EFFECT OF HYDROCORTISONE IONTOPHORESIS VERSUS HYDROCORTISONE PHONOPHORESIS ON POST SURGICAL SCAR: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Abstract

Background: Surgical scars are major post-surgical complications that cause significant psychological and physical consequences, compromise the quality of life and need intensive intervention.
Objective: The purpose of this study was to compare the effect of hydrocortisone iontophoresis and hydrocortisone phonophoresis on the treatment of surgical scar and overall scar appearance.
Patients and methods: Sixty patients of both sexes (18 males and 42 females) underwent surgery, and had surgical hypertrophic scar took part in this study. Their ages ranged from 20-35 years and they were recruited from Surgical Department-Mansoura Health Insurance Hospital and Horus University in Egypt. Patients were randomized into three groups of equal number (20 patients for each group): Group A: (Iontophoresis group): They received iontophoresis application of hydrocortisone 1%. Group B: (Phonophoresis group): They received phonophoresis application of hydrocortisone 1%. Group C: (Control group). All patients in all groups received their medical treatment (Polydimethylsiloxane cream [twice daily] and Diclofenac Potassium ampoules [once daily]) as well as their conventional physiotherapy treatment (ultrasound and deep friction massage). All outcome measures were measured for all patients before and after 12 weeks of treatment application through tonometer (for measuring pressure load) and Modified Vancouver scar assessment scale (VSS) (for measuring four skin characters including height, pliability, vascularity and pigmentation).
Results: Post treatment, the one-way ANOVA test found that there was a highly significant improvement in pressure load and overall scores of modified Vancouver scar scale (VSS) in both iontophoresis and phonophoresis groups compared with control group as P-value < 0.001.
Conclusion: Appropriate application of either hydrocortisone iontophoresis or hydrocortisone phonophoresis can induce a significant improvement on height, pliability, vascularity and pigmentation of post-surgical scar.

Keywords: Hydrocortisone iontophoresis, Hydrocortisone phonophoresis, Modified Vancouver scar scale (VSS), Post-surgical scar, Tonometer.

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1. INTRODUCTION

Surgical scars have a complex pathogenesis with dermal fibro proliferative disorders. They include excess fibroblast proliferation (fibrous tissue that replaces normal skin) and excess collagen deposition. A scar forms as a result of biological process of wound healing in the skin and other tissues of the body. Thus, scarring is a natural part of the healing process. (1)

Most surgical scars are prominent, erythematous, firm, inflexible, as well as contracted. Collagen and other extracellular matrix proteins establish their structure. The scar's extracellular matrix lacks matured elastin fibers (2)

It may develop either immediately or within months post-surgical incision. Its mass always remains inside

the boundaries of the original wound and may partially regress after initial rapid growth. (1)

Destructive scarring after surgery can lead to permanent disfigurement, which in turn may result in negative self-esteem, social withdrawal, and employment discrimination. it also has severe rehabilitation outcomes such as Disability, impairment, as well as loss of function (3), (4), (5) and (6)

Compression therapy, local / intralesional corticosteroids, excisional surgery, radiotherapy, cryotherapy, laser treatment, silicone gel sheets, as well as a variety of topical and oral drugs are all used in the management of surgical scars. Treatment strategies may consist of one or more of the aforementioned modalities (2) and (7)

Transdermal drug delivery is a promising substitute for the more common routes of medication administration, such as oral administration and intravenous injection. Implementation of ultrasound or direct electrical current to the skin (phonophoresis as well as iontophoresis) rises its permeability and permits the delivery of different substances into and throughout the skin, despite the stratum corneum acting as a barrier that restricts the penetration of substances throughout the skin (5) and (8)

Both iontophoresis and phonophoresis, in which electrical current or ultrasound is utilized to propel a topical application substance throughout tissues, are recent techniques. These physical modalities provide strategies for improving the percutaneous absorption of some medications, which is useful because many pharmaceuticals are poorly absorbed by the skin via passive diffusion only (5)

Hydrocortisone (HC) also recognized as cortisol is a primary corticosteroid which is naturally excreted by the adrenal cortex. Also, it is considered a mild topical corticosteroid that is used to restrict the reaction to stress, decrease swelling, redness, and itching in various inflammatory skin disorders. (9), (10) and (11)

Hydrocortisone acetate is also used for raised dermal surgical scarring and can be used by both iontophoresis and phonophoresis. Hydrocortisone acetate reduces inflammation, alters collagen gene expression, and blocks collagen, glycosaminoglycan production, as well as fibroblast proliferation, all of which contribute to the regression of keloids and hypertrophic scars after their administration. (12) and (13)

Hydrocortisone (HC) has a potent anti-inflammatory and immuno-suppressive effects that help in scar management via inhibition of fibroblast proliferation, downregulation of collagen synthesis and acceleration of collagen breakdown. (9)

Because rarity of researches that have measured the effectiveness of iontophoresis and phonophoresis of hydrocortisone on post-surgical scar. Therefore, this study was to fill this gab and to examine and compare between the effect of hydrocortisone iontophoresis and hydrocortisone phonophoresis on the treatment of surgical scar and overall scar appearance.

