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COMBINED SURGICAL EXCISION WITH LOCAL INFILTRATION OF VERAPAMIL FOR THE TREATMENT OF KELOID; A CLINICAL STUDY

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Abstract

Keloid scar is one of the most challenging problems for physicians and surgeons. The current treatment of keloids is based on many ways and modalities which includes medical therapy, combined surgical excision with other modalities, physical treatment etc. The optimal curative treatment remains undefined.

This study aimed to evaluate the effectiveness of the surgical excision combined with local infiltration of verapamil to treat patients with keloid.

This prospective study involved 20 patients with keloid scars at different parts of the body. These keloid scars were surgically excised with local infiltration of Verapamil. This study was carried out at Al-Shaheed Ghazii Al-Harriri Hospital, Al-Wasity Hospital in Baghdad and Al-Sadr Teaching Hospital in Basrah Between January 2017 and May 2018. The age of the patients ranged between 11 to 44 years. Fourteen of them were females and 6 were males.

After one year follow-up period, 11 patients had good results, 5 patients had moderate results and 4 patients had poor results. Patient's satisfaction in those who had good results was excellent. No serious complications were recorded, only one patient got local wound dehiscence.

In conclusion, surgical excision of keloid scar combined with post-surgical verapamil infiltration showed promising results in the management of keloid scar and reduction of its recurrence rate.

Key words: Keloid, Scar, Surgery, Excision, Verapamil

Introduction

The skin is the largest organ of the body and one of the most important organs in human being. It is subjected to a large number of insults, one of the main insults is wound[1].

The specific sequences of different processes following wounding has only one common aim, i.e repair or regrowth. This is achieved by very complex and dynamic procedures, in which tissues are degraded (catabolic phase) and newly synthesized tissue replaced lost one (anabolic phase)[2].

Normal tissues stops signal that halt the repair process when the dermal defect is closed and the epithelialization is complete. When these signals are absent or ineffective, the repair process may continue and result in excessive scar tissue formation. The underlying regulatory mechanisms leading to excessive scarring and repair are not known yet[3].

Keloid scar, is defined as excessive formation of scar tissue that extends beyond the boundaries of the original incision or wound[4]. The unsightly and sometimes painful keloid is an inappropriate over reaction of the healing process. Keloid (spot-like) have been called cancroid (cancer-like, crab-like) and cheloids (claw-like) because of it's specific feature of aggressive expansion[5]. For unknown reasons, keloid and hypertrophic scar formation are unique for man, attempts to develop animal

models for abnormal scar formation have always proved unsuccessful[6].

Patients and methods

Between January 2017 and May 2018, twenty patients with keloid in different sites of the body were included. All patients were treated by surgical excision and intralesional infiltration with verapamil (calcium channel blocker). This study was carried out in Al–Shaheed Gazi Al–Hariri hospital and Al-Wasity Hospital in Baghdad, and Al–Sadr Teaching Hospital in Basrah, Iraq.

Patients with large keloid that cannot directly and primarily closed at the time of surgery were excluded from this study, also, those patients who had history of previous attacks of sever hypotension or those with history of heart failure and pregnant women, were excluded. In this study, verapamil ampule (5mg/2ml or 2.5mg/1ml) was used. The patient's primary concern was the aesthetic appearance of their scars; but some of them had itching, pain and tenderness. None of the patients reported definite functional impairment due to keloid scar.

Figure1: Large keloid which is excluded from the study.

Pre-operative investigations were done for all the patients like blood tests, ECG, echocardiogram in patients who gave cardiac problem history. Photographs were taken in preoperative, postoperative and follow-up periods.

Informed consent was taken from all patients for medico-legal purpose.

Table I: Patient's data collected in this study

Patient number	Age years	Gender	Duration	Site	Etiology	Size of keloid (length, width, height)
1	15 y	Female	1 year	Earlobe	Ear pierce	2cm×2cm×1cm
2	25 y	Male	1.5 years	Right forearm	Burn	5cm×1cm×7mm
3	20 y	Male	1 year	Post auricular	Surgical excision	3cm×1cm×1cm
4	16 y	Female	2 years	Earlobe	Trauma	2cm×1.5cm×1cm
5	17 y	Female	3 years	Left forearm	Burn	3cm×2cm×1cm
6	30 y	Female	2 years	Earlobe	Ear pierce	2cm×1cm×8mm
7	40 y	Female	2 years	Ear (helical rim)	Previous surgery	1.5cm×1.5cm×7mm
8	35 y	Female	2 years	Earlobe	Ear pierce	1.5cm×1cm×4mm
9	40 y	Male	2 years	Chest wall	Previous surgery	3cm×1.5cm×1cm
10	30 y	Female	2 years	Earlobe	Ear pierce	1cm×1cm×5mm
11	35 y	Female	3 years	Ear (anterior surface)	Trauma	2cm×2cm×7mm
12	11 y	Male	2 years	Preauricular region	Trauma	1.5cm×1.5cm×8mm
13	44 y	Male	6 years	Anterior chest wall	Previous surgery	3cm×2cm×1cm
14	36 y	Female	6 years	Ear (helix)	Burn	2cm×2cm×1cm
15	20 y	Female	2 years	Earlobe	Ear pierce	2cm×1cm×1cm
16	37 y	Male	3 years	Shoulder	Burn	2cm×1.5cm×1cm
17	16 y	Female	2 years	Ear (helix)	Burn	2cm×1.5cm×5mm
18	23 y	Female	2 years	Earlobe	Ear pierce	2cm×1cm×7mm
19	26 y	Female	2 years	Post auricular	Trauma	2cm×2cm×1cm
20	31 y	Female	4 years	Forearm	Burn	3cm×2cm×1cm

