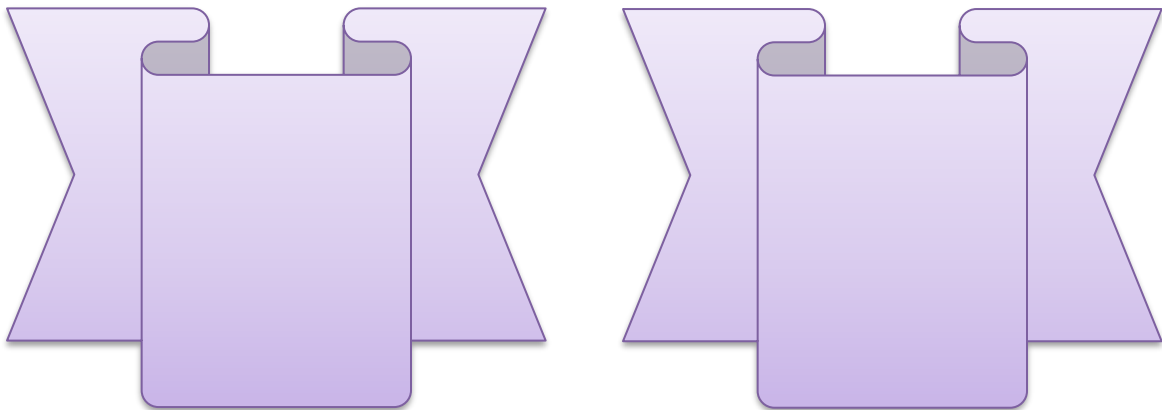


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## Original Article

# Efficacy of Trichloroacetic Acid in Patients with Alopecia Areata: A Clinico-Histopathological Study

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## ABSTRACT

### Article information

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**Background:** Alopecia areata is an autoimmune disorder caused by a breakdown in the follicular immune privilege system, resulting in non-scarring hair loss. Many therapeutic options have been tested with variable results.

**Aim of the work:** To assess the efficacy of trichloroacetic acid [TCA] 35% in patients of alopecia areata.

**Patients and Methods:** This prospective cross-sectional study included 40 patients recruited from department of dermatology and venereology, Al-Hussein hospital. Every patient was treated by 3 sessions of TCA 35% with one-month intervals. The assessment was done by clinical, trichoscopy, and histopathological examination.

**Results:** The study included 40 patients, 22 males [55%] and 18 females [45%]. The mean age of studied patients was  $25.6 \pm 8.6$  years with a minimum age of 16 years and a maximum age of 50 years. The duration of the disease ranged between 2 months and 10 years with a mean duration of  $2.7 \pm 2.5$  years. Thirty patients [75%] showed improvement at the end of TCA sessions.

**Conclusion:** Based on our findings, topical application of TCA 35% is a safe and effective treatment option for patients with alopecia areata. Moreover, it can be used in wide areas of the scalp and cases of alopecia totalis.

**Keywords:** Alopecia; Hair loss; Alopecia areata; Trichloroacetic acid.



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## INTRODUCTION

Alopecia areata [AA] is an autoimmune disorder characterized by hair loss in small, irregular areas. Hair loss is most commonly seen on the scalp, although it can also appear in other hairy parts of the body and can manifest in many different patterns. Although it is a benign condition and most patients are asymptomatic, it can cause emotional and psychosocial distress [1].

Alopecia areata can progress to complete loss of scalp hair [alopecia totalis] or loss of all body hair [alopecia universalis] [2]. It can affect children, adults, and hair of all colors, also both sexes equally [3].

The cause of AA remains incompletely understood, but many factors include autoimmune process, genetic susceptibility, environmental factors, psychological stress, and oxidative stress are all suggested to contribute to the disease [4-8].

Alopecia areata is primarily a hair follicle cycle disease [9]. An unexplained trigger is thought to initiate an autoimmune lymphocyte invasion upon a hair bulb in AA. This inflammatory process is particular for anagen hairs and generates anagen arrest, resulting in aberrant anagen hair loss, which is clinically known as dystrophic anagen hair with tapering proximal ends and a paucity of root sheaths. Once AA becomes chronic, hair follicles often stay in a protracted telogen phase with no discernible attempt to revert to an anagen growing phase [10, 11].

