

# A Comparative Study in the Treatment of Solar Lentigines With Trichloroacetic Acid 40% Versus Cryotherapy

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Solar lentigo is local and benign proliferation of melanocytes at the dermoepidermal junction. The major concern of these lesions is related to cosmetic issues. The aim of this study was to compare the efficiency and adverse effects of trichloroacetic acid (TCA) 40% versus cryotherapy in treatment of solar lentigo. This is a study of 68 individuals who suffered from solar lentigines on their hands, one side treated with cryotherapy and the other side with TCA 40% randomly. This treatment was repeated after one month. Photographs of the hands were taken prior to and 2 months following the treatment, and degree of improvement (lightening) of lesions and the resulted adverse effects were collected. The results demonstrated that cryosurgery was more likely to produce lightening of the lentigines than TCA 40% solution, but this difference was not significant ( $P=.32$ ). Cryosurgery was more painful and took longer to heal. Although cryosurgery had better results than TCA 40% in lower Fitzpatrick skin types, the difference was not significant.

Characteristic features of photoaging skin are sallowness mottled pigmentation, dry and rough skin, loss of skin tone, leathery texture, laxity, coarse and fine wrinkles, benign and malignant tumors,

and solar lentigines.<sup>1,2</sup> Solar lentigo is local and benign proliferation of melanocytes at the dermoepidermal junction. These lesions are several yellow or brown ovals or round maculae with obvious margins created at the areas such as back of the hands, forearm, and face, which are exposed to sunlight.<sup>3</sup> Maculae can also be regarded as the first signs of the photoaging process, which can also have a substantial impact on patients. The incidence increases with age, affecting more than 90% of white persons older than 50 years of age. In the differential diagnosis, solar lentigines should be distinguished from ephelides, lentigo simplex, pigmented actinic keratosis, flat seborrheic keratosis, melanocytic nevus, and malignant melanoma. These can be differentiated based on clinical appearance.<sup>4</sup> Considering that solar lentigo is

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most seen in exposed parts of the body such as the face, neck, hands, and forearm, negative effects of these lesions on affected people should not be overlooked. On the other hand, these lesions can impose further mental pressure on the patient considering that they can be the first sign of the aging process resulting from sun damage. At the same time, the major concern of these lesions is related to cosmetic issues and most of the people may be looking for treatment.<sup>4,5</sup> Therapy for solar lentigines can be divided into 2 broad categories: physical therapy and topical therapy. Physical therapy of solar lentigines includes cryotherapy, laser therapy, pulsed light, and chemical peels. These are frequently used with excellent outcome. A range of topical therapies are currently in use, including hydroquinone (HQ), tretinoin, adapalene, and more recently, a stable fixed combination of Mequinol and tretinoin.<sup>6,7</sup> Trichloroacetic acid (TCA) is a chemical agent that causes epidermal necrosis by protein precipitation. Trichloroacetic acid has been shown to be effective in treating facial lentigines and photodamaged skin.<sup>8,9</sup> Few studies have been conducted on the effects of this drug and its comparison with other treatments. Contradictory results have been obtained in studies by Lugo-Janer et al<sup>9</sup> and Reziee,<sup>10</sup> showing that the effects of TCA were less than ones of cryotherapy and in another study, its effects have been reported less effective than Q-switched Nd:YAG laser.<sup>11</sup> But, in the Sezer study,<sup>12</sup> the effects of TCA and glycolic acid combination with cryotherapy was comparable. Considering high prevalence of solar lentigines, lack of proved treatment without adverse effects and contradictory of current studies on effects of TCA, we decided to conduct the present study aimed at comparing efficiency and adverse effects of TCA 40% versus cryotherapy in the treatment of solar lentigines.

### METHODS

In this clinical trial study 68 patients (56 females and 12 males), aged 24 to 86 years (mean  $44 \pm 12/24$ ), and with solar lentigines participated from March 2007 to March 2010. Written consent was obtained from all participants. Every patient should have at least 5 lesions on each hand. Individuals with warts, recurrent herpes, sensitivity to light, Reynaud phenomenon, pregnancy, and lactation were disqualified. Those patients with primarily actinic keratoses or seborrheic keratoses; sunburn within recent 2 to 3 days; those who have received treatments such as surgery, cryotherapy, radiotherapy and psoralen plus UVA therapy within the last 6 weeks; and isotretinoin during last 6 months were excluded from the study. This study was approved by the ethics committee of our university. Images were taken of lesions with a digital camera before treatment.

