Standard guidelines of care: Keloids and hypertrophic scars

Somesh Gupta, V. K. Sharma

ABSTRACT

Keloids and hypertrophic scars (HTS) are the result of overgrowth of fibrous tissue, following healing of a cutaneous injury, and cause morbidity. There are several treatment modalities which are useful for the management of keloids, though no single modality is completely effective. The most commonly used modalities are pressure, silicone gel sheet, intralesional steroids, 5-fluorouracil (5 FU), cryotherapy, surgical excision, and lasers. They may be used either singly or, as is done more commonly, in combinations. Any qualified dermatologist who has attained postgraduate qualification in dermatology can treat keloids and HTS. Some procedures, such as cryosurgery and surgical excision, may require additional training in dermatologic surgery. Most modalities for keloids, including intralesional injections and mechanical therapies such as pressure and silicone gel based products, can be given/ prescribed on OPD basis. Surgical excision requires a minor operation theater with the facility to handle emergencies. It is important to counsel the patient about the nature of the problem. One should realize that keloid will only improve and not disappear completely. Patients should be informed about the high recurrence rates. Different modalities carry risk of adverse effects and complications and the treating physician needs to be aware of these and patients should be informed about them.

Key words: Hypertrophic scars, keloids, steroids, cryosurgery

INTRODUCTION

Keloids and hypertrophic scars (HTS) are the result of an overgrowth of fibrous tissue following healing of a cutaneous injury. Keloids extend beyond the margins of the original wound, do not usually regress spontaneously, and tend to recur after excision, while HTS do not expand beyond the boundaries of the initial injury and may undergo partial spontaneous resolution.

RATIONALE AND SCOPE

No single treatment is uniformly effective in all patients and multiple treatment options may be needed in a patient. These guidelines review current evidence for the efficacy of each treatment modality and provide basic recommendations based on them, so that the physician can choose the treatment modality appropriate for an individual patient while taking efficacy, adverse effects, therapeutic and cosmetic outcome, feasibility, patient’s preference, and cost into consideration.

PHYSICIAN’S QUALIFICATION AND FACILITY

Physicians involved in the management of keloids and HTS should have a postgraduate qualification in dermatology or super-specialization in plastic surgery. The management of keloids and HTS is challenging.
and often requires additional clinical skills such as specialized training in dermatologic surgery. Radiotherapy needs to be delivered by a specialist. Some of the procedures, such as intralesional injections or surface cryosurgery, can be done in the physician’s treatment room. More invasive modalities like surgical excision require more specialized care such as a minor OT with a trained nurse as an assistant. The minor OT should have a tray with emergency medications, oxygen cylinder and intravenous catheter. An anesthetist should be ready on call.

**COUNSELING**

Patients should be informed in detail about the nature and course of the disease, available treatment options suitable to an individual patient, their efficacy and adverse effects, and cost. They should be informed about the possibility of recurrences after treatment. The final decision to undertake treatment should lie with the patients. Informed consent should be obtained in all cases. Pretreatment photography is recommended.

**DIFFERENT MODALITIES AND THEIR CURRENT STATUS IN THE MANAGEMENT OF KELOIDS**

It is important to note that it is difficult to eradicate keloids and most of the modalities are associated with some adverse effects. While these modalities have evidence of variable degree, there are problems in finding and categorizing evidence from the literature, as most studies suffer from subjective evaluation of treatment outcome, limited or no follow-up, and poor study design. Many studies have not differentiated HTS from keloid, which responds more readily to study design. Many studies have not differentiated treatment outcome, limited or no follow-up, and poor as most studies suffer from subjective evaluation of finding and categorizing evidence from the literature, evidence of variable degree, there are problems in

The primary goals while planning a treatment protocol should be a low recurrence rate, significant cosmetic and symptomatic improvement and minimal adverse effects. In the guidelines, we have included treatment modalities with at least two published studies/case series that include one good quality study.

