

Postburn Hypertrophic Scar Response to Potassium Iodide Iontophoresis

SALMA A. MOHAMED, M.Sc.*; MOHAMED M. KHALAF, Ph.D.*; IBRAHIM G. IBRAHIM, M.D.** and NANCY H. ABO EL-NOUR, Ph.D.*

The Department of Physical Therapy for Surgery, Faculty of Physical Therapy and Department of Plastic Surgery, Faculty of Medicine**, Cairo University*

Abstract

Background: Hypertrophic scar is the most common complication of burn injuries that may lead to functional disability. Application of Potassium Iodide iontophoresis can soften and remove collagen, which allows scar to be molded and stretched.

Purpose: The aim of this study was to evaluate the effect of Potassium Iodide iontophoresis in treating hypertrophic scar.

Methods: Thirty patients with age ranged from 25 to 40 years with hypertrophic scar over upper extremity participated in this study. The patients were randomly selected from different clinics and hospitals in Giza and divided into 2 equal groups. Group A (study group): Received in Potassium Iodide iontophoresis and traditional physical therapy (stretching, strengthening exercises, elastic bandage and medication). Group B (control group): Received only traditional physical therapy (stretching, strengthening exercises, elastic bandage and medication) three times per week for 8 weeks. Measurements of scar were done using modified vancouver scar scale and ultrasonography, which collected before treatment and after the end of treatment.

Results: There were no significant difference in scar assessments pre study measures between both groups. Post-treatment there were significant improvement in scar assessments (ultrasonography and modified vancouver scar scale) in study group compared with control group ($p=0.002$ and $p=0.001$) respectively.

Conclusion: Potassium Iodide iontophoresis program was considered as an effective method for hypertrophic scar management in post burned patients in expression of decreasing thickness and firmness.

Key Words: Potassium Iodide (KI) – Iontophoresis (IP) – Hypertrophic scar (HTS).

Introduction

HYPERTROPHIC Scar (HTS) following surgical procedures, trauma and especially burns is a great concern for patients and a challenging problem for clinicians. HTS cause significant functional and cosmetic decrease in quality of life [1].

Scar formation is the most common complication of burn injuries that leads to functional and aesthetic. HTS usually develop within one to three months after injury, in contrast with keloid scars that may appear up to 12 months after injury. HTS is the result of an excessive response to a skin injury which usually occurs 6-8 weeks after the reepithelialization of a burn injury that has involves the reticular layer of the dermis [2].

Iontophoresis which is the facilitated movement of ions across a membrane under the influence of an externally applied small electric potential difference ($0.5\text{mA}/\text{cm}^2$ or less), is one of the most promising novel drug delivery system, which has proved to enhance the skin penetration and the release rate of number of drugs having poor absorption/permeation profile through skin [3].

Potassium Iodide (KI) 10 percent solution is the recommended choice for treating scar and tendon adhesions. Potassium iodide can soften and remove collagen, which allows an area to be molded and stretched [4].

Material and Methods

The study was done in El-Helal Hospital from March 2016 till April 2017. In this study, 30 patients with hypertrophic scar over upper extremity were

Correspondence to: Dr. Salma A. Mohamed, The Department of Physical Therapy for Surgery, Faculty of Physical Therapy, Cairo University

assigned randomly into two equal groups (study and control groups) of equal number. Group (A): The study group received potassium iodide iontophoresis for 8 weeks three times per week in addition to traditional physical therapy program (elastic bandage, R.O.M. exercises, A.D.L. activities, stretching and strengthening exercises) plus routine medical treatment. Group (B): The controlled group received only traditional physical therapy program (elastic bandage, R.O.M. exercises, A.D.L. activities, stretching and strengthening exercises) plus routine medical treatment (Ravi 2 ointment for 3-5 times per day).

Inclusive criteria:

Patient ages ranged from 25 to 40 years in both sexes with hypertrophic scar over upper extremity, they were 3 months or more after burn, they had second degree of burn and all had hypertrophic scar caused by flame burn injury.

Exclusive criteria:

Patients who had any skin abnormalities (cancer, psoriasis), any other degrees of burn (third, fourth), any other types of burn (electric, chemical) and who had skin grafts were excluded.

Ethics:

The protocol of this study was approved by the Ethical Committees of the Faculty of Physical Therapy (Cairo University, Egypt). Every patient applied informed consent before starting the study. All participants were informed about the nature and the effect of the treatment and measurement devices. The patients were also instructed to report any side effects during the treatment sessions.

Measurements:

A- Modified vancouver scar scale:

Clinical assessment tool rated and scored scar according to pliability, vascularity, height, pigmentation, pain and pruritis. It was used before and after the end of treatment (after 2 months) for both groups of patients [5].