All photographs were taken with the same camera and with the same conditions considering magnification, light, and position. Randomly, one side was treated with cryotherapy spray one time so that the tip of the spray had a 3-cm distance from the lesion, and spraying was continued until the surface of the lesion became frosted as a result of spraying. Duration of spraying varied from 2 to 5 seconds regarding the diameter of the lesion. The other side was treated with TCA 40% with a cotton applicator after washing with soap and water. The patients were recommended not to expose skin to sun and frequently use sunscreen provided them freely. Both treatment methods were repeated after one month. During treatment and after the 2-month follow-up period, the patients were studied considering adverse effects of both treatments including blister, permanent and severe pain, dyspigmentation, atrophy, and scarring. The photographs were taken at the end of the 2-month follow-up period. Four blinded observers who were board-certified dermatologists were asked to grade each treated hand. The observers graded the treatment based on before and after pictures. Lesions improvement considering degree of lightening was classification as follows: (1) nonimprovement: lightening  $< 25\%$ ; (2) mild improvement:  $25\% > \text{lightening} < 50\%$ ; (3) moderate improvement:  $50\% > \text{lightening} < 75\%$ ; (4) marked improvement: lightening  $> 75\%$ .

Patients were asked to select the treatment that achieved the best result, the most painful, and the one with faster healing time. Continuous variables are reported as means  $\pm$  standard deviation. Categorical variables are presented as percentages. Log transformation was used for analysis of skewed data. Univariate (2-sided *t* tests and chi-square tests, Pearson correlation) analyses were performed when appropriate.

### RESULTS

Sixty-eight patients were enrolled in the study, but 62 completed the study (52 females and 10 males). Six cases were lost to follow-up. Eight of the patients had Fitzpatrick skin type I, 20 had Fitzpatrick skin type II, 25 had Fitzpatrick skin type III, and 9 had Fitzpatrick skin type IV. Analysis of results in patients' different skin colors found that patients with Fitzpatrick skin type I achieved above-average results. It was found that 87.5% (14 of 16) of the patients with Fitzpatrick skin type I achieved more than 50% improvement compared with 60% (24 of 40), 56.2% (27 of 48), and 55.5% (10 of 18) of the patients with skin types II, III and IV, respectively (Table 1).

Comparing baseline images and ones taken after treatment with cryotherapy, it was concluded that

TABLE 1

## Improvement by Fitzpatrick Skin Type

Fitzpatrick Skin Type	I	II	III	IV
No change	0	7	10	4
Mild improvement	2	9	13	4
Moderate improvement	10	19	21	8
Marked improvement	4	5	6	2

40 cases (64%) had more than 50% improvement (more than moderate improvement), which was statistically significant ( $P < .05$ ). The hand treated with TCA 40% had more than 50% improvement in 35 cases (56%), which was also significant ( $P < .05$ ). Comparing more than 50% improvement of cryotherapy with TCA 40% [40 cases (64%) vs 35 cases (56%)] demonstrated that they had no statistically significant difference ( $P = .32$ ) (Table 2).

More than 75% improvement was in 12 cases (19.3%) in cryotherapy and 5 cases (8%) in TCA 40%. Neither of them were statistically significant. Polling the patients, 40 (64%) stated that cryotherapy was more effective. Twenty-two patients (35%) reported TCA 40% was better and more effective. Forty-eight patients (77%) in the study felt that TCA 40% was the quickest to heal, but 14 of 48 (30%) felt that cryosurgery had the quickest healing. Fifty-two patients (84%) felt that cryosurgery was the most painful treatment (Table 3).

Considering adverse effects observed during treatment, blistering was the most common side effect observed in treatment with cryotherapy. But, hyperpigmentation was the most common side effect seen in those treated with TCA 40%. Comparison of adverse effects observed in the 2 therapeutic groups demonstrated that they have statistically significant difference ( $P < .05$ ) (Table 4).