2. PATIENTS AND METHODS

A prospective, single-blind randomized controlled study with pre-test post-test design was carried out from 10th August 2021 till 20th March 2022, at Mansoura Health Insurance Hospital and Horus University in Egypt. Sixty patients of both sex (18 males and 42 females) suffering from post-surgical scar about 2-3 months post-surgery took part in this randomized controlled study after signing an informed consent form prior to data collection. They're aged from 20-35 years. Patients were only included if they are medically and clinically stable. On the fifth of December 2020, after receiving approval from the Ethics Committee of the Faculty of Physical Therapy, Cairo University (No: P.T.REC/012/003047), recruitment started.

The sample size was calculated considering the difference in the Modified Vancouver scar assessment scale – VSS among the 3 groups to be 0.42 (effect size), significance level= 0.05, and with 80% power. The sample size was calculated to be 20 patients per group, 1:1:1 ratio. The presumed effect size was based on a pilot study of 5 patients in each group. Sample size calculation was conducted using G*POWER statistical software [version 3.1.9.2; Universität Kiel, Germany] and F tests- One way ANOVA.

The patients were randomized into Iontophoresis group (n=20), Phonophoresis group (n=20) as well as control group (n=20) by a blinded research assistant who opened sealed envelopes containing a computer-generated randomization cards.

- **Exclusion criteria**

The following conditions resulted in patient exclusion: Patients having implanted electronic devices, such as cardiac pacemakers, must take special precautions to prevent ultrasound interference. Those with diabetes, cardiovascular problems, or a previous history of skin cancer in the treatment region were also excluded as these disorders may alter sensation, delay healing process and worsen the scar which counteract with the goal of the study. Uncooperative patients and obese patients (BMI $\geq$ 30) were also excluded in order to achieve best results.

- **Inclusion criteria**

The patients took part in this randomized controlled study after signing an informed consent form prior to data collection. The patients were of both sexes and all of them were conscious and ambulant. They're aged from 20-35 years. All patients were suffering from hypertrophic scar about 2-3 months post

abdominal or shoulder surgery. All patients were free from any other pathological conditions or dysfunctions that may affect the study such as hematoma, infection and stitch abscesses. All patients of the study received the same approach of medications. All patients received a good explanation of treatment and measurement procedures. The size of the scar was varied from 5cm*10cm*15cm.

MEASUREMENT PROCEDURES

1. Tonometer:

It is an objective valid and reliable device used for measuring pressure load (mmHg) on scar tissue through measuring scar tissue viscoelastic deformation that provided most useful information about scar pliability (elasticity) and directly reflecting the effect of the scar on movement, function as well as quality of life. (14) and (15)

Following a burn injury (Zhang, 2019) showed that the tonometer had an excellent intra-rater measurement reliability, with ICCs between 0.878 and 0.945 for hypertrophic scarring as well as 0.96 for normal skin. (16)

Because it provides a continuous deformation force with nothing more complicated than a series of small weights, the tissue tonometer is not required to be calibrated on a regular basis. The measurement area is placed directly under the tissue tonometer, which is a weighted device. A blunt piston is pressed into the tissue by the weight, and the resulting output reading is shown. The measurements are proportional to the tissue's pliability. (17)

The tonometer has a 1-mm-diameter plunger and uses a 200-gram weight to create a constant force equal to 29.6 kg / cm2. The depth to which the plunger could be depressed into the tissue indicated the tissue's pliability. An analog dial was used to measure the depth of the skin depression in mm (sensitivity, 0.01 mm). (18)

Principles and procedures of measurement: (16) and (18)

All scar treatments were removed and allow the patient to rest for 5 minutes prior to measurement. All measurement procedures were explained to the patient.

Scar surface (limb) was positioned horizontal as much as probable on a hard surface. The utilization of folded towels as well as sand bags may help. Avoid using soft pillows.

The sites to be measured were divided into multiple points and were marked with a permanent marker on an individual patient transparent template that was positioned directly on the site of the scar. Accurate reevaluations of scar pliability over time require a marking method that remains consistent over time.

