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Analysis of Serum Folate Levels after Narrow Band UVB Exposure

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Abstract

Background: Photodegradation of certain vitamins such as riboflavins, carotenoids, tocopherol, and folate has been well-documented. Previous observations suggest that photochemotherapy (PUVA) may cause folate deficiency. This is of great importance since folate deficiency has important health consequences and has been linked with the development of neural tube defects. UVB Phototherapy is generally recommended by dermatologists as safe to use in pregnant women. Studies on UVB-induced alterations of serum folate levels have not been conducted.

Objective: Investigating the influence of UVB radiation on serum folate levels in vivo.

Methods: Twenty patients undergoing narrow band UVB (NB UVB) phototherapy as well as 20 healthy volunteers were enrolled into the study after excluding factors known to influence serum folate concentrations. Serum folate was analyzed in all subjects at baseline, and after 36 NB UVB exposures in treated patients. Three UVB exposures were performed weekly within 12 weeks (mean cumulative NB UVB dose: 75.95 ± 3.67 J/cm²).

Results: Serum folate values were statistically significantly lower in patients at the end of the study compared to their baseline and control levels.

Conclusion: Cumulative UVB exposure may induce folate catabolism and simultaneous folate deficiency.

Introduction

Folate and folic acid are forms of a water soluble B vitamin. Folate, the

conjugated form of folic acid, occurs naturally in food and is an essential nutrient that is required for amino acid metabolism and DNA biosynthesis. Folic acid is the synthetic form of the vitamin [1],[2]. Folate status may be negatively influenced by inadequate intake, pregnancy, alcoholism, and the use of certain drugs [3]. Photodegradation of folate as well as other vitamins such as riboflavins, carotenoids, and tocopherol; has also been well-documented [4]. Photolysis of folate may be significant especially when serum is exposed in vitro to ultraviolet radiation [5].

Inadequate levels of this vitamin have important health consequences. Apart from macrocytic megaloblastic anemia, potential manifestations of folate deficiency include neurological and neuropsychiatric disorders, and preneoplastic conditions [2],[3]. Furthermore, folate deficiency has been associated with a predisposition to atherosclerotic cardiovascular disease [3],[6],[7]. A connection has also been confirmed between defective folate metabolism and neural tube defects in humans [8],[9]. On the other hand, an association has been described between neural tube defects and sun bed exposure during the first weeks of pregnancy, suggesting that folate photolysis may occur in vivo [10],[11].

Fair-skinned patients undergoing photochemotherapy (PUVA) for dermatological conditions have previously been reported to have low serum folate concentrations [5]. Studies on UVB-induced alterations of serum folate levels however, have not been conducted. Nevertheless, UVB phototherapy is generally recommended by dermatologists as safe to use in pregnant women [12]. Owing to the lack of controlled studies in this field, this trial was performed investigating serum folate levels in patients undergoing a series of narrow band UVB exposures and their comparison with their baseline levels and levels in healthy volunteers.

Patients and Methods

The study was conducted in the phototherapy unit at Ain Shams University dermatology department. Fasting blood samples were obtained from 20 patients undergoing narrow band UVB phototherapy for vitiligo, and from 20 age and sex matched healthy volunteers chosen as controls.

To study photolysis of serum folate relatively independent from photoprotection due to pigmentation, only patients and volunteers with skin types I, II, and III were included in the study. Patients having extensive vitiligo (involving more than 40% of the body surface area), were considered skin type I. Exclusion criteria for the studied subjects included: patients with highly melanized skin (skin types IV, V and VI), current pregnancy, abnormal diets, current use of vitamins or other supplements, any form of UV therapy 3 months prior to the study, systemic illness, and diseases or drugs known to impair folate metabolism as psoriasis, antirheumatic, anticonvulsant, and methotrexate therapy.

A narrow band UVB phototherapy unit was used (Cosmedico

Medizintechnik GmbH, Germany), fitted with 8 standard fluorescent tubes emitting major peak wavelengths of 311 nm (Philips TL-01 100 W). Patients received 3 exposures weekly within 12 weeks. For each patient the initial dose was given based on skin type in accordance with dosage schedules supplied with the device. Vitiligo patients were initially exposed to a dose of 0.21 J/cm². Subsequent dose increments depended on the effect of treatment, the aim was to attain and maintain minimally perceptible non painful erythema. Doses were increased by 10%-20% of the previous well-tolerated dose.

Baseline fasting serum folate levels were initially determined for patients prior to UVB exposure and for controls. Folate levels were again analyzed for patients at the end of the study after 36 NB UVB sessions; 24 hours after the last exposure. Blood samples were protected from light, separated and serum was stored at -70°C before analysis. Determination of serum folate was performed using an automated immunoassay system Ax SYM (Abbott Laboratories, USA). According to this assay serum folate levels were defined as: normal (5.3-14.4 ng/ml), intermediate (3.7-5.2 ng/ml), and deficient (<3.7ng/ml).

For analysis of data, comparison of two independent means was performed using the student's t-test, while comparison of paired means (mean folate values before and after UV exposure) was done using the paired t-test. Differences were considered significant when p was < 0.05.

Results

The following table shows the clinical characteristics and the mean (\pm SD) serum folate levels of the studied subjects.

