Capsaicin Phonophoresis versus Transcutaneous Electrical Nerve Stimulation in the Treatment of Pruritus in Lichen Simplex Chronicus: A Prospective Randomized Controlled Study

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ABSTRACT

Introduction: Lichen Simplex Chronicus is characterized by circumscribed, lichenified, pruritic patches that may develop on the neck, upper thigh, lower legs, ankles, extensor surface of forearms, back, scalp, vulva, pubis, and scrotum.

Aim of Study: To assess the efficacy of capsaicin phonophoresis and the efficacy of transcutaneous electrical nerve stimulation in treatment of pruritus in Lichen Simplex Chronicus and to compare between both modalities which is more effective.

Methodology: Study Design: A prospective, randomized controlled trial. Sample size: 30 Patients; Each group-15. Study setting: Physical therapy department of New Kasr El-Aini Teaching Hospital, Cairo University, Egypt. Duration of Study: The total duration was 8 months. In group 1 patients received capsaicin phonophoresis and in group 2 patients received transcutaneous electrical nerve stimulation, both modalities were applied 3 treatment sessions per week for one month (12 sessions). Outcome measures: 5- D itch scale and Dermatology Life Quality Index which have been collected pre-treatment, post-treatment and follow-up (one month).

Results: Results of within group analysis, showed significant improvement (P < 0.05) in both outcome measures in both groups (pre-treatment, post-treatment and after one month). Results of between groups analysis showed no significant improvement (P > 0.05) in both outcome measures between both groups (post-treatment and after one month).

Conclusion: Capsaicin phonophoresis as well as transcutaneous electrical nerve stimulation may prove to be a useful modality for the treatment of pruritus in Lichen simplex chronicus with no significant difference between them.

Keywords: Lichen Simplex Chronicus, Pruritus, Capsaicin Phonophoresis, Transcutaneous Electrical Nerve Stimulation.

INTRODUCTION

Lichen simplex chronicus (LSC) is an inflammatory skin disorder classified as neurodermatitis) is characterized by a central lichenified plaque thickened and an endogenous eczema, it is characterized by lichenification of the skin as a result of repeated scratching. LSC (circumscribed hyperpigmented, usually surrounded by lichenoid papules and, along the borders with surrounding normal skin, by an indefinite area of slight thickening. [1] The
most common sites are the neck (sides), upper thigh, lower legs, ankles, extensor surface of forearms, back, scalp, vulva, pubis, and scrotum. The peak of incidence is between 35 and 50 years of age, and women are more affected than men (F:M = 2:1). [2]

The marked thickening with leathery skin is secondary to chronic rubbing or scratching from pruritus. Pruritus is defined as a cutaneous sensation that provokes the desire to scratch. [3] LSC may be caused by skin or systemic diseases, infection, local trauma, depression, stress, or anxiety. Patients with atopic dermatitis are more likely to develop LSC. Other causes include insect bites, scars, and allergic contact dermatitis. Some patients have contributing emotional or psychiatric problems that may exacerbate this disease. [4]

LSC has to be differentiated from lichen amyloidosis, atopic dermatitis, allergic and irritant contact dermatitis, cutaneous T cell lymphoma, lichen planus, discoid eczema, plaque psoriasis, seborrheic dermatitis, and stasis dermatitis. [5] Histologic examination demonstrates hyperkeratosis, acanthosis, spongiosis, and patches of parakeratosis in the epidermis. Epidermal thickening of all skin layers, with elongation of rete ridges and pseudoepitheliomatous hyperplasia. Papillary dermal fibrosis with vertical streaking of collagen bundles is characteristic of LSC. [6]

The past recommended treatment of LSC was topical specific antipruritic agents as 1% menthol and phenol in base creams but it was not very helpful. Potent topical glucocorticoid creams or ointments as betamethasone dipropionate or intra-lesional glucocorticoids such as triamcinolone acetonide are often successfully employed. Topical application of capsaicin (0.025–0.1%), can be effective in the very early manifestations. [7] Topical tacrolimus has proved to be effective treatment in LSC. [8]

