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Trichloroacetic Acid (TCA) Peels for Depigmentation in Universal Vitiligo: A Retrospective Analytical Study

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Abstract

Depigmentation is advocated as a treatment option in people with vitiligo when the disease involves the skin on a major portion of the body surface area and is left with residual pigmentation on the face or other exposed body parts. Depigmentation in such patients can be achieved by using topical treatments or procedures like Cryotherapy, Q-switched lasers, or peels. This is a retrospective analytical study on patients with Universal vitiligo in whom the residual pigment was treated with 20-30% Trichloroacetic acid (TCA) peels at our institute over 2 years. Data of about 40 such patients was retrieved including the demographic data, the total number of peeling sessions received, any adverse effects recorded, and the response seen at the end of treatment sessions. Out of 40 patients, 37 patients completed the treatment course and >75% clearance of pigmentation (excellent response) was achieved in 32 patients (86.48%). In addition, 2 patients (5.40%) reported 50-75% clearance of pigmentation (good response) while 3 patients (8.10%) reported poor results. No significant adverse effects were reported in any treated patient and no patient experienced a recurrence of pigmentation over 3 months of post-treatment follow-up.

Keywords: ***Vitiligo; Depigmentation; Peels; Trichloroacetic acid (TCA)***

1. Introduction

Vitiligo is a multifactorial depigmenting disorder characterized by amelanotic, non-scaly, chalky-white macules on the skin and/or mucosae. Vitiligo is classified as an autoimmune disease and is associated with genetic and environmental factors including metabolic factors, oxidative stress, and cell detachment abnormalities [1,2].

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Classification of vitiligo is important primarily because of its prognostic implications. Vitiligo is classified into two major forms: nonsegmental vitiligo (NSV) and segmental vitiligo (SV) [2]. Achieving uniform-colored skin in vitiligo patients is a process that entails repigmentation and camouflaging as well as depigmentation; especially in patients with very extensive body surface area involvement (universal vitiligo) [3].

Universal vitiligo (UV) corresponds to complete or nearly complete depigmentation of the skin and the term is commonly used when NSV gradually progresses to almost complete depigmentation of the skin (>80% body surface area), and sometimes oral/genital mucosae. Small perifollicular, discrete, or coalescent pigmentation may persist in sun-exposed areas in patients with universal vitiligo [2]. This persistent pigmentation on the face and hands can be quite disfiguring for individuals, especially those with skin of color. The psychological impact on the quality of life resulting from this residual pigmentation is as significant as the vitiligo itself. Depigmentation treatment is thus advocated in these patients to clear the residual pigment present. Although monobenzyl ether of hydroquinone (MBEH) cream is the mainstay of depigmentation therapy, it takes a long time to act and can result in complications in some patients [4]. Patients who do not respond fully to MBEH or who are intolerant to the drug can be managed by cryotherapy, Q-switched Nd: YAG laser, Ruby laser, and Alexandrite laser treatment. However, the availability of these laser devices and the cost involved is sometimes an important limiting factor [5,6]. Chemical peels like phenol and trichloroacetic acid (TCA) have also been used as depigmenting therapy in vitiligo. Phenol can achieve the goal of complete depigmentation, although, to avoid systemic absorption and toxicity, the application has to be confined to small areas [7] TCA peel is one of the most commonly used peels in hyperpigmentation disorders and its effect is based on sloughing off of the epidermis and removal of excess melanin along with impairment of melanin synthesis [8].

2. Materials and Methods

This is a retrospective analytical study which was conducted at a private dermatology setup in August 2023 on patients with UV who had undergone serial peeling sessions with TCA from July 2021 to June 2022 for the treatment of residual pigmentation on any part of the body.

Demographic data, the site of the body treated, total number of sessions received, overall response to treatment, topical treatments used in between sessions, and other relevant data were retrieved from the records. Clinical details and repeat digital photographs taken at each clinic visit were used and compared with pretreatment data and photographs to aid the assessment of results. Any adverse effects recorded in the data were also noted down.

All patients had UV involving body surface area >80% with cosmetically unacceptable spotted localized residual pigmentation on the face, hands, forearms, and/or feet. All patients had been photographed at the initial visit and consequent visits, and an informed consent for treatment had been obtained from each one of them before starting the peeling sessions.

