Keloidoscope: in search for the ideal treatment of keloids

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Abstract Although keloids were recognised in the Smith Papyrus of ancient times, the precise definition, cause and management have remained elusive. Several forms of treatment have been used with varying success.

Objectives This study assesses and compares the value of intralesional steroid (Triamcinolone acetonide 40mg/ml), cryotherapy and cryotherapy with intralesional steroid in the treatment of keloids.

Methodology 33 patients were studied, 11 each in the three arms and the volume of the keloids was recorded using wax patterns of alginate impressions of the keloids to note the change in size postoperatively.

Results The best average percentage response was observed in patients who received both Cryotherapy (CRY) and Intralesional Steroid (ILS) (69.02%) followed by patients who received only intralesional steroid (43.98%). Among the patients who received only cryotherapy, the average percentage response was only 39.24%. 72.73% patients who received intralesional steroid with cryotherapy showed more than 50% improvement (good response) while only 9.09% patients who received intralesional steroid alone and cryotherapy alone showed similar improvement.

Conclusion In patients with keloids good response can be obtained with CRY with ILS as compared to ILS alone and CRY alone.

Keywords Keloids · Intralesional steroids · Cryotherapy

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Introduction

The first recognised description of keloids was in the Smith Papyrus around 1700 BC [1]. A keloid is a unique dermal fibroproliferative disorder that occurs after trauma, inflammation, burns, surgery and possibly spontaneously. It extends beyond the confines of the original wound and tends to recur after excision. Although it is not fatal, it is a major cosmetic problem and symptoms like pain and itching can significantly disturb the patient's quality of life.

Despite an increased understanding in the molecular and biochemical mechanisms of keloid formation in recent years, keloids remain difficult to manage. Multiplicity of methods of treatment is an indicator that none of them is entirely satisfactory.

This study assesses and compares the value of Intralesional Steroid (ILS)

(Triamcinolone acetonide 40mg/ml), Cryotherapy (CRY) and cryotherapy with intralesional steroid in the treatment of keloids.

Keloids affect only Homo Sapiens [1]. The incidence of keloid formation is higher in individuals with darker pigmentation [2]. Patients with the highest incidence of keloid development are between the ages of 10 and 30 years. The male to female ratio is approximately 1:1.

A predisposition to keloid formation has been noted in individuals with blood group A [1]. Both constitutional and local factors influence the liability of any scar to keloid change [3]. Constitutional factors include skin colour, race, endocrine activity and heredity. Local factors include the region affected, the orientation of the scar and the nature of the injury.

Areas of highest tension such as pre-sternal area, upper back, shoulders, anterior chest, upper arms and posterior neck are

sites of frequent keloid formation. In contrast, the central third of the face is rarely a site for keloids.

Associated pruritus, dysesthesia or pain as well as restricted range of motion are frequently noted with keloids [1]. Malignant transformation of keloids is rare [4].

A keloid is characterized histologically by the haphazard deposition of collagen fibres within the dermis, with an abnormal type I:III collagen ratio [5] surrounded by a mucinous extracellular matrix with few macrophages and an abundance of eosinophils, mast cells, plasma cells and lymphocytes [1]. Keloids demonstrate a unique pericapillary cell called the myofibroblast. This cell has characteristics of both fibroblasts and smooth muscle cells.

Multiple recommended treatment modalities speak well to the fact that none are ideal:

Surgical therapy

Surgery for the treatment of keloids has been relegated mainly to a second line therapy for lesions unresponsive to steroids or pressure or other topical therapy [6]. The recurrence rates for simple surgical excision of keloids alone vary from 50% to 80%.

Surgical excision with a full thickness graft may provide sufficient microvasculature to allow for anastomosis with the host microvasculature, thus resulting in decreased angiogenesis and fibroblast proliferation.

Radiation therapy

Radiation alone without excision is poorly effective with a recurrence rate between 50% to 100%. Typically, treatment is initiated immediately after surgery, with total doses ranging between 1500 and 2000 rads. Hyperpigmentation is the most common residual effect of radiation and it is also known to be carcinogenic [1].

Radiation therapy is generally reserved for adult patients who have significant symptoms or disability from their keloids.

Pressure therapy

Materials used include silicon gel in the form of compression wraps, tubular support bandages, presized garments, adhesive plasters, pressure earrings, molded splints and self adhering polyurethane sponges.