The base plate of the modified tissue tonometer (MTT) is not transparent and covers the indicated points, so The MTT base plate was applied directly to the tissue via the holes done in the transparent template which were slightly greater than the size of the base plate.

Measurements were achieved by holding MTT vertically, and ensuring no additional downward pressure was done while putting the device on the tissue.

After no more than 6 seconds, measure the depth of the plunger depression in millimeters in order to avoid tissue hypoxia that might be caused from prolonged pressure, provided that the patient must be capable of staying immobile while the MTT is in contact.

Every point measurement was repeated 3 times using the same technique and then the mean of three repeated trials for each point was taken.

Each point should be measured after a minimum of 2 minutes of resting to allow for adequate tissue reconstruction time and for the instrument to be calibrated on a firm surface. For follow up, a larger value of MTT reading (T) indicates more pliable scar and so more improvement.

2. Modified Vancouver scar assessment scale: (19)

Table (1): Modified Vancouver scar assessment scale

Skin characteristics	Parameters
Pliability	
0	Normal
1	Supple
2	Yielding
3	Firm
4	Ropes
5	Contracture
Height	
0	Flat
1	< 2 mm
2	2 - 5 mm
3	> 5 mm

Vascularity/erythema	
0	Normal
1	Pink
2	Red
3	Purple
Pigmentation	
0	Normal
1	Hypo-pigmented
2	Mixed
3	Hyper-pigmented

TREATMENT PROCEDURES

All patients in the treatment groups completed a 12-weeks treatment program (3 sessions / week) consisting of either hydrocortisone iontophoresis (in iontophoresis group) or hydrocortisone phonophoresis (in phonophoresis group) in addition to their medical treatment (in the form of Polydimethylsiloxane cream [twice daily] and Diclofenac Potassium ampoules [once daily]) and also traditional physical therapy program in the form of ultrasound and deep friction massage.

All patients in control group completed a 12-weeks treatment program (3 sessions / week) consisting of their medical treatment (in the form of Polydimethylsiloxane cream [twice daily] and Diclofenac Potassium ampoules [once daily]) as well as their conventional physiotherapy program in the form of ultrasound and deep friction massage only.

Hydrocortisone iontophoresis:

The hydrocortisone saline solution (5 mL of 1% Hydrocortisone) was poured directly onto the sponges of the active rubber electrode (negative electrode) during each session of iontophoresis, which used direct current. (20)

An active (negative) electrode (50-70 cm2) was positioned at the scar site, and a passive (positive) electrode (80-120 cm2) was positioned elsewhere, at a distance appropriate to the passive electrode's size. The drug was transmitted to the skin from the negative pole. (21)

For efficient drug transmission, all patients underwent 36 sessions. The direct current was applied at an intensity of 40 milliamperes per minute (mA/min) for a total of 20 minutes throughout each session. Therefore, the current was raised until the patient felt it, but not higher than necessary. (20)

Hydrocortisone phonophoresis:

The hypertrophic scar was prepared for hydrocortisone phonophoresis by applying a thin film of coupling medium (gel), and then an adequate amount of 1% hydrocortisone was placed over the scar using a syringe. Then, pulsed ultrasound was done by the therapist using 5 cm2 ultrasound head with perpendicular contact with the skin in a slow circular movement. The ultrasound parameters were as the following: (mode: pulsed ultrasound – a frequency of 1 MHz – with an intensity: 0.5 W/cm2 – duration: 5 minutes – treatment duration: 36 sessions with rate of 3 sessions per week). (2)

OUTCOME MEASURES

The primary measures for determining treatment outcomes were pressure load (mmHg) and scores of Modified Vancouver scar assessment scale (pliability, height, vascularity, pigmentation and total score). Patients were assessed in comfortable position and the assessed part was carefully cleaned and hydrated. The measurement tools were Tonometer and Modified Vancouver scar assessment scale. All measures were assessed before treatment application (pre-treatment) and after 12 weeks of treatment application (post-treatment) for each patient in all three groups of the study (iontophoresis group, phonophoresis group and control group).

STATISTICAL ANALYSIS:

Statistical testing was done with SPSS 28.0 (Statistical Package for the Social Sciences).

If the P-value was less than 0.05, the differences were considered significant. Age, height, weight, as well as body mass index were presented as means and standard deviations across all three groups, while the distribution of gender was presented as frequencies and percentages. Paired t-test was utilized to test the differences in measured variables within groups pre and post treatment for parametric data, whereas One-way ANOVA test utilized to test the differences in the measured variables between groups pre and post treatment for parametric data. Pairwise comparisons were conducted using post hoc (Bonferroni) test to compare the differences in outcome measures between groups post treatment in case of overall significance.