Patients were divided into the following groups based on: Age of the patients, Gender ratio, Duration till patient presentation, Etiology of the keloid, Site of the keloid . The patients were studied according to their age and gender. Most of the cases were at age group at the second decade and at fourth decade. Females number are more than double the males. The average age of the patients is 27.4 year. The gender of the patients in this study was 6 males and 14 females, i.e. male: female ratio is 6:14(1:2.33). The duration of the keloid till presentation varies, from one year to more than 6 years.

Table II: Age of the patients

Age	Male	Female	Total
1st decade	-	-	-
2nd decade	2	5	7
3rd decade	1	4	5
4th decade	2	5	7
5th decade	1	-	1
Over	-	-	-
Total	6	14	20

The etiology and the causative agents were equal to 6 in both ear piercing and burn, while it's equal to 4 in each post-operative and trauma.

Table III: Etiology of keloid

Etiology	Number
Ear piercing	6
Burn	6
Post-operative	4
Trauma	4

Keloids in this study were located in different sites of the body. In the majority of the cases it is located on the ear (2 in males and 12 in females) , in three of the cases, keloids were located on the forearm (1 in male and 2 in females) while only 2 male patients got chest keloid but no female case. Finally only one case has it on shoulder (1 male but no female).

Table IV: The site of keloid in different body parts.

Sites	Males No.	Females No.
Ear	2	12
Forearm	1	2
Chest	2	_
Shoulder	1	_

Technique: Following disinfection with povidone iodine solution, 2% Xylocaine with1:100,000 adrenaline was infiltrated around the scar. After waiting for 5-7 minutes, the keloid scar was totally or partially removed by using No.15 blade. The scar was excised up to the healthy tissue or most of the scar bulk. After good hemostasis, the wound was closed primarily. Infiltration of verapamil (2.5 mg\1ml or 5mg \2ml) was done by using 22 gauge needle, the amount of injection vary between 2 to 4 ml depending on the size of the excised lesion. The infiltration includes the closed wound edges with its underlying tissue. After 5-7 days the stitches were removed. The patient's fist visit was after 2 weeks from the time of

surgery to receive the second injection of intralesional Verapamil by the same way as the first injection. The third infiltration was done 2 weeks after the second injection, then the fourth injection was done one month after the third injection. The total amount of infiltration depend on the resultant closed wound.

Patients were kept then on regular follow-up which was extended up to one year following the first verapamil injection.

Figures 2 A-G Shows the surgical procedure in series

Figure 2A- keloid length

Figure 2B-keloid width and height

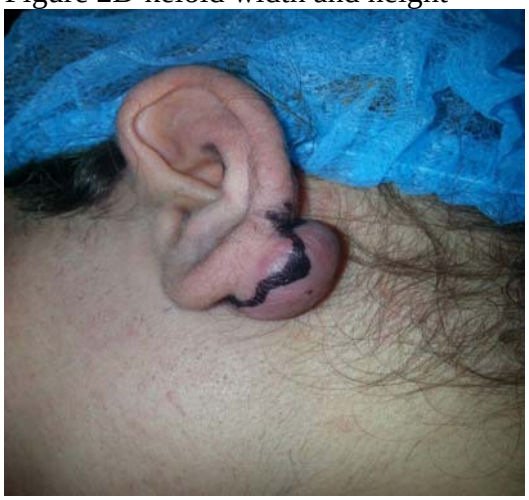

Figure 2C- preoperative marking

Figure 2D- excision of the major keloid bulk

Figure 2E- Defect closure

Figure 2F- the excised keloid

Figure 2G- after verapamil infiltration

Results

This is a prospective study of twenty patients with keloid scars in different parts of the body, collected from two cities of Iraq (Baghdad, Basrah). All patients had surgical excision with verapamil infiltration.

During the follow-up period (1 year), the study evaluates the results depending on the following parameters: Scar size: length, width, height compared to the original scar. Consistency of scar: (if recur) firmness, softness. Symptoms reported itching and pain. And patient satisfaction. According these parameters, the study got the following results and outcome which are summarized in table V below.

