

Evaluation of serum folate level before and after oral PUVA therapy in psoriatic patients

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Abstract

Psoriasis is a chronic, recurrent, and immune-mediated inflammatory disease that affects 2–3% of the world population. The present study aimed to evaluate serum folate level before and after oral PUVA therapy in psoriatic patients. Patient and methods: A total of 40 psoriatic patients without any other morbidities (age ranged from 19 to 63 years, including 20 males and 20 females), All the patients received oral 8-methoxypsoralen at a dose of 0.6 mg/kg, followed 2 hours later by ultraviolet A exposure (oral PUVA therapy), For each patient the therapy will be twice weekly for eight weeks. Patients in the PUVA group were treated twice times weekly with a starting dose of 2 J/cm², increasing by 20% each session, to a maximum of 15 J/cm² per dose. Patients underwent up to 16 sessions. The dosage was adjusted if patients developed erythema. We have measured serum folate levels at baseline and after oral PUVA exposure. Also we use PASI score as objective method to visualize the relationship between improvement of psoriasis and changes in folate serum levels at baseline and after 16 exposures to PUVA for 8 weeks along with subjective methods which were done by photography and adverse effects were also reported. Results: There is statistically significant decrease of folic acid level after 16 sessions of phototherapy by average 20%. According to PASI score, Our results shows that there is statistically significant improvement in PASI score after phototherapy by average 60%. Conclusion: Folate deficiency should be evaluated and corrected in the patients, as it may be aggravated by UV therapy.

Keywords: Psoriasis, 8-methoxypsoralen, Ultraviolet A, Serum folate level.

1. Introduction

Psoriasis is one of the most common chronic inflammatory skin conditions, affecting 3–4% of the adult population that results from a polygenic predisposition with triggering factors, e.g. trauma, infection, drugs and emotional stress. Psoriasis is characterized by sharply demarcated red papules and plaques covered with silvery scales (psoriasis vulgaris), the commonest sites are extensor surfaces of limbs, elbows, knees and sacral region [1].

Untreated psoriasis can reduce social, occupational, and overall well-being. Despite the availability of topical, oral, and systemic treatments, many patients with psoriasis, especially those with moderate-to-severe generalized psoriasis, are not adequately treated with an effective, long-term treatment regimen [1].

Phototherapy with ultraviolet A (UVA) and ultraviolet B (UVB) has been used for different dermatological problems such as psoriasis, vitiligo, generalized morphea, and mycosis fungoides. UVA phototherapy combined with topical or oral psoralen named PUVA therapy is an old method for psoriasis treatment. Psoralen is photo-activated by UVA radiation, which results in inhibition of cellular proliferation [2].

The most usual method of administration is oral 8-methoxypsoralen at a dose of 0.6 mg/kg, followed 2 hours later by ultraviolet A exposure. PUVA therapy has been shown to be beneficial in approximately 90% of treated patients, most of them within 6 to 12 weeks [3].

UV exposure has photo-degradation effects on some vitamins such as folate, riboflavin, tocopherol, and carotenoid in many in vitro studies. It has been reported that UV radiation may cause neural tube defects in embryos of exposed mothers probably due to folate deficiency. On the other hand, UV rays increases vitamin D production [4].

Folic acid and its derivatives are essential micronutrients for DNA and amino acids biosynthesis [5].

Folate deficiency in psoriasis patients is more possible than other skin disorders even prior to phototherapy. It may be due to higher cellular proliferation rate in psoriasis patients and the important role of folate in biosynthesis of DNA. Also, depression and cardiovascular diseases are more frequent in psoriasis patients, which may be aggravated by folate deficiency [6].

Folate deficiency is a common micronutrient deficiency in the world, which has been estimated 10% in the United States and 60% in low socioeconomic countries (Mojtabai, 2004). UV radiation could disintegrate serum folate in vitro, but there are not enough experiences to support similar results in vivo [7].

Folate deficiency could be associated with megaloblastic anemia, cardiovascular diseases, malignancy, depression, and neural tube defects. On the other hand, phototherapy by itself may be associated with cutaneous cancers. Therefore, simultaneous folate deficiency and phototherapy may increase risk of skin cancers [8].