### COMMENT

On the basis of assessment of photographs, both treatments achieved good results, but cryosurgery was clearly

the more effective therapy for the treatment of solar lentigines. Our study suggested that efficiency of TCA 40% can be compared with cryotherapy in the treatment of solar lentigines (more than 50% improvement; 56% vs 64% respectively). Additionally, it has fewer adverse effects than cryotherapy. These results were in contrary with the findings of Lugo-Janer et al<sup>9</sup> and Raziee<sup>10</sup> and in accordance with the Sezer study.<sup>12</sup> The Lugo-Janer et al<sup>9</sup> and Raziee<sup>10</sup> studies used TCA with concentrations of 30% and 33% and more than 50% improvement was seen in 36% versus 12% in their studies. Concentration of material used in pilling is one of the factors affecting depth of pilling and as a result destructive power against melanocytes. In this study, we used TCA 40%, which was more concentrated than one used in Lugo-Janer et al<sup>9</sup> and Raziee<sup>10</sup> studies and can be regarded as one of the justifying factors considering efficiency of TCA 40% in our study. Low percentage of marked improvement and moderate improvement with both modalities show low efficacy of the treatments. However, the cryotherapy in treatment of solar lentigines would be more effective using proper technique and adequate instrumentation. It also would be dependent on the physician's experience in this field.<sup>13,14</sup> Both treatments would be more effective in lighter skin types, and cryotherapy in Fitzpatrick skin type I and II is clearly superior to TCA 40%. The principle of the treatment in solar lentigines is tissue injury by cell freezing. Melanocytes are especially vulnerable to cold injury and can be destroyed by temperatures of  $-48^{\circ}\text{C}$  to  $-78^{\circ}\text{C}$ .<sup>15</sup> We expect that postcryotherapy hypopigmentation is a

TABLE 2

## Response to Treatment

Lightening, %	TCA 40%	Cryotherapy
No change (<20%)	15	8
Mild improvement (20%–50%)	16	10
Moderate improvement (50%–75%)	30	28
Marked improvement (>75%)	5	12

TABLE 3

## Patient Survey Results, N=62

	TCA 40%	Cryotherapy
Best result	22 (36%)	40 (64%)
Healed quickest	48 (77%)	14 (30%)
Most painful	10 (17%)	52 (84%)

frequent complication, but in our study blistering was the most common side effect observed in treatment with cryotherapy. In addition, we repeated the treatments 2 times every month. Repeating treatment results in more destruction of melanocytes and more improvement. Another reason for any difference in outcomes resulting from the studies is related to effects of how to evaluate response to treatment, methods applied for used treatments, and skin type. In contrast to the Raziee et al<sup>10</sup> study where PIH was the main complication, at the end of the trial we observed that in

cryotherapy, blistering was the main complication, and in TCA 40%, hyperpigmentation was the main complication.

Since so few patients showed marked improvement, neither treatment was statistically significant ( $P < .05$ ). It can be stated that cryotherapy and TCA 40% were not effective in the cure of solar lentigines and just led to average improvement.

Although cryotherapy has better results compared with TCA, it is more painful and takes longer to heal dependent on the cryosurgery technique. However,

TABLE 4

## Frequency of the Observed Adverse Effect for Each Therapeutic Group

	TCA 40%	Cryotherapy
Permanent and severe pain	1	3
Blistering	2	8
Permanent erythema and edema	2	4
Hyperpigmentation	4	5
Hypopigmentation	2	4
Scarring	1	3
Severe itching	3	2

cryotherapy with an instrument such as a Kryomed® device would not be painful and cause no open wound so that there is no healing time.<sup>16</sup> Recently other treatments have been used to treat solar lentigines with variable success. Tyrosinase inhibitors in combination with topical retinoid have been shown to achieve good results in lightening solar lentigines.<sup>17</sup> Ablative laser therapy and the newer photoselective lasers lighten the lentigines in a short time but are not cost effective.<sup>18-20</sup> Better cryotherapy instrumentation and experience of the treating physician has already been shown to improve the results in solar lentigines.<sup>13,16</sup>

This study demonstrated that TCA 40% is equal to cryotherapy in the treatment of solar lentigo. Additionally, it has less adverse effects and repeating treatment does not result in increasing frequency or severity of the adverse effects.

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