PUVA-bath therapy with 8-methoxypsoralen for the treatment of psoriasis vulgaris

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SUMMARY

Systemic PUVA therapy is being successfully used for the treatment of a variety of skin diseases for nearly two decades. In 1976 Fischer and Alsins published their article on PUVA bath therapy using trioxsalen (TMP) as photosensitizer for the treatment of psoriasis vulgaris. Since then PUVA bath therapy has proven itself as an effective alternative form of PUVA therapy. It has no systemic side effects and when compared with systemic PUVA therapy the same therapeutic effect requires smaller cumulative UVA doses and a smaller number of exposures. This article reviews the author's experience with PUVA bath therapy for the treatment of psoriasis vulgaris.

Introduction

Psoralen and ultraviolet A (PUVA) bath therapy is an alternative form of PUVA in which the psoralen is delivered highly diluted in bath water solution rather than orally prior to UVA treatment. Topical delivery of psoralen in bath water has many advantages over oral delivery of 8-methoxypsoralen (8-MOP) in PUVA: elimination of nausea, low (possibly zero) risk of cataracts, less total UVA irradiation and possible reduced risk of PUVA-induced cutaneous cancers (1).

The indication for PUVA bath therapy is moderate-to-severe psoriasis, in which 20% or more of body surface area is involved. The PUVA bath therapy is also successfully used in the treatment of cutaneous T-cell lymphomas (2,3), lichen planus (2,3,4), granuloma annulare disseminatum (4), urticaria pigmentosa (4) and localized scleroderma (4).

Before starting the PUVA bath therapy a careful evaluation of the patient is necessary. There are a number of situations in which PUVA bath treatment is relatively or absolutely contraindicated (1). Absolute contraindications include psoralen allergy, displastic nevus syndrome, simultaneous existence of photosensitivity-producing conditions (systemic lupus erythematosus, porphyria, etc), inability to comply safety precautions and pregnancy and lactation; relative contraindications include simultaneous use of a photosensitizing drug or topical preparation (sulfonamides, tetracyclines, coal tars, etc), presence of

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previous history of squamous cell carcinoma or melanoma and history of exposure to arsenic or ionizing irradiation.

The patient must be able to understand the safety precautions that are necessary for PUVA bath treatment. These include wearing glasses in the light box to protect the eyes, avoiding the careless splashing of psoralen-containing water in the eyes or mouth. Patients should avoid sun exposure at least 24 hours after bathing in psoralen. Although psoralen delivered by bath water should not affect the eyes, the patients should wear protective sunglasses for 24 hours after the treatment.

Pregnant women and mothers who are breast-feeding should be excluded (1).

Materials and methods

6 female and 5 male patients with moderate-to-severe psoriasis between 26 and 72 years of age (mean age 51,7) were admitted for treatment with PUVA bath therapy. All patients had been treated more that 1 year with topical agents (corticosteroids, calcipotriol) or systemic retinoids without success.

The patients bathed for 15 minutes in psoralen water solution with final concentration 1,0 mg/L (made of Oxsoralen caps., containing 10mg 8-MOP in one capsule, Gerot Pharmazeutika, Wien, Austria) to wet all psoriatic lesions below the neck.

Immediately after the patient's exit from the bath UVA irradiation with Waldmann PUVA 3001 box containing 14 pcs special lamps TL 85W/09T fluorescent bulbs, with a peak emission of 365 nm (Waldmann Medizintechnik, Villingen-Schwenningen, Germany) was administered (1). The starting dose of UVA irradiation was based on the patient's minimal phototoxic dose (MPD). Immediately after bathing in 8-MOP (at concentration 1,0 mg/L) patches of the patient's skin were irradiated at doses ranging from 0,5 to 6 J/cm^2. The starting dose of UVA should be the test dose just bellow the MPD. Therefore therapy was started with 0,25 to 0,5 J/cm^2 corresponding to the previously determined MPD. We generally increased the UVA dose by 0,5J for every second or third treatment, provided no phototoxicity had been produced by the preceding dose. When a threshold for mild phototoxicity had been reached, we maintained the next UVA dose at the level of the previous dose and increased the UVA dose more slowly with subsequent treatment. PUVA therapy was administered three times per week (on Monday, Wednesday and Friday) with gradually increased doses of UVA over the course of therapy.

