Treatment of pityriasis versicolor using 1% diclofenac gel and clotrimazole cream (comparative therapeutic study)

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Abstract  Background: Pityriasis versicolor is a superficial fungal infection of the skin. Multiple modalities of therapy have been used including both topical and systemic agents, such as imidazoles, triazoles and allylamines.

Objective: To evaluate the effectiveness of topical 1% diclofenac gel in the treatment of pityriasis versicolor in comparison with topical clotrimazole cream and aqua rosa cream as a placebo control.

Patients and methods: This is a single-blinded, comparative therapeutic trial of topical 1% diclofenac gel in the treatment of pityriasis versicolor in comparison with topical 1% clotrimazole cream and aqua rosa cream as a placebo control group was conducted at the Department of Dermatology – Baghdad Teaching Hospital during November 2006–November 2008.

This study included 75 patients (39 males and 36 females). They were divided randomly into three groups, each containing 25 patients. Group A patients treated with diclofenac gel: include 15 (60%) males and 10 (40%) females. Their ages ranged from 15 to 44 (23.72 ± 6.52) years, while the duration of the disease ranged from 1 to 24 (4.28 ± 5.79) months. Group B patients treated with
1. Introduction

Pityriasis versicolor is a mild chronic infection of the skin caused by Malassezia yeast, and characterized by discrete or concrecent, scaly, discolored or depigmented areas mainly on the upper trunk (Hay and Moore, 2004).

Several modalities have been used in the treatment of pityriasis versicolor with both topical like imidazoles, selenium sulphide shampoos and lotions, ciclopirox olaamine, zinc pyrithione shampoos, sulphur preparations, salicylic acid preparations, propylene glycol lotions, tretinoin cream, terbinafine solution, benzyl peroxide, zinc sulphate lotion and lactic acid lotion, and systemic antifungal like itraconazole, fluconazole and ketoconazole with different mechanisms of their action (Gupta et al., 2002; Sharquie, 1991; Sharquie et al., 2008, 2009; Al-Tereihi, 2007).

Topical diclofenac gel is a non-steroidal anti-inflammatory drug. In dermatology 3% diclofenac gel is used for the topical treatment of actinic keratosis (Rivers et al., 2002; Kose et al., 2008). Diclofenac gel also used in treatment of genital porokeratosis (Kluger et al., 2007), rosacea (Weiss et al., 2008) and alopecia areata (Sharqie et al., 2006).

The aim of the present work is to evaluate its effectiveness in the treatment of pityriasis versicolor in comparison to clotrimazole cream and aqua rosa cream as a placebo control group.

2. Patients and methods

This is a single-blinded, comparative therapeutic study of 1% diclofenac gel in comparison to 1% clotrimazole cream and aqua rosa cream as a placebo control group in the treatment of pityriasis versicolor. The study was carried out in the Department of Dermatology and Venereology – Baghdad Teaching Hospital from November 2006 to November 2008. Seventy-five patients with pityriasis versicolor were included in this study. Full history was taken from each patient regarding: age, sex, duration of disease, family history, seasonal variation, previous personal history of the disease and any previous treatment used for it.

Examination of the patients and assessment of the disease were performed by:

- Clinical examination of the lesion, reporting the site, size, color, presence of the scales and erythema.
- Wood’s light examination: to confirm the diagnosis through showing yellow fluorescence of the lesions, this test was positive, also to determine the site, extent of the lesions.
- Skin scraping test by dissolving the scales in 10% KOH solution, the test is considered positive when it reveals short stubby hyphae and yeast forms.
- Examination of the patients and assessment of the disease were performed by:

Group A patients treated with diclofenac gel: Patients included in this group were 15 (60%) males and 10 (40%) females.

Group B patients treated with clotrimazole cream: Cases involved in this group were 13 (52%) males and 12 (48%) females.

Group C patients treated with aqua rosa cream: Patients composed in this group were 11 (44%) males and 14 (56%) females.