B- Ultrasonography:

GE Voluson E6 Ultrasound System was used to evaluate the thickness of the affected area in relation to a fixed point for every measurement to determine changes in skin thickness from the start of the study. Measurements were performed by the same investigator. Measurements were taken before and after the end of treatment (after 2 months).

Treatment procedures:

Group A (Experimental, KI group). The patient was placed in suitable position and was asked to take off the clothes in the treated area only, the patients received potassium iodide iontophoresis in addition to the medication and traditional physical therapy program in the following steps: 1) The treatment was applied for 20min., 3 times per week for 8 weeks. 2) The current was slowly increased to initial desired amplitude (1-2mA) for (3-5min.) then increased to higher level (3-4mA) for the rest of treatment time. They received also traditional physical therapy.

Group B (control group): Patients in the control group received only traditional physical therapy as stretching exercises for the tightened muscles using stretch relax techniques for 10 minutes, strengthening exercises for surrounding muscles using dolerme technique for 10 minutes, elastic bandage were worn for 18-24h. And moisturizing cream for 3-5 times per day.

Statistical procedures:

Descriptive statistics and *t*-test were conducted for comparison of subject characteristics between groups. *t*-test was conducted to compare mean values of scar thickness and MVSS between both groups; and paired *t*-test was conducted to compare between pre and post-treatment mean values of the measured variables in each group. The level of significance for all statistical tests was set at $p < 0.05$. All statistical tests were performed through the Statistical Package for Social Sciences (SPSS) Version 19 for windows (IBM SPSS, Chicago, IL, USA) [6].

Results

All the patients involved in the study have been continued the study until the end of it. None refused or withdrawn. The study group consisted of 15 patients (5 males and 10 females). Their ages ranged from 25-40 years with a mean value of 31.06 ± 4.28 , the control group consisted of 15 patients (4 males and 11 females) with a mean value of ages 33.6 ± 4.92 . There were no significant differences between both groups in the mean value of patients' ages and sexes.

- Within group comparison:

There was a significant decrease in scar thickness and MVSS post-treatment in the study group compared with that pre-treatment ($p=0.0001$). The percent of decrease in scar thickness and MVSS

were 20.31% and 27.1 respectively (Table 2) & Fig. (1).

Regarding control group, there was a significant decrease in scar thickness ($p=0.0001$) and significant decrease in MVSS ($p=0.001$) post-treatment compared with that pre-treatment. The percent of decrease in scar thickness and MVSS were 9.05% and 11.96 respectively (Table 1) & Fig. (1).

Comparison between groups:

There was no significant difference between both groups in scar thickness and MVSS pre-treatment ($p>0.05$). Comparison between groups post-treatment revealed a significant decrease scar thickness ($p=0.002$) and MVSS ($p=0.001$) of the study group compared with that of the control group, (Table 2) & Fig. (1).

Table (1): Comparison of scar thickness and MVSS between pre and post-treatment in study and control groups.

	$\bar{X} \pm SD$		MD	% of change	t-value	p-value
	Pre-treatment	Post-treatment				
<i>Study group:</i>						
• Scar thickness (mm)	15.06±0.96	12±1.19	3.06	20.31	11.5	0.0001 **
• MVSS	10.33±1.54	7.53±1.92	2.8	27.1	10.69	0.0001 **
<i>Control group:</i>						
• Scar thickness (mm)	14.8±1.14	13.46±1.18	1.34	9.05	7.13	0.0001 **
• MVSS	11.2±1.32	9.86±1.68	1.34	11.96	4.18	0.001* *

\bar{x} : Mean. MD : Mean Difference. **: Significant.
SD : Standard Deviation. p-value : Probability value.

Table (2): Comparison of scar thickness and MVSS between study and control groups pre and post-treatment.

	$\bar{X} \pm SD$		MD	t-value	p-value
	Study group	Control group			
<i>Pre-treatment:</i>					
• Scar thickness (mm)	15.06±0.96	14.8±1.14	0.26	0.69	0.49*
• MVSS	10.33±1.54	11.2±1.32	-0.87	-1.65	0.11*
<i>Post-treatment:</i>					
• Scar thickness (mm)	12±1.19	13.46±1.18	-1.46	-3.37	0.002 **
• MVSS	7.53±1.92	9.86±1.68	-2.33	-3.53	0.001 **

\bar{x} : Mean. MD : Mean Difference. *: Non significant. **: Significant.
SD : Standard Deviation. p-value : Probability value.