Phonophoresis is the use of ultrasound waves (US) to enhance the absorption of topically applied drugs by increasing skin permeability to topical medications. The major advantages of phonophoresis are the introduction of medication to a local area without invasion of the skin and the synergistic interaction of US and drugs. [9] Capsaicin was the active ingredient in hot chili peppers, its initial application in human is analgesic, repeated application leads to desensitization, and a high concentration can block C fiber conduction velocity and result in long lasting sensory deficits. These properties of capsaicin explain its effect in the treatment of some painful condition such as cluster headache, reflex sympathetic dystrophy, LSC, pruritus, post herpatic neuralgia and diabetic neuropathy. [10]

Transcutaneous electrical nerve stimulation (TENS) is a non-invasive analgesic technique that is used to relieve pain such as nociceptive, neuropathic, and musculoskeletal. [11] No definitive pathway for itching has been shown, but it is thought that TENS may work in a similar way in its effect on pain control. [12]

The aims of the present study were to assess the efficacy of capsaicin phonophoresis as well as the efficacy of TENS in treatment of pruritus in LSC and to compare between both modalities in treatment of pruritus in LSC.

MATERIALS AND METHODS

Subjects

This study was carried out on 30 patients (22 female and 8 male) suffering from pruritus due to LSC. The study was designed as a prospective, randomized controlled trial with pre-treatment, post-treatment and follow-up (one month after finishing treatment) evaluation. The data were collected between May to December 2012 at physical therapy department of New
Kasr El-Aini Teaching Hospital, Cairo University, Egypt. Subjects were assessed and informed consent with ethical approval was taken. Subjects were assigned into 2 groups of equal number fifteen for each, patients who received capsaicin phonophoresis (group 1) and those who received TENS (group 2) using a computer generated table of random numbers.

All patients suffered from localized itching attacks to one area leading to severe scratch or rub to this area. The following criteria were used for inclusion: age between 35 to 50 years and presence of lichenified plaques of at least 5 cm in width, characteristic of localized LSC, on the following sites: extensor surface of forearms, upper thighs, lower legs or ankles for a period of at least 1 year, which did not respond to local treatment with corticosteroids and moisturizers. Exclusion criteria were other inflammatory skin diseases, cardiovascular diseases including cardiac pacemaker and loss of sensation at the treatment site, diabetic patients and patients with systemic diseases that may cause itching. The diagnosis of LSC was made with clinical examination and lesions secondary to predisposing skin disorder were excluded.

Outcome Measures

There were 2 outcome measures included in this study first the 5-D itch scale and second Dermatology Life Quality Index (DLQI) which have been collected pre-treatment, post-treatment and follow-up (one month).

5- D itch scale

The 5-D itch questionnaire was specifically developed to be a measure of itch that is brief, easy to complete, easy to score (either manually or electronically), sensitive to the multidimensional nature of pruritus and its effect on quality of life, applicable to multiple diseases, and capable of detecting change over time. The ‘5-D itch scale’ was titled according to 5 domains: duration, degree, direction, disability and distribution. The duration, degree and direction domains each included 1 item, while the disability domain had 4 items. All items of the 1st four domains were scored from 1 to 5. The distribution domain included 16 potential locations of itch, including 15 body part items and one point of contact with clothing or bandages. The total score was calculated by summing the score of all items resulting in a minimum score of 5 (no pruritus) and maximum score of 25 (most severe pruritus). The 5-D has demonstrated ease of use, content validity, test-retest reliability, internal consistency and ability to detect change in itch over time in patients with skin disease, pruritus, liver disease, kidney disease and burns.\textsuperscript{[13]}