The treatment was applied twice daily as a thin coating to the entire lesion and to normal skin around the lesions.

Re-evaluation was done for each patient by performing physical examination, skin scraping test and Wood’s light examination every 2 weeks during the month of the study and for the second month of follow up to report clinical and mycological responses and any signs and symptoms of local and systemic side effects.

Preparations: Diclofenac gel (Voltaren Emulgel®). Each 100 g of the gel contains the active substance diclofenac.
diethylamine, which corresponds to 1 g diclofenac sodium as well as propylene glycol and flavoring agents. The base of Voltaren Emulgel is a fatty emulsion in an aqueous gel to which isopropanol and propylene glycol have been added. Emulgel is 20 g tubes. It is manufactured by: NOVARTIS PHARMA, Switzerland.

Clotrimazole cream is obtained from MEDICO LABS, Syria 20 g tubes each 1 g contains 10 mg of clotrimazole.

The clinical response score was performed depending on Sharquie et al. score (Sharquie et al., 2008; Al-Tereihi, 2007):

- **No response:** There is no response on clinical examination and on skin scraping test examination.
- **Partial response:** There is some clinical improvement (decrease in scales) or skin scraping test change to negative results.
- **Complete response:** Both clinical and skin scraping test examinations indicate resolution.

Improvement of pigmentedary changes was not a criterion for response to treatment; this is because return of normal pigmentation may take several weeks after the clearance of pityriasis versicolor.

Statistical analysis was done by EP16 system, $\chi^2$ matching between the groups. $P$ value of less than 0.05 was considered significant.

3. Results

In general for all patients, the diagnosis proved was by clinical, mycological and Wood’s light examinations. This study included 75 patients (39 (52%) males and 36 (48%) females).

**Group A:** The clinical response in patients treated with topical diclofenac gel.

After 2 weeks of treatment, 4 (16%) patients showed complete improvement (clinically and mycologically), while the response after 4 weeks of treatment was 14 (56%) patients with complete improvement (Yates corrected $\chi^2 = 7.03$, $P$ value = 0.008).

**Group B:** The clinical response in patients who were treated with topical clotrimazole cream after 2 weeks of treatment was 14 (56%) patients with complete improvement, while the result after 4 weeks of treatment was 23 (92%) patients with complete healing (Yates corrected $\chi^2 = 38.9$, $P$ value < 0.00000001). The difference in clinical response in patients between 2 weeks and 4 weeks was significant (Yates corrected $\chi^2 = 6.65$, $P$ value = 0.009) (Fig. 1).

The difference in clinical response in patients between 2 weeks and 4 weeks was significant (Yates corrected $\chi^2 = 7.03$, $P$ value = 0.008).

**Group C:** The clinical response in patients who were treated with topical aqua rosa cream, no patients showed either partial or complete improvement after 2 or 4 weeks of treatment.

In comparison between groups A and B there was significant difference at 2 weeks (Yates corrected $\chi^2 = 7.03$, $P$ value = 0.008) and at 4 weeks (Yates corrected $\chi^2 = 6.65$, $P$ value = 0.009).

In comparison between groups A and C there is no significant difference at 2 weeks (Yates corrected $\chi^2 = 2.45$, $P$ value = 0.1) but significant difference at 4 weeks (Yates corrected $\chi^2 = 16.77$, $P$ value = 0.00004) (Tables 1 and 2).

4. Discussion

Pityriasis versicolor is a common yeast infection of the skin encountered in daily practice affecting adult people with unacceptable cosmetic effects pityriasis versicolor, which recurs frequently despite adequate initial therapy (Hay and Moore, 2004).

There are many therapeutic agents effective for treatment of pityriasis versicolor who are either topical like clotrimazole, ketoconazole, oxiconazole, terbinafine, selenium sulphide, tretinoin, ciclopirox olamine, zinc sulphate and lactic acid or systemic including itraconazole, fluconazole and ketoconazole. Despite these many therapies there is no standard therapy with complete cure rate (Gupta et al., 2002; Sharquie, 1991; Sharquie et al., 2008, 2009; Al-Tereihi, 2007).

