Methotrexate plus narrowband UVB phototherapy versus narrowband UVB phototherapy alone in the treatment of plaque-type psoriasis: A randomized, placebo-controlled study

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Background: Combining phototherapy with topical and oral agents allows clinicians to treat recalcitrant psoriasis with reduced number of treatments and cumulative UV exposures.

Objective: This study was designed to determine the number of treatments necessary to clear plaque-type psoriasis when narrowband (NB) UVB is administered with methotrexate (MTX) or placebo in a randomized, controlled fashion.

Methods: MTX (15 mg/wk) or placebo was administered 3 weeks before standard NB UVB phototherapy was started. Treatments with the oral agent and phototherapy were continued until Psoriasis Area and Severity Index scores were reduced to less than 10% of the original scores or 24 weeks. Follow-up was performed until lesional scores returned to 50% of the original ones.

Results: A total of 24 patients were enrolled and 19 patients completed the study. Kaplan-Meier analysis revealed that the median time to clear psoriasis in the MTX/NB UVB group was 4 weeks, which was significantly less than that for the placebo/NB UVB group.

Limitations: Our sample size was relatively small (24 patients) with 5 dropouts. In addition, the study was conducted in skin types III to IV, Asian patients. Follow-up was limited to 4 to 6 months after completion of phototherapy.

Conclusion: MTX pretreatment allows physicians to clear psoriasis in fewer phototherapy sessions than when phototherapy is administered alone. (J Am Acad Dermatol 2006;54:1013-8.)

Treatment for psoriasis is not totally harmless. The use of methotrexate (MTX) is notoriously associated with liver toxicity especially when long-term treatment is used. Retinoids are teratogenic and cause a plethora of adverse effects, although mostly pharmacologic and dose-related. Cyclosporin A is nephrotoxic. UV therapies can cause skin to age prematurely and, more significantly, skin cancers.

Because most of the adverse effects from the above-mentioned modalities occur after prolonged treatments, rotational,[1] sequential,[2] and combination therapies are often recommended. Combining two or more modalities often allows treating physicians to clear psoriasis faster, thereby exposing patients to fewer doses of each treatment.

Abbreviations used:

DLQI:	Dermatology Life Quality Index
MED:	minimal erythema dose
MTX:	methotrexate
NB:	narrowband
PASI:	Psoriasis Area and Severity Index
PUVA:	psoralen–UVA

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Table I. Baseline characteristics of study patients

Characteristics	MTX/NB UVB (n = 11)	Placebo/NB UVB (n = 13)	*P* value
Age, y			
Range	19-73	30-62	
Mean ± SD	40.36 ± 16.46	47.62 ± 11.74	.24*
Sex			
Male	6	9	.46†
Female	5	4	
Skin type			
III	3	4	.85†
IV	8	9	
Mean duration of disease (mo) ± SD	77 ± 69.69	106.15 ± 89.38	.38*
PASI score at baseline			
Range	7.6-37.4	5.7-25.2	
Mean ± SD	18.05 ± 10.39	14.61 ± 7.23	.35*
PASI score after 3 wk of MTX or placebo			
Range	1.6-22.5	5.6-25.2	
Mean ± SD	9.16 ± 6.08	12.78 ± 6.37	.17*
PASI score at the end of NB UVB treatment			
Range	0-1.4	1.2-13.8	
Mean ± SD	0.31 ± 0.44	4.62 ± 3.57	.002*
Mean DLQI score ± SD	9.91 ± 5.05	10.27 ± 5.35	.87*

DLQI, Dermatology Life Quality Index; *MTX*, methotrexate; *NB*, narrowband; *PASI*, Psoriasis Area and Severity Index.
*Student *t* test.
†Chi-square test.

In the developing countries, retinoids, cyclosporine, let alone biologics, are often times prohibitively expensive. MTX is, thus, the mainstay when costs are taken into consideration. Phototherapy is a relatively safe and very effective treatment modality. However, several weeks are often required to achieve satisfactory clearing of lesions. Our study was designed to evaluate the efficacy of MTX plus narrowband (NB) UVB phototherapy, the combination that has never been tested to clear plaque-type psoriasis.

METHODS

The study protocol was approved by the our ethics committee. Informed consent was obtained from each participant.

Patients with plaque-type psoriasis, with at least 20% of body surface area involvement, whose disease activity had been stable in the 3 months before entering the study were eligible. Patients had to have discontinued systemic treatments, including psoralen–UVA (PUVA), for the past 8 weeks, UVB phototherapy for 4 weeks, and all topical treatments for 2 weeks before entering study. Patients with known history of MTX intolerance, photosensitivity, immunosuppression, and alcohol abuse, and those who were pregnant or lactating were excluded.

Patients were randomized by way of randomization cards to receive either MTX or placebo, which were identical in appearance. MTX (15 mg) or placebo was given in 3 divided weekly doses for 3 weeks before starting NB UVB phototherapy. The oral medications were given on weekends and continued until clearance or end of 24-week study period. At the end of the 3-week run-in period and before starting phototherapy, minimal erythema dose (MED) was determined in all patients. The fluences used at MED testing were 0.28, 0.40, 0.56, 0.80, and 1.12 J/cm^2. Total body irradiation was administered thrice weekly using stand-up cabinets (Daavlin Spectra 311, Bryan, Ohio; TL-01 100-W lamps, Philips, Eindhoven, The Netherlands). Before each phototherapy session, liberal use of mineral oil was encouraged. Starting UVB dose and dose escalations were standard as used in many treatment centers, ie, initial UVB dose was 70% of the MED then increased by 20% if no reactions developed from previous treatment, 10% if minimal reactions occurred, and 0% if erythema lasting longer than 24 hours developed. If no erythema developed from MED determination, UVB fluence was started at 0.70 J/cm^2 (rounding down from 0.78 J/cm^2, which was 70% of the highest fluence given at testing) for safety reasons. Dose increments continued until lesion clearance, which was defined as 90% reduction in Psoriasis Area and Severity Index (PASI) scores. At clearance or 24 weeks, all forms of therapy were discontinued without tapering or maintenance.