Dermatology Life Quality Index

The DLQI was developed to assess limitations related to the impact of skin disease and its treatment. It consists of 10 items and covers 6 domains including: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. Response categories include “not at all”, “a little”, “a lot”, and “very much” with corresponding scores of 0, 1, 2 and 3 respectively; the response “not relevant” (and unanswered items) are scored as “0”. A total score is calculated by summing the score of all items, resulting in a maximum score of 30 and a minimum score of 0. High scores indicate more impairment. The DLQI has well established reliability and validity when used in generalized pruritus, atopic eczema, psoriasis and others.\textsuperscript{[14]}

Treatment Procedures

Group 1: Fifteen LSC patients suffered from pruritus were treated by capsaicin phonophoresis via Ultrasound (SONOPULS 434, ENRAF-NONIUS®, Netherland). Initially, topical gel containing capsaicin (each100 grams contains 25 mg. of
capsicum) was applied circularly with a thickness of 2–3 mm. Then, ultrasound with a 5-cm-diameter applicator was applied over the affected areas (6 extensor surface of forearms, 3 upper thighs, 2 lower legs and 4 ankles) with continuous mode of 1 MHz frequency and 1.5 Wt/cm² power and the treatment duration was 10 minutes. The treatment protocol consisted of 3 treatment sessions per week (day after day) for one month (12 sessions).

**Group 2:** Fifteen LSC patients suffered from pruritus were treated by TENS with high-frequency (50–100 Hz) applications of 30 min duration with a pulse width 40–75 µs were given from a dual-channel portable TENS unit (BioMed Plus TENS Machine, Biomedical Life Systems Inc., Vista, CA, USA) with four 4 X 5 cm surface carbon electrodes. These were applied over the affected areas (7 extensor surface of forearms, 5 upper thighs, and 3 ankles), using a gel based coupling agent for the transmission of electrical impulses. The intensity of TENS was adjusted until the patient reported tingling sensation. The treatment protocol consisted of 3 treatment sessions per week (day after day) for one month (12 sessions). The patients were carefully examined at each session to evaluate any side-effects such as erythema, swelling, irritation or numbness.

**Post-Study Follow-up**

After one month from the end of the treatment procedures for both groups, a follow-up intervention of 5-D itch scale and DLQI were performed to investigate the long lasting effect of capsaicin phonophoresis and TENS in pruritus of LSC patients.

**Statistical Analysis**

All statistics were calculated by using the statistical package of social sciences (SPSS) version 16. Descriptive statistics (mean and standard deviation) were computed for all data. One way repeated measures of ANOVA using Greenhouse-Geisser test was used to assess the difference within each group in 5-D itch scale and DLQI and Bonferroni test to determine the significant difference between measurements time of evaluation (pre-treatment and post-treatment, pre-treatment and follow-up time, post-treatment and follow-up time). Un-paired t-test was used for age, duration of pruritus in years, 5-D itch scale and DLQI between group 1 and group 2. P-values less than 0.05 were considered to be statistically significant.

**RESULTS**

The mean age of the subjects in group 1 was 42.33±5.26 and in group 2 was 42.93±4.57 with p-value of 0.74 which mean no significant difference between the 2 groups in age. The mean duration of pruritus in years of the subjects in group 1 was 2.87±1.13 and in group 2 was 2.80±1.26 with p-value of 0.88 which mean no significant difference between the 2 groups in duration of pruritus in years. So there was a homogenous between the two groups of the study.