The present study aimed to evaluate serum folate level before and after oral PUVA therapy in psoriatic patients.

2. Patient and Method

The study is an interventional clinical study. The study was approved by local ethics committee on research involving human subjects of Benha Faculty of Medicine.

A total of 40 psoriatic patients without any other morbidities (age ranged from 19 to 63 years, including 20 males and 20 females) were participated in this study. They were recruited from outpatient clinic of department

of Dermatology, Venereology and Andrology, Benha University Hospitals, Egypt.

2.1 Inclusion criteria

- Patients with psoriasis vulgaris (plaque psoriasis).
- Psoriatic patients without any associated disease to exclude other factors that decrease folate level.
- Age more than 18 years old.

2.2 Exclusion criteria

- Patients with serious infectious disease, history of hypertension, diabetes, kidney or liver dysfunction, heart disease, and abnormal increase in transaminase or cancer.
- Patients on oral folate supplement, methotrexate and anticonvulsants medication.
- Age < 18 years old.
- Pregnant and lactating women.
- Smoking and alcoholism
- Previous phototherapy in the last two months

All patients were subjected to Complete general examination to exclude other diseases. Complete dermatological examination to evaluate the clinical type and severity of psoriasis (PASI) and Fitzpatrick: to assess skin phototype.

In all groups, the procedure included the following:

- All the patients were receive oral 8-methoxypsoralen at a dose of 0.6 mg/kg, followed 2 hours later by ultraviolet A exposure (oral PUVA therapy), For each patient the therapy was twice weekly for eight weeks.

Patients in the PUVA group were treated twice weekly with a starting dose of .5 J/cm², increasing by 20% each session. Patients underwent up to 16 sessions.

Oral psoralen and ultraviolet A (PUVA)

- UVA machine: Waldmann-UV 7002 cabine. whole body exposure units fitted with 24 UVA lamps, intensity (11.1 mW/cm²) was measured monthly.
- Psoralene: Oral 8-methoxypsoralen at a dose of 0.6 mg/kg 2 hours before phototherapy.

Serum folate level was evaluated in venous blood samples drawn after 12 hr fasting in an individual laboratory using Human Folic acid ELISA kit. For providing photo-protection, blood samples tubes were concealed with an opaque aluminum foil until final step of the measurements. We requested our patients for no significant change in their diet and not taking any multivitamins or folate supplement during course of treatment. Serum folate levels were measured in all patients at the first visit before initiation of phototherapy and after 16 PUVA phototherapy sessions within 30 minutes of the last exposure.

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 25

3. Results

In our study we have 20 males and 20 females, with ages ranging from 19 to 63 years old, median age in males is 36 yrs old while in females is 43 years old .

In our study the most dominant skin phototype was type (4) by 35%, and the least was type (5) by 15%.

From these results we conclude that significant decrease in folic acid levels after phototherapy in patients with skin photo type (2, 3) .While there were no significant changes in folic acid levels after phototherapy in patients with skin phototype (4,5) .

The minimum pre-phototherapy PASI score was 0.8 while after phototherapy it become 0.48, also the mean PASI score before phototherapy was 8.88 (±4.68) become 5.32 (±2.8).

Our results shows that there is statistically significant improvement in PASI score after phototherapy by average 60% (P.value < 0.000001)

In our results the mean folic acid level before phototherapy was 8.77 (±3.38) while the mean after 16 sessions of phototherapy is 7.02 (±2.7)

There is statistically significant decrease of folic acid level after 16 sessions of phototherapy by average 20%

The maximum disease duration in our study was 20years, while the minimum duration was 1 year, while the mean disease duration was 6.125 years.

We have 11 patients with disease duration more than 10 years, and 29 patients with disease duration less than 8 years.

In our results the mean folic acid level before phototherapy was 8.77 (±3.38) while the mean after 16 sessions of phototherapy is 7.02 (±2.7) so the mean folic deficiency is 1.75 (±0.68).