Topical diclofenac gel is a non-steroidal anti-inflammatory drug. In dermatology 3% diclofenac gel is used for the topical

![Figure 1](A) Before treatment by diclofenac gel. (B) After 4 weeks treatment with diclofenac gel.
treatment of actinic keratosis (Rivers et al., 2002; Kose et al., 2008). Diclofenac gel also used in treatment of genital porokeratosis (Kluger et al., 2007), rosacea (Weiss et al., 2008) and alopecia areata (Sharqie et al., 2006).

The results of the present work showed that both diclofenac gel and clotrimazole cream were effective in clearing the lesions of pityriasis versicolor. At 2 weeks of therapy, diclofenac gel cleared 16% of the patients while clotrimazole cream cleared 56% of patients. After 4 weeks of therapy, diclofenac gel cleared 56% of patients while clotrimazole cream was more effective which cleared 92% of patients.

Diclofenac gel appeared to be more effective at 4 weeks than at 2 weeks (P value = 0.008). Clotrimazole cream also appeared to be more effective at 4th weeks than at 2nd weeks (P value = 0.009).

Diclofenac gel in comparison to placebo appeared to be highly effective at 4th weeks of therapy (P value = 0.00004).

In previous Iraqi studies: Sharquie showed that tretinoin cream is highly effective in the treatment of pityriasis versicolor with cure rate 100% after 2 weeks of therapy but with noticeable side effects like erythema and itching (Sharquie, 1991). Sharquie et al. showed that zinc sulphate in 15% topical solution is highly effective treatment of pityriasis versicolor with cure rate 100% at 3 weeks therapy (Sharquie et al., 2008).

Also, Al-Tereihi showed that zinc sulphate in 10% topical solution is an effective treatment of pityriasis versicolor with cure rate 68% after 4 weeks of therapy (Al-Tereihi, 2007).

Sharquie et al. showed that 10% lactic acid solution is highly effective in treatment of pityriasis versicolor with cure rate 100% after 4 weeks of therapy (Sharquie et al., 2009).

While, clotrimazole, as an imidazole antifungal agent exerts its activity by altering the cell membrane permeability by inhibiting the 14-alpha-demethylation of lanosterol which inhibits ergosterol necessary for normal cell membrane permeability. Diclofenac may act via an effect on matrix metalloproteinases which have been elevated with diclofenac. Over expression of metalloproteinases would have keratolytic action capable of degrading collagen and epidermal cytoskeletal elements (Kose et al., 2008).

The residual post-inflammatory hypopigmentation occurred in both drugs similarly. To the best of our knowledge, this is the first work showing the effectiveness of topical diclofenac gel in the treatment of pityriasis versicolor and apart from minimal irritation in few cases it lacks any other side effects in contrast to many other topical therapies like tretinoin cream and sulphur which are associated with marked irritation, but still it was much less effective when compared with clotrimazole, zinc sulphate, lactic acid and selenium sulhide.

### Table 1

| Group | At 2 weeks | | | | | | At 4 weeks | | | | |
|-------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|       | No response | Partial response | Complete response | | No response | Partial response | Complete response | | | | |
| A     | 2 | 8 | 19 | 76 | 4 | 16 | | 1 | 4 | 10 | 40 | 14 | 56 |
| B     | 0 | 0 | 11 | 44 | 14 | 56 | | 0 | 0 | 2 | 8 | 23 | 92 |
| C     | 6 | 24 | 19 | 92 | 0 | 0 | | 5 | 20 | 20 | 80 | 0 | 0 |

### Table 2

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<th>Group</th>
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5. Conclusion

In conclusion, diclofenac gel seems to be effective, cosmetically accepted and safe treatment for pityriasis versicolor with acceptable cure rate but in the present concentration (1%) it cannot compete with other much superior topical drugs. Further studies are highly recommended to have more confirmation of the present findings.

References