The mean changes in 5-D itch scale and DLQI of group 1 (capsaicin phonophoresis) and group 2 (TENS) are summarized in table 1. There was a statistically significant difference within group in 5-D itch scales (F= 151.311, P < 0.05) in group 1. Pairwise comparison test using Bonferroni correction revealed that a high improvement in pruritus from pre-treatment, post-treatment and follow-up time (22.67±1.54, 7.60±5.69, and 6.87±4.94, respectively) with p < 0.05 between pre-treatment & post-treatment, pre-treatment & follow-up which mean a high significant difference. There was non-significant difference p > 0.05 in post-treatment & follow-up time which revealed that the improvement of pruritus was continued after
finishing treatment by one month (follow-up time) table 2. In group 2, there was a statistically significant difference within group in 5-D itch scales (F= 61.684, P < 0.05). Pairwise comparison test using Bonferroni correction revealed that a high improvement in pruritus from pre-treatment, post-treatment and follow-up time (22.60±1.72, 9.20±7.51, and 9.60±7.42, respectively) with p < 0.05 between pre-treatment & post-treatment, pre-treatment & follow-up which mean a high significant difference. There was non-significant difference p > 0.05 in post-treatment & follow-up time which revealed that the improvement of pruritus was continued after finishing treatment by one month (follow-up time) table 2. In group 2, there was a statistically significant difference within group in DLQI (F= 59.460, P < 0.05). Pairwise comparison test using Bonferroni correction revealed that a high improvement in pruritus from pre-treatment, post-treatment and follow-up time (16.73±3.08, 4.67±8.32, and 4.93±8.36, respectively) with p < 0.05 between pre-treatment & post-treatment, pre-treatment & follow-up which mean a high significant difference. There was non-significant difference p > 0.05 in post-treatment & follow-up time which revealed that the improvement of pruritus was continued after finishing treatment by one month (follow-up time) table 2. Comparison revealed that there were non-significant differences in mean changes of 5-D scales pre-treatment, post-treatment and follow-up time (p > 0.05) between group 1 and group 2.

There was a statistically significant difference within group in DLQI (F= 116.584, P < 0.05) in group 1. Pairwise comparison test using Bonferroni correction revealed that a high improvement in pruritus from pre-treatment, post-treatment and follow-up time (16.67±2.89, 3.13±6.60, and 2.87±6.97, respectively) with p < 0.05 between pre-treatment & post-treatment, pre-treatment & follow-up which mean a high significant difference. There was non-significant difference p > 0.05 in post-treatment & follow-up time which revealed that the improvement of pruritus was continued after finishing treatment by one month (follow-up time) table 2. Comparison revealed that there were non-significant differences in mean changes of DLQI scales pre-treatment, post-treatment and follow-up time (p > 0.05) between group 1 and group 2 which revealed that both treatment procedures, capsaicin phonophoresis and TENS, had the same effect in improvement of pruritus due to LSC. Fig. 1 demonstrates the mean values difference of 5-D scale pre-treatment, post-treatment and follow-up time in both groups. Fig. 2 demonstrates the mean values difference of the DLQI scales pre-treatment, post-treatment and follow-up time in both groups.

Table 1: 5-D itch scale and DLQI pre-treatment, post-treatment and follow-up time between group 1 and group 2.

<table>
<thead>
<tr>
<th>Scores</th>
<th>5-D itch scale</th>
<th>DLQI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>Pre-treatment</td>
<td>22.67±1.54</td>
<td>22.60±1.72</td>
</tr>
<tr>
<td>Post-treatment</td>
<td>7.60±5.69</td>
<td>9.20±7.51</td>
</tr>
<tr>
<td>Follow-up</td>
<td>6.87±4.94</td>
<td>9.60±7.42</td>
</tr>
<tr>
<td>p-value</td>
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<td>0.005</td>
</tr>
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</table>

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Table 2: The significant difference between time of evaluation of 5-D itch scale and DLQI within group 1 and group 2.

