Keloids: Current Therapies in Barbados
OJ Nelson1, J Ward2, AL Forde3, N Ojeh1

ABSTRACT
Keloids are characterized by scar tissue overgrowth on the skin beyond the borders of the original wound following an abnormal wound healing process and tend not to regress. These disfiguring scars can cause pain, itching and inflammation in the patient leading to an emotional and psychological impact and a sub-standard quality of life. A variety of treatments, using surgical and non-surgical approaches, exists that have been reported to be beneficial. However, no one treatment currently stands out as the most optimal due to a number of factors including different keloid subtypes. Often, a combinational approach to its treatment generates the best results. The incidence of keloid and hypertrophic scarring is very high in African, Hispanic and Asian populations and as yet, the multifactorial aetiology of this disorder is still not clear. Very few published studies on keloid scarring among the Caribbean population and, in particular, the Barbadian population has been reported to-date. The aim of this review is to explore and discuss the current literature of the various keloid treatment modalities typically used in Barbados along with keloid management. These treatments include: the intralesional corticosteroid injection and the triamcinolone acetonide, imiquimod, excision, pressure dressing, cryotherapy, silicone gel sheeting and radiation. Regarding keloid management, a well-planned treatment strategy tailored to suit the individual patient’s needs by an experienced healthcare physician is key in achieving the best outcome with improved cosmesis. The management of the patients’ symptoms as well as patients’ compliance with post-treatment care, is also an important factor to consider.

Keywords: Keloids, recurrence review, treatment, wound healing

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RESUMEN
Los queloides se caracterizan por un crecimiento excesivo del tejido de la cicatriz en la piel más allá de los bordes de la herida original, tras un proceso anormal de cicatrización de la herida, sin tendencia a la reversión. Estas cicatrices desfigurantes pueden causar dolor, pica-zón e inflamación en el paciente, que producen un impacto emocional y psicológico y conducen a una calidad de vida subestándar. Existe una variedad de tratamientos, basados en métodos quirúrgicos y no-quirúrgicos, reportados como beneficiosos. Sin embargo, ningún tratamiento sobresale actualmente como el más óptimo, debido a un número de factores, incluyendo...
diferentes subtipos de queloides. A menudo, un enfoque combinado de su tratamiento genera los mejores resultados. La incidencia de cicatrices queloides e hipertróficas es muy alta en las poblaciones africanas, hispanas y asiáticas, y hasta el momento, la etiología multifactorial de este trastorno aún no está clara. Hasta la fecha, se han reportado muy pocas publicaciones de estudios sobre la cicatrización de queloides entre la población caribeña, y en particular, la población de Barbados. El objetivo de este estudio es explorar y discutir la literatura actual de las varias modalidades de tratamiento del queloide usadas típicamente en Barbados junto con el manejo del queloide. Estos tratamientos incluyen: acetónido de triamcinolona, inyección de corticoesteroide intralesional, imiquimod, escisión, apósito de presión, crioterapia, recubrimiento con gel de silicona, y radiación. En cuanto al manejo de los queloides, una estrategia de tratamiento bien planificada adaptada a las necesidades de cada paciente por un médico experimentado es clave para lograr el mejor resultado con cosmesis óptima. El manejo de los síntomas de los pacientes, así como la conformidad de los pacientes con la atención del post-tratamiento, es también un factor importante a considerar.

Palabras clave: Queloides, revisión de la recurrencia, tratamiento, cicatrización de la herida

INTRODUCTION

Wound healing is an organized and complex series of processes, which results in the restoration of tissue structure integrity and functions of the damaged tissue. It is temporally categorized into three overlapping phases namely, inflammation, granulation tissue formation and tissue remodelling (1). Any defects that occur during any of the wound healing phases can give rise to the development of keloids.

