surgery is used alone, but surgery can be curative when used in combination with other treatments (e.g. intralesional steroid injections, peri- or post-operative radiation)
Intradermal sutures may benefit scars disposed to tension
Discuss the risks of surgery, the potential for generating new keloids and expected post-operative pain with the patient
Cryotherapy
Minimally invasive with relatively few contraindications
Efficacy rates in keloids are ≈51–74 % [13, 14], although only partial scar eradication is generally achieved
Most effective for smaller lesions, such as keloids resulting from acne [2]; superior to intralesional triamcinolone injections for small, highly vascular keloids [15]
Use in combination with intralesional steroid injections to improve outcomes
Potential adverse effects include temporary dysaesthesias, hyperpigmentation, alopecia, atrophy, cartilage necrosis and hypopigmentation; use caution, especially in dark-skinned individuals
Laser therapy
Laser therapy technologies used in the treatment of keloids and hypertrophic scars continue to evolve
Types of lasers used in treatment include: high-energy, short-pulsed CO_2 lasers, scanned continuous wave CO_2 lasers, neodymium:yttrium-aluminium-garnet (Nd:YAG) continuous wave lasers, pulsed dye lasers and fractional lasers
Current recommendations suggest early use of laser therapy [1, 16]
Early initiation of therapy may modify the inflammation phase of wound healing and alter fibroblast migration, preventing or reducing scar proliferation [16]
Laser treatment may also induce alterations in microcirculation at the wound, preventing excessive scar formation [16]
Newer fractional or pulsed dye lasers place minimal mechanical stress on the tissues, further supporting earlier use [16]
Consider use of laser therapy in erythematous lesions
Common adverse effects include blistering, erythema and transient hyper- or hypo-pigmentation

and silicone gel sheeting (Table 2) as first-line options [1, 2]. Cryotherapy (Table 3) may be effective for smaller lesions (e.g. acne keloids) [2]. In general, outcomes appear to be improved when combination therapy is used [1–3].

Further therapies are available or emerging

Less common treatments for keloids and hypertrophic scars include interferon-α-2b, mitomycin C, onion extract, radiotherapy, vitamins A and E, verapamil, polyurethane dressing, botulinum toxin and photodynamic therapy [1]. Emerging therapies that have shown promise include topical and intradermal immune modulators, anti-transforming growth factor-β antibodies, and micro RNA (miRNA) and small interfering RNA (siRNA)-based methods [1]. Nonetheless, it is clear that keloids and hypertrophic scars still provide significant clinical challenges, and further research in this field is required [1].

Compliance with ethical standards

The article was adapted from the *American Journal of Clinical Dermatology* 2016;17(3):201–23 [1] by salaried employees of Adis/Springer and was not supported by any external funding.

References

1. Trace AP, Enos CW, Mantel A, et al. Keloids and hypertrophic scars: a spectrum of clinical challenges. Am J Clin Dermatol. 2016;17(3):201–23.
2. Juckett G, Hartman-Adams H. Management of keloids and hypertrophic scars. Am Fam Physician. 2009;80(3):253–60.
3. Robles DT, Moore E, Draznin M, et al. Keloids: pathophysiology and management. Dermatol Online J. 2007;13(3):9.
4. Perdanasari AT, Lazzeri D, Su W, et al. Recent developments in the use of intralesional injections keloid treatment. Arch Plast Surg. 2014;41(6):620–9.
5. Wu W-S, Wang F-S, Yang KD, et al. Dexamethasone induction of keloid regression through effective suppression of VEGF expression and keloid fibroblast proliferation. J Invest Dermatol. 2006;126(6):1264–71.
6. Chowdri NA, Masarat M, Mattoo A, et al. Keloids and hypertrophic scars: results with intraoperative and serial postoperative corticosteroid injection therapy. Aust N Z J Surg. 1999;69(9):655–9.
7. Haurani MJ, Foreman K, Yang JJ, et al. 5-Fluorouracil treatment of problematic scars. Plast Reconstr Surg. 2009;123(1):139–48.
8. Jacob SE, Berman B, Nassiri M, et al. Topical application of imiquimod 5 % cream to keloids alters expression genes associated with apoptosis. Br J Dermatol. 2003;149(Suppl 66):62–5.
9. Tyring S. Imiquimod applied topically: a novel immune response modifier. Skin Ther Lett. 2001;6(6):1–4.
10. Naeini FF, Najafian J, Ahmadpour K. Bleomycin tattooing as a promising therapeutic modality in large keloids and hypertrophic scars. Dermatol Surg. 2006;32(8):1023–9.

11. Saray Y, Güleç AT. Treatment of keloids and hypertrophic scars with dermojet injections of bleomycin: a preliminary study. Int J Dermatol. 2005;44(9):777–84.
12. Sawada Y, Sone K. Treatment of scars and keloids with a cream containing silicone oil. Br J Plast Surg. 1990;43(6):683–8.
13. Rusciani L, Rossi G, Bono R. Use of cryotherapy in the treatment of keloids. J Dermatol Surg Oncol. 1993;19(6):529–34.
14. Zouboulis CC, Blume U, Büttner P, et al. Outcomes of cryosurgery in keloids and hypertrophic scars: a prospective consecutive trial of case series. Arch Dermatol. 1993;129(9):1146–51.
15. Layton AM, Yip J, Cunliffe WJ. A comparison of intralesional triamcinolone and cryosurgery in the treatment of acne keloids. Br J Dermatol. 1994;130(4):498–501.
16. Oliaei S, Nelson JS, Fitzpatrick R, et al. Laser treatment of scars. Facial Plast Surg. 2012;28(5):518–24.