Alopecia areata frequently occurs in association with other autoimmune disorders such as vitiligo, thyroid disease, type 1 diabetes mellitus, pernicious anemia, Addison's disease, lupus erythematosus, atopic dermatitis, and psoriasis [12-15]. A hallmark of active alopecia areata is the presence of peribulbar lymphocytes around the bulb region of anagen hair follicles upon histopathological examination [10].

The stimulated synthesis of cytokines and growth factors [particularly platelet-derived growth factors, keratinocyte derived growth factor, vascular endothelial growth factor [VEGF], and IL-10] may be the postulated action mechanism of Trichloroacetic Acid [TCA] in AA. IL-10 has an anti-inflammatory effect, and its concentration was raised after

treating with diphenylcyclopropanone. Moreover, VEGF induces new blood vessels formation, so enhancing the follicular nutrition. Immunomodulatory effect via sensitization and elimination of reactive T lymphocytes is another possible method of action [16].

In this study, we aimed to assess the therapeutic effect of trichloroacetic acid [TCA] 35% in patients with alopecia areata.

## PATIENTS AND METHODS

### Study design and population

This study is a prospective cross-sectional study that included 40 patients recruited from the department of Dermatology and Venereology, Al-Hussein hospital.

The study was approved by the local ethical committee of Al-Azhar University [0000030]. Informed consent was signed by each patient after explaining the nature of the study.

**Inclusion criteria:** All clinical forms of alopecia areata affecting the scalp [monolocularis, multilocularis, ophiasis and alopecia totalis].

**Exclusion criteria:** Age more than 60 years old, patient receiving any other line of treatment within the last 2 months, pregnant and lactating females.

### Treatment protocol

All patients were subjected to full history taking followed by clinical examination of the scalp to evaluate the clinical forms and the severity of alopecia. The region to be treated was cleaned with 70% alcohol, then a semi saturated cotton tip was applied in 2-3 layers till frosting. Patients received a total of 3 regular sessions of TCA 35% one month apart. Patients were advised to use topical antibiotic cream twice daily for one week and desquamation occurred within 5 days of treatment.

### Clinical evaluation

All patients were subjected to evaluation by MacDonald hull and Norris grading system<sup>17</sup> for density, pigmentation, and texture of growing hair before treatment, after every session, and at the end of treatment protocol.

Serial photographs using Nikon D5300 camera with lens [18-55] were taken, and to reduce potential bias, scoring was performed by two independent blinded dermatologists.

**Dermoscopic evaluation:** All patients were examined using DermLite DL4 handheld dermoscope, attached to iPhone 13 Pro camera and was evaluated by non-treating blinded dermatologist pre- every- and 3 months post procedural to assess exclamation marks, dystrophic hairs, yellow dots and black dots.

**Patient satisfaction:** On a quartile scale, patients rated their progress at the end of the study [markedly improved  $\geq 75\%$ , significantly improved 50%–74%, moderately improved 25%–49%, and slightly improved 25%].

### Histological evaluation

From the scalp lesion to be treated, a 2-mm punch biopsy [down to the level of subcutaneous tissue to fully evaluate the follicular area] was obtained at the first visit and 4 weeks after the last session. Each biopsy was fixed in 10% formalin solution at 4 °C overnight, dehydrated with alcohol, and embedded in paraffin, sectioned, and then examined histologically using hematoxylin and eosin [HE] stain [staining epidermis and dermis]. Specimens were graded descriptively and examined by two dermatopathologists. AA of the face was excluded as most patients would refuse the biopsy from face due to cosmetic reasons.

All parameters [epidermal changes, sebaceous glands, hair follicle structure, number of hair follicles, collagen deposition around hair follicle and cellular infiltrate] were assessed in each of the stained sections.

**Follow-up:** During sessions, weekly follow-up was performed to examine any side effects like pain, erythema, dyspigmentation, and/or scarring. After the end of sessions, a monthly follow-up evaluation was done for 3 months to assess the results and exclude the relapse of treated patches of AA.