Keloid scars are proliferative and largely disfiguring scars that result owing to events such as a cutaneous injury, inflammation, surgery, elective cosmesis, burns, foreign body reactions, or occur spontaneously. They are characterized by their shiny, hard, smooth, often dome-shaped appearances that may develop years after the initial insult and rarely regress. These benign fibrous growths are characterized by scar tissue overgrowth beyond the borders of the original wound and tend to recur after excision (Fig. 1).

The over-proliferation of the dermal fibroblasts, the over-production of collagen fibres and other extracellular matrix or decreased degradation of collagen can lead to keloid or hypertrophic scar formation (2).

Keloid pathophysiology

The aetiology of keloids is poorly understood. However, the cell and molecular events implicated in keloid pathology are now being elucidated. Fibroblast-specific growth factors such as transforming growth factor-beta (TGF-β), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), connective tissue growth factor (CTGF) and platelet-derived growth factor (PDGF) (3, 4) are among some of the factors that have been implicated in the development of keloids. Studies have also shown that nutrition may be a contributing factor in keloid formation (5).

Genetics and incidence of keloids

A number of chromosomal loci have been identified that are linked with the risk of developing keloids (6). Moreover, familial aggregation and twin studies have reported various modes of inheritance (7) suggesting a genetic component and predisposition to keloid development. The role of human leukocyte antigen (HLA) subtypes has also been implicated (8). In keeping with
the proposed genetic model of the disease, keloids occur most frequently in persons of 10‒30 years of age. There is also an equal risk in both males and females, with females showing a slightly higher incidence. This is likely due to the higher levels of cosmetic procedures undertaken by females, such as ear piercing. They are predominantly reported in persons of darker skin, with studies demonstrating a 15 times higher-risk in this population (9). The incidence of keloid and hypertrophic scarring is high in African, Hispanic and Asian populations and estimated to be 4.5%‒16% (10) although, it may occur in any ethnic group particularly after surgery or trauma to the chest or shoulder region.

**Anatomical location and histopathology of keloids**

The most common anatomical sites for keloids include: the chest, shoulders, upper arms, cheeks, skin overlying joints, with earlobes being reported with the highest frequency. Of note, the anatomical site of a keloid appears to affect its morphological characteristics. The major source of histopathology in keloids is found in the reticular layer of the dermis. It is composed of dense connective tissue including collagen and fibroblasts. The damage to this layer leads to the deposition of thick hyalinised collagen. Furthermore, recent research has provided three distinct findings only present in keloid specimens namely: (a) the presence of a tongue-like advancing edge underneath normal-appearing epidermis and papillary dermis, (b) horizontal cellular fibrous band in the upper reticular dermis and (c) prominent fascia-like band (11).

**Studies on keloids in the Caribbean**

To-date, there are very few published studies on keloid and hypertrophic scarring among the Caribbean population and, in particular, the Barbadian population. Bayat and co-workers (12) examined the site-specific morphology of keloid scars in Afro-Caribbean people in Jamaica (12). Bayat et al (13) studied the clinical characteristics of 211 cases of keloid scarring in Afro-Caribbeans in Jamaica (13). Another study investigated the genetic predisposition to keloid formation in the Jamaican population (14). More recently, a study investigated the association of HLA-DRB1* and keloid disease in an Afro-Caribbean population (15). Ashcroft and co-workers (16) assessed the influence of HLA class I and class II loci on the prevalence of keloid disease in Jamaican Afro-Caribbeans (16). In Barbados, Smith and McGrouther (17) carried out a study on a total of 126 keloids from patients in Barbados and Manchester to evaluate the natural history and spontaneous resolution of keloid scars to develop prognostic information for the patients and to provide the baseline for future treatment trials (17). Narakula and Shenoy [2008] (18) conducted a prospective clinical study of 46 ear keloids in 31 patients in Barbados using three protocols for keloid treatment including keloid excision and postoperative intralesional triamcinolone injection, keloid excision followed by postoperative superficial X-ray, and keloid excision and a combination of superficial X-ray therapy and intralesional triamcinolone.

