

SHORT REPORTS

Serum Levels of 8-Methoxypsoralen
2 Hours after Oral AdministrationI. Steiner, T. Prey, F. Gschnait,¹J. Washüttl and F. Greiter²*Institute for Botany, Technical University of Vienna,*¹*Department of Dermatology, University of Vienna,*²*Greiter Research Laboratories, Weidling,
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Abstract. Serum levels of 8-methoxypsoralen (8-MOP) were determined 2 hours after oral administration and found to vary considerably among psoriatic patients. There was no definite correlation between the 8-MOP serum level, the dose of 8-MOP/kg body weight ingested, and the minimal phototoxic UVA dose.

Key words: 8-methoxypsoralen; Serum level; Photochemotherapy; PUVA

The phototoxic response to orally administered 8-methoxypsoralen (8-MOP) depends on the patient's individual skin sensitivity, the amount of UVA energy applied and on the actual 8-MOP serum level at the time of irradiation (4).

In the present study, serum levels of 8-MOP were determined 2 hours after oral administration and correlated with the dose of 8-MOP/kg body weight ingested and with the UVA energy necessary to elicit a barely perceptible phototoxic reaction (=minimal phototoxic dose=MPD).

MATERIAL AND METHODS

Sera from 37 psoriatic patients, who were checked for normal liver and kidney function, were examined 2 hours after ingestion of 8-MOP. 8-MOP was administered on a mg/kg body weight basis according to the schedule employed in PUVA treatment (1, 3, 5). Oxsoralen® 10 mg capsules (GEROT-Pharmazeutika, Vienna) were used. Blood and sera were kept and handled in the dark.

8-MOP was determined quantitatively after extraction of 10 ml serum with 1 N HCl by preparative thin-layer chromatography using Di-iso-propylether/concentrated acetic acid 90:10 as developing solvent (2). The chromatogram was evaluated *in situ* by means of a chromatogram spectrophotometer. Determinations were made in duplicate.

The MPD was determined 2 hours after 8-MOP intake (4) according to the principles of phototesting in photochemotherapy, employing a modified system of dose increments adjusted for the experimental needs of this study.

RESULTS

Table I shows the values obtained in 37 patients. The 8-MOP serum levels varied within wide limits (0.1-9.3 µg/10 ml); mean: 2.8 ± 2.4 µg/10 ml. The average dosis of 8-MOP (mg/kg body weight) ad-

Table I. 8-MOP serum levels, MPD, and 8-MOP dose/kg body weight in 37 psoriatic patients

Patient no.	8-MOP doses (mg/kg body weight)	MPD (Joule/cm ²)	8-MOP serum level (µg/10 ml)
1	0.60	2.9	6.9
2	0.65	1.7	3.3
3	0.63	3.2	5.7
4	0.57	2.8	5.2
5	0.65	1.9	0.3
6	0.60	2.2	2.7
7	0.60	5.4	1.9
8	0.59	0.7	3.3
9	6.62	5.4	8.1
10	0.56	1.3	4.1
11	0.65	5.0	9.3
12	0.58	5.1	5.5
13	0.62	0.7	0.1
14	0.52	3.0	1.7
15	0.56	1.4	3.4
16	0.63	0.9	0.4
17	—	6.3	2.8
18	0.58	4.1	0.1
19	0.50	2.7	0.8
20	0.50	1.3	2.4
21	0.64	2.0	0.6
22	0.55	4.1	0.1
23	0.66	4.1	2.3
24	0.55	1.3	2.0
25	0.63	1.3	3.4
26	0.51	2.6	3.2
27	0.59	3.5	1.7
28	0.58	3.3	0.4
29	—	—	1.5
30	0.55	1.6	1.9
31	0.71	1.6	0.8
32	0.66	4.1	1.4
33	0.72	4.1	1.4
34	0.50	2.7	1.3
35	0.57	0.5	7.6
36	0.60	1.0	5.7
37	0.75	1.2	0.5

ministered was 0.60 ± 0.06 , the average MPD (Joule/cm²) being 2.6 ± 1.5 .

No definite correlation was found between 1) the doses of 8-MOP ingested and the 8-MOP serum level, 2) the 8-MOP serum level and the MPD, or 3) the doses of 8-MOP ingested and the MPD.

