
Folate and phototherapy: What should we inform our patients?



Myron Zhang, MD,^a Gregory Goyert, MD,^b and Henry W. Lim, MD^a
Detroit, Michigan

Background: Ultraviolet (UV) degradation of folate has been studied in vitro and in vivo, but comprehensive reviews of the subject and recommendations for supplementing folate are lacking, especially for women of childbearing age, in whom decreases in folate predisposes newborns to neural tube defects.

Objective: We reviewed the effects of phototherapy on folate and provide a recommendation for women of childbearing age on phototherapy.

Methods: PubMed was searched for in vivo studies comparing folate levels before and after phototherapy.

Results: There is no evidence of decreased folate levels after UVA exposure. Decreased folate levels after sun exposure were limited to subjects taking folate supplements. Studies using narrowband UVB showed mixed results, potentially explained by dose-dependent degradation of folate; exposure $>40 \text{ J/cm}^2$ cumulatively and $>2 \text{ J/cm}^2$ per treatment were associated with 19%-27% decreases in serum folate levels, while lower doses did not affect folate levels.

Limitations: Extensive variability in results from studies and lack of considering confounders.

Conclusions: We recommend all women of childbearing age on phototherapy take 0.8 mg/day of folate supplements, as suggested by current guidelines for women of childbearing age, to reduce the risk of neural tube defects in unplanned pregnancy. (J Am Acad Dermatol 2017;77:958-64.)

Key words: folate; folic acid; narrowband ultraviolet B; neural tube defects; phototherapy; psoralen plus ultraviolet A; ultraviolet A1.

Narrowband (NB) ultraviolet (UV) B (311-312 nm), psoralen plus UVA (PUVA), and UVA1 (340-400 nm) are used to treat psoriasis, vitiligo, mycosis fungoides, and atopic dermatitis, among other dermatoses,¹⁻⁴ with a favorable side effect profile compared to systemic alternatives. Of note, while PUVA is a form of photochemotherapy, for simplicity, in this article, phototherapy will also be used to refer to PUVA.

One seldom-mentioned issue related to phototherapy is the potential to decrease folate levels, which is of interest to women of childbearing age, as birth defects, including neural tube defects (NTD),

Abbreviations used:

5MTHF:	5-methyltetrahydrofolate
NB:	narrowband
NTD:	neural tube defect
PTB:	per ten thousand births
PUVA:	psoralen plus ultraviolet A
UV:	ultraviolet

cardiac defects, and facial clefting have all been noted to be increased in women with folate deficiency.⁵⁻⁷ While Murase et al and others have previously mentioned the potential effect of UV on serum

From the Department of Dermatology^a and Women's Health Services,^b Henry Ford Hospital, Detroit.

Funding source: None.

Conflicts of interest: None declared.

Accepted for publication October 7, 2016.

Reprints not available from the authors.

Correspondence to: Henry W. Lim, MD, Department of Dermatology, Henry Ford Medical Center — New Center One, 3031 West Grand Blvd, Suite 800, Detroit, Michigan 48202, USA. E-mail: hlim1@hfhs.org.

0190-9622/\$36.00

© 2016 by the American Academy of Dermatology, Inc.

<http://dx.doi.org/10.1016/j.jaad.2016.10.016>

folate levels,^{8,9} in practice, many dermatologists and obstetricians are unaware that an interaction exists between phototherapy and folate. Moreover, providers who are aware of this interaction are often unsure of how to treat their patients because of the lack of formal recommendations or reviews on the topic. We present a review of the effects of phototherapy on folate and provide a recommendation for supplementing folate in women of childbearing age receiving phototherapy.