**The Treatment of keloids in Barbados**

Various forms of treatment exist for keloids including intralesional steroids, topical corticosteroids, silicone gel sheeting, pressure therapy, surgical excision, cryotherapy, laser therapy, radiation, photodynamic therapy, calcineurin inhibitors, immune response modulators, chemotherapy agents: interferon, 5-fluorouracil, mitomycin C and bleomycin. However, no current single treatment has been shown to completely eradicate keloid scars effectively due to the various factors such as age, ethnicity, gender and anatomical location of the keloid (19). Almost all of the available therapies have significant adverse effects and/or are painful. Therefore, patients often have to live with their symptoms which include pain and pruritus as well as the emotional and psychological impact of these disfiguring scars. Currently, there are a number of treatment options available for keloids in Barbados. This review will explore and discuss the current literature of these treatment modalities along with keloid management.

**Intralesional steroids**

Corticosteroids, and in particular intralesional corticosteroid injections, are considered the first-line of approach for the treatment of keloids. There are a number of mechanisms that are thought to be responsible for reducing scar formation, the central one being the suppressive effect on the inflammatory process (20). Others include: the inhibition of collagen synthesis and fibroblast growth, enhancing collagen degradation, reducing TGF-β1 and inducing vasoconstriction causing tissue hypoxia (20).

For the treatment of keloids, several corticosteroids can be used including: hydrocortisone acetate, methyl prednisolone and dexamethasone. However, the most commonly used intralesional corticosteroid is triamcinolone acetonide [10‒40 mg/mL] (Fig. 2).
Three injections are given every three to four weeks for up to six months or more (21). Intralesional corticosteroid therapy has had some success in studies with response rates varying from 50 to 100%, with reported recurrence rates varying from nine to 50% (22, 23). This form of treatment has been reported to be used alone or as part of a combinational therapy with 5-fluorouracil, surgery, pulsed-dye laser, radiation therapy and cryotherapy (24, 25).

A number of issues have arisen concerning the use of intralesional corticosteroids. Pain resulting from injection is common and may be managed by the administration of intralesional lidocaine (26). Others reported are atrophy, telangiectases, ulcerations, and hypopigmentation (27). Darker-skinned patients present with higher occurrence of hypopigmentation and should be advised accordingly. In Barbados, depending on a number of keloid parameters, triamcinolone acetonide injection at a concentration of 40 mg/mL is the preferred treatment method and is generally used as a monotherapy. However, in the cases of bulbous keloids with significant cosmetic deformity, using a combined approach of surgical excision and triamcinolone acetonide is more efficacious. Close monitoring of the scar site is essential to avoid a recurrence (personal observations). Indeed, the use of triamcinolone acetonide as an adjunct therapy to both surgical excision and combined surgical excision and radiotherapy has been published with positive treatment outcomes in Barbados (18).

**Surgical excision**

The surgical excision of keloids is amongst the most practical methods of keloid removal. However, excision results in a new wound where aggressive collagen synthesis can lead to a similar or even larger keloid. It has been found that the likelihood of recurrence is between 50 and 100% (28); hence, surgical excision is not recommended as a monotherapy. Instead, it should be combined with other treatment modalities such as corticosteroid injection, radiotherapy, interferon injection and pressure therapy. Silicone gel has also been used in conjunction with keloid excision with varying degrees of success (29). Different methods exist for the surgical removal of keloids as well as flattening and reducing keloid scars and the method employed depends on many factors including: keloid size, location, patient’s age and skin type. Some of the surgical methods include: W-plasty, Z-plasty, excision with grafting, linear closure and flap coverage (30). The experience of the operating surgeon and technique used are often directly correlated with the final scar cosmesis (31). In Barbados, the surgical excision of pinna keloids tends to be used as an effective monotherapy without keloid recurrence provided that all the keloid tissues is removed (Fig. 3).
However, close monitoring of the scar site by both the patient and the doctor is important to prevent a recurrence. For all other keloids, surgical excision is often combined with corticosteroid injection, radiotherapy (18), silicone gel / liquid or imiquimod cream (personal observations).

