Therapeutical Options for Keloids

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ABSTRACT

The keloid is a pathology that affects exclusively the human being and can not be reproduced in any other animal species. Therefore, the knowledge regarding this pathology is limited and, several times, controversial. The ideal option for its treatment has not been completely established and there are several therapeutical methods. In this article we tried to develop a critical review of the literature making the current used methods evident and, therefore, discussing its major advantages and disadvantages.

INTRODUCTION

There are several doubts regarding the differential diagnosis, ethiology and correct management of keloids [1,2]. Once the keloids affect only the human being, some of this difficulty is due to its irreproducibility in animal trials[3]. There are no differences in the incidence regarding the sex[2, 3, 4]. They are more frequent in black individuals and they have never been described in albinos[2, 5, 6]. The keloids present a familiar tendency and a dominant autossomic pattern that has been described as a possible responsible[2]. Some differences pointed

out between the hypertrophic scar and the keloid lead us to believe that the they are two different pathologies and that they required different treatments[7, 8, 9]. According to Ehrlich et al.[7], some immunological alterations appear to be more frequent in the patients with keloids. The immunoglobulines seem to be altered, especially the IgM and IgG, which are increased, and the IgA, which is frequently decreased. There are no changes at the complement[2, 10]. The alpha and gamma interferon and beta tumoral necrosis factor production are highly decreased in the patients presenting keloids[10]. The immunology role at the keloid development, however, is still obscure. According to Piérard et al.[11], the dendrites have a high concentration of the XIIIa factor, which is able to limit the collagen accumulation at the scars. The deficiency of these cells can be related to the keloids advent[11].

This purpose of this revision is to allow an objective view of the major current therapeutical options.

THERAPEUTICAL OPTIONS

SURGERY

The surgery, as an isolated treatment modality, has been almost abandoned due to the high recidivation rates, which are near 100% and generally occur within the first postoperative year[6, 10, 12, 13]. The surgical excision – together with postoperative corticoids injections, radiotherapy or compression – presents better results and each combination will be singly discussed as follows.

BETATHERAPY

Some authors present response rates varying from 16%[10] to 94%[14], when this therapy is singly used. When associated to the surgery, the results seem to be better and more consistent[13, 14]. The carcinogenic induction probability at the irradiated wound has not been totally set aside[13, 14]. The method advocates are supported by the fact that, up to this date, no carcinoma case has been unequivocally correlated to this therapeutical modality[14]. The available data are still not sufficient to determine its safe use in children. According to Norris et al.[14], the age inferior limit has not been yet defined and the irradiation possible implications on the epiphysis or bone growth area are not totally clear. According to Van der Beck[15], there is an interference at the bone growth of children with keloids treated with radiotherapy. Up to this moment, this therapeutical modality in children and the bone growth area irradiation avoidance is recommended. Klumpar et al.[13] report a work with 126 patients that received postsurgical radiotherapy treatment. The follow up period was of 12 years, where 83% of the patients presented a good control of their keloids with this associated modality. In the study, a higher keloid recidivation rate was observed at the infected wounds and in the patients with a positive familiar history. The betatherapy, associated with the surgery, has been shown as a useful and effective method of keloid treatment, particularly in those cases resistant to the other therapeutical modalities[13, 14].

CORTICOIDS

The corticoids can be applied in a topic or intralesional way[1, 3, 10]. The hydrocortisone cream presents a positive response in only 20% of the patients[10] and is not frequently used currently. The intralesional tryamcinolone presents a response rate near 100% with an approximated recurrence of 10-40%[10]. Sherris et al.[5] described the corticoid effect as a decrease of the collagen and glycosaminoglycans synthesis and the wound inflammatory process, producing the fibroplasia inhibition[5]. According to Stucker and Shaw[1], these medications present no risks. The major adverse effects are: local tissue atrophy, dyschromia, tubercle reactivation, teleangiectasia, immunosupression and others[1, 5, 7, 15, 16, 17]. According to Tang et al.[9], many of these effects are temporary. The corticoids are considered as a first line treatment for the recent keloids, with no more than one year of existence[1, 5, 18, 19, 20]. They can be singly used or together with other modalities[20]. The excision associated with the corticoids injection was extensively studied and presents a recidivation rate near 50%[9, 10, 13].

COMPRESSION

The isolated or associated compression was one of the firsts methods described[7, 10, 14]. The surgery, associated with postoperative compression, presents a lower recidivation rate than the isolated surgery [10]. In general, this method consists of a mesh of elastic tissue or spandex applied during 12-24 hours per day, during 12-36 uninterrupted months. Up to 60% of the patients presented some kind of response, with a decrease of approximately 75% of

the lesion's original volume[10]. However, with the long use, the meshes are uncomfortable, hot, and can cause pruritus or allergic reactions[10, 14]. The compliance rate can fall after the 3-4 first months, especially in the summer, if the patients are not well-orientated[14].

