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ORIGINAL ARTICLE

Dermoscopic Evaluation of the Efficacy of Topical Trichloroacetic acid 70% Versus Methoxsalen 0.2 % Paint in Acral Vitiligo, A comparative Cross-Sectional Study

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Abstract

Background: ***Vitiligo, an acquired disorder characterized by depigmentation, has an unidentified etiology. The pathogenesis of this condition has been the subject of various hypotheses, such as autoimmune, neurohumoral, and autocytotoxic theories.***

Aim and objectives: ***To evaluate dermoscopically the efficacy of topical Trichloroacetic acid 70% versus methoxsalen 0.2 % paint in acral vitiligo, a comparative cross-sectional study.***

Patients and methods: ***This comparative cross-sectional study evaluated dermoscopically the efficacy of topical Trichloroacetic acid (TCA) 70% versus methoxsalen 0.2 % paint in stable acral vitiligo. Response to the treatment was determined dermoscopically by marginal pigmentation appearance of the reticular network, marginal pigmentation, perifollicular pigmentation, and mixed re-pigmentation patterns. This study included 50 patients suffering from stable acral vitiligo divided into 2 equal groups: Group A (n=25) received topical methoxsalen 0.2 % every other day for 3 months, with a dermoscopic follow-up every 2 weeks. Group B (n=25) received topical TCA 70% application at the clinic every two weeks for 3 months with dermoscopic follow-up.***

Results: ***All cases of non-re-pigmentation dermoscopically showed no clinical improvement. In contrast, one case showed marginal pigmentation and the appearance of a reticular network, and this case showed mild clinical improvement. Also, in two cases with mixed repigmentation, one showed moderate clinical improvement, and the other showed good clinical improvement.***

Conclusion: ***TCA demonstrates a notably better response and higher patient satisfaction compared to methoxsalen. Consequently, TCA 70% emerges as a preferable recommendation for acral vitiligo treatment over methoxsalen. TCA 70% had a lower effective rate (6 cases only improved of a total of 25 cases).***

Keywords: Dermoscopic evaluation; Topical Trichloroacetic acid 70%; Methoxsalen 0.2 %; Acral vitiligo

1. Introduction

The quality of life, self-esteem, marriage, and work are all significantly impacted by vitiligo, particularly for those with darker skin tones and those who reside in culturally diverse nations.[1]

Actually, the disorder's skin depigmentation results from the death of melanocytes, which produce the melanin pigment found in the skin, the hair, mucous membranes, and retina 2, wherein several erratic white spots develop on various skin areas.

Primary patches typically form on sun-exposed areas, such as the face and dorsal hands.[3]

While the precise cause of vitiligo remains unknown, a number of theories have been proposed, including autoimmune, genetic, neurological, biochemical, and self-destruction.[4]

Dermoscopy can help in noninvasive confirmation of the diagnosis by ruling out other illnesses that mimic vitiligo. Vitiligo is basically a clinical diagnosis. More significantly, dermoscopy is becoming more and more used as a valuable supplemental instrument for assessing disease activity.[5]

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Even with the most recent advancements in vitiligo treatment, many patients still experience insufficient or no response to medication, and results are still generally disappointing. TCA has not been extensively studied in clinical trials for repigmentation in cases of stable vitiligo. In summary, TCA appears to be a viable, reasonably priced, and well-tolerated therapy choice for the management of vitiligo in both adult and pediatric patients.[6]

This comparative cross-sectional study compares the effectiveness of topical TCA 70% versus methoxsalen 0.2% paint in treating acral vitiligo from a dermoscopic perspective.

2. Patients and methods

This comparative cross-sectional study evaluated dermoscopically the efficacy of topical TCA 70% versus methoxsalen 0.2 % paint in stable acral vitiligo. The patients were consecutively recruited from the outpatient clinic

of Dermatology of Al-Hussein University Hospital in the period from

November 2022 to November 2023.

Study procedure:

The study includes 50 patients presenting with stable acral vitiligo, divided into two groups of 25 patients. Group (A) received topical methoxsalen 0.2 % every other day for 3 months with dermoscopic follow-up every 2 weeks. Group (B) received topical TCA 70% applied at the clinic every two weeks for 3 months with dermoscopic follow-up.

