lichenoides chronica eine neue Indikation zur PUVA-Therapie? Dermatologica *59*: 451, 1979.
6. Nigra, T. P. & Soter, N. A.: Pityriasis lichenoides. *In* Dermatology in General Medicine (ed. Fitzpatric), 2nd ed., p. 665. McGraw-Hill, 1979.
7. Cormane, R. H., Hamerlinck, F. & Siddiqui, A. H.: Immunologic implications of PUVA therapy in psoriasis vulgaris. Arch Dermatol Res *265*: 245, 1979.
8. Faber, W. R. & Van Joost, Th.: Pityriais lichenoides, an immune complex disease? Acta Dermatovener (Stockholm) *60*: 259, 1980.

A Retrospective Study of Cataract Formation in 96 Patients Treated with PUVA

Ole Hammershøy[1] and Flemming Jessen[2]

[1]*Department of Dermatology and Venerology and* [2]*Department of Ophthalmology, Odense University Hospital, DK-5000 Odense C, Denmark*

Received October 14, 1981

Abstract. Studies in guinea pigs have shown formation of cataract when they are treated with 8-methoxypsoralen (8-MOP) and UVA irradiation. 96 patients treated with PUVA between 1975 and 1980 were examined to observe if cataract formation had occurred more frequently in these patients. No patient developed cataract during the PUVA treatment period and these findings were found to correspond to those in a "standard population".

Key words: PUVA treatment; Cataract formation

Studies in guinea pigs treated with 8-methoxypsoralen (8-MOP) in doses corresponding to 140 times the therapeutic dose, followed by prolonged exposure to ultraviolet light (UVA), have demonstrated cataract formation in the animals (2, 3).

Up till now, no reports are available showing cataract formation in patients treated with PUVA. The present study comprised 96 patients treated with PUVA during the period 1975–80. The aim was to establish whether this group of patients suffered more frequently from cataract than might be expected in a "standard population".

MATERIALS AND METHODS

During the study period, 120 patients were treated with photochemotherapy and of these, 96 patients satisfied the requirements to enter the present study.

The 96 patients were 42 women and 54 men, aged 18 to 81 years (average 49 years). In the different age groups the patients were divided into subgroups according to the ophthalmologic findings at the latest examination. The definition were: "no cataract", "unchanged cataract" or "change in cataract" (Table I).

Initially the PUVA treatment was given four times a week, and subsequently twice a week or once a week. Two hours before treatment the patient ingested 0.4–0.6 mg 8-methoxypsoralen (Meladinine®) per kg. During treatment the patients had their eyes protected by dark glasses and were requested to wear protection glasses (Black-Ray UVC-303) for 24 hours after treatment.

The ophthalmologic examination included visual acuity, ophthalmoscopy, slit lamp examination and photo of the lenses. All examinations were made in mydriasis. Before starting and during the treatment the following haematological parameters were performed: erythrocyte sedimentation rate, haemoglobin, leukocyte count, thrombocytes, creatinine, carbamide, alkaline phosphatase and alanine-amino-transferase.

Before and during the treatment the skin was examined to search for carcinomas.

RESULTS

No patient developed cataract during the PUVA treatment. Of the 96 patients, 36 (37.5%) had cataract when commencing the PUVA treatment. The remaining 60 patients (62.5%) were free from any sign of cataract both before and after the PUVA treatment. 28 (77.8%) of the 36 patients had "unchanged cataract". In the remaining 8 patients slit lamp examination gave the impression of cataract growth. The distribution regarding age, length of observation time and the visual acuity results in these 8 patients are shown in Table II.

DISCUSSION

In 1974 Parrish et al. (9) introduced the treatment of psoriasis with psoralen given orally and followed by UVA irradiation (PUVA treatment). Since then this treatment form has increasingly been used for the treatment of various diseases of the skin. However, the observations of Cloud et al. (2, 3) have given cause to reconsider whether PUVA treatment might cause cataract formation.

El-Mofty & El-Mofty (5) described 11 patients treated with photochemotherapy. They were aged 20–40 years. The duration of therapy was 5–23

Table I. *Cataract formation in 96 patients treated with PUVA*

	<40 years	41–50 years	51–60 years	61–70 years	>70 years	Total
No cataract	29 (85.4%)	14 (73.8%)	9 (49.6%)	8 (50.0%)	0	60 (62.5%)
Unchanged cataract	4 (11.7%)	4 (21.0%)	6 (33.6%)	6 (37.5%)	8 (89.0%)	28 (29.2%)
Changed cataract?	1 (2.9%)	1 (5.2%)	3 (16.8%)	2 (12.5%)	1 (11.0%)	8 (8.3%)
Total	34	19	18	16	9	96
Frequency of cataract	14.7%	26.3%	50.0%	50.0%	100%	
Frequency of cataracta senilis (average of 3 investigations		33.9%	63.3%	78.8%	92.0%	

years, and the dose of 8-MOP, 40–120 mg/day. No signs of cataract formation were found in the patients.

