Modified goeckerman technique: A new therapeutic modality for early stage mycosis fungoides: A pilot study

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Introduction

William Goeckerman was the first to acknowledge the efficacy of utilization of coal tar followed by exposure to ultraviolet (UV) radiation in the treatment of psoriasis [1]. The mechanism by which topical coal tar induce amelioration of psoriatic lesions has not been clearly elucidated. The following effects have been postulated: reduction of the hyperproliferative state of the epidermis, modulation of pro-inflammatory cytokines, depletion of T-lymphocytes and inhibition of angiogenesis [2].

The use of conventional Goeckerman technique is based on the use of broadband UVB after tar application [3]. However, the absorption spectrum of UVB (280-320nm) is not consistent with the action spectrum of tar which lies between (330-350nm). The use of UVA which has an absorption spectrum extending from 320nm to 340nm would be more...
effective in increasing the activity of local coal tar application.

So based on this fact, we are currently using coal tar and UVA instead of UVB (modified Goeckerman technique) for the treatment of psoriasis. We noticed that post-irradiation follow up biopsies of psoriatic lesions treated with modified Goeckerman technique exhibited marked depletion of lymphocytes in comparison to pre-irradiation biopsies.

Accordingly we hypothesized that modified Goeckerman technique could deplete epidermotropic as well as superficial dermal lymphocytes from MF lesions. Therefore we decided to try modified Goeckerman technique for early stage MF and compare its effects to those of PUVA.

Materials and Methods

The present prospective comparative randomized study was conducted in outpatient clinic, Dermatology Department, Cairo University. Thirty participants diagnosed as early stage Mycosis Fungoides [MF] (stages Ia, Ib, Ila) signed an informed written consent prior to their enrollment in this trial. Contraindications to phototherapy, intake of systemic therapy or photochemotherapy 6 months prior to inclusion, pregnancy and age less than twelve years were all considered exclusion criteria. Dermatology Research Ethical Committee (REC) approved the conduction of the study.

All patients were subjected to a pretreatment work-up including complete history taking, full clinical examination to detect the extent and type of MF and skin type of patient. Two skin biopsies with a 5 mm punch were taken from the suspected lesions to confirm the diagnosis by Hematoxylin and eosin stain (H & E). Lymph node examination and biopsy were done when indicated. Laboratory investigations (complete blood picture, liver & kidney function tests, fasting and 2 hours postprandial blood sugar, lactate dehydrogenase) and chest-x-ray and abdominal ultrasound examinations were carried out.

All patients were randomly (using envelope concealment method) divided into two groups. **Group A** included 15 patients who received modified Goeckerman technique (Tar +UVA). Patients were instructed to take a shower, apply crude coal tar 2.5% in petrolatum to the whole body and avoid the face and genitals then to leave the tar for at least 6 hours and then remove it before irradiation by vegetable oil taking care not to remove the whole application, then they received irradiation with UVA at a starting dose of average 2 J/cm² according to Fitzpatrick’s skin type and gradually increased by 20% increments according to patients’ response and tolerance. Finally the patients were instructed to take a shower after irradiation and apply a lubricant. The procedure was repeated 6 days / week for 3 months. Radiation source used was “Waldmann lighting” cabin “Germany”, which comprised 26 UVA light sources, having a radiation spectrum spectrum of 315 nm to 400nm and a peak of 365nm. **Group B**: included 15 patients who received 8-methoxypsoralen at a dose of 0.7mg/kg 2 hours before the sessions; the radiation source used and the dose received were the same as group A. The treatment period lasted for 3 month for both groups.

The primary outcome measure was the clinical response which was graded as excellent (75-100% improvement), very good (50-75% improvement), fair (25-50% improvement), and poor (0-25% improvement). The clinical evaluation was subjective and carried out by two independent blinded dermatologists by observing the extent of erythema, scaling, induration, extent and poikilodermia of the MF lesions in each patient. This was carried out every 2 weeks throughout the study period (3 months).

The secondary outcome measure was the histopathological response which was graded as excellent (75-100% improvement), very good (50-75% improvement), fair (25-50% improvement) and poor (0-25% improvement).

Histopathological assessment was carried out by two qualified dermatopathologists as regards epidermotropism and density of dermal lymphocytic infiltrate.

Statistical methods

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 20 for windows; SPSS Inc, Chicago, IL, USA). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. Data was described as mean, standard deviation (± SD) and range for parametric numerical data, and frequency and percentage of non-numerical data. Quantitative variables of the studied groups were compared using Mann Whitney U test for independent samples. For comparing categorical data, Chisquare (χ²) test and McNemar test were performed. Exact test was used instead when the expected frequency is less than 5. A probability value (p value) less than 0.05 was considered statistically significant.

Results

Thirty patients [20 males (66.7%) and 10 females (33.3%)]-diagnosed with early stage MF (Ia, Ib and Ila) were
recruited in and completed the current study. Twenty five of these patients (75%) were suffering from classic MF while 5 patients (25%) presented with hypopigmented MF. The mean duration of MF in patients of group A (Tar+ UVA) was 8.20±6.041 months, while the mean duration for patients of group B (PUVA) was 7.53±5.303 months.

At baseline evaluation there was no significant difference between both groups as regards their demographic data or clinical evaluation (Table 1).

**Primary outcome measure:**

After three months of treatment both groups showed significant clinical improvement. However there was no statistically significant difference between the two groups clinically (P= 0.833) (Table 2, Fig 1)

Group A (Tar+ UVA) patients showed excellent response in 4 patients (26.7%), very good response in 5 patients (33.3%), fair response in 4 patients (26.7%) and poor response in 2 patients (13.3%).

Whereas group B (PUVA) patients showed excellent response in 2 patients (13.3%), very good response in 6 patients (40%), fair response in 5 patients (33.3%)and poor response in 2 patients (13.3%).