First, either Septisol or Hibiclens is used to clean the skin. Once the skin feels dry, either acetone or alcohol is used to remove any remaining oils and scale.[7] The skin is then treated with TCA solution in separate layers using cotton-tipped applicators until frosting, or visible blanching, of the skin is attained. When the TCA strength is chosen carefully, one to three passes are typically enough to create icing. Antibiotic ointment is applied topically after the TCA self-neutralizes within the dermis.

Blanching disappears quickly after application and is replaced by erythema and edema. Excessive penetration areas are more likely to experience difficulties and may remain pale.[8] The individual should be advised that modest edema and erythema are normal and will usually go away soon after the procedure. Applying ice and taking a brief course of a topical mid-potent steroid together can help reduce post-treatment inflammation. The few patients who experienced isolated infections and erosions that cleared up a few days later were the only minor adverse effects observed in our cases.[6]

EthicalConsiderations:

After the approval of the Ethics Committee of the Faculty of Medicine,

Al-Azhar University, all participants signed an informed consent after

explaining to them the objective of the study, treatment strategy, anticipated outcomes and adverse consequences, and comparable evaluations of viable substitute therapies.

History taking: Complete a full personal history (name, age, sex, occupation, and residency), including a family history of vitiligo or alopecia areata. Also, complete a medical history to exclude any other skin disease or systemic morbid disease (HTN, DM, Dyslipidaemia, and thyroid disease) and no history of medication for any medical or psychic problem.

All patients will be subjected to Full clinical examination, including estimation of (the VASI score) and (VIDA score), daylight photography+photography under dermoscopy for confirmation of the diagnosis, dermoscopic examination for acral vitiliginous lesions to ensure the stability of these lesions, and lab work (CBC, LIVER PROFILE, LIPID PROFILE, THYROID HORMONES).

Inclusion Criteria: Age 10-50 years, sex: both, stable acral vitiligo for the last (6-12 months), and no history of topical medication for acral vitiligo for the last 3 months.

Exclusion Criteria: Pregnant or breastfeeding females, children below 10 years and patients above 50 years, patients taking any medication for acral vitiligo for the last 3 months, patients who have new lesions or an increase in the size of existing lesions

in the last 6 months or positive Koebner phenomenon, patients with other autoimmune diseases, individuals who have previously had hypertrophic or keloidal scars, as well as those using steroids or other drugs for other systemic disorders, NSAID, immunomodulation drugs, patients with a history of any malignancies and patients with systemic co-morbid condition.

Evaluation of the treatment:

Three months after treatment, clinical and dermoscopic assessments were performed regarding repigmentation response, patient satisfaction, and side effects.

Repigmentation Assessment clinically:

The entire lesion was given a 0% score prior to treatment to show a baseline of no repigmentation and a second percentage that was calculated at the conclusion of the study to represent the degree of repigmentation. This allowed for the determination of response to the treatment based on the quartile grading scale. Two independent dermatologists mindlessly assessed each site's treatment outcome using a 4-point repigmentation percentage scale, classifying the results as "0, absent" (0%), "1, poor" (1-25%), "2, moderate" (26-50%), "3, good" (51-75%), and "4, excellent" (>75%) based on visual comparisons with a pretreatment photo taken in

the same lighting.

Repigmentation Assessment dermoscopic ally:

Response to the treatment was determined by marginal pigmentation appearance of the reticular network, marginal pigmentation, perifollicular pigmentation, and mixed re-pigmentation patterns.

Patient's Satisfaction:

Patients' levels of satisfaction were classified as unsatisfied, partially satisfied, satisfied, or extremely satisfied.

Side Effects:

The patients were to report any problems, including erythema, discomfort, ulceration, burning sensation, ecchymosis, infection, kernelization, and allergy symptoms.

Follow-up assessment:

Following the conclusion of therapy sessions, all patients were observed for three months to identify any worsening (change of color in pigmentation lesions) or recurrence (emergence of new lesions) of the lesions.

