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Prevention and Treatment of Keloids with Intralesional Verapamil

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Key Words

Keloids · Verapamil hydrochloride · Topical silicone

Abstract

Background: The current treatment of keloids is based on surgery, medical therapy and physical treatment. The optimal treatment remains undefined. **Objective:** This clinical study determines the effectiveness of verapamil hydrochloride on the prevention and treatment of keloids. **Methods:** Two groups of patients with keloids were divided according to lesion site and age. The first group was treated by perilesional surgical excision of keloids and topical silicone, combined with adjuvant treatment of intralesional 2.5 mg/ml verapamil hydrochloride injections administered at timed intervals. The second group served as control, receiving the same treatment except the verapamil hydrochloride. **Results:** A periodical examination to check specific clinical parameters and an 18-month follow-up determined that keloids were cured in 54% of the cases in the first group, compared to 18% in the second group. Moreover, in the remaining 36% of patients in the first group in whom keloids recurred, there was an improvement in size and above all in consistency. **Conclusion:** These findings suggest that verapamil hydrochloride is an effective tool for the prevention and therapy of keloids.

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Introduction

Excessive cutaneous scarring (keloids) is a defective wound healing process. Keloids (from the Greek 'kelè' meaning crab pincers) are considered idiopathic fibroblast tumors either arising from different skin lesions such as burns, wounds, caustications, acne, granulomas, ear-lobe piercings, vaccinations, microtraumas or spontaneously with no definable cause.

Most lesions occur on the upper trunk, the earlobes, the neck or the chin. Keloids are clinically characterized by fibrous tissue that initially takes on a common scar appearance tending to hypertrophy. Later the scar tissue accumulates fibrous tissue, rises above the plane of the skin and takes on a papular, nodular, sessile, peduncular or patchy aspect extending beyond the borders of the primary lesion into surrounding tissue. On palpation the scar is woody and fibrotic, often painful or itchy.

On histology keloids appear as fibroblast proliferation of the reticular dermis sometimes involving the papillary dermis. Fibroblast activity determines densely packed collagen fibers and the absence of elastic tissue. The fibers weld into hyaline cords, while resident fibrous connective tissue cells fill the gaps between the meshwork.

The current line of treatment for keloids is founded on surgery, medical therapy (intralesional steroids, interferon, topical cyclosporin, retinoids, topical silicone) and physical treatment (pressure, cryotherapy, irradiation, laser therapy) [1–11].

The aim of this study was to determine the effectiveness of intralesional verapamil hydrochloride injection in

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Table 1. Patients of first group (*with* intralesional verapamil hydrochloride injections)

Patients out of 22	Keloid location	Absence of result (keloid recurrence)	Partial result (improvement in size and consistence)	Complete result (keloid free)
10	back	0	4 (40%)	6 (60%)
6	deltoid	0	2 (33%)	4 (66%)
6	sternum	2 (33%)	2 (33%)	2 (33%)
Global results of first group		2 (9%)	8 (36%)	12 (54%)

the treatment and prevention of keloids. A calcium antagonist decreases collagen production in the extracellular matrix and stimulates collagenase synthesis reducing fibrous tissue production [12–18].

Intralesional verapamil hydrochloride (at 10 mg/ml) has already been successfully used in the past for keloids, hypertrophic scars and other afflictions featuring the overproduction of fibrous tissue [19, 20].

Based on this experience, it was our intent to exploit the Ca²⁺ blocking to prevent and treat keloids.

After having tested local intralesional infiltrations of verapamil hydrochloride in stabilized keloids to soften scars, with poor results, and in agreement with the literature reporting less effectiveness than local cortisone, we then proceeded to determine the effectiveness of the drug in preventing keloids in susceptible individuals. We examined whether verapamil hydrochloride could be used at an early phase of scar healing to prevent keloid formation.

Materials and Methods

Data concerning keloids of 44 patients (28 men and 16 women; age range 22–45 years) were examined as evaluated with respect to size (range 2–6 cm) and duration (range 2–5 years) in typical sites. Specifically 20 subjects presented lesions on the back, 12 had sternal scars and the remaining 12 had deltoid keloids.

