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EFFECT OF CRYOTHERAPY ON HYPERTROPHIC SCAR

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ABSTRACT

Background: Hypertrophic scar formation is a major clinical problem in the developing and industrialized worlds, Cryotherapy is the local or general use of low temperatures in medical treatment.

Purpose: The purpose of the study was to evaluate the therapeutic effect of cryotherpy in treating hypertrophic scar.

Method: Sixty patients who had hypertrophic scar participated in this study. Their ages ranged from 20 to 40 years. The participants were selected from Deraya university outpatient clinic and EL Minia University Hospital. They were randomly distributed into two equal groups. Group A (control group): This group received routine medical treatment and routine physical therapy including (stretching Exercises, Positioning and splinting, Pressure Therapy and Massage). Group B (study group): This group received cryotherapy for 10 minutes at -14 degree, 2 sessions per week, for 10 weeks in addition to routine medical and physical therapy treatment. Measurements were done using MAPS and were recorded in the first visit as a base line and after 3 months of treatment.

Results: There was a statistically significant difference between groups in the study group compared with the control group regarding post treatment data of surface, height, thickness, color, pigmentation and the total score of MAPS where p value equals (0.005, 0.0001, 0.0005, 0.0021, 0.00016, < 0.00001) respectively.

Conclusion: Cryotherapy had significant effect in improving the outcome and treating hyper trophic scar.

Key words: Cryotherapy / hyper trophic scar / MAPS / burn.

Introduction

Hypertrophic scars and keloids are anomalous injury reactions in which connective tissue react to injury, irritation, medical procedure, or burns[1].

The primary challenge to scar treatment starts with the straightforward distinguishing proof and conclusion of the risky anomalous of wound, Hyper trophic

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scars are regularly raised, ruddy or pink, and sometimes pruritic but don't pass the edges of the initial wound, though keloids penetrate into encompassing normal tissue[2].

Chronic inflammation or infection due to the severity of the injury cause prolonged wound healing process and contributes to severe scarring and this is common mechanism that make patients sometimes end up with hypertrophic scar (HTS) formation[3].

Due to their capacity to produce excessive collagen in irregular wound healing conditions, fibroblasts and myofibroblasts play an important role in hypertrophic scar formation[4].

There is growing evidence indicates that other cells, such as keratinocytes and mast cells, are actively involved in scar pathogenesis when co-cultured with keratinocytes, fibroblasts showed substantial proliferation behavior[5].

Intercommunication of epidermal keratinocytes may also promote the proliferation of dermal fibroblasts while decreasing collagen output[6].

The process of cryotherapy was primarily required to transfer the cold to tissues. Owing to intracellular hyperosmotic conditions, cell damage starts when the freezing shock has just entered the tissues leading to Rapid transfer of electrolytes, thus growing the intracellular portion that has been accused of destroying cell proteins and enzyme systems, thrombosis has been observed as a cause of irreversible tissue loss even in mild freezes in the microcirculation system. In addition, inflammation eventually leads to necrosis, sequence repetitions increase cell deaths[7].

Melanocytes have been referred to begin the depletion process between -4 and -7 ° C, while death of keratinocytes and connective tissue cells occurs only at -14 ° C. Regarding the basic mechanism, this procedure has been used at lower temperatures, and is also available with high success rates for certain dermatological conditions[8].

The cryotherapy used to facilitate subzero temperature freezing of the tissue, resulting in tissue damage and subsequent second-intention healing[9].

The purpose of the study was to evaluate the therapeutic effect of cryotherpy in treating hypertrophic scar.

Furthermore the need of this study was developed from the lack in the quantitative knowledge and information in the published studies about the effect of cryotherapy on hypertrophic scar.

Subjects and Methods

Sixty patients who had hypertrophic scar participated in this study. Their ages ranged from 20 to 40 years. The participants were selected from Deraya university outpatient clinic and EL Minia university hospital, randomly distributed into two equal groups.

Group A (control group): This group included 30 patients who received routine medical treatment and routine physical therapy as (Stretching exercises, Positioning and splinting, Pressure Therapy and Massage) 2 sessions per week.

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Group B (study group): This group includes 30 patients who received cryotherapy for 10 minutes at -14 degree, 2 sessions per week, for 10 weeks in addition to routine medical and physical therapy treatment as (Stretching exercises, Positioning and splinting, Pressure Therapy and Massage). Measurements were done using MAPS (Matching Assessment of Scars and Photographs) and were recorded in the first visit as a base line and measured at the end of treatment after 3 months of treatment.

Statistical Analysis:

Statistical analysis was done using SPSS, version 23 for Windows; SPSS Inc., Chicago, Illinois, USA. Descriptive statistics for patients' ages were calculated as mean and standard deviation while, the dependent variables were calculated as a median. Chi square test of association was conducted to assess the distribution of males and females within groups. The Mann-Whitney test was conducted to compare the mean ranking of the study and control groups. Wilcoxon sum ranking test was conducted to compare the pretreatment and posttreatment data of the same group. The alpha level of significance was set less than or equal 0.05.