**Statistical analysis:** Data were fed to the computer and analyzed using SPSS version 20.0. [Armonk, NY: IBM Corp]. Proper tests were performed according to each variable.

## RESULTS

The study included 22 males [55%] and 18 females [45%]. The mean age of our studied patients was  $25.6 \pm 8.6$  years with a minimum of 16 years and a maximum of 50 years of age. The duration of alopecia among our patients ranged between 2 months and 10 years with a mean duration of  $2.7 \pm 2.5$  years. Eight patients [20%] had a family history of alopecia, and 10 patients [25%] were smokers. There were 4 diabetic patients [10%] and 2 hypertensive patients [5%]. Multilocularis type was the most clinical presentation [45%] other types were as follow: ophiasis [20%], monocularis [20%], and alopecia totalis [15%] [Table 1].

There was non-significant statistical difference of overall response as regard age, sex, history of smoking and chronic disease. The treatment showed a response in 30 patients [75%]. Response was graded according to MacDonald hull and Norris grading system as follow: minimal response in 8 patients [20%], moderate response in 12 patients [30%], good response in 6 patients [15%], and excellent response in 4 patients [10%], while there was no response in 10 patients [25%]. All cases of monocularis type showed response to the treatment [Table 2].

All patients that had active alopecia areata on dermoscopic examination 14 patients [35%] responded to treatment. We also found that response increased with sessions among our patients [35%, 62.5% & 75% in 1st, 2nd & 3rd sessions respectively].

Regarding histopathological examination, there was an increased number of hair follicles after treatment [ $2.35 \pm 1.5$ ] when compared with number of hair follicles before treatment [ $1.35 \pm 0.7$ ]. Regarding inflammatory infiltrate before treatment, it was minimal in 12 patients [30%], mild in 20 patients [50%] and moderate in 8 patients [20%] while after treatment, it was minimal in 36 patients [90%], mild in 2 patients [5%] and there was no infiltrate in 2 patients [5%] showing highly statistical significant [p-value < 0.001] decrease of infiltrate around hair follicles was found after treatment. No statistically significant difference [p-value > 0.05] was found as regard changes in epidermis, sebaceous glands, and collagen deposition around hair follicles before and after treatment [Table 3].

**Table [1]:** Response to treatment according to the type of AA

Alopecia type		Response				Stat. test	P-value
		No [n = 10]		Yes [n = 30]			
	Ophiasis	2	20%	6	20%	X <sup>2</sup> = 3.5	0.314
	Monolocularis	0	0%	8	26.7%		
	Multilocularis	6	60%	12	40%		
	Alopecia totalis	2	20%	4	13.3%		

**Table [2]:** Overall response to treatment according to MacDonald hull and Norris grading system

Studied patients [n = 40]			
Overall response	No	10	25%
	Yes	30	75%
Response grade	No	10	25%
	Minimal	8	20%
	Moderate	12	30%
	Good	6	15%
	Excellent	4	10%
Developed hair	No	10	25%
	Normal coarse hair	10	25%
	Fine villous hair	8	20%
	Intermediate hair	12	30%
Pigmentation	No	10	25%
	Normally pigmented	10	25%
	Partially pigmented	8	20%
	Moderately pigmented	12	30%
Density	No hair growth	10	25%
	1 – 25% growth	8	20%
	26 – 50% growth	12	30%
	51 – 75% growth	6	15%
	76 – 100% growth	4	10%

**Table [3]:** Histopathological findings before and after treatment

		Follow				Stat. test	P-value
		Before [n = 40]		After [n = 40]			
Epidermis	Normal	32	80%	34	85%	X <sup>2</sup> = 0.34	0.556
	Atrophy	8	20%	6	15%		
Infiltrate	No	0	0%	2	5%	X <sup>2</sup> = 36.7	< 0.001
	Minimal	12	30%	36	90%		
	Mild	20	50%	2	5%		
	Moderate	8	20%	0	0%		
Sebaceous gland	Normal	16	40%	24	60%	X <sup>2</sup> = 3.2	0.074
	Atrophy	24	60%	16	40%		
Hair follicle structure	Normal	20	50%	32	80%	X <sup>2</sup> = 7.9	0.005
	Atrophy	20	50%	8	20%		
Collagen deposition	Normal	24	60%	22	55%	X <sup>2</sup> = 0.2	0.651
	Thickened	16	40%	18	45%		
Number of hair follicle	Mean ± SD	1.35 ± 0.7		2.35 ± 1.5		MW = 458	< 0.001