DISCUSSION

This study demonstrates that 8-MOP serum levels, determined 2 hours after oral administration of the drug, vary considerably in different psoriatic patients. Moreover, no definite correlation was found between MPD and 8-MOP serum level, thus indicating that the patient's individual sensitivity to PUVA depending on the skin type, is of major importance in the phototoxic response to 8-MOP.

Since in addition no correlation exists between the 8-MOP serum level 2 hours after 8-MOP administration and the dose of 8-MOP per kg body weight administered, a variable resorption and/or excretion rate for 8-MOP may be assumed, differing from one psoriatic patient to another.

Our failure to demonstrate a correlation between the three different parameters investigated in this study underlines the importance and absolute necessity of phototesting (4) prior to PUVA treatment.

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REFERENCES

1. Parrish, J. A., Fitzpatrick, T. B., Tanenbaum, L. & Pathak, M. A.: Photochemotherapy of psoriasis with oral methoxsalen and long-wave ultraviolet light. *N Engl J Med* 29: 1207, 1974.
2. Steiner, I., Prey, T., Washüttl, J., Greiter, F. & Wolff, K.: Eine dünn-schichtchromatographische Bestimmungsmethode für 8-Methoxypsoralen im Humanserum. *Microchim Acta* 1: 119, 1977.
3. Wolff, K., Fitzpatrick, T. B., Parrish, J. A., Gschnait, F., Gilchrist, B., Hönigsmann, H., Pathak, M. A. & Tanenbaum, L.: Photochemotherapy for psoriasis with orally administered methoxsalen. *Arch Dermatol* 112: 943, 1976.
4. Wolff, K., Gschnait, F., Hönigsmann, H., Konrad, K., Parrish, J. A. & Fitzpatrick, T. B.: Phototesting and dosimetry for photochemotherapy. *Br J Dermatol* 96: 1, 1977.
5. Wolff, K., Hönigsmann, H., Gschnait, F. & Konrad, K.: Photochemotherapie bei Psoriasis. Klinische Erfahrungen an 152 Patienten. *Dtsch Med Wschr* 100: 2471, 1975.

Periodic, Functional Disuse of Limbs: Report of a Case

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Abstract. The case is presented of a patient who developed periodic loss of function in individual limbs, and associated cyanosis and hyperkeratosis. Investigation excluded organic disease, and the condition responded to physiotherapy.

Key words: Functional disuse; Cyanosis; Hyperkeratosis

Prolonged inactivity of a limb may induce oedema, cyanosis, hyperkeratosis and ulceration. The appearance may mimic a number of cutaneous, neurological and vascular disorders.

CASE REPORT

A 16-year-old boy was referred in November 1974 with a 12-month history of periodic attacks of cyanosis, coldness and weakness affecting the right hand. These attacks began immediately after a fall on the right elbow, although there had been no fracture nor ulnar nerve injury. The patient was a non-smoker; there was no history of exposure to ergot, vinyl chloride or vibrating machinery.

By October 1975 the right arm had gradually returned to normal, but similar episodes affected the left leg. The problems with his limbs forced our patient to lose jobs as a gardener and hotel porter.

In March 1976 the left arm was involved, an episode which persisted for 6 months. Below the elbow, the arm became cold, swollen and blue. Hyperkeratosis of the hand and forearm developed (Fig. 1). Peripheral pulses were normal. There was subjective sensory impairment, but no objective sensory loss. Power of all muscle groups was normal, although use of the limb produced considerable discomfort. There were no signs attributable to parietal lobe dysfunction. After a period of observation it became clear that the patient was neglecting the affected arm; it was carried limply by his side and the patient (a nail biter) ceased to bite the nails of his left hand.

Routine investigations gave either normal or non-contributory findings. Skull X-ray, Brain Scan, E.E.G. and right subclavian and brachial arteriography were also normal. Sweating tests indicated no disturbance of central, peripheral or end-organ mechanisms. Skin thermometry indicated that the basal temperatures were only low in the limbs when they were clinically affected; reflex vasodilation in the hands was normal at all times.

The patient formed a good relationship with his physicians and the medical social worker. Although quiet and