

Utility of different modality in the treatment of keloid scar

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ABSTRACT

Background : Keloids constitute an abnormal benign fibro-proliferative wound healing response to any type of skin injury. it has high influence on Patient's psychology and cosmetic view. It has high prevalence in African-American subjects. Until now there is no definitive treatment.

The aim of study : to assess the response in three different groups using three different modalities (intralesional steroid, cryotherapy, and both).

Patient and method : This was a randomized controlled clinical method with equivalent intervention assignment study, which was done on 16 patients (105 lesions), who attended Ibn Sina Teaching hospital, Mosul, Iraq, from January 2019 to January 2021.

Results : there were significant responses to the three modalities (p-value less than 0.05). and the response assessed for each patient according to Vancouver Score Scale (VSS), Patient and Observer Scar Assessment Scale (POSAS), and 2 diameters assess.

Conclusion: The results of this study showed that the combination of cryotherapy with intralesional steroids is more effective than steroid or cryotherapy alone in treating keloids.

Keywords: keloid , scar , steroids , cryotherapy , treatment .

استخدام وسائل المتعددة لعلاج ندوب الجدرية

هالة نذير السلطان

فرع الطب الباطني ، كلية الطب ، جامعة الموصل ، الموصل ، العراق

الخلاصة

الخلفية : تشكل الجدرية استجابة غير طبيعية لالتئام الجروح الليفية التكاثرية لأي نوع من إصابات الجلد. له تأثير كبير على نفسية المريض ووجهة نظر التجميل. ينتشر بشكل كبير في الموضوعات الأمريكية الأفريقية. حتى الآن لا يوجد علاج نهائي.

الهدف من الدراسة : هو تقييم الاستجابة في ثلاث مجموعات مختلفة باستخدام ثلاث طرق مختلفة (الستيرويد داخل الآفة ، والعلاج بالتبريد ، وكلاهما).

المريض والطريقة : كانت هذه طريقة إكلينيكية عشوائية مضبوطة مع دراسة تخصيص تدخل مكافئ ، والتي أجريت على 16 مريضاً (105 آفات) ، الذين حضروا إلى مستشفى ابن سينا التعليمي ، الموصل ، العراق ، من كانون الثاني (يناير) 2019 إلى كانون الثاني (يناير) 2021.

النتائج : كانت هناك استجابات كبيرة للطرائق الثلاثة (قيمة p أقل من 0.05). وتم تقييم الاستجابة لكل مريض وفقاً لمقياس درجات فانكوفر (VSS) ، ومقياس تقييم المريض والندبة (POSAS) ، وتقييم قطرين.

الخلاصة : أظهرت نتائج هذه الدراسة أن الجمع بين العلاج بالتبريد والستيرويدات داخل الآفة أكثر فعالية من العلاج بالستيرويد أو العلاج بالتبريد وحده في علاج الجدرية.

الكلمات المفتاحية : الجدرية ، الندبات ، المنشطات ، العلاج بالتبريد ، الجدرية ، الندبات .

INTRODUCTION

Keloids constitute an abnormal benign fibro-proliferative wound healing response, that grows overly and invasively under the original wound borders invading an adjacent normal tissue as a response to skin injury (like cutaneous injury and irritation, including trauma, insect bite, burn, surgery, vaccination, skin piercing, acne, folliculitis, chickenpox, and herpes zoster infection)¹.

A scar is the last step in the physiology of wound healing (start with hemostasis “coagulation”, inflammation “mononuclear cell infiltration”, proliferation “epithelialization, fibroplasia, angiogenesis, and formation of granulation tissue” and lastly maturation “collagen deposit or scarring tissue formation”), manifest as non-functioning fibrotic tissue, which may improve over time².

Morphologically, described as well-demarcated, raised cutaneous nodule variable in size and shapes and maybe bosselated lesion³, may be accompanied by intense pain, itching, stiffness, scar contractures, tenderness, and other physical, and psychosocial symptoms.