Statistical Analysis

SPSS 26 for Windows was used to gather, tabulate, and statistically analyze all of the data (SPSS Inc., Chicago, IL, USA). The Shapiro Walk test was used to determine if the data were normally distributed. Frequencies and relative percentages were used to display the qualitative data. The difference between the qualitative variables was calculated using the chi-square test (x2) and Fisher exact. For parametric data, quantitative data were expressed as mean ± SD (standard deviation); for non-parametric data, they were expressed as median and range. For parametric and non-parametric variables, respectively, the difference between the quantitative variables in the two groups was calculated using the Independent T-test and the Mann-Whitney test. To ascertain the degree of relationship between various parameters, Pearson correlation analysis was performed. In order to forecast clinical progress, regression analysis was performed. Every statistical comparison had two tails and was considered significant. P-values less than 0.05 are considered significant, p less than 0.001 denotes a highly significant difference, and P greater than 0.05 denotes a non-significant difference.

3. Results

Table 1. Information on the two groups under study's demographics

		GROUP (A) (METHOXSALEN) (N=25)	GROUP (B) (TCA) (N=25)	STATISTICS	P VALUE
AGE (YEARS) MEAN ± SD RANGE		26.5±12.9 10:48	24±13 10:48	t=0.66	0.51
GENDER N(%)	Female	12 (48%)	10 (40%)	X^2=0.32	0.569
	Male	13 (52%)	15 (60%)		
FAMILY HISTORY N(%)	Negative	14(56%)	17(68%)	X^2=0.76	0.38
	Positive	11(44%)	8(32%)		
SKIN TYPE N(%12	3	12(48%)	9(36%)	X^2=0.73	0.39
	4	13(52%)	16(64%)		

Regarding age, sex, family history, and skin type, there is no discernible difference between the groups under study (p value>0.05).

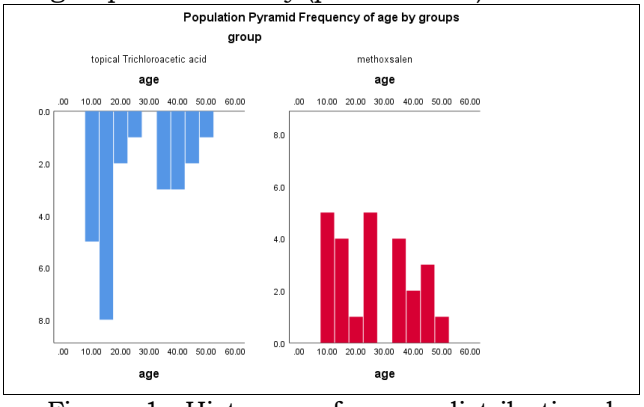

Figure 1. Histogram for age distribution by groups.

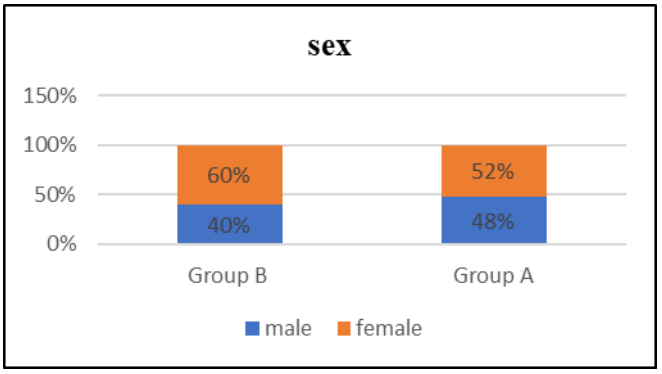

Figure 2. Stack bar chart represent comparison between studied groups regarding sex.