Lasers

Abergel et al. [7] demonstrated a photobiological effect of laser light on collagen metabolism using Neodymium: Yttrium-Aluminium-Garnate (Nd:YAG) 1064nm continuous wave laser.

Astler and Williams showed improvement of keloid scars after 585 nm pulsed dye laser treatments [8]. There is evidence of more rapid improvement of keloids using combination laser treatment with the simultaneous use of intralesional corticosteroid injections and 585 nm pulsed dye laser irradiation [9].

Corticosteroids

Intralesional corticosteroid injections may be used alone or in combination with other

Graph 1 Percentage improvement 1st month post treatment

Graph 2 Average percentage response to therapy

modalities such as cryotherapy and surgery. Immediately following excision, the wound edges may be injected with triamcinolone acetonide and sutures may be left in place for an extra week to minimize the potential of wound dehiscence. Corticosteroid injection is then repeated every 3 to 4 weeks postoperatively.

Cryotherapy

Liquid nitrogen at a temperature of -196°C was introduced as the cryogen of choice in the late 1950s and mid 1960s. Vesiculobullous reactions can occur

following cryosurgery. Pigmentary changes are usually transitory.

Intralesional corticosteroid injections are often combined with cryotherapy.

Material and method

A total number of 33 patients presenting with keloids were included in the study, in whom the lesions:

- were present for 2 years or more.
- did not show symptoms and signs of regression.
- extended into the surrounding normal skin.

- were not given intralesional steroid (ILS) or Cryotherapy (CRY) during the past three months.

Patients with a known history of tuberculosis and diabetes mellitus were not given intralesional steroid.

The materials required were alginate dental impression material, modeling wax, skin marking pencil and measuring cylinder. The keloid was first delineated using skin marking pencil and then an impression of the keloid was obtained using alginate dental impression material. Wax pattern of the keloid was then obtained by pouring molten modeling wax into the impression obtained. Measurement of the volume was then carried out by measuring the displacement of the water when the wax pattern was dipped into the measuring cylinder and the percentage improvement was recorded. The volume was recorded before treatment and then at the first month, second month and third month post treatment.

Patients were randomly selected for ILS (Triamcinolone acetonide 40mg/ml), CRY and CRY+ILS. Only one treatment sitting was given.

ILS (Triamcinolone acetonide 40mg/ml) was given directly into the keloid, delivering 0.1ml to 1 sq.cm upto a maximum of 10 sq.cm using insulin syringe.

CRY was given with liquid nitrogen using a Cryogun. The spray was done in a paint brush fashion with a freeze time of 10 seconds for 1 sq.cm upto a maximum of 10 sq.cm. It was allowed to thaw for one minute. Two such freeze thaw cycles were given.

In CRY+ILS, cryotherapy was given first followed after five minutes by intralesional steroid.

Result and observation

In our study of 33 patients, there were 26 male (78.79%) and 7 female patients (21.21%). The sex ratio was 3.71:1, indicating male predominance. The commonest age group affected was between 21–30 years (54.54%).

A positive family history of keloid was present in 5 patients (15.15%). 18/33 patients (54.54%) had blood group A followed by blood group B noticed in 8 patients (24.24%).

Spontaneous onset was recorded in 23 patients (69.7%). Acne vulgaris was the most common predisposing factor present in 8/10 patients (80%) followed by trauma in 2/10 patients (20%).

Graph 3 Overall response to therapy

Itching was the most common associated feature present in all the 33 patients (100%) followed by burning sensation in 11 patients (33.33%). Hyperaesthesia was present in 9 patients (27.27%) and pain in 8 patients (34.24%).

In the present study, 11 patients were administered intralesional steroid (ILS) alone, 11 cryotherapy (CRY) alone and 11 CRY with ILS.

In the patients who received only intralesional steroid, the maximum response observed was 100% (objective flattening) and the minimum improvement noticed was 20%. Among the patients who received only cryotherapy, the maximum response observed was 60% and the minimum was 20%. Among the patients who received cryotherapy with intralesional steroid, the maximum response observed was 100% (objective flattening) and the minimum response noticed was 40% (Graph 1).

This response to therapy is one month post treatment was maintained in the 2nd and 3rd month in all the three groups.