## DISCUSSION

Before making a decision on the most appropriate treatment for alopecia areata, the patient's age in addition to the extension of the condition should be taken into account. **Chikhalkar et al.** [18] carried out a prospective trial in 2011 using topical phenol 88% for patchy areas of AA and reported a 78% improvement in hair regrowth. The most

common adverse reaction was hypo-pigmentation. Additionally, lactic-acid 15% was applied topically every other day and shown to be effective. The most prevalent side effect was transitory erythema [18].

The first trial to use TCA topically in treating alopecia was done by **Mahgoub et al.** [19] and they reported a significant improvement.

Our study included 22 males [55%]. Al-Dhalimi *et al.* [20] in his study included also more male patients [60%]. Also, El-Husseiny *et al.* [21], Majid *et al.* [22] and Vila *et al.* [23] showed the same percentage [60%] of males among patients with alopecia in their studies. Zaher *et al.* [24] showed even higher percentage of males among his patients [67%].

The mean age of our studied patients was  $25.6 \pm 8.6$  years. El-Husseiny *et al.* [21] showed that the mean age was 30 and the age range was between 18 and 47 years. While in Majid *et al.* [22], the age ranged between 11 and 48 years, and Wang *et al.* [25] showed higher mean of age among patients with alopecia [34 years]. Even higher mean of age was seen among patients in the study conducted by Al-Dhalimi *et al.* [20] for the study of fractional laser in treatment of alopecia which was 45 years.

The duration of alopecia among our patients ranged between 2 months and 10 years, with a mean duration of  $2.7 \pm 2.5$  years. El-Husseiny *et al.* [21] and Zaher *et al.* [24] showed the mean duration [13.2 months & 1.8 years] respectively. In Wang *et al.* [25]'s study, the mean duration of the disease was much higher [7 years].

There was a statistically significant difference regarding the duration of alopecia. Patients with shorter duration of alopecia responded to our treatment better than those with longer duration of the disease.

Among our patients, 8 [20%] had a family history of alopecia. It was slightly higher in El-Husseiny *et al.* [21] study, where about 25% of the patient reported family history of alopecia. In Zaher *et al.* [24] there was no family history among the patient [15 patients], and this could be explained by the smaller number of the patients in their study.

In this study, minimal response was found in 8 patients [20%], moderate response in 12 [30%], good response in 6 [15%], and excellent response in 4 [10%] while there was no response in 10 patients [25%]. According to Mahgoub *et al.* [19], 63.6% of cases showed excellent outcome to TCA, 18.2% showed good outcome, 4.5% showed fair result, and 13.6% showed poor result.

The higher percentage of response in the present study was observed in patients with active alopecia [14 patients, 100%] when

compared to patients without active alopecia [16 patients, 61.5%] with statistically significant difference. This could be explained that an early treatment when the hair follicles are not destroyed, will give the ability of successful hair regrowth.

Trichoscopic evaluation in our study showed marked reduction of dermoscopic finding of AA as follow exclamation mark [EM], yellow dot [YD], brown dot [BD] and dystrophic hair [DH] and coincided with Mahgoub *et al.* [19] who showed that trichoscopic features were substantially reduced, denoting disease activity.

Histopathological evaluation of our study showed marked reduction of lymphocytic infiltrates around the bulb region of anagen hair follicles [swarm of bees] in active case of alopecia areata and there was an increase in the diameter and number of hair follicles.

Although our study has limitations such as: single center study, lack of immunohistochemistry, small number of subjects, and short duration of follow-up.

**Conclusion:** Our study shows that topical TCA 35% is a simple, in-office, safe, and efficient line of therapy in cases with AA. It's considered a good option in wide area of the scalp and alopecia totalis. Moreover, TCA 35% is a great option for children with AA as it's nearly painless technique and doesn't include needles.

**Conflict of interest disclosure statement:** The authors have no potential conflict of interest to declare.

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