Results

Clinical evaluation of patients showed marked improvement during PUVA bath therapy in all patients.

Patients had between 18 and 25 treatments. A mean cumulative UVA dose was 36,4 J/cm^2 (range, 21,5 to 51 J/cm^2) and a single dose ranging from 0,25 to 6 J/cm^2.

After 8 to 15 treatments the majority of psoriatic plaques in all 11 patients had been largely reduced to hyperpigmented patches. The skin was darkly pigmented. At the and of the PUVA bath therapy 7 patients showed complete resolution of psoriasis, but in 4 patients a few small plaques remained (most evident on the legs, specially the knees, and the elbows). Some residues of psoriasis remained also in 5 patients on the scalp. All patients showed slight to dark postinflammatory hyperpigmentation, whereas 1 patient showed also relative hypopigmentation around former plaques of psoriasis on the back and the legs.

During the treatment 4 patients showed erythema (on the back and buttocks) and 2 patients complained of increased itching in psoriasis lesions. None of them showed nausea, vomiting, dizziness or phototoxicity of the face.

Discussion

Systemic PUVA therapy has been successfully used for the treatment of psoriasis for many years. It is an effective therapy, but it has many short-term and long-term side effects.

In 1976 Fischer and Alsins published their article about PUVA bath therapy with trioxsalen for the treatment of psoriasis vulgaris. In 1996, Lowe introduced this therapy in the United States, using primarily 8-MOP. Since 1997 we have used PUVA bath therapy also in our department for a variety of skin diseases, but mainly for moderate-to-severe psoriasis, using 8-MOP (Oxsoralen capsules, Gerot Pharmazeutika, Wien, Austria).

Topical delivery of psoralen in bath water has many advantages over oral delivery of 8-methoxypsoralen (8-MOP) in PUVA. The topical application selectively concentrates 8-MOP in the epidermis and produces low concentrations of 8-MOP in dermis or serum compared with oral dosing. The concentrations in the epidermis are 10-100 times higher than that in the dermis (5,6,7,8). It is probable that such low plasma/serum levels of 8-MOP after bath application contributes to the lack of nausea and decreased phototoxicity when compared to oral administration (1,5).

The PUVA bath therapy has no systemic side effects and when compared to systemic PUVA therapy the same therapeutic effect requires smaller cumulative UVA doses and lower numbers of exposures (9,10). In our group of patients the cumulative UVA doses in PUVA bath therapy were ranging from 21,5 to 51J/cm^2 (com-

pared to systemic PUVA therapy 55-90 J/cm^2). The total number of exposures during PUVA bath therapy was between 18 and 25 in comparison to 30 exposures during systemic PUVA therapy.

During the PUVA bath therapy patients usually do not have many side effects. The most common short-term side effect is phototoxicity. Some patients complain over pruritus (1,2,4,5,9,10). The patients in our group also did not have many short-term side effects; 4 patients showed erythema and 2 patients complained of increased itching in psoriasis lesions.

According to the data from the literature long-term side effects include possible induction of squamous cell carcinomas, basal cell carcinomas, melanomas, an accelerated photoaging (9,11,12). The total UVA dose required with the bath water delivery of 8-MOP is significantly less than those with oral delivery of 8-MOP - up to 100% lower (10,11,12). Because of that the incidence of squamous cell carcinomas in the bath PUVA patients is significantly lower than it is in the oral PUVA patients (11,12). The systemic absorption of 8-MOP in PUVA bath treatment is very low, so the risk of cataract practically does not exist (1).

We have not seen any of these long-term side effects yet, but the time that we have used PUVA bath therapy is too short to make final conclusions.

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