There were 11 patients who had good results (no keloid recurrence at all), while 5 of the patients had moderate results (keloid recur after 6 months) but smaller in size and less symptomatic i.e. itching, pain than the original keloid. Only 4 patients had poor results (keloid recurs after 4 months) with the same size and symptoms of the original keloid. The patient's satisfaction of those good and moderate results was excellent, accepted in order, while patients with poor results were dissatisfied.

Table V: The results and outcome

Result	Patient number	Patient satisfaction
Good result (no keloid recurrence)	11	Excellent
Moderate result (keloid recur after 6 months)	5	Accepted
Poor result (keloid recur after 4 months)	4	Dissatisfied

The complications and outcome after the treatment were shown in table VI. In 11 patients there were no complications seen after one year of follow-up, which make it 55% of the cases. Only one patient (5%) got wound dehiscence during the follow-up period. All patients had experience minimal tolerable pain during infiltration, and no systemic complications such as hypotension or allergy to verapamil were reported. Only one of the patients had developed a major wound complication which was wound dehiscence, no patient got wound infection.

Table VI: The complications and outcome

Complications	Patient number
No complications	11
Recurrence after 6 months	5
Recurrence after 4 months	4
Wound dehiscence	1

Figures 3 shows examples of the study results (Good, moderate, poor).

Before treatment

After one year (good result)

before treatment

one year later (moderate result)

before treatment

After one year (bad result)

Discussion

In addition to its aesthetic disfigurement, the keloid scar can lead to distressing symptoms such as pain and itching, and it may interfere with function when it is on a joint or distorting an orifice. All these will lead to impairment of the life quality of the patient. Management of keloid represents one of great challenge, since surgical removal alone is associated with more than 60% recurrence rate[7].

This prospective study was done on a limited and small sample to try a way to treat keloid using a combination of surgical excision and intralesional infiltration of Verapamil postsurgery.

This study was based on the study done by Eray Copcu et al[8], they used combination of surgery and intralesional verapamil for treatment of keloid in 21 patients. After 2 years of follow-up, two

patients had keloid with lesser diameter than the original lesion, and 2 patients had lesions with hypertrophic appearance, with rate of patient satisfaction was 6.4. Lee and Ping were the first to demonstrate in 1990 that calcium channel blocker such as verapamil depolymerize the filaments of actin so that it will modify fibroblast both in normal tissue and keloid scar. Calcium channel blocker also acts by degraded collagen by stimulating collagenase production, which results in reducing fibrous tissue production. This mode of action explained its effect on the treatment of collagen overproduction, such as occur in keloid scar[9].

Experimentally it was observed that when fibroblast of human dermis were incubated in culture media that contain either 100 micromol\L Verapamil or 10 micromol\L Trifluoperazine, there will be alteration in the shape of fibroblast with change from bipolar to spherical shape. During change to round shape fibroblast, the calcium channel blocker or calcium antagonist will depolymerized actin filaments without disruption of microtubule. This depolymerization of actin filament that occurs when cell is rounding will apparently turn on procollagenase gene expression in normal human fibroblast without affecting or reduction in cell viability[10].

Some authors investigate whether topical application of verapamil will inhibit excessive scar formation after surgical repair of the nerve. In their experiment, they transected sciatic nerve of rats, and then wrapped the stoma with gelfoam soaked in verapamil solution for 4 weeks. The result showed that the use of verapamil reduced keloid scar formation and it promote growth of axon after peripheral nerve repair[11].

In study which was conducted by Muhammad Uzair et al, they did a comparison study between intralesional triamcinolone and intralesional verapamil in the management of keloid in eighty patients. They observed in their study that in group received triamcinolone injection there were 58.28% reduction in baseline of score of keloid in comparison with 36.75% reduction in group receive verapamil. They concluded that treatment of keloid with using of triamcinolone is better than intralesional verapamil. Their study however cannot be compared with this study, since combination of surgical excision and intralesional verapamil were used and this combination lead to better results as Uzair et al observed that side effects were observed more with using of triamcinolone as compared with intralesional verapamil such as pain, hypopigmentation and menstrual disturbances. They appreciated that the reason why verapamil is less effective than triamcinolone since the corticosteroids has additional anti-inflammatory effect on the scar tissue together with collagen and glycos-aminoglycan synthesis inhibition[12].

A study by Zhouna Li and Zhehu Jin concluded that there is no difference between verapamil and non-verapamil application for treatment of keloid and hypertrophic scar[11]. Same conclusion was also observed by Dhanvaj p et al[13].

Conclusion and Recommendation:

Surgical excision of keloid scar with postsurgery Verapamil infiltration showed promising results in this series. Although, a small sample collected, it give an encouraging results in management of keloid scar and reduction of it's recurrence rate. We recommend a further study to be done with larger sample size together with longer follow-up period.

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