We noticed that there is more folic deficiency with increased disease duration (p value <0.0001) as the mean folic deficiency in the 11 patients with disease duration more than 10 years was 2.4±0.6.

While the mean folic deficiency in the 29 patients with less than 8 years disease duration was 1.6±0.3

In our results the mean folic acid level before phototherapy was 8.77 (±3.38) while the mean after 16 sessions of phototherapy is 7.02 (±2.7) so the mean folic deficiency is 1.75 (±0.68).

We noticed that there is more folic deficiency with increased Age of the patients (p value <0.003) as the mean folic deficiency in the 16 patients with age more than 40 years old was 2.6±1.1.

While the mean folic deficiency in the 24 patients with ages less than 40 years old was 1.4±0.2

In our study we have 20 males and 20 females, there is no statistically significant correlation between gender and mean folic deficiency (p value 0.5).

As the mean folic acid deficiency in males was 1.8±0.4, while in females was 1.7±0.2.

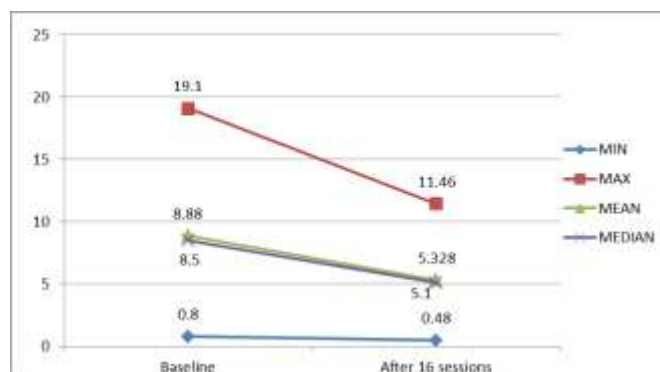


Fig (1) PASI score pre and post 16 sessions phototherapy.

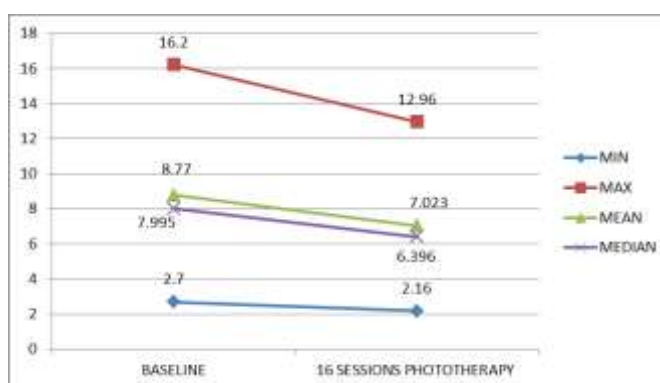


Fig (2) folic acid level pre and post 16 sessions of phototherapy

4. Discussion

To the best of our knowledge, this is the first study to evaluate the effect of oral PUVA (photochemotherapy) on serum folate levels in psoriatic patients. In [9] study, they use bath PUVA. [10] study, they use Goeckerman therapy (crude coal tar and ultraviolet radiation) and measure the levels of serum homocysteine, vitamin B12 and serum Folic acid in patients with severe psoriasis vulgaris.

In Weber et al, 2020 [11] study, they measure serum levels of folate, 25-hydroxyvitamin D3 and cobalamin during UVB phototherapy in 101 patients had at least 12 NB-UVB exposures, 34 patients has psoriasis vulgaris. In [6] study, Serum folate levels were measured at baseline, and after exposure to 18 and 36 sessions of NB-UVB irradiation. [7] study, 30 patients had ECP (extracorporeal photopheresis therapy) on two consecutive days and the FA (folic acid) levels were measured in the extracorporeal collected plasma prior to and after UVA exposure. Of these patients 11 had systemic sclerosis, eight GvHD, five cutaneous T-cell lymphoma, four were after lung transplantation, one had erosive lichen planus and one nephrogenic fibrosing dermopathy. [12] study, 35 psoriatic patients subjected to minimum of 18 exposures to NB-UVB and the serum and red cell folate levels were measured at baseline and after phototherapy.