1. **Intralesional corticosteroids:** This is the most frequently used modality, the steroid most commonly used, being depot preparation of triamcinolone acetonide. The concentration of triamcinolone acetonide depends upon the size and site of the lesion and age of the individual. Generally, it is used in a concentration of 10–20 mg/ml, though it can be given at a dose of 40 mg/ml for a tough bulky lesion. It is important to inject the steroid at a correct depth in mid-dermis, otherwise it may lead to irreversible atrophy of the epidermis. Injections are repeated once in 3–4 weeks depending on the bulk of keloid and therapeutic response. The total number of injections depends on the response and possible side effects. Pain during injection is an important limiting factor. Triamcinolone injection alone is effective in reducing the volume of lesions in a majority of patients (LEVEL A).[1] Ardehali et al.[2] reported that mean scar volume reduced from 0.73 ± 0.701 ml at baseline to 0.14 ± 0.302 ml after monthly intralesional injections of triamcinolone acetate (LEVEL A). Combination 5-fluorouracil (5-FU)/triamcinolone seems to be superior to intralesional steroid therapy alone in the treatment of keloids (92% average reduction in lesion size with combination compared with 73% with steroid alone).[3] Postoperative intralesional triamcinolone after surgical excision seems to prevent recurrence (LEVEL B). With these evidences available, intralesional steroids should be considered as the first line treatment for keloids and hypertrophic scars.[4]

**REFERENCES**


2. **5-Fluorouracil (5-FU) intralesional injections:** This treatment is increasingly becoming popular. 5-FU alone is effective in the treatment of keloids
In summary, intralesional injection of 5-FU is considered as a safe and effective treatment, when used either alone or in combination with intralesional injection of corticosteroids and surgical excision.

REFERENCES

3. Bleomycin: Intralesional injection of Bleomycin appears to be an effective therapy in the treatment of keloids, with almost three-fourth of the patients showing good to excellent results (LEVEL B). It is administered either by intralesional injections or by multiple punctures using 22-G needle.[1-4] The reported adverse events include hyperpigmentation in a small proportion of patients (LEVEL B).[5] However, it is more expensive as compared to steroids and 5-FU and this may be a limiting factor.

REFERENCES

4. Interferon α-2b: Intralesional injection of combination of interferon α-2b with triamcinolone has been reported to be superior to triamcinolone alone in reducing the depth and volume of keloids (LEVEL C).[1] However, contradictory results have also been reported.[2] Current evidence is therefore not unequivocal to recommend the routine use of interferon α-2b. It may be used in selected cases, particularly when the more established intralesional injection modalities described above have failed.

REFERENCES

5. Verapamil: Experimentally, it has been shown to stimulate the synthesis of procollagenase, thus increasing collagenase activity, thereby leading to a reduction in fibrous tissue production. However, there has been limited clinical data showing its efficacy in keloids (LEVEL C). Thus, more studies are needed before it is recommended as a routine treatment for keloids.[1-2]

REFERENCES
2. Xu SJ, Teng JY, Xie J, Shen MQ, Chen DM. Comparison of the

6. **Imiquimod**: Imiquimod 5% cream is a novel immune modulator with localized therapeutic effects at the drug application site, capable of enhancing local production of immune-stimulating cytokines such as interferons, tumor necrosis factor, and interleukins. In a few studies,[1-3] imiquimod cream has been used in conjunction with surgical excision, with an objective of preventing recurrence after surgical excision. However, the antifibrotic effect seems to be short-lived and lesions recur after discontinuation of keloids. There are conflicting data about its efficacy. The evidence is thus not adequate to establish the efficacy and the role of imiquimod in the prevention of recurrence of keloids after surgical excision (LEVEL B).[1-3]