SILICONE PLATES

According to Sawada and Sone[21], the method's beneficial effects are not due to the pressure, temperature or capillar occlusion, but to the corneal extract occlusion and hydration, which would be the major related factors[13, 20, 21, 22]. Several authors reported this modality's efficiency at the hypertrophic scars and keloids[7, 17, 20, 21, 22]. Gold[17] assessed the method's efficiency applying a silicone plate covering only half of the area to be treated. After 4 weeks, approximately 20% of the patients did not show evidences of improvement in their lesions, but in the authors' assessment, approximately 95% of the patients presented some kind of positive response. The plates can be singly used or as a prophylactic way at the postoperative[10, 20, 21, 23, 24]. The patient shall apply them for at least 12 hours/day[17]. It is a painless and easy to apply method, except for the scars at irregular surface zones due to problems with the plate adhesion[20]. According to Palmieri et al.[22], the results can be higher if vitamin E is associated. Up to this date, the obtained response is not enough to justify its use as a monotherapy, but some studies support its use as an assistant at the surgical treatment[17, 20, 21, 22]. The lower price silastic plate's efficacy has not been proved and there are no works comparing the two plates[25].

LASER

The response to the carbon dioxide laser varies from 39 to 92%[10, 26, 27, 28, 29]. Similar controversial rates were identified for the argon laser, between 45-93%[10, 29]. In experimental trials, the laser surgical excision has shown a high capacity of delay in the collagen synthesis[29]. Unfortunately, according to Henderson[29], this effect is only temporary and the advantages demonstrated *in vitro* have not been confirmed at the clinical trials. Norris et al.[26] have demonstrated the laser's ineffectiveness. The initial responses were followed by recidivations treated with corticoids. Therefore, the laser's use at the keloids has not been defined.

CRYOTHERAPY

The cryotherapy as an isolated form of treatment presents a positive response in 55-70% of the patients and, at the majority of the cases, two sessions, with a 20 days interval, are required[10]. The associated use with corticoids produce a satisfactory response in up to 84% of the patients. According to Zouboullis et al.[24], the basis is the cellular layers' destruction by means of anoxia due to the microvascular disturbs caused by the contact with the cold. The recidivation rates have not been totally defined[22, 24].

CALCIUM CHANNEL BLOCKERS

The calcium channel blockers reduce in 50% the incorporation of the proline tritiated to the extracellular matrix[10, 30, 31]. They seem to induce meaningful changes at the fibroblasts configuration and formation and, therefore, increase the extracellular matrix degradation[30, 31]. Lee et al.[30] reported the hypertrophic scars control with intralesional verapamil. These pharmaceuticals deserve new studies for a better assessment[30].

INTERFERONS

The interferons' use has been recently studied and presented consistent results[10, 28, 29, 32]. They act decreasing the type I, II, III and possibly IV collagen production[28, 32]. Its use is intralesional, with weekly applications of up to 0.05 mg. The studies presented decreases of up to 50% at the linear dimensions, with the flattering of the elevated lesions[32]. Headaches are most frequent reported adverse effect [28, 32]. According to Gransten et al.[28] changes at the dermis and epidermis can occur. The epidermis presents a slenderness of the suprapapillar plates and the corneal extract presents a focal hyperkeratosis with the vacuolation of the basal layer. The authors have demonstrated a meaningful decrease of the collagen bundle number and an increase at the mucine quantity at the dermis and epidermis. The use of this pharmaceuticals as a routine is prevented due to the necessity of preliminary results confirmation[10, 28, 32].

OTHER AGENTS

The minoxidil, the pentoxiphilyne and the topic putrescine are some of the tested agents that had dem-

onstrated some clinical response[33, 34, 35]. More recently, Schierle et al.[36], in an experimental trial, could verify a meaningful difference at the testosterone receptors quantity per milligram of tissue between the active keloid tissue and the normal tissue. The author suggests that the increased level of testosterone receptors occur in the active tissue and that a possible treatment line could include topic antiandrogenics. The results must be assessed with skepticism until new studies are performed.

CONCLUSION

While the surgeons have no knowledge of the keloids' physiopathology, they will continue to have unsatisfactory and temporary results[37, 38, 39, 40].

The corticoids are the most frequently used pharmaceuticals and with a good experience. From all the modalities, the surgery associated with the corticoids is the one with the highest clinical experience and must be considered as an option for the great majority of the keloids[9, 16]. Very big or long evolution lesions, however, present a bad response to the corticoids and, in these cases, the surgery associated with the radiotherapy must be stressed as a possible first line[15, 16]. The cryosurgery presents uneven results and scarce clinical experience becoming, therefore, least attractive[10, 16]. The silicone plates, when used as a prophylactic way at the postoperative, reduce meaningfully the recidivation[10]. Its use is beneficial to the keloid, as well as to the hypertrophic scars but it hasn't been established as an isolated treatment modality[20, 23]. The use of laser did not bring evident clinical advantages in the majority of the studies[2, 26, 27]. The verapamil, the pentoxyphiline, the minoxidil, the topic putrescine and the interferon require further studies for their role's definition at the therapy[30, 31, 33, 34, 35].

The controversies regarding this subject are far from the end and the keloids are still representing one of the biggest enigmas of the plastic surgery[36, 37, 38, 39, 40].

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