In our study, according to skin phototype; the most dominant skin phototype was type (IV) by 35%, and the least was type (5) by 15% while type 2 and 3 phototype

25%. Our results revealed significant decrease in folic acid levels after phototherapy in patients with skin phototype 2 and 3 more than skin phototype 4 and 5, this comes in agreement with [9] study, decrease in folate levels was more significant in patients with Fitzpatrick's phototype 3 (III) compared with Fitzpatrick's phototype 4, 5 (IV, V).

According to folic acid level in our present study; the mean level before phototherapy was $8.77 (\pm 3.38)$ while the mean level after 16 sessions of phototherapy was $7.02 (\pm 2.7)$. There is statistically significant decrease of folic acid level after 16 sessions of phototherapy by average 20%.

In consistent to our study results, [9] study, twenty-three patients (71.9% of cases) had a decrease in folate level after bath PUVA therapy. also, [11] study reported a significant decrease of mean serum folate (-1.0 nmol/L; $P = 0.03$) after 12 NB-UVB exposures which is consistent with our results, also they interestingly revealed alterations in folate levels seemed to depend on the type of skin disorder treated. also, [6] study, there were significant decreases in mean serum folate levels after NB-UVB exposure. After exposure to 18 and 36 sessions the decreases were 19% and 27%, respectively.

In contrast to our results, [10] study results showed insignificant differences in serum folic acid were obtained when the data before and after the treatment were compared (12.0 vs. 11.6 nmol/L, $p = 0.082$). In contrast to our results, [13] study revealed no evidence of decreased folate levels after UVA exposure.

Rose et al, 2009 [12] study reported no significant difference in serum and red cell folate levels after NB-UVB.

In our study before treatment, according to PASI score, 40 patients who completed the treatment, the minimum pre-phototherapy PASI score was 0.8 while after phototherapy it become 0.48, also the mean PASI score before phototherapy was 8.88 (± 4.68) become 5.32 (± 2.8). Our results shows that there is statistically significant improvement in PASI score after phototherapy by average 60% (P.value < 0.000001). While we revealed no relationship between improvement of PASI score and change of serum folic acid levels before and after therapy. (10) study, the median value of psoriasis area and severity index score was 19, and after therapy, the median PASI score decreased to five, also, (14) study, 60% in the PUVA group achieved 75% or more improvement in PASI score after 12 weeks of treatment, (15) study, Within 6 weeks bath PUVA reduced the median PASI by 74% (16.4 to 4.2) while system PUVA did so by 62%. their results is consistent to our results.

We noticed that there is more folic deficiency with increased age of the patients (p value < 0.003) as the mean folic acid deficiency in the 16 patients with age more than 40 years old was 2.6 ± 1.1 . While the mean folic deficiency in the 24 patients with ages less than 40 years old was 1.4 ± 0.2 . While, according to gender; there is no statistically significant relation between gender and mean folic deficiency (p value 0.5). As the mean folic deficiency in males was 1.8 ± 0.4 , while in females was 1.7 ± 0.2 .

According to psoriasis course duration in our study results, the maximum disease duration was 20 years, while the minimum duration was 1 year, while the mean disease duration was 6.1 years. We had 11 patients with disease duration more than 10 years, and 29 patients with disease duration less than 8 years, so the mean folic deficiency is $1.75 (\pm 0.6)$. We noticed that there is more folic deficiency with increased disease duration (p value < 0.0001) as the mean folic deficiency in the 11 patients with disease duration more than 10 years was 2.4 ± 0.6 . While the mean folic deficiency in the 29 patients with less than 8 years disease duration was 1.6 ± 0.3 .

In our study, we have shown that oral PUVA administration in treatment of psoriasis leads to improvements in PASI score and decrease in serum folic acid level.

5. Conclusion

Folate deficiency should be evaluated and corrected in the patients, as it may be aggravated by UV therapy. Considering the protective effect of folate against cancers and higher rate of skin cancers in PUVA-treated patients, it seems appropriate to evaluate serum folate status before treatment.

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