**REFERENCES**


7. **Pressure therapy**: Though it is a popular treatment modality for keloids and HTS, there is no proven mechanism of its action in keloid treatment. The expert recommendation is to apply 20–40 mm Hg pressure for 24 hours a day. While several studies have documented its efficacy, other studies reported no difference in the results after pressure therapy. Pressure therapy alone is considered effective for prevention of hypertrophic burn scars (LEVEL C). Pressure may alleviate itching and pain and may cause early scar maturation (LEVEL C).[1,2]

Pressure loss, discomfort from heat and sweating, swelling of limbs, rashes, eczema, friction, and poor compliance are the problems associated with pressure therapy (LEVEL B).[3]

**REFERENCES**

1. Leung P, Ng M. Pressure treatment for hypertrophic scars resulting from burns. Burns 1980;6:244 (LEVEL C).

8. **Silicone products**: Silicone is available as cream, gel sheet, silastic sheet, and orthosis garment. The mechanism of action of silicone therapy has not been completely determined, but is likely to involve occlusion and hydration of the stratum corneum with subsequent cytokine-mediated signaling from keratinocytes to dermal fibroblasts (LEVEL C).[1] The sheet may result in flattening of lesion, increased malleability and softening of the scar, though one study showed that there was no difference in the results with silicone and non-silicone gel sheet dressing (LEVEL C).[2] Vitamin E added to silicone gel has been reported to be beneficial in one study, though not enough evidence is available for its efficacy (LEVEL C).[3] Silicone products have the advantages of ease of administration and being noninvasive, without side effects. Further, their use is supported by some published studies.[4] However, the data available are of poor quality and additional controlled clinical trials with large patient populations are needed to generate further evidence for the efficacy of silicone based products in the treatment and prevention of hypertrophic and keloid scars (LEVEL B).[5,6]

**REFERENCES**


9. **Onion extract**: The topical preparation containing onion extract and allantoin is being marketed and frequently used for keloids and HTS. However,
there is only limited evidence of its efficacy (LEVEL C).\textsuperscript{[1]} In a study by Hosnuter et al., it was found to be ineffective in improving scar height and itching\textsuperscript{[2]} (LEVEL C).

\textbf{REFERENCES}


10. Radiotherapy: Radiotherapy has been used as a monotherapy or as an adjuvant to surgical excision. A combination of surgery followed 24 hours later by radiotherapy is thought to be the most effective approach for the management of extensive HTS and keloids which causes significant morbidity/limitation of movement/contracture, with a recurrence rate varying from 9 to 72\% (LEVEL B), which generally depends on the total dose of radiation and duration of follow-up.\textsuperscript{[1-4]} A relatively high dose must be applied in a short overall treatment time\textsuperscript{[5]} (LEVEL B). A scheme with a Biologically Effective Dose of 30–40 Gy seems to be sufficient to prevent recurrences of keloid after surgical excision (LEVEL B).\textsuperscript{[6]} Electron beam irradiation is considered the most effective; however, strontium 90 brachytherapy has also shown low recurrence rate (LEVEL C).\textsuperscript{[7]} Recently, 32p-patch contact brachytherapy has been introduced for keloids and found to be effective (LEVEL C).\textsuperscript{[8]} Radiation is associated with the risk of carcinogenesis, and there is hesitation and apprehension about its use for a benign condition such as keloids. However, there are only few reports in the literature of malignancies arising from the treatment of keloid scars with radiotherapy.\textsuperscript{[9-12]} Other adverse reactions include skin redness, skin peeling, telangiectasia and permanent skin color changes, generally hypopigmentation (LEVEL B).\textsuperscript{[11]}

In summary, while there are a large number of studies available in recent literature on the use of radiation therapy in keloids, its current use in routine practice is limited both because of the nonavailability of the modality in most centers and also a general apprehension about its use. However, it may be an effective option for recalcitrant and large keloids not responding to other treatments in centers where facilities are available, particularly, in combination with surgical excision.