3. RESULTS

The aim of this study was to compare the impact of hydrocortisone iontophoresis and hydrocortisone

phonophoresis on the treatment of surgical scar and overall scar appearance.

This study was intended to present the collected data as patients' demographic data, scores of Modified Vancouver scar assessment scale (pliability, height, vascularity, pigmentation as well as total score) and pressure load (mmHg). Scores of Modified Vancouver scar assessment scale (pliability, height, vascularity, pigmentation as well as total score) and pressure load (mmHg) were assessed before and after 3 successive months of intervention for each patient in all groups of the study.

Demographic and clinical characteristics of patients

The demographic data of the patients in all groups, such as age, weight, height, as well as BMI, were compared using a one-way ANOVA test, and the results showed no significant differences among groups ($p > 0.05$), as demonstrated in **Table (2).**

Gender distribution of patients

The frequency distribution of gender between groups, was compared using a Chi-squared test, and the results showed no significant difference among groups (p-value > 0.05, as demonstrated in **Table (2).**

Table (2): Demographic and clinical characteristics of patients in all groups

Variables	Age (years)	Height (cm)	Weight (kg)	BMI (Kg/m^2)	Gender [N (%)]	
					Male	Female
Group A (20) ($\bar{x}$ ± SD)	25.73 ± 3.71	165.26 ± 6.47	73.6 ± 8.84	26.88 ± 1.85	8 (40 %)	12 (60 %)
Group B (20) ($\bar{x}$ ± SD)	26.6 ± 4.27	168.46 ± 6.15	72.0 ± 7.76	26.12 ± 1.13	6 (30 %)	14 (70 %)
Group C (20) ($\bar{x}$ ± SD)	25.73 ± 3.82	166.33 ± 4.8	73.46 ± 6.78	26.52 ± 1.72	4 (20 %)	16 (80 %)
F-Value	0.241	1.16	0.192	0.852		
P-Value	0.787	0.826	0.323	0.434	0.757	
χ^2					0.556	
Sig.	NS	NS	NS	NS	NS	

$\bar{x}$: Mean χ^2: Chi square test P-Value: Probability value
SD: Standard Deviation f-value: one-way ANOVA test NS: Non-significant.

Pre and post treatment comparison in mean scores of all outcome measures for each group (within groups)

In each group (group A, B and C), "Paired t-test" showed that there was a highly substantial difference in mean scores of all outcome measures within each group after 12 weeks of treatment application (post treatment) when compared to pre-treatment ($P < 0.05$) **Table (3).**

Comparison of pre-treatment values in all outcome measures between groups

One-way ANOVA test showed that there was no substantial difference among groups in all outcome measures pre-treatment as P-value = 0.774. **Table (3).**

Comparison of post treatment values in all outcome measures between groups

One-way ANOVA test showed that there was a highly substantial difference among groups in all outcome measures post treatment as P-value < 0.001. **Table (3).**

Table (3): comparison of pre and post treatment values in all outcome measures for all groups (within & between groups)

Variables	Group A (20) ($\bar{x}$ ± SD)	Group B (20) ($\bar{x}$ ± SD)	Group C (20) ($\bar{x}$ ± SD)	F-Value	P-Value	Sig.
VSS (Pliability)						
Pre	4.40 ± 0.50	4.50 ± 0.51	4.53 ± 0.52	0.257	0.774	NS
Post	1.25 ± 0.44	1.60 ± 0.50	3.30 ± 0.47	107.52	< 0.001*	S
t-value	38.45	42.13	8.72			
P-Value	< 0.001	< 0.001	< 0.001			
Sig.	S	S	S			
% of change	↓ 72.59 %	↓ 64.44 %	↓ 27.15 %			