The peeling sessions were done only in those cases of universal vitiligo who had not responded satisfactorily to MBEH therapy or were intolerant to it. The peeling sessions were repeated at 2-week intervals till complete depigmentation or a maximum of 6 sessions at each site. The end point of peeling process was the appearance of a uniform, white frosting at the application sites. If at 20% concentration of TCA, no frosting occurred, the concentration was increased to 30%. Topical antibacterial ointment

twice daily and daily application of a broad-spectrum sunscreen with SPF 50+ was advised. Patients were strictly advised to avoid sun exposure, heat, rubbing, scratching, or picking at the scab. Patients were instructed to continue MBEH treatment in between the peeling sessions.

3. Clinical Response

Response was evaluated from the data available and from repeat digital photographs after each session. The degree of depigmentation was rated as excellent (>75% resolution of pigment), good (50%-75% resolution of pigment) or poor (<50% resolution of pigment).

4. Results

A total of 40 patients with UV, having an involvement of >80% body surface area had been enrolled for the treatment out of which 37 patients (11 males and 26 females) completed the course of treatment. The age of patients ranged from 15 - 64 years with a mean of 37.1 years.

Out of these 37 cases, 32 patients (86.48%) reported excellent response with >75% clearance of pigmentation (FIG. 1a,b), 2 patients (5.40%) reported 50% - 75% clearance of pigmentation (good response) while 3 patients (8.10%) reported <50% clearance of pigmentation (poor response) (TABLE 1).

Face was a site treated in all patients (37) and thus, was the most common site for the TCA peeling sessions. The treatment of residual pigmentation on other sites included, hands (11), feet (11), and forearms (8) respectively. Each of these sites received one to six sessions. of TCA peeling. No site received more than 6 sessions. Face responded well to 20% TCA peel while in case of the hands, feet, and forearms, 30% TCA was needed in the majority of cases. The average number of peeling sessions for each site ranged from 2 to 5 (mean=3.2).

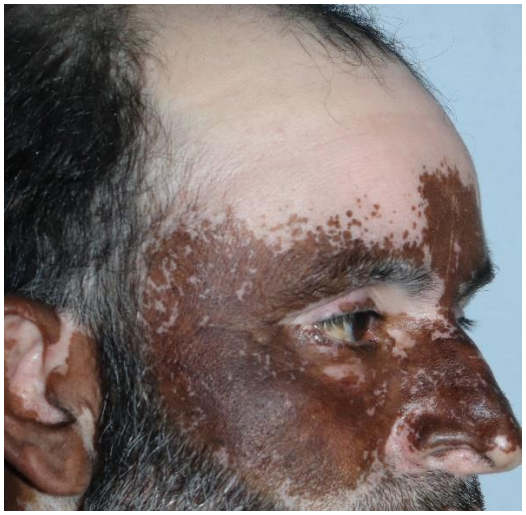

FIG. 1a.

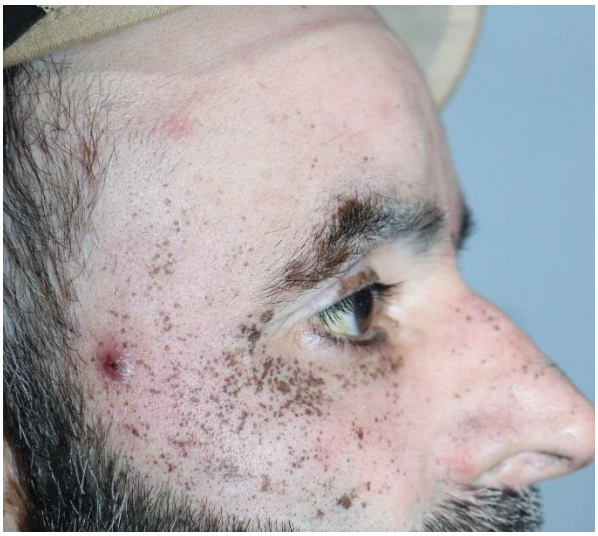

FIG. 1b.

TABLE 1. **Clinical response assessed among the studied cases.**

TREATMENT CASES	**CLINICAL RESPONSE**		
	EXCELLENT (>75% DEPIGMENTATION)	GOOD (50% - 75% DEPIGMENTATION)	POOR (<50% DEPIGMENTATION)
n=37	32	2	3
%	86.48%	5.40%	8.10%

TABLE 2. **Sites treated with TCA peels.**

Treatment site		**Total number (n)**	**Percentage of patients treated**
Face		37	100%
Hands		11	29.7%
Forearms		8	21.6%
Feet		11	29.7%

No significant adverse effects were reported, and the procedure was termed as 'tolerable' by all patients. All patients experienced a mild tingling sensation during the peeling sessions. There were no serious post-treatment sequelae in any patient. None of the patients reported the development of colour mismatch at the treated sites.