\textbf{REFERENCES}


11. Lasers: Carbon dioxide laser monotherapy has a recurrence rate as high as 90\% and is therefore not recommended (LEVEL B).\textsuperscript{[1,2]} Pulsed Dye Laser (PDL) has been reported to decrease transforming growth factor-beta1 (TGF-beta1) induction and up-regulation of matrix metalloproteinase (MMP) expression in keloid tissue (LEVEL C).\textsuperscript{[3,4]} This may be responsible for the keloid regression with PDL treatment. PDL seems to regress majority of keloids (LEVEL C); however, a case of rapid recurrence has also been reported (LEVEL C).\textsuperscript{[5,6]}
REFERENCES


12. Surgical excision: Surgical excision alone is associated with recurrence in 50–100% of patients; however, an exception is earlobe keloid which recurs much less frequently (LEVEL B).[1] Thus, after excision of keloid, an adjuvant should always be used (LEVEL A). Radiation, intralesional steroid and 5-FU prevent recurrence more efficiently than topical imiquimod and interferons (LEVEL B). Topical mitomycin, an antimetabolite, made no difference in the prevention of keloid recurrence after excision when topically applied (LEVEL C).[2] The keloid core extirpation and subtotal keloid excision may be helpful in preventing keloid recurrence; however, the evidence is limited (LEVEL C).[3] Postoperative pressure therapy designed to suit the individual patient needs is important to prevent the recurrences.

REFERENCES


13. Cryosurgery: Cryosurgery with liquid nitrogen leads to total or partial success in almost two-third to three-fourth of keloids after at least three sessions (LEVEL B).[4-8] Hypopigmentation, blistering, delayed healing and infection are the major side effects (LEVEL A).[4] A combination of liquid nitrogen cryosurgery and intralesional steroids seems to have a synergistic effect over liquid nitrogen cryosurgery alone (LEVEL B).[5] Liquid nitrogen cryotherapy done prior to the intralesional injection softens the keloid and makes the injection more easier and leads to uniform dispersal of the drug into pathological tissue. Cryotherapy induces edema and cellular breakdown, causing a decrease in the density of fibrous tissue so that the injection can be given easily. Intralesional cryosurgery seems to provide better esthetic results and cause less hypopigmentation in comparison to surface cryosurgery; however, no comparative studies are available, only case series are available (LEVEL C).[6-9]

REFERENCES


14. Other therapies: Various growth factors and cytokines, such as basic fibroblast growth factor, transforming growth factor-β, and interleukin-10, extracellular matrix modulators such as prolyl 4-hydroxylase inhibitors and tissue transglutaminase inhibitors, and intralesional injection of botulinum toxin, collagenase,
hyaluronic acid, have been suggested as potential therapeutic options; however, enough evidence is not available for the taskforce to recommend their use in the treatment of keloids.

**CONCLUSIONS**

The evidence available for many therapeutic modalities for keloids is poor and high quality randomized studies are not available. This may be due to difficulty in blinding, lack of interest of funding agencies and pharmaceutical industry in supporting research on keloids.

Good evidence of efficacy in keloids is available for intralesional steroids, 5-FU, bleomycin, cryosurgery, and surgical excision combined with radiotherapy. The evidence for efficacy of onion extract, imiquimod, interferons, pressure therapy, and silicone products is weak. Surgical excision and carbon dioxide laser should never be used alone in the management of keloids. Overall, there is enough evidence that several therapies have a synergistic effect when used together. In spite of several limitations, significant improvement is achievable with the available treatments.

The final decision to choose a particular therapy depends on the size and site of lesion, age of the patient, reported recurrence rate, esthetic outcome, treating physician’s experience with a particular treatment modality, availability, and above all, an informed patient’s preference. All the available therapeutic options should be discussed with the patient and they should be allowed to take a decision.

In spite of the availability of a large number of treatment modalities, keloid remains a difficult condition to treat. High recurrence rates, painful treatments, cosmetically unacceptable adverse effects remain a problem in the management of keloids.