VSS (Height)						
Pre	2.75 ± 0.44	2.90 ± 0.30	2.91 ± 0.31	1.163	0.320	NS
Post	1.0 ± 0.0	1.20 ± 0.41	2.0 ± 0.46	44.33	< 0.001*	S
t-value	17.61	16.17	13.07			
P-Value	< 0.001*	< 0.001*	< 0.001*			
Sig.	S	S	S			
% of change	↓ 63.63 %	↓ 58.62 %	↓ 31.27 %			
VSS (Vascularity)						
Pre	2.65 ± 0.49	2.70 ± 0.47	2.90 ± 0.30	1.891	0.160	NS
Post	0.75 ± 0.44	1.30 ± 0.47	2.80 ± 0.41	115.108	< 0.001*	S
t-value	19.0	12.45	1.45			
P-Value	< 0.001*	< 0.001*	< 0.001*			
Sig.	S	S	S			
% of change	↓ 71.70 %	↓ 51.85 %	↓ 3.44 %			
VSS (pigmentation)						
Pre	2.80 ± 0.41	2.81 ± 0.40	2.83 ± 0.43	0.01	0.998	NS
Post	1.20 ± 0.41	1.40 ± 0.50	2.60 ± 0.51	51.063	< 0.001*	S
t-value	14.23	9.20	2.18			
P-Value	< 0.001*	< 0.001*	< 0.001*			
Sig.	S	S	S			
% of change	↓ 57.14 %	↓ 50.17 %	↓ 8.13 %			
VSS (total score)						
Pre	12.65 ± 0.74	12.90 ± 0.55	13.10 ± 0.72	2.216	0.118	NS
Post	4.20 ± 0.41	5.50 ± 0.68	10.70 ± 0.66	661.088	< 0.001*	S
t-value	45.77	65.84	21.35			
P-Value	< 0.001*	< 0.001*	< 0.001*			
Sig.	S	S	S			
% of change	↓ 66.80 %	↓ 57.36 %	↓ 18.32 %			
Pressure load (mmHg)						
Pre	11.40 ± 1.90	12.69 ± 1.65	12.70 ± 3.63	1.712	0.190	NS
Post	4.40 ± 0.41	5.98 ± 1.16	10.26 ± 4.51	661.088	< 0.001*	S
t-value	15.82	15.12	3.78			
P-Value	< 0.001*	< 0.001*	< 0.001*			
Sig.	S	S	S			
% of change	↓ 61.40 %	↓ 53.11 %	↓ 19.21 %			

P-Value: Probability value NS: Non-significant
F-Value: one-way ANOVA test S: Significant

Pairwise comparisons were conducted using post hoc (Bonferroni) test to compare the differences in all outcome measures between groups post treatment and revealed that there was a highly substantial difference among group A & group C in favor of group A. Additionally, there was a highly substantial difference among group B & group C in favor of group B. While, in comparing group A & group B there was no substantial difference among them post treatment as regard VSS pliability, height, pigmentation and pressure load (mmHg), but as regard VSS vascularity and total score there was a substantial difference among group A and B post treatment in favor to group A. **Table (4).**

Table (4): comparison of the difference in all outcome measures between groups post treatment

Multiple pairwise comparisons between both groups (group effect)				
VSS (Pliability)				
Group effect		**MD**	**P-value**	**Significance**
Post-treatment	Group A vs. Group B	-0.35	0.068	NS
	Group A vs. Group C	-2.05	< 0.001*	S
	Group B vs. Group C	-1.70	< 0.001*	S
VSS (Height)				
Group effect		**MD**	**P-value**	**Significance**
Post-treatment	Group A vs. Group B	-0.20	0.241	NS
	Group A vs. Group C	-1.0	< 0.001*	S
	Group B vs. Group C	-0.80	< 0.001*	S
VSS (Vascularity)				
Group effect		**MD**	**P-value**	**Significance**
Post-treatment	Group A vs. Group B	-0.55	< 0.001*	S
	Group A vs. Group C	-2.05	< 0.001*	S
	Group B vs. Group C	-1.50	< 0.001*	S
VSS (pigmentation)				
Group effect		**MD**	**P-value**	**Significance**
Post-treatment	Group A vs. Group B	-0.20	0.562	NS
	Group A vs. Group C	-1.40	< 0.001*	S
	Group B vs. Group C	-1.20	< 0.001*	S
VSS (total score)				
Group effect		**MD**	**P-value**	**Significance**
Post-treatment	Group A vs. Group B	-1.30	< 0.001*	S
	Group A vs. Group C	-6.50	< 0.001*	S
	Group B vs. Group C	-5.20	< 0.001*	S
Pressure load (mmHg)				
Group effect		**MD**	**P-value**	**Significance**
Post-treatment	Group A vs. Group B	-1.58	0.209	NS
	Group A vs. Group C	-5.86	< 0.001*	S
	Group B vs. Group C	-4.28	< 0.001*	S

P-Value: Probability value MD: mean difference
NS: Non-significant S: Significant

4. DISCUSSION

This study was carried out to discover therapeutic effects of hydrocortisone iontophoresis and hydrocortisone phonophoresis on surgical scar and compare the effect of hydrocortisone iontophoresis and hydrocortisone phonophoresis on the treatment of surgical scar and overall scar appearance.