It’s very antique as it was described in an ancient Egyptian Medical Practice⁴. Mostly, it affects the individuals who are aged between (10-30) years, frequently the pigmented-skin persons “high reports in African, Afro-Caribbean, Afro-American, Hispanic, or Asian ancestry”⁵. It Commonly affects sites such as the anterior chest, shoulders, back and earlobe, with those on the pre-sternum and shoulder regions developing under high tension.

Many theories had been supposed to explain the pathology of keloids formation, including elevated skin tension, hypoxia, chronic inflammation, autoimmune genetics, and vascular factors, none of which, however, are independently sufficient to do so⁶⁻¹¹.

Chin GS et al reported 2001 another theory that Keloid fibroblasts express higher Receptor Tyrosine Kinase signals compared to normal skin-derived fibroblasts. This increased cellular signaling may influence cell growth, differentiation & survival, all are linked to cancer development when the signal dysfunction. Also, they found that “Nanog” (a gene that consults self-replication abilities to cells) is absent in somatic cells. , recently found to be up-regulated in keloid Associated Lymphoid Tissue (KALT)^{12,13}.

Aims

Determine the efficacy, improvement of keloid scar with different methods (intralesional injection of triamcinolone, cryotherapy, and both).

PATIENTS AND METHODS

This is a randomized controlled clinical trial was done on 16 patients (105 lesions), who attended Ibn Sina Teaching hospital, Mosul ,Iraq, from January 2019 to January 2021. This study was approved by the local ethics committee of the University of Mosul. The patients' age group was 21-43 years.

Full history had taken from each case about the number of lesions, duration of disease, symptoms associated with scar, family, and drug history. Every patient had been examined by a dermatologist to exclude hypertrophic scar from keloid, depending on the scar growth duration, starting before or after a skin injury, enduring stable or continue growing, shape and the extension to surrounding normal tissue (more or less than 0.5cm) assess the size (width and deepness) using hardened stainless-steel ((150mm Digital Vernier Caliper)) “Kincrome Pty Ltd, Scoresby, Australia” with a liquid-crystal display (LCD) screen to read a precise measure to the nearest (0.02mm), the texture and pliability, vascularity, pigmentation and measure each lesion in 2 dimensions using Vancouver Score Scale (VSS) as shown in table (1). The erythematous color had been assessed using a Hand-held Colorimeter ((ChromaMeter CR-200; Minolta, Ramsey)). A higher erythematous color indicates more saturation toward red.

Table (1): Vancouver Score Scale (VSS) we assess each parameter with number scale to have score

Score	Texture	Pliability	Vascularity	Pigmentation
4	Stony hard	Attached to skin	<7 blood vessels	Dark red or hyper-pigmented
3	Hard mass	Movable hardly	5-7	Red or brown
2	Soft mass	Movable easily	3-5	Pink
1	Normal skin	Normal skin	0-3 small blood vessels	Normal skin color

Then we added all of them to have the score, we did the scoring each visit then we measured the mean improvement between the first and last visit then we assessed the improvement in each group.

Regarding the measurement, we took the 2-dimension measures and assessed the improvement in each modality between the first and last visit.

Also, we used the patient & observer scar-assessment scale (POSAS) to assess each patient in three visits according to six items assessments

(The scores of the patient will range from 6 for the best imaginable scar to 60 for the worst scar imaginable) this done by two board-certificated dermatologists then the average score recorded¹⁴.