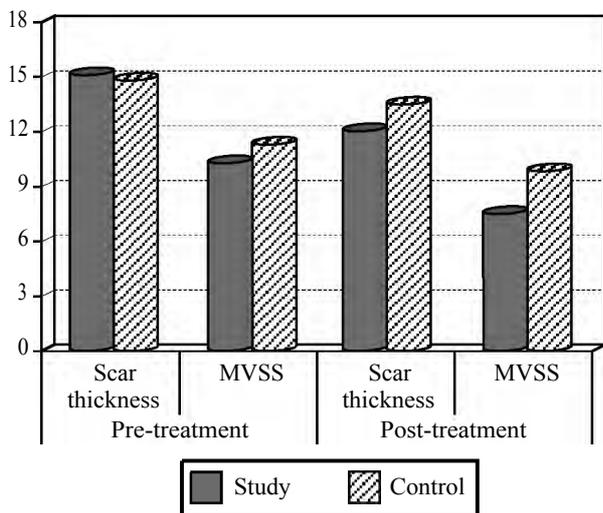


Fig. (1): Mean scar thickness and MVSS of the study and control group pre and post-treatment.

Discussion

A total of 100 million patients develop scars in the developed world alone each year as a result of 55 million elective operations and 25 million operations after trauma [7] Burn injuries, traumatic injuries, and surgical procedures can give rise to exuberant scarring that results in permanent functional loss and the stigma of disfigurement [8].

Excessive scars form as a result of aberrations of physiologic wound healing and may develop following any insult to the deep dermis, including burn injury, lacerations, abrasions, surgery, piercings and vaccinations. By causing pruritus, pain and contractures, excessive scarring can dramatically affect a patient's quality of life, both physically and psychologically [9].

The transdermal route has become one of the most successful and innovative focus for research in drug delivery. Transdermal delivery of drug through the skin to the systemic circulation provides a convenient route of administration for variety of clinical indications. In the development of new transdermal drug delivery the object is to obtain controlled, predictable, and reproducible release of drug into the blood stream of patient. Transdermal device act as drug reservoir and controls the rate of drug transfer [10].

Potassium Iodide (KI) 10 percent solution is the recommended choice for treating scar and tendon adhesions. Potassium iodide can soften and remove collagen, as its antioxidant characteristic which works as a scavenger of hydroxyl radicals that can induce apoptosis and inhibit fibroblast proliferation in tissues which allows an area to be molded and stretched. A patient can increase range of motion and strengthen the overloaded muscle. Using negative polarity for three to six weeks, you can deliver iontophoresis three times weekly. You should expect to see results after 8 to 10 treatments [4].

So this controlled randomized study was conducted to determine the effect of potassium iodide iontophoresis on postburn hypertrophic scar, the results of this study revealed that there were significant differences in scar thickness between the study and control group b p -value $p=0.002$ & $p=0.001$ in ultrasonography & MVSS assessments respectively.

Results of this study concerning the response of hypertrophic scar to potassium iodide iontophoresis come in agree and confirm the observations of Derry, [11]; Manda et al., [12]; Derry, [4]; Curdy et al., [13]; Costa et al., [14], Anghelescu et al., [15].

Derry, [11] presented the use of topical iodine in the form of Lugol's solution (iodine in water) is applied daily to human scars and then covered with plastic wrap, regeneration begins within 2:3 days. Scar improved by 23% after using lugol's solution. Regeneration stops gradually over a few days when iodine applications are stopped. If iodine applications are stopped, a normal adult scar forms that is compatible with the current state of regeneration.

Manda et al., [12] found that feasibility of drug delivery by iontophoresis across the scar skin epidermis was investigated as a potential method for treating scars. The biophysical difference between scar and normal skin epidermis was inves-

tigated as well. Scar and normal skin epidermis excised from the thigh region of human cadaver (female, 41 years life time) supplied by Science Care (Phoenix, Arizona) was stored at -20°C and used within a week. Sodium fluorescein (molecular weight 376.27) was obtained from Sigma-Aldrich Inc. (St. Louis, Missouri). Phosphate-Buffered Saline (PBS) with phosphate buffer concentration of 0.01 M, sodium chloride concentration of 0.154 M, and pH 7.4 were purchased from Sigma-Aldrich Inc. All other chemicals and reagents used were of analytical grade and were procured from Sigma-Aldrich Inc. Scar and normal skin epidermis was mounted between the donor and receiver compartments of the Franz diffusion cell. The receiver compartment was filled with 5mL of PBS and allowed to equilibrate for 2h at $37 \pm 1^{\circ}\text{C}$. The poor absorption of therapeutic agents into the scar as compared with the normal skin is one of the major factors responsible for poor success rate of topical therapy of scars.

Derry, [4] supported the proposed hypothesis potassium iodide iontophoresis initiates, controls, and completes human scar regeneration as his study discussed control of regeneration and wound healing are scientific and clinical objectives. Topical iodine solution applied daily for 3 days to a 50 year old facial scar lead to hyperemic scar tissue and marked improvement. As a working hypothesis, antioxidant characteristic that remove hydroxyl radicals and induce apoptosis, the author proposed topical iodine could initiate, control and complete human scar regeneration.