This study was carried out on sixty patients of both sex. They were suffering from post-surgical scar about 2-3 months post-surgery. They're aged from 20-35 years and they were recruited from Surgical department-Mansoura Health Insurance Hospital and Horus University in Egypt. The study was carried out from 10/8/2021 till 20/3/2022.

Modified Vancouver scar assessment scale (VSS) and tonometer were conducted before and after 12 weeks of treatment application for each patient in all groups.

The result of the present study revealed that there was a significant improvement of post-surgical scar characters in all 3 groups post-treatment. There was highly substantial difference among group A and group C in favor of group A. Additionally, there was a highly substantial difference among group B and group C in favor of group B. Whereas, in comparing group A and group B there was no substantial difference among them post treatment as regard VSS pliability, height, pigmentation and pressure load (mmHg), but as regard VSS vascularity and total score there was a substantial difference among group A and B post treatment in favor of group A.

The result of this study also revealed that hydrocortisone 1% has a potent anti-inflammatory and immuno-suppressive effects that help in scar management via inhibition of fibroblast proliferation, downregulation of collagen synthesis and acceleration of collagen breakdown via inhibition of

the potentially damaging effect of inflammatory cells in non-infected tissues.

Therefore, appropriate application of either iontophoresis or phonophoresis of hydrocortisone 1% can induce a significant effect on post-surgical scar when compared with the traditional physical therapy protocol.

On other hand, there is no substantial difference between the impact of iontophoresis and phonophoresis on the treatment of surgical scar and overall scar appearance. So, the results of this study accept the null hypothesis.

(De Leeuw et al., 2016) studied the effectiveness of hydrocortisone in severely burned patients (septic burn patients who were catecholamine dependent). 39 patients of both sexes were collected and included in the study. The result of this study revealed that there was significant improvement in both inflammation and cosmetic appearance in hydrocortisone group compared to control group post treatment. They concluded that Hydrocortisone as anti-inflammatory drug can diminish capillary leakage, improve hydration status, decrease proteinuria, and decrease amount of fluid administration. So, this study agreed with the results of my study. (22)

(Morsoleto et al., 2015) studied the effect of Hydrocortisone phonophoresis on regeneration of skeletal muscles injuries in twenty Wistar rats. They found significant improvement in Hydrocortisone phonophoresis group in comparison with control group post treatment. The result of this study agreed with my study as they revealed that there were synergetic effects of both ultrasound wave and Hydrocortisone. The ultrasound itself can damage the exposed tissues and drive the inflammatory cells into the treated area. While Hydrocortisone can increase the fibroblast activity, increase collagen deposition and inhibit the potentially damaging effect of inflammatory cells in non-infected tissues. (23)

(Taskaynatan et al., 2007) compared the impacts of hydrocortisone iontophoresis against electrotherapy (ET) on 47 patients having bicipital tendonitis. All patients were given the conventional treatment program of hot packs (15 minutes), ultrasonic (for 5 minutes, with intensity 1.5 w/cm2), as well as exercise. We measured pain, range of motion, and patient satisfaction before, during, and after treatment, as well as a month later. The authors found that there was statistically significant improvement in all of the assessment parameters post-treatment as well as one month later ($P < 0.05$) in the hydrocortisone iontophoresis group compared to electrotherapy group. They found a combination effects of both interferential current as a pain modality and Hydrocortisone as potent anti-inflammatory. Also, they found more deeper penetration of Hydrocortisone due to iontophoresis application that overcome stratum corneum layer of the skin and allow more mobilization of the drug molecules that consisted and agreed with the results of my study. (24)

(Dakowicz and Latosiewicz, 2005) studied the effect of Hydrocortisone iontophoresis as a conservative treatment in 40 patients (35 women and 5 men) with unilateral carpal tunnel syndrome (CTS). By the end of treatment, it was found that there was significant decrease in pain and paresthesia in iontophoresis group compared to control group. This was due to the synergetic anti-inflammatory action of both hydrocortisone and ultrasound that may improve nerve conduction by reducing edema in tissue that surrounds the median nerve. So, the result of this study consisted with the result of my study. (25)

(Koeke et al., 2005) studied and compared the effect of topical application of hydrocortisone, therapeutic ultrasound (US) and Hydrocortisone phonophoresis on 40 male rat's Achilles tendon repair process after tenotomy. They found significant improvement in both ultrasound and Hydrocortisone phonophoresis groups compared to other groups, but the Hydrocortisone phonophoresis group was more superior and more significant than ultrasound group.

The most significant results in Hydrocortisone phonophoresis group were due to piezoelectric features of ultrasound waves that create electrical potentials of low amplitude on collagen tissues. The interaction between ultrasonic waves and collagen molecules increases the fibroblast activity, production of collagen and fibers deposition in the site of injury that stimulates tissue repair process.