Then we divided the patients into three groups. First group treated with intralesional triamcinolone acetonide 40mg/ml [suspension (Kenacort A®) diluted with lidocaine hydrochloride 2% to prepare a dose of 20mg/mL] alone. The second group was treated with intralesional cryotherapy spray [using Nitrogen at -196°c sprays 2 times in 15 seconds with an interval of 5 minutes in between covering the lesion with 1mm beyond margin]. The last group was treated with cryotherapy and after 2-5 minutes we injected diluted triamcinolone. We had a group (1) three patients who had 3 scars in different parts of their bodies; we treated each lesion with a different modality (3 ways) to evaluate the effect of each method on the same person to eliminate the individual response variability and to declare homogeneity between treatment methods. Then we had a group (2) nine patients with 2 scars also we used 2 different methods like 3 patients treated with method (1 &2), the other 3 patients treated with method (1, 3), last 3 patients treated with method (2,3). Then group 3 we used to each patient a method. We randomized sored the lesions to which method we used.

All the cases had been reviewed and retreated every four weeks apart for 3 sessions, with the usage of the same method, each session we assessed all the parameters, photos taken, record the improvement & asked the individuals to evaluate and score patient's satisfaction about the treatment we used using a "four points scale" (no improvement gave 0, little improvement gave 1, good gave 2, excellent response gave3). During this period of treatment, patients were not allowed to use additional keloid treatments.

We excluded patients who had lesions less than 6 months, pregnant, patients with Fitzpatrick skin type (4, 5 & 6), hypertrophic scar, use of systemic chemotherapeutics or chronic use of systemic steroids or immunosuppressive treatment also patients with history for hypersensitivity to local anesthetics, adrenaline, or triamcinolone.

Treatments used in the study were conformist rather than experimental. The hospital's local safety procedures were monitored. The possible side effects had been treated according to current best practices. We didn't face any serious side effects during the period of treatment.

Ethics

The protocol was approved by the Medical Ethics Committee of Mosul University.

RESULT

There were 16 patients were included in the research were 105 keloid scars caused by different causes (piercing, post chickenpox, burn, surgery, and acne scar). The patients were divided into three groups (group 1 treated with intralesional steroid, (group 2 with cryotherapy) and (group 3 treated with both cryotherapy then intralesional steroid). For patients with more than one lesion, we used more than one method of treatment.

All cases had been followed every month for a new session for three sessions and assessed the improvement using Patient and Observer Scar Assessment Scale (POSAS) and Vancouver Score Scale (VSS). We found in G1, there were about 9 points full POSAS after three sessions and about 29% improved in the 2 diameters measure and significant improvement in Vancouver Score Scale (in all parameters).

In G2, the POSAS was decreased by 12 points, and about 34% decrease in scar 2 diameter measures and also significantly decrease in all Vancouver Score Scale (VSS).

Lastly, in the third group, there were 20 points improvement in (POSAS), 69% improvement in diameters and significant decrease in Vancouver Score Scale as shown in tables 2, 3 and 4.

As it shown in photos.

Table 2: The patient and observer scar-assessment scale (POSAS) and the difference in each visit in every group

Group	patient and observer scar-assessment scale (POSAS)		
	First visit	Second visit	Third visit
G1	43.4	39.1	34.3
G2	41.1	35.4	29.9
G3	48.2	38.7	28.5

Table 3: showed the mean improvement between the first and last sessions in Vancouver Score Scale in each parameter in every group.

Group	Mean improvement between first and last session in Vancouver Score Scale (VSS).				P value
	Texture	Pliability	Vascularity	Pigmentation	
G1	1.9	2.1	2.7	1.1	<0.05
G2	2.1	1.6	1.2	0.4	
G3	2.6	2.4	3.1	1.7	

Table 3: show t The 2 diameter of scar tissue and the mean difference between the first and last sessions in all three groups.