These patients were assigned – based on a waiting list – to two equal groups of 22 persons. Patients were matched for lesion site and age. The final analysis was based on comparisons of case-control matched pairs.

In the first group, keloids were treated by surgical excision, topical silicone applied in sheets and intralesional verapamil hydrochloride injections at the operation and at timed intervals. The second group, the controls, received the same treatment except that no verapamil hydrochloride was administered. In both groups, the surgical excision of keloids was performed perilesionally. Topical silicone was applied at the first signs of scar formation (7–14 days) and lasted for 6–9 months. The first group received 2.5 mg/ml of verapamil hydrochloride with doses varying from 0.5 to 2.0 ml depending on the size of the keloid. We used the following treatment schedule: intralesional infiltrations on postsurgical days 7, 14, 28 and during the second month. This was always followed by application of silicone sheets.

All patients were examined on the 28th postoperative day, in the second month, in the third month and at the 18-month follow-up to evaluate size, thickness, texture and subjective symptomatology (e.g. burning, pruritus).

Results

The results indicate that at the 28-day follow-up only 10 of the 22 patients (45%) in the first group had the beginnings of visible abnormal scar formation.

In the second month, 12 patients (54%), of whom 6 of 10 (60%) had previous keloids on the back, 2 out of 6 (33%) prior sternal keloids and 4 of 6 (66%) deltoid keloids, showed resolution of the problem with unremarkable scar tissue.

Of the remaining subjects, 8 (36%) had partial resolution with recurrence of smaller and softer keloids than those removed by surgery, while only 2 cases (9%) presented with worse keloids than before. At the 18-month follow-up, nothing had changed (table 1).

In the second group at the 28-day follow-up, 18 patients (82%) presented an initial reappearance of the abnormal scar and gradual worsening until full-blown keloids developed. At 18 months, such keloids were worse in 6 (27%) of the cases and matched initial lesions in 12 patients (55%), whereas an amelioration of the lesion could be demonstrated in only 4 cases (18%). No complete regression of the keloids occurred in any subject (table 2).

Discussion

Although optimal treatment of keloids remains undefined, good results can be obtained through a multimodality approach [1–11].

The combined use of surgery and intralesional corticosteroid infiltration is still today a successful treatment and provides the best means of support [1–11]. Together with this therapy, applied pressure and topical silicone sheets

Table 2. Patients of the second group (without intralesional verapamil hydrochloride injections)

Patients out of 22	Keloid location	Absence of result (keloid recurrence)	Partial result (improvement in size and consistence)	Complete result (keloid free)
10	back	7 (70%)	3 (30%)	0
6	deltoid	5 (83%)	1 (17%)	0
6	sternum	6 (100%)	0	0
Global results of second group		18 (82%)	4 (18%)	0

have been useful [3, 10]. In agreement with the literature, our experience with these techniques has been subjective, inconstant and not without atrophic outcomes [11]. In our series, treatment of keloids by perilesional surgical excision and topical silicone, followed by adjuvant treatment with intralesional verapamil hydrochloride injection at timed intervals, offered a higher rate of resolution than other therapeutic strategies and some other series [21], without any significant difference in recurrence rates related to sex and age, while in the sternum location there was a higher percentage of recurrence (tables 1, 2). This is the second study which has proved the effectiveness of this treatment with a success rate of more than 50% in keloids [20], but in contrast to the experience of Lawrence, we did not use a combined pressure therapy, we compared two equal groups of patients treated with and without verapamil, we did not examine earlobe keloids

and in our study keloids were completely cured in 54% of cases and there was an improvement in size and above all in consistence in 36% of cases, with a global satisfactory response in 91% of cases.

In 1990, Lee and Ping [17] first demonstrated that calcium antagonists such as verapamil depolymerize actin filaments and consequently modify fibroblasts in normal scars as well as keloids. They also stimulate collagenase production, thus reducing fibrous tissue production [12–18]. This explains why the drug is effective in conditions with overproduction of collagen, such as keloid scars.

In conclusion, intralesional infiltration of verapamil hydrochloride at 2.5 mg/ml, following the treatment strategy offered, associated with topical silicone layering, begun right after surgical extirpation with adjacent tissue, is a sound approach to treat keloids. This should be confirmed by a larger randomized clinical trial.

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