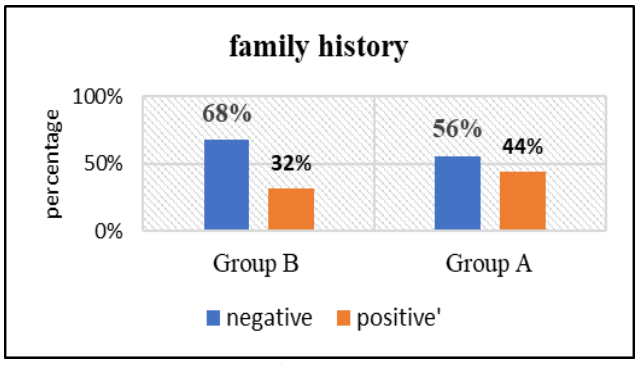

Figure 3. Bar chart represent comparison between studied groups regarding family history.

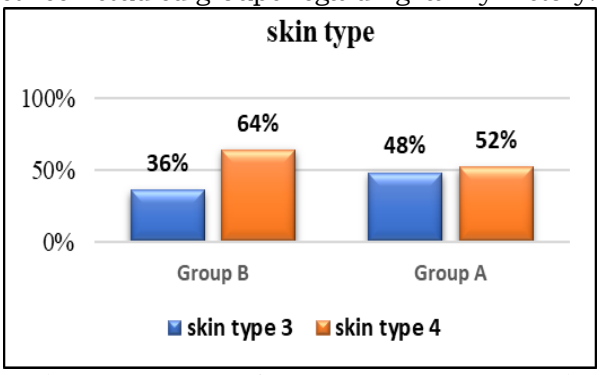

Figure 4. Bar chart represent comparison between studied groups regarding skin type.

Table 2. Comparison between both groups regarding duration of disease and age of onset.

	GROUP (A) (METHOXSALEN) (N=25)	GROUP (B) (TCA) (N=25)	T	P VALUE
DURATION OF DISEASE (YEARS) MEAN±SD RANGE	3.98±2.31 1:10	3.42±1.77 1:7	0.96	0.34
AGE OF ONSET IN YEARS MEAN±SD RANGE	22.5±12.7 7: 46	20.7±13 6 : 46	0.51	0.60

The length of the disease and age of onset do not significantly differ between the two groups, as this table demonstrates (p value > 0.05).

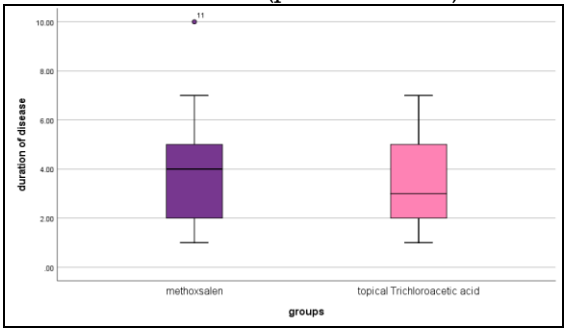

Figure 5. Box plot represent comparison between both groups regarding duration of disease.

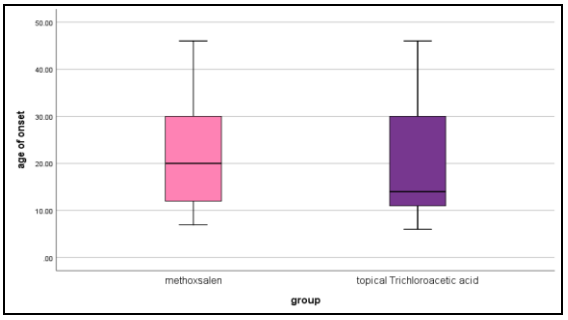

Figure 6. Box plot represent comparison between both groups regarding age of onset of disease.

Table 3. comparison between both groups regarding clinical improvement and satisfaction.

	GROUP (A) (METHOXSALEN) (N=25)	GROUP (B) (TCA) (N=25)		P VALUE
CLINICAL IMPROVEMENT				
NO IMPROVEMENT	24(96%)	19(76%)	X^2=4.5	
MILD IMPROVEMENT	1(4%)	4(16%)	X^2=2	0.04*
MODERATE IMPROVEMENT	0	1(4%)	X^2=NA	0.15
GOOD IMPROVEMENT	0	1(4%)	X^2=NA	-----
EXCELLENT IMPROVEMENT	0	0	X^2=NA	-----