Curdy et al., [13] showed the objective of the effect of the iontophoresis in the recovery of human skin impedance. A series of metal chloride aqueous solutions (NaCl, KI, CaCl₂, and MgCl₂) was investigated: First at the same concentration (133 mmol/L) and then at the same ionic strength as a NaCl solution at 133mmol/L. The influence of hydration alone was also examined as a control. The recovery of human skin impedance was followed in the frequency range 1-1,000Hz, over a 30-minute period after iontophoresis during which 3 impedance spectra were recorded. The results revealed that at $t=30$ minutes post-iontophoresis, skin impedance was approximately 3 times greater than the value immediately after the cessation of current passage.

Costa et al., [14] showed the versatility of an old drug Potassium Iodide (KI) that continues to be a safe and effective therapeutic option for the treatment of scar, as long as it is properly prescribed and administered. Study performed on 15 patients

with scar and showed marked improvement. It is assumed that potassium iodide has an important anti-oxidant role in inhibition of fibroblastic proliferation, since the patients that show better response for scar. This can be evidenced in the formulations recommended by WHO or even by some reference books and scientific articles on pharmacology, which define the concentration of the saturated solution of potassium iodide as 1 g/mL. They probably use already prepared saturated solutions and dilute them to obtain a concentrated solution (not saturated) of 1 g/mL. In Brazil, we typically use the pure potassium iodide salt (PA) in the therapeutic formulations.

Anghelescu et al., [15] studied the effect of potassium iodide iontophoresis on adhesion and contraction of Hemifacial Spasm (HFS). The actual case refers to a 62 years old Caucasian woman, with a typical progressive left side HFS, manifested at the age of 55. She was treated in a conservative manner, using iontophoresis with potassium iodide (KI) applied to the twitched hemiface, for 10 days, in two therapeutic sequences. After the second treatment session, the patient noticed a 47% global reduction of her disturbances, reflected by the self-assessment questionnaires scores.

Conclusion:

From the previous discussion of these results and according to reports of researches in the field related to the present study, it could be concluded that Potassium Iodide iontophoresis was considered as an effective method for hypertrophic scar management in postburn patients in expression of decreasing thickness and firmness.

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إستجابة ندبات ما بعد الحروق لإنتقال يوديد البوتاسيوم الأيوني

المستخلص: تطبيق الإنتقال الأيوني ليوديد البوتاسيوم لندبات ما بعد الحروق يحفز تليين وإزالة الكولاجين مما يؤدي إلى إستطالة وقولبة الندبات.

الهدف: لمعرفة فاعلية الإنتقال الأيوني ليوديد البوتاسيوم لعلاج ندبات ما بعد الحروق.

الطرق والأساليب: قد أجرى البحث على ثلاثين مريض ممن يعانون من ندبات ما بعد الحروق وتتراوح أعمارهم ما بين ٢٥ إلى ٤٠ عاما وقد تم إختيارهم عشوائيا من مختلف العيادات الخارجية والمستشفيات بمحافظة الجيزة. تم تقسيم الحالات إلى مجموعتين متساويتين المجموعة التجريبية والمجموعة الضابطة. تم تقييم الندبات عن طريق ميزان فانكوفر المعدل والسونار. لقد تم وضع برنامج العلاج لمدة ثمانية أسابيع: المجموعة الأولى: (المجموعة التجريبية): تكونت من ١٥ مريض شاركوا في العلاج بالإنتقال الأيوني ليوديد البوتاسيوم بالإضافة إلى برنامج العلاج الطبيعي التقليدي المكون من (تمارين إستطالة + تمارين تقوية + رباط ضاغط) + (دواء) لمدة ٨ أسابيع ٣ جلسات أسبوعيا بفاصل زمني يوم واحد بين كل جلسة.

المجموعة الثانية: (المجموعة الضابطة): تكونت من ١٥ مريض شاركوا في برنامج العلاج الطبيعي التقليدي المكون من (تمارين إستطالة + تمارين تقوية + رباط ضاغط) + (دواء) لمدة ٨ أسابيع ٣ جلسات أسبوعيا بفاصل زمني يوم واحد بين كل جلسة.

النتائج: وقد أسفرت النتائج عن وجود دلالة إحصائية لتأثير العلاج بالإنتقال الأيوني ليوديد البوتاسيوم في الندبات في المجموعة التجريبية في مقابل المجموعة الضابطة.

الخلاصة: من هذه النتائج يمكن إستدلال أن الإنتقال الأيوني ليوديد البوتاسيوم له تأثير مباشر على تحسن ندبات ما بعد الحرق.