Modified combined methotrexate PUVA therapy in the treatment of recalcitrant psoriasis: A preliminary report

Sir,

Methotrexate probably reduces the thickness and scaliness of psoriatic plaques, altering the photo-optical properties of the diseased skin so as to increase the penetration of UVA radiation, resulting in the marked reduction in the total cumulative exposure

to UVA radiation necessary to achieve remission.[1,2] Thus, the main advantage of using a combination of methotrexate and PUVA therapy is the marked reduction achieved in the total cumulative exposure to UVA radiation necessary to achieve remission.[1] This was the basis of our trial of this combination therapy on three cases of recalcitrant psoriasis.

Three male adults of Fitzpatrick skin type V with recalcitrant psoriasis with a minimum PASI score of 20 (on various topical and systemic treatments) were recruited between December 2003 and March 2005 and those with contraindications for PUVA and methotrexate and on active systemic therapy in the past 8 weeks were excluded. Informed consent was taken from all the patients and the protocol had the approval of the institutional ethical committee. All patients were investigated and followed up as per guidelines for methotrexate usage and PUVA therapy. Complete remission was defined as 'greater than 90% reduction in PASI from baseline' and partial remission as 'more than 75% reduction from the baseline'. Relapse was defined as 'a PASI score that is 50% more as compared to the baseline'.

These patients were started on tablet methotrexate 10 mg/week for a period of 4 weeks. PUVA therapy using 8-methoxypsoralen crystalline tablets at a dose of 0.6 mg/kg body weight was instituted twice a week from week 5 onwards along with the same dose of methotrexate. UVA radiation was delivered with a Dermalight 6000® model (from Dr. Honle, Munchen, Germany) chamber having an irradiance of 14 mw/cm^2 with a starting dose of 3 J/cm^2. The UVA dose was incremented by 0.5 J/cm^2 every second or third sitting depending on the patient's response to therapy.

Once complete remission had occurred, the patient was put on a maintenance dose of PUVA (last clearance dose administered once a week for a period of 4 weeks) along with methotrexate. On completion of the maintenance dose of PUVA, methotrexate was tapered by 2.5 mg every week. The patients were then followed up monthly for a minimum period of 3 months.

Partial remission was achieved in all the cases by 7.6 weeks and complete remission by 10.6 weeks. At the time of complete remission, the total number of UVA exposures was 13.3 per person, the mean UVA cumulative dose was 58.3 J/cm^2, the final clearance dose of UVA was 5.16 J/cm^2 and the mean cumulative dose of methotrexate was 106.6 mg [Table 1]. Monthly follow-up after the end of the maintenance period of 3 months did not see any relapse. The only adverse events noticed were nausea in two patients and mild pruritus in three patients.

The mean cumulative dose of methotrexate and maximal UVA doses in our report were similar to the study by Morison *et al*.[2] In the present report, the number of PUVA exposures and clearance times were much higher, which could be on account of our cases being recalcitrant in nature, belonging to skin type V, being on lower initial doses of methotrexate, with slow increment in UVA doses and twice weekly PUVA administration and consequently, had no instance of acute or subacute phototoxicity (in comparison to Morison *et al*.[2] study).

Shehzad *et al*.,[3] utilizing the combination of methotrexate and PUVA therapy, observed that the mean number of PUVA sessions needed for clearance was 10 and the mean time was 2.5 weeks. PUVA administered four times a week may have allowed for faster clearance times in the above studies. Twice-weekly PUVA treatment used by us for psoriasis was proved to be as effective as treatment given more

Table 1: Results of combined methotrexate PUVA therapy at the end of complete remission and at the end of the maintenance period

No.	Age	Sex	Duration (years)	PASI	PR (weeks)	CR (weeks)	TD (weeks)	Methotrexate CD (mg)		UVA CD dose (J/cm^2)		Final UVA (J/cm^2)
								CR	TD	CR	TD	
1	47	M	4	28.1	8	10.5	17.5	105	160	57.5	79.5	5.5
2	39	M	1	28.7	7	10	17	100	155	50.5	68.5	4.5
3	42	M	3	20.5	8	11.5	18.5	115	170	67	89	5.5

PASI, Psoriasis area severity index; PR, partial remission; CR, complete remission; TD, Total duration at the end of maintenance; CD, Cumulative dose

frequently and probably more safe.[4]

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Diagnosis of delayed pressure urticaria

Sir,

Delayed pressure urticaria (DPU) is a physical urticaria in which pressure is the physical stimulus that causes whealing. Pressure (defined as the force applied to a unit area of surface) induces reproducible whealing in DPU. Delayed cutaneous erythema and edema occur in association with marked subcutaneous swelling after the application of a sustained pressure stimulus to the skin. These signs occur as early as 30 min and typically 4 to 6 h later. Lesions may persist for up to 48 h. The response is dependent on the degree of pressure; duration of the stimulus; body site affected; and activity of the disease, which is variable in intensity.[1] Sites that previously have reacted to pressure have been found to be refractory to an additional pressure stimulus for at least 24 to 48 h. Most patients with DPU have chronic idiopathic urticaria (CIU) and angioedema. DPU should be considered in all patients with CIU whose disease is unresponsive to antihistamines. The disease is variable and remissions and exacerbations occur.

In DPU, a positive response after any form of pressure challenge consists of the appearance of palpable lesions after at least 30 min. Because most positive responses occur at 6 h, observers usually read pressure tests at 6 h. There is no standard method of pressure testing for DPU. Hence, I used simple and easily available implements like a 2 kg weight and a blood pressure cuff to test for DPU in 50 patients of CIU.

Fifty adult patients with chronic urticaria attending a private skin centre at Navi Mumbai were enrolled in this study. All antihistamines and oral steroids were stopped 48 h prior to the test. A 2 kg of weight, available at a general store, was placed on the right forearm of patients and a blood pressure cuff was strapped tightly around the weight to give sustained pressure [Figure 1]. The pressure in the cuff is raised to 100 mm of Hg and is maintained for 1 min or till patient feels discomfort, whichever is earlier. Reading is taken after 30 min and at 6 h for visible and palpable swelling.

The 50 cases comprised of 33 male and 17 female patients (age range 18-80 years, mean age 43 years). Three patients (2 male and 1 female), out of the 50, tested positive with this instrument at 30 min and at 6 h. Positive test was seen as a palpable and visible swelling on right forearm at the site of pressure at the end of 30 min and at 6 h. These patients had typical history of swelling at the site of pressure, like waist and palms and soles.

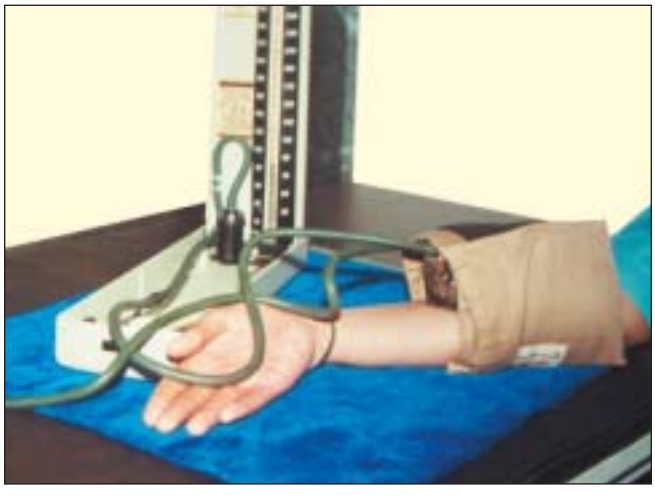

Figure 1: Blood pressure cuff tied with 2 kg weight around right forearm