Results:

I. Demographic data of patients:

Mann Whitney test revealed that there was no statistically significant difference between groups regarding age, weight, height, and body mass index (BMI) where p value equals (0.553, 0.484, 0.727, 0.399) respectively.

Variable	Control group	Study group	T value	P value	significance
Age (year)	29.07± 3.84	28.4± 4.76	0.597	0.553	NS
Weight (Kg)	77.1± 11.22	75.13± 10.41	0.704	0.484	NS
Height (Cm)	172.93 ± 6.94	172.3 ± 7.06	0.35	0.727	NS
BMI (Kg/M^2)	25.67 ± 2.44	25.19 ± 1.83	0.848	0.399	NS

II. Gender distribution:

Chi square test of association revealed that there was no statistically significant difference between groups regarding gender distribution where p value equals 0.438.

Variable	Control group	Study group	Total
Male	14	17	30
Female	16	13	30
Total	30	30	60 (Grand Total)

The chi-square statistic is 0.6007. The p-value is 0.438 (NS)

III. Matching Assessment of Scars and Photographs (MAPS) results:

As presented in Table (3), Mann Whitney test revealed that there was no statistically significant difference between groups regarding pretreatment data of surface, height, thickness, color, pigmentation, total score of Matching Assessment of

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Scars and Photographs where p value equals (0.077, 0.089, 0.28, 0.896, 0.992, 0.153) respectively. regarding post treatment data of surface, height, thickness, color, pigmentation, total score of Matching Assessment of Scars and Photographs**,** Mann Whitney test revealed that there was a statistically significant difference between groups where p value equals (0.005, 0.0001, 0.0005, 0.0021, 0.00016, < 0.00001) respectively.

Table (3): Between groups MAPS results

Variable		Control group	Study group	Z value	P value	significance
Surface	Pre	3	4	-1.767	0.077	NS
Height		3	3	-1.7	0.089	NS
Thickness		3	3	-1.079	0.28	NS
Color		3	3	0.126	0.896	NS
Pigmentation		2	2	0.0073	0.992	NS
Total score		14	14	-1.434	0.153	NS
Surface	Post	2	2	2.79	0.005	S
Height		2	2	3.84	0.0001	S
Thickness		2	1	3.47	0.0005	S
Color		2	1	3.07	0.0021	S
Pigmentation		2	1	3.76	0.00016	S
Total score		11	7	5.18	< 0.00001	S

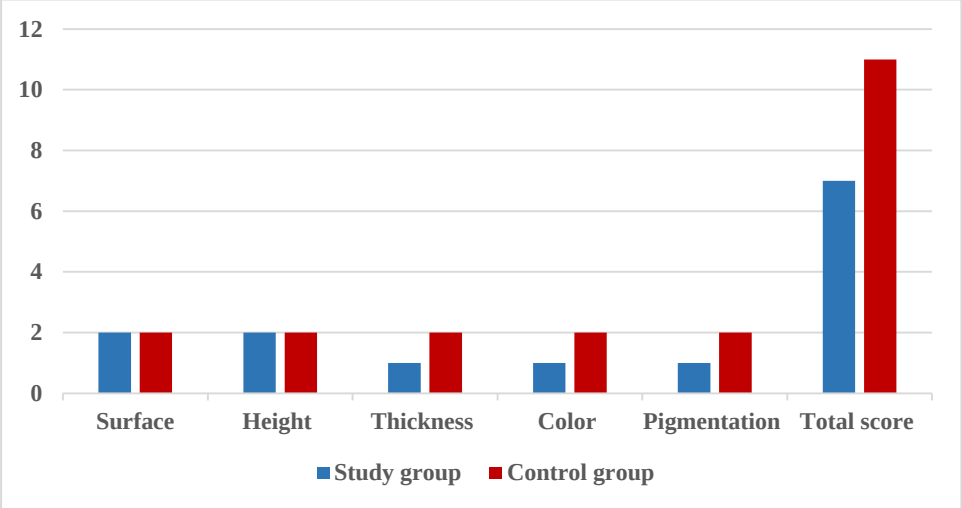

Figure (1): posttreatment median values of surface, height, thickness, color, pigmentation, total score of both groups

In addition, Wilcoxon sum ranking test revealed that there was a statistically significant difference between pretreatment data and posttreatment data of surface, height, thickness, color, pigmentation, total score of Matching Assessment of Scars and Photographs in control group where p value equals (< 0.00001, 0.00096, 0.0034, 0.00096,

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0.0051, <0 .00001) respectively. Furthermore, Wilcoxon sum ranking test revealed that there was a statistically significant difference pretreatment data and posttreatment data of surface, height, thickness, color, pigmentation, total score of Matching Assessment of Scars and Photographs in the study group where p value less than 0.00001 as shown in table (4).