Silicone based products
Silicone gel sheeting has been employed since the 1980s in the treatment of keloids and hypertrophic scars; it is now considered the first-line of treatment for small keloids and hypertrophic scars (32). The underlying mechanism of this therapy is not entirely understood although a few hypotheses have been proposed. The dominant opinion states that silicone-based products enhance the hydration of the corneum stratum, reduce collagen synthesis and increasing fibroblast regulation (33). It is also thought that silicone-based products increase the temperature and oxygen tension (34). A study reported that 60% of the patients receiving the treatment experienced the flattening of the keloid. In addition, other beneficial effects such as reduced pain, tenderness and pruritus left 90% of the patients satisfied with the outcomes of the treatment (35). Studies have shown that best results are attained if the silicone sheeting is worn for 12 to 24 hours a day for two to three months (36). Despite the recorded response rates, there has been some controversy regarding silicone-based products. Recently, a Cochrane review concluded that the studies provided weak evidence in the treatment and prevention of keloid scarring using silicone gel sheeting and that the studies investigating this therapy were of poor quality (29). Of note, although this leaves a question as to the efficacy of silicone-based products, studies are continuing to produce convincing support in favour of their applications (37, 38). Various forms of topical silicone exists other than silicone sheeting such as creams, spray, gel cushion and liquid. The forms of the topical silicone used in Barbados are silicone gel sheeting and silicone liquid (personal observations).

Pressure therapy
Pressure therapy has been used as a means of treating and managing keloids and hypertrophic scars for decades. Compression techniques are widely used in the treatment of burn and hypertrophic scarring. This is also the case in Barbados (personal observations). It is hypothesized that increased pressure to the scar surface limits perfusion, and reduced oxygen to the site of injury results in decreased collagen synthesis (39). It is also thought that pressure reduces scar hydration stabilizing mast cells and reducing angiogenesis (40). There is, however, still much uncertainty regarding the underlying mechanism. The application of pressure can be achieved via a number of methods ranging from bandages to buttons. The recent developments in magnet-applied pressure therapy have proven successful, with the overall recurrence-free rates of 89.4% (41). A continuous pressure of 20–25 mmHg for 12–23 hours per day for more than six months is recommended (42). One central constraint of this treatment pertains to the scars anatomical location. Not every scar may present in an appropriate site, either due to psychological distress or difficulties associated with attaching a pressure garment. Due to the latter issue, the pressure garment is predominantly used for auricular keloids (43, 44). A significant beneficial outcome of pressure therapy is that it bypasses the issue of pain that tends to accompany intraleisional therapies.

Radiation therapy
The use of radiation therapy for the treatment of keloids was first introduced in the early 1900’s. Since then, it has been used as a monotherapy to a lesser extent (22) and more commonly, as an effective adjunct therapy following surgical excision (45) with success rates of 67% to 98% (46). When used as a combined therapy with surgery, the recurrence rates of keloids have been shown to decrease (45, 47). Radiation therapy has been shown to effectively reduce pain, pruritus and tenderness that are often associated with keloids (48). Different types of radiation have been used as adjunct therapy postsurgical excision and include: superficial X-rays, brachytherapy and electron beam with varying degrees of success (45). Radiation has been shown to work by reducing fibroblast proliferation by inducing apoptosis and restoring the balance between the production and degradation of scar collagen (49, 50). The recommended dose for radiation for the treatment of keloids varies from three to 40 Gy (46) depending on the anatomical site (28). Some of the side-effects of radiation include: hyperpigmentation, scarring radiation dermatitis, atrophy and the increased risk of cancer. Due to the latter, the use of radiation therapy has been restricted to adults only as well as the low carcinogenic areas that do not include the thyroid and breast.