In the follow-up period of 3 months, all 34 of the positive responders (91.8%) were able to preserve the therapeutic benefit of the treatment. The patients' level of satisfaction was quite high, with most patients being highly satisfied with the treatment offered. (32/37).

5. Discussion

Depigmentation is a practical solution for UV and subjects living with extensive NSV who are unresponsive to all medical management options [6]. The nature of this treatment is prolonged, and results are permanent which makes patient selection and screening important. This retrospective study assessed the efficacy and safety of TCA in patients of UV who did not respond to or were intolerant to topical treatment with MBEH.

MBEH is a hydroquinone derivative that has been used as a depigmenting agent in a wide range of pigment disorders [9]. It is the only US FDA-approved treatment for depigmentation in vitiligo [5]. It acts through the formation of quinone products and ROS to induce specific T-cell response against melanocytes [3]. Depigmentation is mostly irreversible and histologically associated with the loss of melanosomes and melanocytes [3]. Gradual lightening of the skin occurs over 4 to 12 months with this topical therapy [3]. MBEH can be used at different concentrations: 10% on the face, 5% on the neck, 20% on the arms and legs. For patients who do not respond to 20% MBEH for 3 to 4 months, the concentration can be increased to 30% and up to 40% if there is no response, primarily on the extremities, especially the elbows and knees. Concentrations greater than this must not be encouraged [3].

Successful management of residual pigment in extensive non-responding vitiligo was first described by Ole Rordam et al in 2012 in a patient with slowly progressive, enlarging, depigmented areas on the pectoral area, upper arms, legs, and face [10]. However, MBEH has been used judiciously since its potential negative side effects such as skin irritation, contact dermatitis, ocular side effects, exogenous ochronosis became known [9,11]. When treating patients who experience the burden and stigma of ubiquitous vitiligo with significant residual pigmentation, its potential cosmetic benefits should always be taken into consideration [12] A longer duration of therapy and higher concentrations may be required if the disease has been stable for many years [13].

Chemical peels are used to treat hyperpigmented skin disorders through controlled chemical burns of epidermis and/or dermis. TCA acts by precipitation of proteins, coagulation, and necrosis in the epidermis. A well-known side effect of TCA peels is post-inflammatory hypopigmentation [14]. The release of inflammatory cytokines induced by inflammation of the skin can cause cessation of melanogenesis, and severe inflammation leads to complete loss of melanocytes causing permanent hypopigmentation [15]. El-Mofty et al. [6] evaluated the use of TCA (25%, 50%) to remove residual facial pigmentation in 20 Egyptian patients with extensive vitiligo. They reported better results with TCA 50% and suggested that using higher concentrations disrupt the dermoepidermal junction leading to koebnerization and better depigmentation. They reported that patients with active vitiligo had better outcomes than those with less active disease. Alternatively, in 2021, Nofal A et al. [16] attempted the use of TCA 100% for the removal of residual pigmentation of face in 50 patients of universal vitiligo, of which 80% showed excellent response and 12% cases had partial depigmentation. A median number of two sessions was required to achieve complete depigmentation. Minor adverse effects such as burning sensation, erosions and local infection were reported. Comparatively, depigmentation therapy done with TCA 100 % used by Ahmad Nofal et. al, had better results compared to the tested subjects with TCA 25% and 50% used by El-Mofty et al [6]. This outcome was possibly due to the use of higher concentrations by the former.

Based on the findings of these previous studies, we hypothesised that the use of TCA peel in combination with MBEH might aid in avoiding the negative side effects associated and yield more prolonged and better depigmentation as compared to monotherapy with either modality. Therefore, we retrospectively analysed the usage of TCA 20% - 30% to induce complete depigmentation in 40 patients with vitiligo universalis who had recalcitrant pigmented spots on the face, hands, forearms, and feet and who started using MBEH two weeks prior to and in between the peeling sessions. Patients older than twelve years were included in our study. 37 patients completed the study and 32 patients (86.48%) showed excellent response (>75%), 2 patients (5.40%) showed good response (50% - 75%). The average number of peeling sessions for each site ranged from 2 to 5 (mean=3.2) and face responded well to 20% TCA peel while for the hands, feet and forearms, 30% TCA was needed in majority of cases. No significant adverse effects were reported by any of our studied case.