Group	Thickness/mm	Length/mm
G1	-0.3	-1.5
G2	-0.4	-1.7
G3	-0.9	-2.5

Photo 1: Patient had been treated with interlesional steroid, (A) first session, (B) second session after 1 month and (C) third session after another 1 month. (see the skin atrophy)

Photo 1

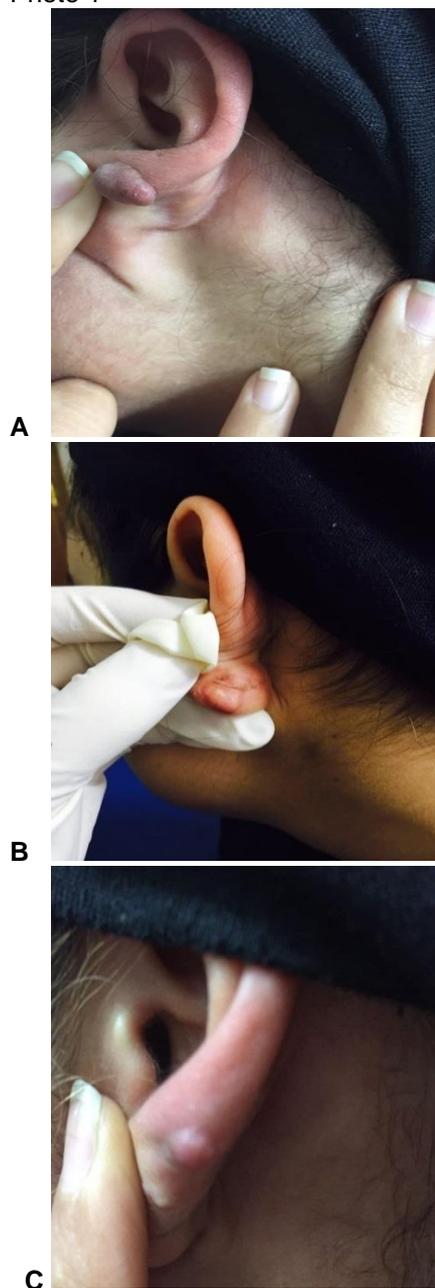


Photo 2 : Patient had been treated with cryotherapy (group2) , (A) first session, (B) second session after 1 month and (C) third session after another 1 month. (see the post inflammatory hypopigmentation)

Photo 2

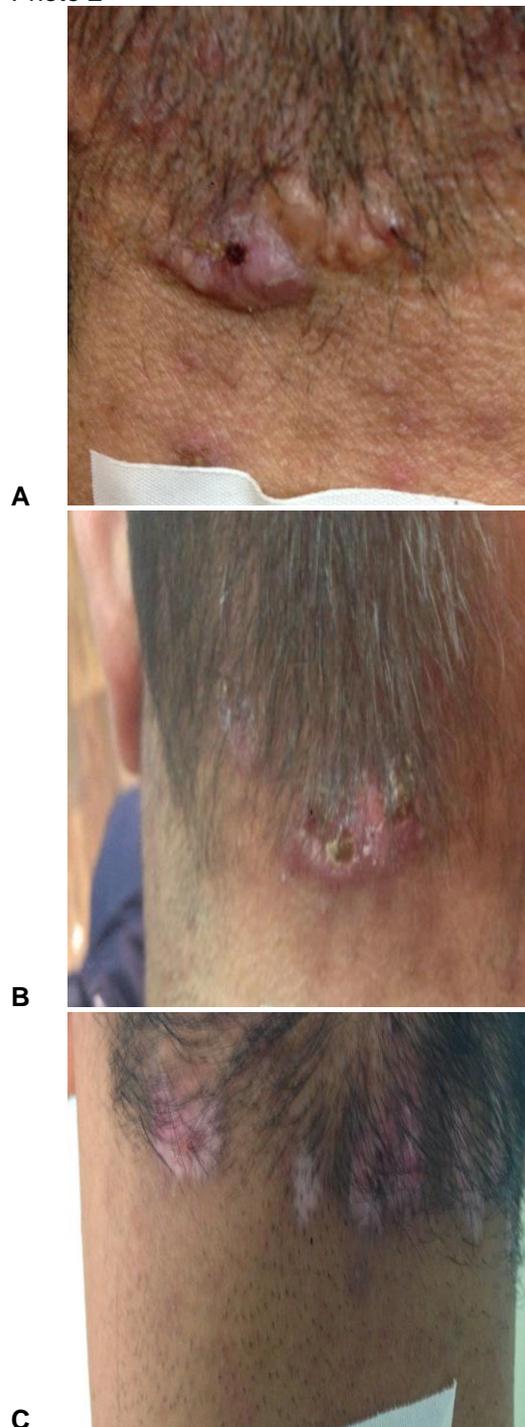


Photo 3 : Patient had been treated with cryotherapy then intralesional steroid (group3) , (A)first session, (B) second session after 1 month and (C) third session after another 1 month.