Table (3): Within group MAPS results

Variable	Group	Median (pre)	Median (post)	Z value	P value	significance
Surface	Control group	3	2	-4.29	< 0.00001	S
Height		3	2	-3.29	0.00096	S
Thickness		3	2	-2.93	0.003	S
Color		3	2	-3.29	0.00096	S
Pigmentation		2	2	-2.8	0.0051	S
Total score		14	11	-4.7	<0 .00001	S
Surface	Study group	4	2	-4.703	<0 .00001	S
Height		3	2	-4.782	<0 .00001	S
Thickness		3	1	-4.623	<0 .00001	S
Color		3	1	-4.541	<0 .00001	S
Pigmentation		2	1	-4.541	<0 .00001	S
Total score		14	7	-4.782	<0 .00001	S

Discussion

This study was conducted to evaluate the therapeutic effect of cryotherpy in treating hypertrophic scar.

The results of the present study revealed that cryotherapy had a significant effect regarding post treatment data of surface, height, thickness, color, pigmentation, total score of Matching Assessment of Scars and Photographs where p value equals (0.005, 0.0001, 0.0005, 0.0021, 0.00016, < 0.00001) respectively. As shown in table (3) and Fig. (3).

Height, surface and pigmentation of hypertrophic scar were the most improved.

Blume[10] stated that Cryotherapy, which is freezing scar tissue, is used in conjunction with other therapies, such as intralesional corticosteroids, as a mono treatment for hypertrophic and keloid scars. A strong response during 32 months of follow-up was demonstrated in 76 percent of patients with hypertrophic scars without recurrence.

The results of this study is in accordance with **Harshai**[11] who stated that after treatment in hypertrophic scars and keloids with cryotherapy, more than 50 percent reduction in scar volume was recorded without recurrence during 18 months of follow-up, cryotherapy is thought to affect the process of wound healing collagen remodeling.

Kuflik and Kuflik[12] agreas with that theory and suggested that Initially, water passes out of the cell through osmosis, causing internal dehydration and cell damage, causing cell injury with water crystallising outside the cell. Internal crystal formation

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and further cell disruption are caused by freezing. The thawing process contributes to the creation of larger crystals. The longer the freeze thaw periods, the colder the temperature, the greater the cell damage, the longer the thawing time.

The results of this study were in accordance with **Lawrence and Tefler**[13] who stated that repeated freeze-thaw cycles, fast freezing, and gradual thawing are considered the best treatment, the thaw time is usually two or three times longer than the freeze time.

Necrosis typically occurs at the center of the application region, where the temperature vary between -14 C and -20 C There is a rim of partially damaged tissue, and some cells remain alive in the peripheral areas, but with such injury that causes subsequent apoptosis, the temperature does not need to be measured because clinical studies indicate that for the most common skin lesions, the horizontal spread of freezing is also important and relates to the freezing of the skin cells beyond the lesion edges[14].

When cooled to a temperature of -14°C, mammalian cells are killed (-4F), The formation of ice crystals, both intracellular and extracellular, starts with primary injury then the Intracellular crystals rupture the cell's outer membrane and the ice formation outside the cell dehydrates the cellular environment resulting in lethal concentrations of electrolytes and changes in pH, the cell fails to monitor the permeability of ions when organelles are damaged and cell death provokes[15].

With cell death at -4 C to -7 C, melanocytes are the most susceptible to freezing depigmentation may occur, especially in more pigmented patients, The death of keratinocytes requires -10 to -20 C, fibroblasts are more freeze-resistant and need temperatures ranging from -14 C to -30 C to lead to cell death[16].

Kimura and Kishimoto[17] stated that Cryotherapy was performed locally, causing changes in the amount of systemic cytokines. Indeed, both LC techniques also decreased IL-17A plasma levels while equally repressing local IL-6, IL-17A and IL-1β gene expression and protein levels, while only ice decreased IL-6 plasma levels. The levels of IL-6 protein appeared to decrease in plasma as well, it is hypothesize that ice produced a greater local and systemic anti-inflammatory influence, as indicated by the evolution of the clinical parameters, which were positively linked with plasma IL-6 and IL-17A.

Harshai[11] stated that cryotherapy may be less desirable to patients than other treatments, because of the resulting pain, skin atrophy and hypopigmentation, especially with the use of surface techniques (e.g. contact and spray probes and because of the high frequency of treatment.

There were limitations in the study like the small sample size, using only one technique of assessment and the side effects of cryotherapy.

In the future studies in the same scope, we recommend using larger sample size, different ways of subjective and objective assessment and combining cryotherapy with other innovative ways in treating hypertrophic scar.

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