Patient selection before starting treatment is of paramount importance as it stands the risk of complications. Therefore, patients with a history of hypertrophic scar or keloidal tendency, heavy occupational exposure to sun such as field workers were excluded from our study. Care should be taken during the application of TCA peels to avoid accidental spillage on the surrounding skin or near the eye in case of periorbital application. Instructions should be given to avoid sun exposure. The patient should be informed that mild erythema and/or edema are to be expected, which usually resolve after the procedure. In our studied cases, none of the patients reported any adverse events except a mild tingling sensation on application of the peel. Ice application along with a short course of a topical mid-potent steroid can help suppress the post-treatment inflammation. In our studied cases, a topical antibacterial ointment twice daily till the formation of a crust and daily application of a broad-spectrum sunscreen with SPF 50+ was advised. Patients were strictly advised to avoid sun exposure, heat, rubbing, scratching, or picking at the scab. Another common side effect of depigmenting therapies is the development of colour mismatch at the treated sites. However, this was not reported by any of our patients either during treatment or within the follow-up period.

Over the years, many different methods have been used to achieve complete depigmentation in vitiligo patients [17]. Phenol 88% is one such depigmenting agent, but it is not suitable for extensive depigmentation due to the risk of hepatic and cardiac toxicity with systemic absorption, in contrast to TCA peels which have no such adverse effects [18].

Physical measures like cryotherapy and laser devices, are targeted to melanocytes and can be applied when rapid depigmentation is required especially on the face [7]. Small areas should be treated in a single session as aggressive cryotherapy for large areas carries the risk of blistering and scarring [3]. Laser therapy is effective in depigmenting residual patches in patients of vitiligo within a short duration of time. Several devices like Q switched ND YAG, Ruby and alexandrite lasers have been in use [19]. A study [6] compared the use of TCA 25%, 50% with Q switched ND YAG and demonstrated a higher response with laser therapy (75% of the patients showed excellent depigmentation with an average number of 1-3 sessions). They stated that laser therapy needed fewer sessions (median 3) compared to TCA 25%, 50% (median 5, 4 respectively). The peels turned out to be a better option for depigmentation of larger areas. In our study, complete depigmentation was noticed in 86.4% of patients with a median number of 3 sessions. Moreover, depigmentation of large areas using laser therapy can be very painful necessitating pre-treatment anaesthesia and will require multiple, expensive treatment sessions [4]. The advantages of TCA treatment as compared to the previously mentioned modalities are that TCA is a cheap, readily available and cost-effective

method which can be performed in outpatient clinics. It has no risk of systemic absorption and reduced downtime with minimal adverse effects.

Repigmentation or relapse of therapy is a major problem after depigmentation therapy especially in areas with greater follicular distribution [3]. In a study, relapse rate in patients with excellent depigmentation was 20% (8 out of 40 patients) after a six-month follow-up period as reported by Nofal A et al. in 2021. In a study by Njoo et al. [20] who compared 4-methoxyphenol and Q-switched Ruby laser for depigmentation in vitiligo, the relapse rate was 36% and 44% respectively. In our study, the relapse rate in patients with excellent depigmentation were 0 % after the three-month follow-up period. The most likely cause for repigmentation in patients is frequent sun exposure along with negligent or incorrect use of topical sunscreen. Suppression of neomelanogenesis can be achieved with proper care and counselling. This can reduce the risk of repigmentation after treatment.

In our study, no statistically significant correlation was found between the therapeutic response and the different clinical variables.

6. Limitations

The limitations of this study include the retrospective design, the limited number of patients studied, and the lack of comparison with other depigmenting methods. Furthermore, the follow-up period of the study was too short to provide insight into the long-term effectiveness of the treatment provided.

7. Conclusion

In summation, our study is the only of its kind, to the best of our knowledge, that emphasizes the importance of early aggressive treatment of vitiligo universalis and helps determining that topical treatment with monobenzyl ether of hydroquinone is suitable for cases and when used in conjunction with TCA peel, can effectively manage residual pigmentation. Therefore, this fast, effective, and safe treatment is essential to reduce the burden of the disease and improve their quality of life.

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