In Barbados, the use of radiotherapy as an adjunct therapy following surgical excision is commonly used as second line therapy approach. Typically, superficial X-ray of 12 Gy in three fractions on three consecutive days, ideally starting from the first operative day,
A prospective clinical study of 46 ear keloids in 31 patients was conducted in 2006 at the Queen Elizabeth hospital, Barbados, using three protocols for keloid treatment. Following keloid excision, a postoperative intralesional triamcinolone injection at monthly intervals was given, a postoperative superficial X-ray of 12 Gy in three fractions on three consecutive days, was performed or a combination of superficial X-ray therapy and intralesional triamcinolone were given. The results obtained from the study demonstrated that, surgical keloid excision followed by radiotherapy and / intralesional triamcinolone as adjunct therapies, were reliable methods with few complications. Regular clinical follow-up was found to be an important factor for preventing keloid recurrence.

Imiquimod
Imiquimod 5% cream is a topical immune response modulator approved for the treatment of warts, actinic keratosis and basal cell carcinoma in adults. It is thought to work by inducing the pro-inflammatory cytokine interferon-alpha (interferon-α) which enhances collagen degradation and by causing pro-apoptotic effects. Imiquimod has been successfully used postoperatively following keloid excision. Conversely, another study also reported the recurrence of presternal keloids following keloid excision and imiquimod treatment indicating the need for more controlled studies to be conducted to gain a full insight into the efficacy of imiquimod treatment of keloids. In Barbados, imiquimod cream is typically used on small keloids with varying degrees of success.

Cryotherapy
Cryotherapy applies low temperatures to the keloid. The effects of freezing causes vascular injury that ultimately results in tissue necrosis. This therapy has proven most successful when combined with other treatments, especially intralesional triamcinolone acetonide injections. It is common to administer cryotherapy before intralesional triamcinolone acetonide injection for the best outcomes. The positive effects of liquid nitrogen and cryotherapy have been reported in a number of studies, with success rates varying from 32 to 74% and better outcomes with hypertrophic scars compared with keloids. The recommendations for treatment include: two freeze-thaw cycles of 15 to 30 seconds every three weeks for up to 10 visits.

Recently, an intralesional cryoneedle has been developed. Superior results have been reported using the cryoneedle over contact/spray probes. Studies have shown volume reductions up to 67% in a single session. The usefulness of cryotherapy is limited to newer scars, as older scars tend not to exhibit sufficient vascularization necessary for the treatment’s mechanism of action. A number of adverse effects are associated with cryotherapy including: pain, atrophy and hypopigmentation, which is common amongst dark-skinned patients. A case study presented at the Caribbean Dermatology Association in Jamaica reported that the use of cryotherapy on a large pinna keloid on a patient led to its reduction but resulted in hypopigmentation (unpublished data). In Barbados, cryotherapy is used but is not a common mode of treatment.

CONCLUSION
Keloids are problematic scars that are difficult to treat and remove. This present review has explored and discussed the current literature of the various modes of keloid therapies available in Barbados along with keloid management. Intraleisonal triamcinolone acetonide injection, imiquimod, surgical excision, pressure dressing, silicone gel sheeting and radiation are among the modalities commonly used. Cryotherapy, although used, is not a common mode of treatment. A combinational approach is considered the most effective. Despite there being a greater array of treatments that are not currently used in Barbados, those employed are among the most...
traditional and reliable treatment methods. It is possible in the foreseeable future that other forms of therapy will become available in Barbados. Of crucial importance, however, is the management of keloids. A well-planned treatment strategy that takes into account the patient’s needs by a highly experienced healthcare physician is instrumental in the eradication of keloids. Factors like keloid size and location, skin type and the age of the patient, have to be taken into consideration before deciding on the best-line of treatment which should also be tailored to the specific needs of the patient. Patient pain, pruritus and inflammation management, close clinical monitoring, as well as patient compliance with post-treatment care are also equally important.

AUTHORS’ NOTE
The authors have no conflicts of interest to disclose.

AUTHORSHIP
NO conceived the study. NO and OJN participated in its design, coordination and drafting of the manuscript. JW and ALF helped draft the manuscript. All the authors were involved in writing the paper and gave approval for the submitted version.

REFERENCES