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Long-term outcome of severe chronic plaque psoriasis following treatment with high-dose topical calcipotriol

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Summary We have previously reported the effectiveness of high-dose calcipotriol in extensive psoriasis. We now report the long-term outcome in patients following this treatment. Twenty-eight patients with severe psoriasis were treated as in-patients with high-dose topical calcipotriol for 2 weeks. There was a mean reduction in the psoriasis area and severity index of 65%. Sixty-nine per cent were controlled for 3 months and 42% for 6 months. The relapse rate was comparable with that following Ingram's regimen, the in-patient stay was shorter and the treatment more acceptable. Careful monitoring of calcium homeostasis is mandatory.

Current treatments for extensive chronic plaque psoriasis vulgaris include phototherapy, chemotherapy and photochemotherapy (PUVA). The mainstay of treatment in the U.K. is either short wavelength ultraviolet radiation (UVB) combined with dithranol or tar (Ingram's and Goeckerman's regimens),[1,2] or PUVA. Alternatively, systemic treatments can be used: these are effective but potentially toxic.

Calcipotriol is a well-established treatment in mild to moderate psoriasis.[3] We have previously reported that calcipotriol is an effective, rapid in-patient treatment for extensive psoriasis.[4] Hypercalcaemia and hypercalciuria were the principal side-effects, which were dose-dependent and rapidly reversible.[4,5] None of the patients who developed hypercalcaemia or hypercalciuria was symptomatic. We now report the long-term follow-up and relapse rates in patients treated with this regimen.

Patients and methods

Men and women over the age of 18 years with extensive psoriasis (greater than 15% body surface area) were admitted to hospital for treatment.[4,5] These patients participated in one of two studies investigating the clinical and biochemical effects of high-dose calcipotriol (50 μg/g) ointment. In the first study, patients applied 200 g of calcipotriol for 1 week followed by 300 g for the second week.[4] In the second, the dose was tailored to the extent of the psoriasis up to a maximum of 360 g.[5] Patients were excluded if there was a history of renal impairment or renal calculi, or if they were pregnant, breast-feeding, or taking thiazide diuretics or other systemic treatment, including PUVA, for their psoriasis. Psoriasis area and severity index (PASI) was recorded at baseline and after 2 weeks. Serum total adjusted calcium was measured three times weekly and 24 h urinary calcium was measured twice weekly during and for 1 week after the high-dose regimen. In the event of hypercalcaemia or hypercalciuria, calcipotriol was omitted until the calcium returned to normal and then restarted at a lower dose. Following discharge, patients used calcipotriol within the licensed dose (100 g/week) for residual psoriasis.

Follow-up was assessed retrospectively using patient notes. Control was defined as the ability to control psoriasis at home without second-line treatment. Wilcoxon's test for paired differences was used to analyse the PASIs.

Results

Twenty-eight patients were treated: their mean age was 47 years (range 18–83) and the sex distribution was equal. Nineteen patients had had psoriasis for more than 10 years. Four patients were diagnosed within 1 year of treatment. All patients had received topical preparations (steroids, tar or dithranol), three UVB, and 10 systemic treatment (PUVA, etretinate or methotrexate). Mean PASI (range) fell from 21·4 (8·2 to 53·7) to 7·8 (1·2–32·9) ($P < 0·0001$), with a mean reduction of 65% (range 32–87%). Eighteen patients (64%) had a PASI of $< 7·5$ (mean 4·8) after treatment. Follow-up details were unavailable in one patient.

One patient did not respond to the regimen. Of those

patients who responded, eight (31%) relapsed within 3 months, requiring UVB (three patients), PUVA (three), methotrexate (one) or acitretin (one). Five (19%) relapsed between 3 and 6 months requiring UVB (one patient), PUVA (two) or acitretin (two). Two remained clear at 3 months but failed to attend subsequent appointments. Eleven (42%) remained controlled for 6 months or more, of whom two have been discharged and two remain controlled at 8 months and 5 years, respectively. Three patients relapsed within 8 months requiring UVB, acitretin and repeat high-dose calcipotriol followed by acitretin. Two patients relapsed at 1 year requiring UVB and high-dose calcipotriol with PUVA. Two patients who responded were alcoholics. Outcome was independent of severity, duration and previous treatment.

Five patients developed hypercalcaemia (range 2·66–2·94 mmol/L); none was symptomatic. Treatment was stopped and values returned to normal within 3 days.[5] All patients had received a dose greater than 5 g/kg per week. Nine patients became hypercalciuric during treatment and two patients did so in the following week. Two patients were hypercalciuric at baseline and had a further rise during treatment. Hypercalciuria correlated poorly with the dose of calcipotriol.

Discussion

We have found high-dose calcipotriol to be an effective in-patient treatment for extensive psoriasis. Cunliffe *et al.*[6] found that 61·2% of patients with mild to moderate psoriasis showed clearance or marked improvement of their psoriasis when treated with topical calcipotriol. In their study topical calcipotriol ointment (50 μg/g) was applied to a maximum of 100 g/week for 6 weeks. This response rate is similar to our study, in which 65% of patients with extensive psoriasis, treated with the high dose regimen, responded.

Of those patients who responded, 69% were controlled for 3 months, 42% for 6 months, and 23% for a year. These rates are comparable with those following Ingram's regimen.[7,8] However, it is difficult to compare directly with other studies where the severity of psoriasis was assessed by area rather than PASI, and treatment was continued until clearance; and in the study by Monk *et al.*[8] there was no indication of the severity of psoriasis in the pretreatment group. Monk *et al.*[8] defined relapse as a recurrence of 50% or more of the pretreatment area of psoriasis. Seventy-nine per cent of his patients remained controlled at 3 months, 42% at 6 months and 19% at 1 year, compared with 69%, 42% and 23%, respectively, in our patients. Two of our patients were alcoholics in whom high-dose calcipotriol has proven a highly effective non-hepatotoxic treatment.

The main concern with this regimen is hypercalcaemia and vitamin D toxicity.[5] All patients who developed hypercalcaemia had received a dose greater than 5 g/kg per week. We have since changed our policy and permit a maximum of 5 g/kg or 360 g/week of calcipotriol. The second concern is hypercalciuria, which correlated poorly with the dose of calcipotriol. However, the hypercalciuria was reversible on stopping calcipotriol, and it is generally accepted that in individuals with no predisposition to renal calculi, hypercalciuria is unlikely to be a problem in the short term. In view of this we now advise patients to drink plenty of non-milky drinks during treatment. In-patient treatment and close monitoring of serum and urine calcium is important.

Topical calcipotriol does not stain and is more convenient to apply than dithranol. The in-patient stay was 2 weeks, compared with a mean of 18·5 days with Ingram's regimen.[8] Patients found it easier to continue calcipotriol as maintenance treatment. We have shown that high-dose topical calcipotriol is an effective, safe treatment in extensive psoriasis with relapse rates comparable with those found in conventional in-patient topical regimens.

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