On other hand, heat and cavitation are the mechanisms which facilitate the transdermal drug delivery in phonophoresis process. Heat can increase the kinetic energy of the drug molecules, increase the circulation in treated areas, dilate hair follicles and sweat glands. These physiological changes can overcome the stratum corneum layer and facilitate the penetration as well as diffusion of the drug molecules. Cavitation can make structural disorders on the epidermis layer which in turn facilitate the penetration as well as diffusion of the drug molecules. (26)

The findings of this study come in contradiction with the findings of (Bare et al., 1996) who measured cortisol levels in order to evaluate whether or not hydrocortisone phonophoresis improved the absorption of hydrocortisone through the skin. 16 subjects between 18 and 33 years old without symptoms of any ongoing inflammatory conditions were included in this study. The authors found that there was no substantial difference in serum cortisol level after application of hydrocortisone phonophoresis. hence, we draw the conclusion that hydrocortisone does not penetrate the epidermis and enter the underlying vasculature. This might be due to short treatment duration as all subjects had one session of ultrasound therapy alone and one session of hydrocortisone phonophoresis and this was totally

differed from my study with a 12 weeks of total treatment duration and so it was not enough to elicit desired results. (27)

(Melo-Silva Junior et al., 2018) studied the efficacy of Losartan (0.1 mg / mL), Hydrocortisone (0.2 mg / mL) and Acetylsalicylic acid (ASA) (3 mg / mL) in preventing the development of fibrous scar tissue in skeletal muscles of Wistar rats.

The authors found that there was a significant difference in Losartan group (LG) in the form of presence of smallest fibrotic area compared to both Hydrocortisone (HG) and Acetylsalicylic acid groups (ASA). Additionally, there was no substantial difference among Hydrocortisone group (HG) and Acetylsalicylic acid group (ASA). This was in contradiction with the results of my study and this might due to small concentration of Hydrocortisone solution (0.2 mg / mL) that was totally differed from Hydrocortisone concentration in my study (1 mg / mL). (28)

Limitations of the study

Much effort was made with each patient to minimize the effect of any errors that might have been introduced by the nature of the study itself. the study was limited by the following: Sample size is insufficient, Human error in administering diagnostic or treatment processes; patients' cooperation during the treatment.

5. CONCLUSION

On the basis of the present data, it is possible to conclude that application of either hydrocortisone iontophoresis or hydrocortisone phonophoresis in combination with traditional physical therapy treatment (in the form of ultrasound and deep friction massage) on post-surgical scar can cause more significant improvement of overall scar characters such as Height, Pliability, Vascularity, and Pigmentation than traditional physical therapy alone.

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Conflicts of interest

There is no conflict of interest

6. REFERENCES

1. **Song J., Li X., & Li J. (2020):** "Emerging evidence for the roles of peptide in hypertrophic scar". Life sciences. (241): 117-174.
2. **Wahba E., Hamada H., and Khatib, A. (2019):** "Effect of silicone gel versus Contractubex or corticosteroid phonophoresis for post-burn hypertrophic scars: a single-blind randomized controlled trial". Physiotherapy Quarterly, 27(1): 1-5.
3. **Tosa M. and Ogawa R. (2020):** "Photodynamic therapy for keloids and hypertrophic scars: a review". Scars, Burns & Healing (6), 2059513120932059.
4. **Wafaa H., Salah el-din M., Eman M. and Moataz M. (2016):** "Contractubex Versus Corticosteroid Phonophoresis on Burn Hypertrophic Scar". Med. J. Cairo Univ., 84 (2): 63-67.
5. **Gerd G., Gauglitz, Hans C., Korting, Tatiana P., Thomas R., Marc G. and Jesch K. (2011):** "Hypertrophic Scarring and Keloids: Pathomechanisms and Current and Emerging Treatment Strategies". Mol. Med., (17) (1-2): 113-25.
6. **Engrav H., Loren, Garner L., Warren and Tredget E. (2007):** "Hypertrophic Scars". Journal of Burn Care & Research, 28: (4).
7. **Anthonissen M., Daly D., Janssens T. and Kerckhove E. (2016):** "The effects of conservative treatments on burn scars: a systematic review". Burns.; 42 (3): 508–518.
8. **Aharon A., Luai K., Giora E. and Joseph K. (2014):** "Ultrasound mediated transdermal drug delivery". Advanced Drug Delivery Reviews; (72): 127-143.
9. **Tou K., Cawley A., Bowen C., Sornalingam K., & Fu S. (2022):** "Measurements of hydrocortisone and cortisone for longitudinal profiling of equine plasma by liquid chromatography–tandem mass spectrometry". Drug Testing and Analysis. 14 (5): 943-952.
10. **Papp K., Papp A., Dahmer B. and Clark C. (2012):** "Single-blind, randomized controlled trial evaluating the treatment of facial seborrheic dermatitis with hydrocortisone 1% ointment compared with tacrolimus 0.1% ointment in adults". J Am Acad Dermatol; 67: e11–5.
11. **Rovelli F., Mercuri S. and Naldi L. (2011):** "Seborrheic dermatitis in clinical practice". Recenti Prog Med; 102: 126–33.
12. **Jalali M. and Bayat A. (2007):** "Current use of steroids in management of abnormal raised skin scars". Surgeon; 5:175–80.
13. **Ud-Din S. and Bayat A. (2013):** "Strategic management of keloid disease in ethnic skin: a structured approach supported by the emerging literature". Br. J. Dermatol. 169 Suppl (3) 71–81.
14. **Magliaro A. and Romanelli M. (2003):** "Skin hardness measurement in hypertrophic scars". Wounds (15): 66–70.
15. **Sara U. and Ardeshir B. (2014):** "New Insights on Keloids, Hypertrophic Scars, and Striae". Dermatol. Clin. (32): 193–209.
16. **Zhang W., (2019):** "Objective assessment of the Pliability of Hypertrophic Scar, a Systematic Review". Oral presentation at The 12th Asia-Pacific Burn Conference, Singapore.