SATISFACTION				
NOT SATISFIED			X^2=4.5	0.04*
PARTIALLY SATISFIED	24(96%)	19(76%)	X^2= 2	0.15
COMPLETELY SATISFIED	1(4%)	4(16%)	X^2=NA	-----
	0	2(8%)		

Significant at p value 0.05; NA can't be estimated; X 2 chi square

The study groups differed significantly in terms of no improvement (p value<0.05), with 76% of patients receiving TCA and 96% receiving methoxsalen demonstrating no improvement. While the improvement in patients receiving TCA was mild, moderate, and good (16, 4%, and 4%), the change in patients receiving methoxsalen (4, 0, 0) was statistically non-significant (p value>0.05).

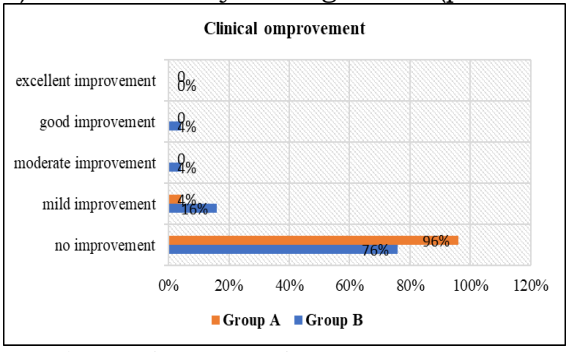

Figure 7. Bar chart represent comparison between studied groups regarding clinical improvement.

Table 4. Comparison between studied groups regard Pigmentation pattern of dermoscopic examination and site of lesion.

	GROUP (A) (METHOXSALEN) (N=25)	GROUP (B) (TCA) (N=25)	STATISTICS	P VALUE
PIGMENTATION PATTERN OF DERMOSCOPIC EXAMINATION				
NO RE-PIGMENTATION	24(96%)	19(76%)	x^2=4.5	0.04*
MARGINAL PIGMENTATION AND APPEARANCE OF RETICULAR NETWORK	1(4%)	3(12%)	x^2=1	0.29
PERIFOLLICULAR PIGMENTATION AND APPEARANCE OF RETICULAR NETWORK	0	1(4%)	NA	----
MIXED	0	2(8%)	NA	----
SITE OF LESION				
RIGHT HAND	8(32%)	4(16%)	x^2=2.1	0.55
LEFT HAND	5(20%)	8(32%)		
RIGHT FOOT	6(24%)	7(28%)		
LEFT FOOT	6(24%)	6(24%)		

Significant at p value 0.05; NA can't be estimated; X 2 chi square

When it comes to no re-pigmentation, there is a substantial difference between the examined groups (p value<0.05), with 76% of patients receiving TCA and 96% of patients receiving methoxsalen showing no re-pigmentation. Although the pigmentation of patients receiving TCA (12%, 4%, and 8%) was either marginal, perifollicular, or mixed, the pigmentation of patients receiving methoxsalen (4%, 0, 0) was not statistically significant (p value >0.05).

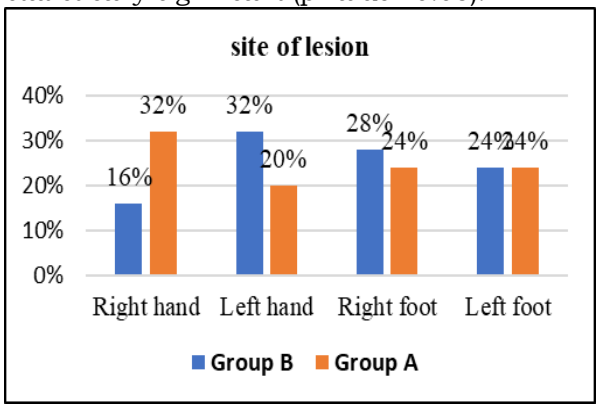

Figure 8. Bar chart represent comparison between studied groups regarding site of lesion.

Table 5. correlation between clinical improvement and other parameter.

