Trichloroacetic Acid Peel 15% + NB-UVB Versus Trichloroacetic Acid Peel 25% + NB-UVB for Stable Non-Segmental Vitiligo

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Abstract

Background: No single treatment proved to be satisfactory for vitiligo, therefore, dermatologists are still searching for innovative therapeutics and combinations.

Objectives: To evaluate the efficacy of combined trichloroacetic acid peel 15% (TCA) + NB-UVB versus TCA 25% + NB-UVB for cases with stable, non-segmental vitiligo.

Patients and Methods: Ten patients with stable, non-segmental and non-acral vitiligo were recruited. Two lesions per patient were treated: The 1st with TCA 15% + NB-UVB, whereas, the 2nd with TCA 25% + NB-UVB. Clinical assessment was done before and after treatment.

Results: The 1st lesions treated with TCA 15% + NB-UVB showed marked improvement in 70% of patients, moderate improvement in 10% and minimal response in 20%. While the 2nd treated lesions with TCA 25% + NB-UVB revealed marked improvement in 20% of patients, moderate improvement in 40%, mild improvement in 10% and minimal in 30%. No koebnerization or disease activation has been reported.

Conclusion: Initiation of vitiligo therapy with TCA 15% can enhance the clinical response achieved by NB-UVB.

Recommendations: TCA should be tried on a large scale of patients as monotherapy and combined therapy.

Key Words: Vitiligo – Combined treatment – Trichloroacetic acid – NB-UVB.

Introduction

TREATMENT of vitiligo represents a major dermatological challenge and many patients remain in a refractory state inspite of availability of different conventional therapies such as NB-UVB (311-313nm) which is considered the cornerstone therapy for vitiligo [1]. Therefore, combination approaches and incorporation of new modalities are required.

Apart from the famously known Koebner’s phenomenon in vitiligo patients (development of isomorphic lesions at traumatized uninvolved skin of patients with cutaneous diseases), [2] it is widely known that there is wound-associated pigmentation in normal individuals. The latter could be explained by two major processes; the first is incontinentia pigmenti, which occurs after destroying the basal cell layer resulting in accumulation of melanophages in the upper dermis, whereas the other process involves an epidermal inflammatory response induced by injury ranging from early tyrosine kinase induction to the late upregulation of growth factors, proteases, and extracellular matrix components, resulting in the release and oxidation of arachidonic acid to prostaglandins and leukotrienes. These mediators alter the activity of melanocytes and immune cells. This leads to increase in the synthesis of melanin and transfer of pigment to surrounding keratinocytes [3].

Other reports documented that there is a reverse Koebner's phenomenon in vitiligo in which there is spontaneous repigmentation of vitiligo patches following skin grafts [4].

These facts (wound-associated pigmentation together with the reverse Koebner's phenomenon) paved the way for the entrance of new modalities for vitiligo treatment: Physical trauma induced by dermabrasion, [5] thermal trauma by using fractional laser therapy [6] and chemical trauma by phenol and Trichloroacetic Acid (TCA) (Chemical peeling) [7].
Aim of the study:
To assess the efficacy of TCA chemical peel (15% and 25% concentrations) followed by NB-UVB in treatment of stable, Non-Segmental Vitiligo (NSV).

Patients and Methods

The current study was conducted in the Outpatient Clinic, Dermatology Department, Faculty of Medicine, Cairo University (Kasr Al-Ainy Hospital) from March 2014-March 2015. After approval by the Dermatology Research Ethical Committee (Derma REC), an informed written consent for participation in the study and photography were taken.

Ten patients with stable, NSV and fulfilling the inclusion criteria were recruited and subjected to complete medical history, detailed assessment of vitiligo and photography taking. Two vitiligo lesions/patient were chosen and given numbers (1 and 2) and they were treated with TCA 15% + NB-UVB and TCA 25% + NB-UVB respectively.

Inclusion criteria:
Patients of both sexes, older than twelve years with stable NSV (VIDA +1, 0 or 1) having at least two discrete vitiliginous patches, not on acral parts and each measuring from 3 to 5 cm in diameter.