<table>
<thead>
<tr>
<th>Time of evaluation</th>
<th>5-D itch scale</th>
<th>DLQI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td></td>
<td>Group 1 p-value</td>
<td>Group 1 p-value</td>
</tr>
<tr>
<td></td>
<td>Group 2 p-value</td>
<td>Group 2 p-value</td>
</tr>
<tr>
<td>Pre-treatment &amp; post-treatment</td>
<td>22.67±1.54</td>
<td>3.13±6.60</td>
</tr>
<tr>
<td></td>
<td>7.60±5.69</td>
<td>4.67±8.32</td>
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<td></td>
<td>0.001</td>
<td>0.001</td>
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<tr>
<td>Pre-treatment &amp; follow-up</td>
<td>22.60±1.72</td>
<td>16.73±5.08</td>
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<td>9.20±7.51</td>
<td>4.93±8.36</td>
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<tr>
<td></td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Post-treatment &amp; follow-up</td>
<td>7.60±5.69</td>
<td>3.13±6.60</td>
</tr>
<tr>
<td></td>
<td>6.87±4.94</td>
<td>4.67±8.32</td>
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<tr>
<td></td>
<td>0.067</td>
<td>0.311</td>
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<tr>
<td></td>
<td>9.20±7.51</td>
<td>2.87±6.97</td>
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<tr>
<td></td>
<td>9.60±7.42</td>
<td>4.93±8.36</td>
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</tr>
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</table>

**DISCUSSION**

The present study was a prospective, randomized controlled trial done on thirty patients who had pruritus due to LSC, they assigned into two groups of equal number fifteen for each; capsaicin phonophoresis (group 1) and TENS (group 2). The purposes of this study were to assess the efficacy of capsaicin phonophoresis as well as the efficacy of TENS in treatment of pruritus in LSC and to compare between both modalities in treatment of pruritus in LSC with the long term relief of pruritus.

Pruritus is an orphan symptom since it was considered in the past as a subset of pain. While both pain and itch are induced by chemical messengers that excite unmyelinated C fibers, the current weight of evidence supports the view that a unique subpopulation of these fibers is activated by pruritus-inducing stimuli. [3] Certain parts of the skin are highly sensitive to itch. Removing the nerve fibers in the immediate subdermal tissue of these anatomical sites will leave pain sensation intact but eliminate the capability of responding to pruritic stimuli. Pain and itch induce different reflex actions: pain results in withdrawal; itch creates the urge to scratch. [17]

The results of the study showed that there were significant differences pre-treatment & post-treatment and pre-treatment & follow-up time, on the other
hand, there was non-significant difference post-treatment and follow-up time in both groups, that means both modalities capsaicin phonophoresis and TENS were effective in treatment of pruritus in LSC and both had long lasting effect post treatment.

In this study capsaicin phonophoresis was used in group 1. Phonophoresis is the movement of drug molecules through the skin using coupling medium under influence of ultrasound which increase skin permeation of many drugs. [18] Since ultrasound and chemical enhancers individually can increase transdermal drug delivery, Johnson et al., 1996, hypothesized that combination of ultrasound and enhancers may result in greater degree of penetration than that resulting from each method alone. [19]

Capsaicin is the phytochemical (8-methyl-N-vanillyl-6 nonenamide) sourced from various species of the plant genus Capsicum and is the component of chili peppers. Capsaicin cream is indicated for use in post-herpetic neuralgia, painful diabetic neuropathy and pain of osteoarthritis. The effects of capsaicin related to its ability to deplete the neuropeptide substance P, which increased in patients with atopic dermatitis, from local sensory nerve terminals in the skin. [20] Capsaicin is also an inhibitor of vasodilatation. There has been increasing interest in the use of capsaicin in the management of pruritus. The previous studies reported that topically applied capsaicin is effective in the treatment of pruritus. [21] The greater the dose of capsaicin and the more frequent applications, the sooner desensitization will appear and pruritus disappears. Side effect of topical application of capsaicin may be initial burning. [22] Topical capsaicin’s effects have been confirmed in several controlled clinical studies for different pain syndromes, neuropathy and nostalgia paraesthetica, [23] brachioradial pruritus, [24] pruritic psoriasis, and haemodialysis-related pruritus. [25,26] Case reports and case series showed effects in hydroxyethyl starch-induced pruritus, [27,28] prurigo nodularis, lichen simplex, [29] nummular eczema, aquagenic pruritus, and psoralen ultraviolet A (PUVA) associated with pruritus. [30]