CORRELATION	CLINICAL IMPROVEMENT	P VALUE
DURATION OF DISEASE	r= -0.15	0.27
AGE OF ONSET	r= -0.05	0.75
SKIN TYPE	r=0.02	0.84
PATIENT SATISFACTION	r=0.98	<0.001*

*significant at p value 0.05; r: mean correlation coefficient

There are strong positive correlation between clinical improvement and patient satisfaction as correlation coefficient 0.92 and p value<0.01. On other hand no significant correlation was found with duration of disease, age of onset and skin type.

Table 6. Relation between clinical improvement and pattern of pigmentation dermoscopically.

		CLINICAL IMPROVEMENT				TOTAL	P VALUE
		N0	Mild	moderate	good		
PATTERN OF REPIGMENTATION DERMOSCOPICALLY	no re-pigmentation	43	0	0	0	43	
		100.0%	0.0%	0.0%	0.0%	86.0%	
	marginal pigmentation and appearance of reticular network	0	4	0	0	4	
		0.0%	80.0%	0.0%	0.0%	8.0%	
	perifollicular pigmentation and appearance of reticular network	0	1	0	0	1	
		0.0%	20.0%	0.0%	0.0%	2.0%	
	Mixed pattern of repigmentation	0	0	1	1	2	
		0.0%	0.0%	100.0%	100.0%	4.0%	
TOTAL		43	5	1	1	50	<0.001*
		100.0%	100.0%	100.0%	100.0%	100.0%	

X^2=100

MEASURE OF ASSOCIATION (ETA)=0.98

Significant at p value 0.05; X2 mean chi square

There is significant association between pattern of pigmentation and degree of clinical

improvement (p value<0.05) and Eta=0.98 this mean strong association was found.

Table 7. Binary logestic regression for predictors of clinical improvement.

		CRUDE OR	P VALUE	(95% CI) OF OR
SEX	Female	1	0.38	1
	Male	0.46		(0.08: 2.6)
SKIN TYPE	4	1		1
	3	1.04	0.99	(0.20 :5.2)
DURATION OF DISEASE		1		
		0.71	0.17	(0.43:1.1)
FAMILY HISTORY	Positive	1		1
	Negative	0.79	0.77	(0.15 :3.9)

Cases with negative family history are 0.79 times liable for improvement compared to positive case, also male are less liable for improvement than female (OR=0.46). While for skin type there is no difference between skin type 3 and 4 regarding improvement.

4. Discussion

Regarding no improvement, there is a substantial disparity between the groups under study. (p-value is 0.04), 76% of patients who received TCA showed no improvement compared to 96% of patients who received methoxsalen. That made TCA better than methoxsalen. While 16%, 4%, and 4% of patients who received TCA had shown mild, moderate, and good improvement, respectively, compared to 4%, 0%, and 0% in patients who received methoxsalen, respectively; statistically speaking, there was no difference (p-value>0.05).

Nonsatisfied patients were statistically significantly higher with methoxsalen than TCA, with 96% and 76%, respectively (p-value=0.04). While partially satisfied patients were statistically insignificantly higher with TCA than methoxsalen, with 16% and 4%, respectively (p value=0.14). Two patients (8%) in the TCA group were completely satisfied, yet no one was completely satisfied in the methoxsalen group.

Regarding the pigmentation pattern of dermoscopic examination and site of lesion in the studied groups, the pigmentation pattern of dermoscopic examination was categorized as no re-pigmentation, marginal pigmentation, and appearance of the reticular network, perifollicular pigmentation, and mixed re-pigmentation patterns.

Regarding no re-pigmentation, there is a significant difference between the groups under study (p-value=0.04), as 76% of patients who received TCA had shown no re-pigmentation compared to 96% of patients who received methoxsalen. While 12%, 4%, and 8% of patients who received TCA had re-pigmentation either marginal, perifollicular, or mixed, respectively, compared to 4% had marginal re-pigmentation in patients who received methoxsalen, and this difference was statistically non-significant between the groups (p-value>0.05). This previous finding supports the higher repigmentation results of TCA compared to methoxsalen.