	Sex	Age (years)	Skin Type	Cumulative NB UVB dose (J/cm ²)	Baseline Serum Folate (ng/ml)	Serum Folate after 36 NB UVB sessions (ng/ml)
NB UVB exposed patients (n=20)	13F 7M	25.5 \pm 3 (19-39)	I:9 II:3 III:8	75.95 \pm 3.67 (70.79-79.88)	8.1 \pm 2.6 (4-14)	5.9 \pm 1.5 (2.6-8.6)
Non exposed controls (n=20)	11F 9M	25.65 \pm 8 (18-36)	II:5 III:15		8 \pm 1.9 (3.8-13.3)	

Values=mean \pm standard deviation (range)

Table 1: Characteristics of patients and controls and mean (\pm SD)

serum folate levels (ng/ml) at baseline and at the end of the study

In all patients and controls, at baseline, serum folate levels were within the normal and intermediate range and no statistically significant difference was found between both groups ($p>0.05$). Serum folate values were however significantly lower in patients at the end of the study compared to their baseline values and control values ($p<0.05$).

Discussion

Data obtained from the study suggest that serial UVB exposures can significantly influence serum folate levels. B randa and Eaton [5] previously reported that exposure of human plasma in vitro to solar-simulated radiation causes 30-50% loss of folate within 60 minutes. In vitro studies have also shown that various folate vitamers (polyglutamates) may be detected using fluorescence detection at UV excitation of different wavelength, e.g. 290 nm or 360 nm[13]. These folate vitamers can be characterized by different absorption spectra. It was observed that apart from spectral absorbance of certain folate vitamers within the UVA range, there is also considerable absorbance within the UVB and UVC range (fig-1)[14].

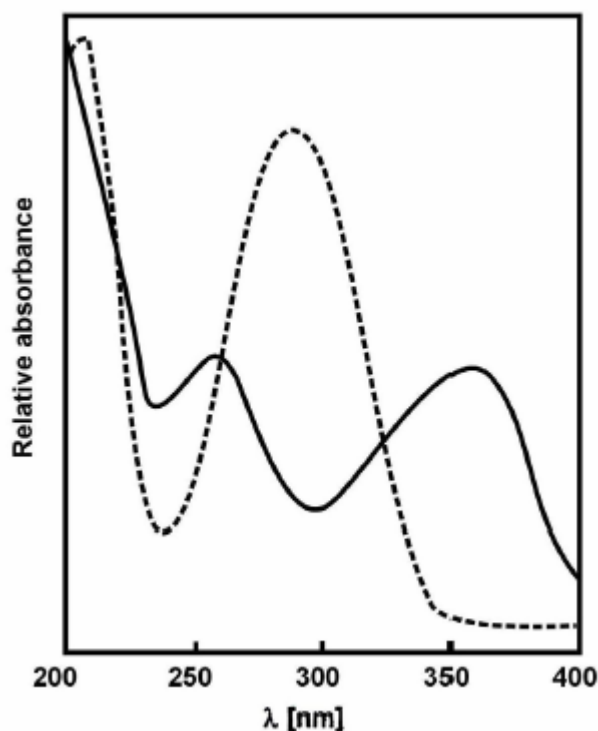


Fig-1: UV absorption spectra of tetrahydrofolate (- - -) and 10 formyltetrahydrofolate (—) assessed with high-performance liquid Chromatography and a UV diode array detection system [14].

It has been described that UVB radiation, because of its minor dermal penetration depth, has probably no significant influence on serum folate levels[15]. In the present study however, the abnormally low folate concentrations detected in the studied patients after narrow band UVB exposure, suggest that folate photodegradation may also be induced in vivo after high and/or cumulative UVB exposure.

The vitamin folate is vital for all living creatures as it regulates one-carbon transfer essential for normal cellular metabolism and is a cofactor for a variety of genetic pathways [2], [16]. Numerous investigators have described the relationship of folate metabolism to various disease processes [3],[6],[7],[16].

Folate deficiency is especially strongly linked with the development of neural tube defects [8],[9]. Low prevalences of severe folate deficiency and neural tube defects have been observed in native Africans and African Americans. It has been hypothesized that the heavily melanized skin in those races is of great importance in protecting against UV induced photolysis of folate [17]. Although folate deficiency is common in pregnant women and may arise both from inadequate dietary intake and from increased utilization of the vitamin during pregnancy, yet it has been argued that photolysis of folate by UV light may, especially in fair-skinned women, precipitate a folate deficiency sufficient to cause a neural tube defect [18],[19]. Lapunzina[11] observed three patients with neural tube defects whose mothers had sunbed exposures (UVA) during the first weeks of their pregnancies. All three mothers were young and healthy. Although folate deficiency of the mothers was not proved, the author speculated that sunbed exposure may have caused teratogenesis in these three patients. Based on epidemiological data Van Rootselaar[10] also suggests that UV radiation may cause neural tube defects in embryos of exposed mothers.

Ultraviolet B phototherapy is generally recommended by dermatologists as safe to use in pregnant women [12]. However, based on our findings in the current study we assume that exposure to high and/or cumulative NB UVB radiation can induce folate catabolism. It would therefore be suggested that intense or prolonged periconceptual exposure of women to NB UVB radiation for therapeutic reasons should be avoided especially if a connection between in vivo folate photolysis, clinical folate deficiency, and neural tube defects is established. This could be investigated in future studies in which it would be of interest to include other parameters of folate catabolism such as red cell folate and genetic polymorphism.

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