Folate, also known as vitamin B₉, is an essential nutrient that facilitates the transfer of one-carbon groups in DNA synthesis and other biosynthetic reactions.¹⁰ Humans cannot synthesize folate *de novo* and must therefore obtain adequate amounts through diet. Naturally occurring folate is found primarily in the form of 5-methyltetrahydrofolate (5MTHF) in leafy vegetables and other foods.¹¹ This form of folate is biologically active and readily participates in reactions, such as the conversion of homocysteine to methionine and 2'-deoxyuridine-5'-phosphate to 2'-deoxythymidine-5'-phosphate, a nucleotide component of DNA. Folic acid is the synthetic, oxidized form of folate found in the majority of supplements.¹¹ Folic acid must first be reduced by dihydrofolate reductase in intestinal or liver cells to dihydrofolate then tetrahydrofolate, which can then participate in the biosynthetic reactions above.

Both folate and folic acid undergo degradation upon exposure to UV. The *in vitro* inactivation of folate by sunlight has been described as early as 1947.¹² In 1978, Branda et al showed degradation of folate in human plasma by 36%-38% after 1-hour exposure to 360 nm UVA.¹³ *In vitro* studies since then have evaluated the effects of UV on both naturally occurring folate and synthetic folic acid. Steindal et al reported first order degradation of 5MTHF, a naturally occurring folate, into 5-methyldihydrofolate and then *p*-aminobenzoyl-L-glutamic acid by broadband UVB.¹⁴ Others have shown degradation of 5MTHF by broadband UVA in the presence of endogenous photosensitizers such as riboflavin¹⁵ and uroporphyrin,¹⁶ but not by UVA alone. Focused studies of the photodegradation spectrum for 5MTHF have not been performed. Two studies showed degradation of folic acid by UVC (254 nm peak)¹⁷ and UVA (365 nm peak)¹⁸ lamps into *p*-aminobenzoyl-L-glutamic acid, 6-formylpterin,

and pterin-6-carboxylic acid via zeroth-order kinetics, with a subsequent rate accelerated by photosensitization by degradation products. The action spectrum for folic acid photodegradation spans the UVA, UVB, and part of UVC range (260-400 nm), with a maximal degradation around 270 nm.¹⁹ Importantly, common wavelengths used in phototherapy, such as NB-UVB and UVA1, are within the degradation spectrum.

CAPSULE SUMMARY

- Photodegradation of folate has been demonstrated in laboratory studies.
- The effect of ultraviolet radiation on folate levels in humans is still inconclusive.
- Women of childbearing age on phototherapy should receive standard-amount folate supplements to prevent potential neural tube defects.

METHODS

We searched PubMed from 1946 to July 30, 2016, for [folate or folic acid] and [phototherapy, light, UV, UVA, UVB, or PUVA], limiting to studies that measured folate levels in the same patients before and after phototherapy. Additional articles were also found by following citations in relevant articles. Epidemiologic studies of NTDs were searched from the same database and dates using the terms [neural tube defects] and [seasonal or geographic or epidemiology]. Search results were reviewed for comparisons of NTD prevalence between seasons or locations with different sun exposure.

RESULTS

Tables I and II summarize the studies found for serum and erythrocyte folate levels, respectively. These will be further discussed below.

UVA

Gambicher et al found no significant changes in serum folate (in fact, a slight increase was observed) after a cumulative broadband UVA dose of 96 J/cm² over 6 sessions.²⁰ Der-Petrossian et al measured serum folate in the setting of extracorporeal photopheresis (using 8-methoxypsoralen and UVA) and likewise found no significant change.²¹

NB-UVB

Two of 6 studies, by Shaheen et al²² and El-Saie et al,²³ demonstrated significant decreases in serum folate levels in 20 vitiligo patients and 30 psoriasis patients, respectively, after 1 course of 36 treatments of NB-UVB (Table I). Of note, these two studies used higher cumulative doses (76 J/cm² and 118 J/cm²) than 3 of the 4 negative studies (all <46 J/cm² over 9-20 treatments).²⁴⁻²⁶ The remaining study found no decrease in 52 vitiligo patients after comparable

Download English Version:

<https://daneshyari.com/en/article/5647698>

Download Persian Version:

<https://daneshyari.com/article/5647698>

[Daneshyari.com](https://daneshyari.com)