Similarly, Nofal et al.[6] Analyze the safety and effectiveness of TCA at various dosages for the management of persistent localized vitiligo. There were one hundred patients with stable vitiligo, including acral and nonacral. Every two weeks, or for a maximum of six treatment sessions, trichloroacetic acid was applied as a monotherapy to the vitiliginous patches at varying concentrations based on the treated site until full repigmentation. For six months, there was a follow-up every month to look for any recurrence. The face, trunk, and extremities responded to TCA treatment the best, with eyelid vitiligo showing the highest response (good improvement in 80% of patients). There were reduced response rates in the vitiligo of the hands and feet. Few patients experienced minor and transitory adverse effects.

Unlike our finding, In Ibrahim et al.[9] experiments, following skin microneedling with Dermapen and using 70% TCA, assessment of repigmentation was with no effect (8.2%), mild (23.5%), moderate (14.8%), good (38.3%), and excellent (14.7%). Patient satisfaction was not satisfied, satisfied, and very satisfied in 20.5%, 38.2%, and 41.1% of patients. The different results of this previous study may be due to microneedling using dermapen.

Unlike our finding, in another study by El-Mofty et al.[10] 50% of patients were not satisfied with TCA at a dose of 25%, 10% were somewhat pleased, and 40% were highly satisfied. The authors employed TCA at two different concentrations, 25% and 50%. Meanwhile, with TCA, 25% and 15% of patients were not satisfied, 35% were moderately satisfied, and 50% were highly satisfied, which disagreed with our findings. The different results of this previous study are due to acral vitiligo being more resistant to treatment than other types included in the EL-Mofty study so that we may need a higher concentration of TCA.

Khater et al.[11] concluded that combining microneedling plus TCA 70% and intradermal injection of 5-FU can be a straightforward approach to managing vitiligo, yielding satisfactory cosmetic repigmentation outcomes across all age cohorts. This approach can be employed as a relatively safe alternative or an augmenting technique, either before or in conjunction with any established and widely

accepted methods for treating stable, non-segmented vitiligo. The findings of this study suggest that this combination therapy offers a viable option for individuals seeking effective and aesthetically acceptable solutions for their vitiligo-related concerns.

After TCA 70% with micro-needling in the Khater et al.[11] study, his results were contrary due to the use of micro-needling. In 43.8% of patients, the edit was moderate (26–50%); in 18.8% of patients, the improvement was good to exceptional (repigmentation>50%); and in 6.2% of patients, there was no change.

In addition, Elnokaly et al.[12] compared the efficacy of 70% TCA. Specifically, the researchers examined the effectiveness of microneedling combined with TCA compared to micro-needling with tacrolimus in treating 60 patients diagnosed with Vitiligo. The study results indicated a slightly higher repigmentation level observed in the TCA patches, as opposed to those treated with tacrolimus.

Furthermore, an excellent response in terms of repigmentation was observed in approximately 43.3% of the patches treated with TCA. Additionally, 13.3% of the TCA-treated patches showed a noticeable improvement.

Furthermore, 10.0% of the TCA-treated patches showed a substantial improvement, while 13.3% of the TCA-treated patches showed a mild improvement. Thus, these findings shed light on the potential benefits of incorporating 70% TCA in treating Vitiligo patients, particularly when combined with microneedling techniques.

Regarding the correlation between clinical improvement and other parameters, there is a strong positive correlation between clinical improvement and patient satisfaction, with a correlation coefficient of 0.92 and p-value < 0.01. On the other hand, no significant correlation was found with duration of disease (r= -0.15 and p value=0.27), age of onset (r= -0.05 and p value=0.75), and skin type (r=0.02 and p value=0.84).

4. Conclusion

Trichloroacetic acid (TCA) demonstrates a notably better response and higher. Patient satisfaction compared to methoxsalen. Consequently, TCA 70% emerges as a preferable recommendation for acral vitiligo treatment over methoxsalen. TCA 70% had a lower effective rate (6 cases only improved of a total of 25 cases) in this study, so we recommend a trial of a high concentration or microneedling before the application of TCA to achieve a better response. The dermoscopic examination is helpful in noticing early repigmentation and early improvement during the treatment of vitiligo, in addition to its use in the assessment of vitiligo activity.

Disclosure

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Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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