17. **Oliveira G., Chinkes D., Mitchell C., Hawkins H. and Herndon D. (2005):** "Objective assessment of burn scar vascularity, erythema, pliability, thickness, and planimetry". Dermatol Surg; 31:48.
18. **Lye I., Edgar D. and Wood F. (2006):** "Tissue tonometry is a simple, objective measure for pliability of burn scar: Is it reliable?". J. Burn Care Res. (1): 82–5.
19. **Lee K., Bamford A., Gardiner F., Agovino A., Horst B., Bishop J., Grover L., Logan A. and Moiemen N. (2020):** "Burns objective scar scale (BOSS): Validation of an objective measurement devices based burn scar scale panel". J. Burns. (46): 110-120
20. **Seda B., Arzu R., Ebru K. and Kerem B. (2018):** "The short-term effectiveness of low-level laser, phonophoresis, and iontophoresis in patients with lateral epicondylosis". Journal of Hand Therapy: 1-8.
21. **Simsek N. and Kirdi N. (2016):** "Elektroterapide Temel Prensipler". Ankara: Hipokrat.
22. **De Leeuw K., Niemeijer S., Eshuis J., Nieuwenhuis K., Beerthuizen M., and Janssen T. (2016):** "Effect and mechanism of hydrocortisone on organ function in patients with severe burns". Journal of critical care. (36): 200-206.
23. **Morsoleto M., Morsoleto F., Alves de Matos A., Morgado F. and Anaruma C. (2015):** "A Study of the Effects of Phonophoretic Application of Hydrocortisone on the Regeneration of Injuries to Skeletal Muscle". Microscopy and Microanalysis. 21 (S5): 77-78.
24. **Taskaynatan A., Ozgul A., Ozdemir A., Tan K. and Kalyon A. (2007):** "Effects of steroid iontophoresis and electrotherapy on bicipital tendonitis". Journal of Musculoskeletal pain. 15(4): 47-54.
25. **Dakowicz A. and Latosiewicz R. (2005):** "The value of iontophoresis combined with ultrasound in patients with the carpal tunnel syndrome". Rocz Akad Med Bialymst. (50): 196-198.
26. **Koeke P., Parizotto N., Carrinho P. and Salate, A. (2005):** "Comparative study of the efficacy of the topical application of hydrocortisone, therapeutic ultrasound and phonophoresis on the tissue repair process in rat tendons". Ultrasound in medicine & biology, 31(3): 345–350.
27. **Bare A., McAnaw M., Pritchard A., Struebing J., Smutok M., Christie D. and Seal L. (1996):** "Phonophoretic delivery of 10% hydrocortisone through the epidermis of humans as determined by serum cortisol concentrations". Physical therapy, 76(7): 738-745.
28. **Melo-Silva Junior O., Nunes C., Corrêa T., Silva M., Freitas L. and Alberti L. (2018):** "Comparison of the efficacy of losartan, hydrocortisone and acetylsalicylic acid (ASA) in preventing the development of fibrous scar tissue in skeletal muscle". Revista Brasileira de Medicina do Esporte. 24: 418-421.