Capsaicin phonophoresis was used in the treatment of chronic neck pain in study by Durmus et al., 2014, a total of 61 patients with definite chronic neck pain were included in this study. The patients were randomized into 3 groups; Group 1 (n = 21) received capsaicin phonophoresis and exercises. Group 2 (n = 20) received placebo capsaicin phonophoresis and exercises. Group 3 (n = 20) was given only exercises. All of the programs were performed 3 days a week, for 6 weeks. They concluded that a combination of capsaicin phonophoresis with exercise therapy can be used to obtain optimal clinical results regarding improving pain, disability, depression, and sleep quality in the patients with chronic neck pain. [15]

In the present study, it is the first time to use capsaicin phonophoresis in treatment of pruritus in LSC patients. A topical gel containing capsaicin was used. Capsaicin phonophoresis was effective treatment and had a long lasting effect, as patients after finishing the treatment by one month had a good result and no longer suffering from pruritus without side effects. The results of the current study also showed that there was great improvement in group 2 that used TENS in treatment of pruritus in LSC and also had long lasting effect post treatment without side effects. This confirms the efficacy of TENS in relieving pruritus in LSC patients and these findings may attribute to the mechanism of TENS.

The main mechanisms of the antipruritic action of TENS are unknown.
One possible mechanism is a peripheral nociceptive effect of electrical current on itching and pain fibers. TENS at rates of 50–100 Hz produces analgesia that is not reversible by naloxone. Stimulation of large myelinated fibers blocks nociceptive transmission at the level of the spino-thalamic tract cell bodies. TENS can produce neuro-modulation by three ways: (i) presynaptic spinal cord inhibition; (ii) direct inhibition of excitation of abnormally firing nerves and (iii) restoration of afferent input. \[31\]

This findings supported by Engin et al., 2009, investigated the use of TENS treatment in relieving pruritus in LS. A total of 22 patients with LS underwent conventional TENS mode. TENS was performed for all patients for 1 h / treatment 3 times per week for 4 weeks. By the end of the study, 18 (80%) of the subjects experienced a reduction in pruritus intensity of > 50%. They concluded that TENS may prove to be a useful and well-tolerated treatment modality for the treatment of pruritus in patients with LS. \[16\]

In another study by Yuksek et al., 2011, reported the effects of TENS on the DLQI measures and VAS scores in patients with pruritus, in whom LS and macular amyloidosis (MA) were diagnosed. At week 2, there was a significant difference in median VAS scores between baseline in the group of LS. At 4 weeks of therapy, statistically significant differences were observed compared with the baseline and week 2 in the median VAS scores in the group of MA. There was also a statistically significant improvement in median DLQI total scores with respect to baseline, which was achieved as early as week 2 in patients with LS and MA who were on the TENS treatment. \[32\]

Tang et al., 1999, evaluated the short-term efficacy and adverse effects of TENS for decreasing pruritus in patients with dermatoses by a prospective 1-week study using TENS given once daily, they found that a significant reduction of pruritus was obtained without adverse effect referable to TENS treatment, and a subjective reduced use of conventional topical drugs was also reported by all patients. \[33\]

LSC is an irritating itchy dermatosis in which anxiety is common and affects the quality of life (QOL) of the patients. In the present study, more than one methods of evaluation (5-D itch scale and DLQI) were used to confirm the efficacy of capsaicin phonophoresis as well as the efficacy of TENS in treatment of pruritus in LSC and to compare between both modalities in treatment of pruritus in LSC. Both methods of treatment (capsaicin phonophoresis and TENS) were effective in treatment of pruritus of LSC without side effects as there were significant difference between pre-treatment and post-treatment and had long-lasting effect as there were no significant difference between post-treatment and follow-up time. The results of this study showed that there were no significant difference between capsaicin phonophoresis and TENS as pruritus disappeared in both groups.

CONCLUSION

From our clinical observation, capsaicin phonophoresis as well as transcutaneous electrical nerve stimulation (TENS) might prove to be useful modalities for the treatment of pruritus in Lichen simplex chronicus (LSC) with no significant difference between them.

REFERENCES


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