Does Addition of Topical Calcipotriol to UVB Increase the Risk of Irritant Reactions in Psoriasis?

Sir,

The efficacy of both topical application of calcipotriol and UVB in the treatment of psoriasis is well documented. The combination of the two treatments seems to be more effective and to give a higher clearance rate (1, 2). In some cases irritant reactions related to the combined treatment have been reported (3).

The aim of this study was to evaluate irritant reactions related to calcipotriol ointment alone and UVB alone and to the combination of calcipotriol and UVB in the treatment of psoriasis.

MATERIAL AND METHODS

Data from two randomised right/left studies were analysed regarding irritant reactions. Patients included in the studies had chronic stable plaque-type psoriasis with symmetrical lesions on the arms, the legs and/or the trunk.

Series A: One hundred and one patients were treated with calcipotriol on one side and calcipotriol + UVB on the other side of the body (open study) (2).

Series B: Seventy-six patients were treated with calcipotriol + UVB on one side and vehicle + UVB on the other side of the body (double-blind study).

Calcipotriol ointment, 50 μg/g, was applied twice daily and UVB was used 3 times weekly for 8 weeks. The UVB dose was increased from 0.7 × MED prior to start of treatment in rapid steps up to the erythema threshold. Calcipotriol was applied at least 2 h prior to or after UVB exposure.

RESULTS

Irritation, with itching and erythema within the psoriasis lesions, was recorded in 17% of the sites treated with calcipotriol + UVB, in 14% of the sites treated with calcipotriol alone and in 13% of the sites treated with vehicle + UVB. The differences were not of statistical significance.

Seven patients in series B applied calcipotriol immediately after UVB; 3 of these 7 patients experienced UV burning, compared to 7 out of 170 patients in total applying calcipotriol at least 2 h prior to UVB.

The irritant skin reactions were mild to moderate and of the same kind and severity on the side treated with the combination of calcipotriol + UVB, with calcipotriol alone, or vehicle + UVB, except for one case treated with calcipotriol + UVB, who got a reaction with smarting pain and blisters starting 3 weeks after onset of treatment. Following reduction of UVB, treatment was continued in all except for the case with the reaction mentioned, in whom treatment was withdrawn.

There was no difference as regards skin type, PASI or thickness of the lesions prior to the treatment in patients with irritant reactions as compared to patients not irritated by the treatment.

DISCUSSION

Calcipotriol treatment may cause irritation in psoriatic skin, as calcipotriol itself has irritating properties (4, 5). In two studies of calcipotriol ointment alone lesional/perilesional irritation was reported in 19% and 20%, respectively (6, 7). The main side-effect of UVB is irritation and burning. Standard volunteer photocontact allergy and phototoxicity studies conducted in the USA concluded that calcipotriol is unlikely to be associated with phototoxic or phototoxic reactions in clinical use (Data on file, Leo Pharmaceutical).

Four cases of burn reactions were reported recently in patients who were established on UVB phototherapy and subsequently began treatment with calcipotriol ointment (3). Two of the patients were able to continue the combination therapy after reduction of the UVB dosage.

In our two analysed treatment series presented, there was no difference in the rate of irritation related to the treatment of calcipotriol, of UVB or of the combination of calcipotriol and UVB. However, there was an increased risk of irritation when calcipotriol was applied just after UVB irradiation. UVB enhanced the effect of calcipotriol in both the series. The efficacy of the treatment was greater on this side than on sides treated with calcipotriol alone (series A) or vehicle + UVB (series B). The skin on the calcipotriol + UVB-treated sides was thinner and less scaling than on the other sides, allowing more absorption of UVB. The UVB dosage used was relatively aggressive. One likely explanation for the somewhat more irritant events occurring on the calcipotriol + UVB-treated sides is that the UV-related irritant events were mainly caused by the erythrogenic UVB dose itself but enhanced when calcipotriol was applied immediately after exposure to the relatively high UVB doses.

CONCLUSION

Treatment with the combination of calcipotriol ointment and UVB for psoriasis generally does not cause irritation, lesion/ perilesional erythema or itching more often than calcipotriol alone or UVB alone. The risk may be increased, however, when calcipotriol is applied immediately after exposure to relatively high doses of UVB. It is therefore recommended that calcipotriol ointment or cream is not applied immediately after UVB irradiation but preferably several hours later.

ACKNOWLEDGEMENT

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Acta Derm Venereol (Stockh) 77
Cancer Induction by Immunosuppression in Psoriasis after Heavy PUVA Treatment

Sir,

High cumulative dosages of PUVA therapy have been reported to increase the risk of skin malignancies (1, 2). The incidence of non-cutaneous cancers also appears to be increased in PUVA-treated psoriatic patients. Long-term treatment with immunosuppression also implies an increased risk of malignancies (3). The cumulative suppression of the immune system is considered of more importance than the choice of immunosuppressive agents (3, 4). In patients treated with both high cumulative dosages of PUVA and immunosuppression, such as cyclosporine, the risk of cancer development seems to be even more increased (5).

Two cases are presented, in whom cancer was induced by low-dose and short-term immunosuppressive therapy, respectively, after previous heavy PUVA treatment for chronic widespread psoriasis. They were treated with oral PUVA for many years and also received a large amount of natural UV light. Because of UV damage of the skin, PUVA was withdrawn. Immunosuppressive therapy was then instituted.

CASE REPORTS

Case 1

A 49-year-old man with psoriasis since 3 years of age has received over 440 PUVA treatments. From 1991 he was treated with thioguanine in low dosages (6, 7), varying from 40 mg per day to 20 mg 2-3 times per week, giving complete or almost complete remission of psoriasis lesions. After 3 years he suddenly got multiple keratotic tumours on the legs, in the face and on the trunk. New tumours appeared every month, altogether over 15 squamous cell carcinomas. There was a large polycyclic carcinoma in the left inguinal region, which at diagnosis had spread to the lymph nodes.

Case 2

A 59-year-old man with psoriasis since 20 years of age has received over 340 PUVA treatments. Cyclosporine, 3 mg/kg body weight, was instituted in the beginning of 1995. Within some months he presented multiple, very rapidly developing squamous cell and basal cell carcinomas over the trunk and extremities.

DISCUSSION

The cases here presented clearly point at the risk for cancer induction even by mild and short-term immunosuppressive therapy in cases previously treated with heavy oral PUVA. The finding also indicates that there have to be different strategies in the use of immunosuppression in psoriasis. In patients not treated with PUVA, in particular in younger patients with severe psoriasis, immunosuppression by such agents as cyclosporine and thioguanine can be argued as a part of a rotation treatment modality (8). In patients previously treated with PUVA, in particular after heavy oral PUVA, even low-dose immunosuppression has to be used with the greatest caution or, rather, be avoided in this high-risk group of psoriasis patients regarding development of malignancy.

REFERENCES


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