**Secondary outcome measure**

Histopathological response for group A (Tar+ UVA) was as follows: 3 patients (20%) showed excellent response, 4 patients (26.7%) showed very good response, 6 patients (40%) showed fair response and 2 patients (13.3%) showed poor response. As for group B (PUVA) 2 patients (13.3%) showed excellent response, 5 patients (33.3%) showed very good response, 6 patients (40%) showed fair response and 2 patients (13.3%) showed poor response.

There was no statistically significant difference regarding the histopathological response between the two groups (P= 0.958) (Table 3, Figs 2).

### Table 1. Demographic and Clinical data of patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Skin Phototype</th>
<th>Type of MF</th>
<th>Stage of MF</th>
<th>Clinical evaluation</th>
<th>Histopathological evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>12-77</td>
<td>11</td>
<td>73.3%</td>
<td>11</td>
<td>73.3%</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>(42.13±21.692)</td>
<td>4</td>
<td>26.7%</td>
<td>4</td>
<td>26.7%</td>
<td>3</td>
</tr>
<tr>
<td>Group B</td>
<td>18-57</td>
<td>9</td>
<td>60%</td>
<td>8</td>
<td>40%</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>(38.07±12.104)</td>
<td>12</td>
<td>73.3%</td>
<td>11</td>
<td>73.3%</td>
<td>2</td>
</tr>
</tbody>
</table>

### Table 2. Clinical results of both groups

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Response</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>4</td>
<td>2</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>V.Good</td>
<td>26.7%</td>
<td>13.3%</td>
<td>20.0%</td>
<td></td>
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<tr>
<td>Fair</td>
<td>33.3%</td>
<td>40.0%</td>
<td>36.7%</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>46.7%</td>
<td>80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical response</td>
<td>100.0%</td>
<td>100.0%</td>
<td>30</td>
<td>0.833</td>
</tr>
</tbody>
</table>

### Table 3. Histopathological response in both groups

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histopathological response</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>V.Good</td>
<td>20.0%</td>
<td>13.3%</td>
<td>16.7%</td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td>26.7%</td>
<td>33.3%</td>
<td>30.0%</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>40.0%</td>
<td>40.0%</td>
<td>40.0%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>100.0%</td>
<td>100.0%</td>
<td>30</td>
<td>0.958</td>
</tr>
</tbody>
</table>
The average cumulative UV dose received by patients for group A (Tar+ UVA) was 180J/cm² whereas the average cumulative dose for group B was 160J/cm².

The side effects noticed in the study for group A (Tar+ UVA) included tar folliculitis in one patient (6.7%), irritant dermatitis in one patient (6.7%) and burning sensation in two patients (13.3%). Whereas in group B (PUVA) nausea was the most commonly noticed side effect in 7 patients (46.7%) followed by pruritus in 6 patients (40%).

**Discussion**

Modified Goeckerman technique yielded comparable results to the established PUVA regimen for the management of early stage mycosis fungoides [MF] as evidenced by the results demonstrated in the present study. There was no statistically significant difference (clinically and histopathologically) between both groups.

Our modification was the use of UVA instead of UVB. The rationale behind the use of UVA instead of UVB is that the absorption spectrum of tar is 330-350 nm which lies in the UVA and visible light spectrum [4]. Accordingly the maximum suppression of DNA synthesis would occur to a greater extent with UVA rather than with UVB [5].

We noticed that modified Goeckerman technique causes marked depletion of lymphocytes in post treatment biopsies of psoriatic patients, and therefore we assumed that modified Goeckerman technique may be effective in depleting lymphocytes involving the dermis and epidermis in early stages of MF.

In the present study both groups showed similar clinical response. However there was no statistically significant difference between the two groups clinically (p value= 0.833)

Also, there was no statistically significant difference regarding the histopathological response between the two groups (p value=0.958).

The response to PUVA therapy in our study was consistent with the results obtained by EL-Mofty et al., 2005 [6] who achieved clinical improvement (good and very good response) in 60% of cases.
The response to PUVA was also similar to that obtained by Ponte et al., 2010 [7] who found that 62.1% of their patients had a complete response, 25.3% had a partial response and (12.6%) had poor response.

The side effects encountered in both modified Goeckerman technique and PUVA were comparable. One patient in group A (Tar+ UVA) developed folliculitis on his lower limb during treatment. Tar folliculitis is a common side effect, probably because of chlorine-containing ingredient in tar is a follicular irritant. It usually occurs on the lower extremities with tar concentrations greater than 2% [8].

Moreover, in group A (Tar+ UVA) irritant dermatitis occurred in one participant and stinging feeling in another two. These side effects did not necessitate termination of therapy.

On the other hand PUVA therapy (group B) in this study was associated with Nausea in 7 patients (Nausea was not reported by any of the patients treated with modified Goeckerman technique) and pruritus in 6 patients, whereas nobody in the Tar group (group A) complained of pruritus.

When compared with PUVA, the use of coal tar has not been associated with increased risk of cancer [9]. Moreover it does not induce eye complications as PUVA technique would do [10]. Furthermore it can be used safely in patients with liver problems as PUVA therapy might lead to deterioration of liver functions [11] and cause toxic hepatitis in some patients [12].

Finally we can conclude that the response to modified Goeckerman technique is equivalent to PUVA in the treatment of early stage of MF and can be considered an effective alternative to PUVA especially in children and patients with liver or eye problems. It has minimal side effects as folliculitis and burning sensation which usually do not necessitate termination of therapy. Moreover, it spares the patients the hazards and side effects of psoralen as nausea, elevation of liver enzymes and eye complications.

**Conflict of interest**

The authors have declared that no competing interests exist.

**References**