Photo 3

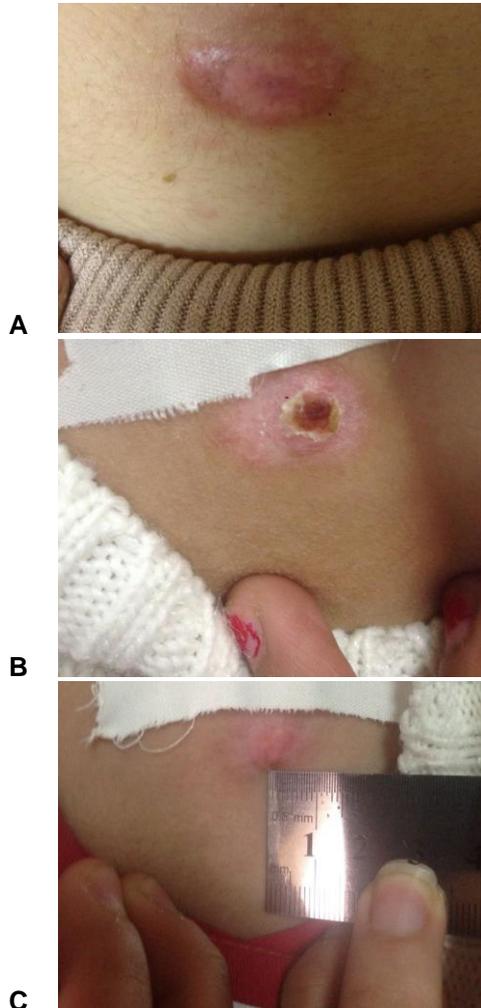
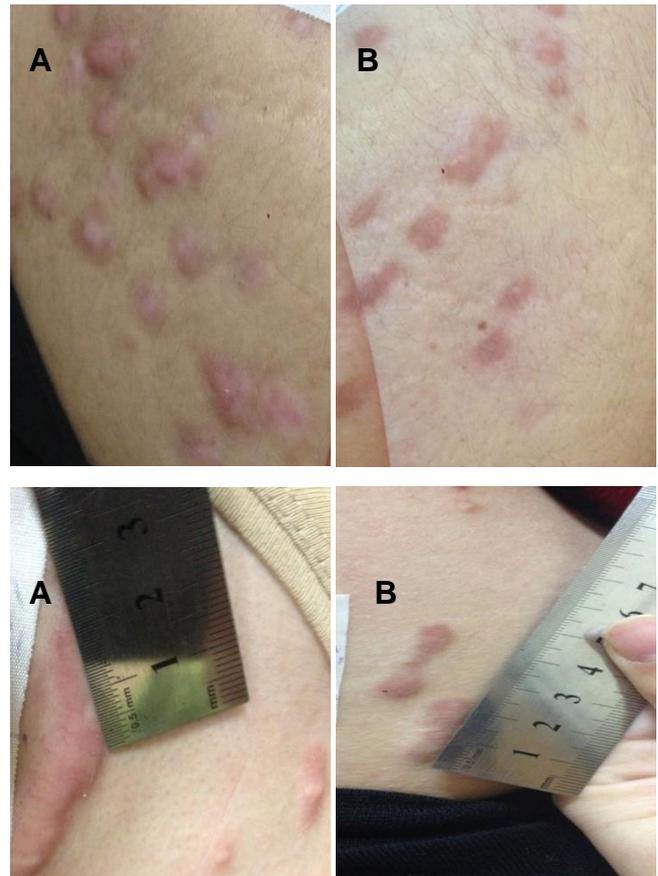
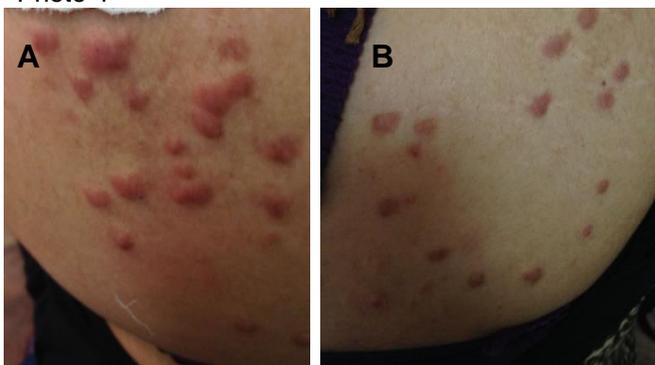