The best average percentage response was observed in patients who received both cryotherapy and intralesional steroid (69.02%) followed by patients who received only intralesional steroid (43.98%). Among the patients who received only cryotherapy, the average percentage response was only 39.24% (Graph 2).

A comparison between the three therapy groups was made and according to Kruskal-Wallis H analysis (equivalent to Chi square), there was a significant difference in response to therapy, between

these groups as the p value was less than 0.01. Cryotherapy with intralesional steroid was better than intralesional steroid or cryotherapy alone.

When the response to cryotherapy was compared with that of intralesional steroid by Student's t-test, the response was not found to be significant (p - more than 0.05).

4 out of 33 patients (12.12%) achieved objective flattening. 72.73% patients who received intralesional steroid with cryotherapy showed more than 50% improvement (good response) while only 9.09% patients who received intralesional steroid alone and cryotherapy alone showed similar improvement. Among the patients who received intralesional steroid with cryotherapy 11 out of 11 patients (100%) showed more than 25% improvement. But, patients who received intralesional steroid or cryotherapy alone, 3 out of 11 (27.27%) had improvement equal to or less than 25% (Graph 3).

Hypopigmentation/depigmentation was noticed in all patients (100%) who received cryotherapy alone and cryotherapy with intralesional steroid. This was not observed in patients who received intralesional steroid alone.

Blistering was noticed in 6/11 patients (54.54%) who received cryotherapy alone and in 7/11 patients (63.64%) who were given cryotherapy with intralesional steroid.

Discussion

Keloids treated with triamcinolone have decreased levels of the proteinase inhibitors

Fig. 1 Keloid treated with intralesional steroid. a) Pre-treatment b) Post-treatment c) Wax patterns pre-treatment, 1 month, 2 months and 3 months post-treatment

Fig. 2 Keloid treated with cryotherapy. a) Pre-treatment b) Post-treatment c) Wax patterns pre-treatment, 1 month, 2 months and 3 months post-treatment

Fig. 3 Keloid treated with combination of intralesional steroid and cryotherapy a) Pre-treatment b) Post-treatment c) Wax patterns pre-treatment, 1 month, 2 months and 3 months post-treatment

alpha₂-macroglobulin and alpha₁-antitrypsin, suggesting that these collagenase inhibitors are removed by corticosteroids [7]. Other mechanisms such as decreased glucose-6-phosphate dehydrogenase activity, increased alanine transferase activity and decreased DNA content in keloid nodules have also been reported [10].

Cryosurgery employs the use of refrigerants to effect cell damage and microcirculatory disturbances leading to stasis, thrombosis, transudation of fluid through damaged microvasculature and cellular anoxia with subsequent tissue necrosis and sloughing followed by tissue flattening [11].

In literature, cryotherapy alone has resulted in complete keloid flattening in 51% to 74% of patients treated [2]. When used in combination with intralesional steroids, an 84% response rate has been traditionally seen, a greater response than

with cryotherapy or intralesional steroid alone [12].

In this study, it was observed that the average percentage response for the patients who received CRY with ILS was 69.02%. For the patients who received ILS alone, it was 43.98% and for those who received CRY alone it was 39.24%. 72.73% of patients who received the combined modality of treatment showed more than 50% improvement. Also, the average percentage response to CRY with ILS was approximately 1.5 times that of ILS alone and CRY alone.

Cryotherapy used alone has variable responses and experimentally, collagen is particularly resistant to cryosurgical damage [11] and it seems likely that this is the explanation for the poor response observed in the cryotherapy group.

Patients tolerated intralesional steroid better after cryotherapy. In addition to facilitating injection, cryotherapy may

provide some degree of anaesthesia before infiltration [2]. The combination of cryotherapy with intralesional steroid may be synergistic and this may be the reason for good response observed in CRY with ILS group.

Conclusion

In patients with keloids, a better response can be obtained with treatment with a combination of CRY and ILS as compared to ILS or CRY alone, although hypopigmentation / depigmentation produced by cryotherapy is less desirable in dark skinned individuals.

Recent years have seen an increased understanding in the molecular and biological mechanisms of keloid formation, allowing for the development of more specific therapeutic options for these lesions but, because many treatments are anecdotal, a consistently effective plan of therapy for keloids remain elusive. Consequently, the treatment of keloids has remained empirical.

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