Exclusion criteria:
Patients who received topical or systemic treatment for vitiligo over the past 6 month. Patients with history of koebnerization or keloidal tendency.

Protocol of therapy:
The area to be treated was degreased by acetone or alcohol. Either TCA 15% (1st lesion) or 25% (2nd lesion) was then gently applied with uniform smooth strokes so as to cover the entire lesion till an ivory white uniform frosting appeared. Feathering of the borders was done by painting from the periphery of the lesion into the surrounding normal skin. Then, lesions were thoroughly washed with saline. Patients were asked to apply zinc oxide ointment twice in a day and not to remove the crustations or the peeled layers of the skin. Four sessions were performed at one-week interval.

After that, patients were referred to Kasr Al-Ainy Phototherapy Unit to start NB-UVB sessions. They received two sessions weekly with a total of forty eight sessions. Starting dose was 700mJ/cm² (skin type III, IV and V). Then, increment was 300mJ/cm² every session if there is no or minimal perceptible erythema. Doses were maintained for cases with clear persistent erythema and sessions were stopped in case of marked erythema till resolution of erythema, then, resumed with the last tolerable dose.

Clinical evaluation:
After every session:
• Patients were asked and examined for possible side effects (discomfort, burning sensation, erythema, infection or desquamation).
• Treated lesions were examined for:
  - Perifollicular, marginal or diffuse repigmentation.
  - Decrease or increase size of the lesion.
  - Development of new lesions.
  - Any koebnerization.

• Clinical response was assessed by this score:
  1- Minimal response: Up to 30%.
  2- Mild response: >30-60%.
  3- Moderate response: >60-90%.
  4- Marked improvement: >90-100%.

Statistical methods:
The statistical package SPSS version 23 was used for data coding. Then, data was summarized using frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Chi square ($\chi^2$) test was performed to compare the data of different categories. Exact test was used instead when the expected frequency is less than 5. \(p\)-values less than 0.05 were considered as statistically significant.

Results
Ten patients were enrolled in this study, eight females (80%) and two males (20%). Their ages ranged from 15 to 60 years.

The 1st and 2nd lesions were subjected to TCA peels 15% and 25% respectively. Two patients (20%) responded to TCA 15%, one with marginal and perifollicular repigmentation Fig. (1B) and the other with diffuse repigmentation. Four patients (40%) showed marginal and perifollicular repigmentation with TCA 25% Fig. (1E).

After peel sessions, participants reported discomfort and burning sensation which were relatively stronger with TCA 25%. These symptoms
were associated with mild to moderate post peel erythema and desquamation/scaling.

Number of patients who responded with marked improvement (>90% repigmentation) were higher with TCA 15% + NB-UVB than those treated with TCA 25% + NB-UVB. In spite of that, when the results of combined TCA 15% + NB-UVB were compared to TCA 25% + NB-UVB, they were not of statistical significance (p-value=0.113).

<table>
<thead>
<tr>
<th>Response</th>
<th>TCA 15% + NB-UVB</th>
<th>TCA 25% + NB-UVB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of lesions</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Minimal response</td>
<td>2 20</td>
<td>3 30</td>
</tr>
<tr>
<td>Mild response</td>
<td>0 0</td>
<td>1 10</td>
</tr>
<tr>
<td>Moderate response</td>
<td>1 10</td>
<td>4 40</td>
</tr>
<tr>
<td>Marked improvement</td>
<td>7 70</td>
<td>2 20</td>
</tr>
</tbody>
</table>

**Fig. (1): Clinical response (patient number 1):**

[A] Pretreatment.
[B] Post treatment with TCA 15% alone: Marginal and perifollicular repigmentation on the central neck lesion after 4 sessions.
[C] Post treatment with TCA15% + NB-UVB: Diffuse repigmentation (100%).

**Fig. (2): Clinical response (patient number 1):**

[D] Pretreatment.
[E] Post treatment with TCA 25% alone: Marginal and perifollicular repigmentation on the flexor aspect of the right forearm after 4 sessions.
[F] Post treatment with TCA 25% + NB-UVB: Diffuse repigmentation (85%).