Photo 4 : These patient had more than 3 lesions we used the three modalities on the lesions, (A) first session and (B) third session.

Photo 4



DISCUSSION

Keloid is one of the distressing dermatological problems that we faced in our practice. the keloidogenesis remains so poorly understood, different hypotheses for the pathogenesis had been supposed; which involved both genetic (like Ethnicity, genetic predilection, sex, age & the body site injured), environmental factors, and cellular abnormalities (the epidermal compartment, keratinocyte, and the immune system role)¹⁵.

Different lines of treatment had been used over time but official guidelines till now are not based. We used three methods in our research to assess the response and improvement.

Intralesional triamcinolone acetonide is recorded as (gold standard in nonsurgical treatment for keloid & hypertrophic scar)¹⁶. Steroids were substantiated to persuade keloid regression by different mechanisms by suppressing the inflammatory processes by inhibiting leukocytes and monocytes phagocytosis & migration or may be through their vasoconstrictor power, thus reducing the delivery of oxygen and nutrients to the wound bed, and may affect re-epithelialization & new collagen creation.

We found that the mean improvement was about (29%) in 3 sessions with (p-value 0.04) which was similar to had been reported by Woraphong¹⁷, the effect was especially in pliability and thickness but less improvement in the color of the scar although the main side effect of this treatment was pain at the site of injection in 71% of cases and 34% complained from telangiectasia as had been recorded in Paul A etal¹⁸.

In the second group with cryotherapy method, the response was 34% response after 3 sessions with (p-value 0.035) especially in thickness, blood vessels, and texture as it had been reported by Barara et al¹⁹ in their research, but less improvement in color even leads to post-inflammatory hypopigmentation in darker skin color patients in 12% of cases, as it has been reported by Har-Shai Y,²⁰.

The last group received both cryotherapy then intralesional steroids, there was 65% improvement in lesion especially the texture and the pliability as had been reported by Bloemen et al²¹. In standings of thickness, scar had been responded significantly better to combined cryotherapy and triamcinolone method versus triamcinolone alone or cryotherapy alone, as has been reported in G Yosipovitch et al in their research.²²

Most patients reported that the pain of intralesional injection significantly was lower when we injected after cryotherapy, also we found the easiness of the injection the scarred tissue, but the main side effect also was the post-inflammatory hypopigmentation as had been reported by Hamideh et al.²³

Study Limitations

The main challenge through the study was the follow-up visits complaint and the few numbers of cases.

There Was No Conflict Of Interest

CONCLUSION

The evidence available for many therapeutic modalities for keloids is limited and high-quality randomized studies are not available. This may be due to difficulty in follow-up. The results of this study revealed that combination of cryotherapy & Intralesional steroids was more effective than steroid or cryotherapy alone in treating keloids and it provides better outcomes in shorter duration with fewer complications.

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