**Discussion**

TCA peel used in this study is relatively safe with neither systemic absorption nor toxicity. It is characterized by transient discomfort and short downtime, [9] as well as no limitations for the applied amount of the solution/session and large areas can be covered with repeated sessions [7].

When applied to the skin, TCA causes coagulation of epidermal and dermal proteins, and necrosis of collagen up to the upper reticular dermis [10].

TCA peel is associated with “hot spots” where it can penetrate deeper for no apparent reason which means that higher TCA concentrations may
induce an unexpected damaging inflammatory response [9,11].

That’s why we used lower concentrations (15% & 25%) than that tried by Puri and Puri (100%) who reported superficial scarring and bacterial infection [7]. In our study, three patients have shown signs of clinical improvement in the form of perifollicular and marginal repigmentation after 4th sessions of TCA 25% peel. Two patients responded to TCA 15%; one with perifollicular and marginal repigmentation, while the other showed diffuse tanning. All patients treated with TCA peel had associated desquamation. None of them developed scarring, infection or koebnerization.

Whether TCA peels works through postinflammatory hyperpigmentation or reverse koebnerization has not been specified and remains to be elucidated, however, treating skin-of-colour patients may favor postinflammatory hyperpigmentation as De Padova and Tosti [12] have reported that TCA peel is commonly associated with PIH in skin type IV and VI, as the elicited inflammation increases both melanogenesis and melanin transfer to adjacent keratinocytes [13] and a variety of inflammatory cytokines are transiently produced by TCA-treated keratinocytes before their necrosis as PDGF (platelet derived growth factor) and other growth factors [14] that may affect melanogenesis. In addition, Kimura and colleagues has documented that TCA peel can induce (pro-opiomelanocortin) POMC and (melanocortin-1) MC1R [15].

TCA peel has the following advantages: Simple office procedure with no complicated surgery or anaesthesia involved. Discomfort and pain are minimal. Repeat peels can be done on these areas if required. One can cover large areas in multiple settings [7].

Puri and Puri applied TCA 100% (repeated once a month if required) and it was followed by PUVA/PUVASOL sessions for 2-3 months. They reported marked pigmentation in 66.6% patients and mild pigmentation in 20% patients [7].

As regards the 1st lesions treated with TCA 15% followed by NB-UVB, marked improvement was seen in 70% of patients, moderate improvement in 10% and minimal improvement in 20%. Concerning the 2nd treated lesions with TCA 25% followed by NB-UVB, clinical responses were; marked improvement in 20% of patients, moderate improvement in 40%, mild improvement in 10% and minimal in 30%.

Conclusion:
Looking for a simple, available, cost-effective alternative or additive method for vitiligo therapy in stable NSV, NB-UVB preceded by TCA peel 15% could be a novel modality with no reported infection, koebnerization, scarring or disease progression. Further studies on large scale of patients are still needed.

References
لملخص العربي

الوصول لافضل النتائج العلاجية لمرض البهاق يقوم الطبي بالبحث المستمر عن طرق علاجية جديدة ويلجأوا لاستخدام أكثر من وسيلة علاجية للفحص المريض.

في هذه الدراسة تم إدراج عشرة مرضى الذين يعانون من البهاق الغير نشط والغير جزئي. وقد تم علاج منطقتين من الاختبار المصاب بالمرض. استخدمت مادة حمض ثلاثي كورور الخليل بتركيز متحيز بين 15% و 25% ببعض جلسات موضعية كل أسبوع لمدة شهر وقد استخدم لكل منطقة تركيز واحد فقط. ثم بدأت جلسات الامض فوق البنفسجية ب-محدودة المدى بواقع جلستين أسبوعيا لمدة أربعة وعشرين أسبوعا. وتبقي النتائج، وجد أن نسبة التحسن القصوى كانت 70% مع مادة حمض ثلاثي كورور الخليل بتركيز 15% مع جلسات الامض فوق البنفسجية ب-محدودة المدى وكانت أقل منها (20%) عندما استخدم تركيز 20% من حمض ثلاثي كورور الخليل.