Bäck et al. (1) described 13 patients with vitiligo, treated with 8-MOP + exposure to natural sunlight. Duration of therapy was 2–12 years. The total dose of 8-MOP was 4–41 g. The patients were not requested to protect their eyes. Even here, no increased frequency of cataract formation was found in the patients, as compared with the frequency of cataract in a "standard population".

In the present study, no patient developed cataract during PUVA treatment. The occurrence of cataract in this study, compared with the prevalence of cataract formation in a "standard population" (4), was found to correspond to the occurrence expected. The 8 patients (Table II) had no visual complaints and had, from the 1st to the later ophthalmologic examination, an unchanged visual acuity.

"Change in cataract" was demonstrated during the slit lamp examination, but could not be found by comparison photography of the lenses. The changes in cataract were localized totally peripherally and could only bee seen when using mydriasis. These areas had during the PUVA treatment been covered by the iris and had consequently not been exposed to UVA irradiation. Hence the changes can hardly be attributed to the PUVA treatment.

Even though the risk for cataract formation seems extremely remote, an ophthalmologic examination should be performed before commencing treatment with PUVA and, furthermore, should also be performed during the treatment, if complaints of changes in visual acuity arise. Lerman et al. (6, 7) have shown that the normal oclular lens acts as a very efficient UV-filter, so aphakic patients need particular caution when considering PUVA treatment.

Lerman et al. (6, 7) recommend that PUVA-

Table II. *Age, observation time, duration of treatment and visual acuity at the 1st and last ophthalmologic examination in the 8 patients with possible change in cataract*

RE = right eye, LE = left eye

Patient no.	Age (yrs)	Observation time (months)	Duration of treatment (months)	Visual acuity at first examination		Visual acuity at second examination	
				RE	LE	RE	LE
1	39	28	28	6/6	6/6	6/6	6/6
2	45	28	60	6/6	6/6	6/6	6/6
3	56	29	8	6/6	6/6	6/6	6/6
4	57	27	47	6/6	6/6	6/6	6/6
5	57	28	31	6/6	6/6	6/6	6/6
6	64	30	10	6/9	6/24	6/9	6/24
7	69	9	10	6/6	6/6	6/6	6/6
8	71	21	21	6/6	6/6	6/6	6/6
Average	57.3	25	26.9				

treated patients should wear dark glasses for protection for 12–24 hours after treatment, since they have demonstrated free 8-MOP in the human lens for at least 12 hours after oral ingestion. These findings are contrary to the findings of Marqversen et al. (8), who could not demonstrate any accumulation of 8-MOP in human lenses up to 72 hours after oral ingestion. There seems to be some confusion about how rigorous a recommended sunglass regimen should be after ingestion of 8-MOP.

REFERENCES

1. Bäck, O., Hollström, E., Lidén, S. & Thorburn, W.: Absence of cataract ten years after treatment with 8-methoxypsoralen. Acta Dermatovener (Stockholm) *60:* 79, 1980.
2. Cloud, T. M., Hakim, R. & Griffin, C.: Photosensitization of the eye with methoxypsoralen. Arch Ophthalmol *64:* 62, 1960.
3. — Photosensitization of the eye with methoxypsoralen. Arch Ophthalmol *66:* 105, 1961.
4. Duke-Elder, S.: System of Ophthalmology XI. Henry Kimpton. London, 1969.
5. El-Mofty, A. M. & El-Mofty, A.: Retrospective ocular study of patients recieving oral 8-methoxypsoralen and solar irradiation for the treatment of vitiligo. Ann Ophthalmol *6:* 946, 1979.
6. Lerman, S.: Potential ocular complications of psoralen-UV-A therapy. Dermatosen *28:* 5, 1980.
7. Lerman, S., Megaw, J. & Willis, I.: Potential ocular complications from PUVA therapy and their prevention. J Invest Dermatol *74:* 197, 1980.
8. Marqversen, J., Axelsen, I., Nielsen, E. & Zachariae, H.: 8-Methoxypsoralen and the eye (in press).
9. Parrish, J. A., Fitzpatrick, T. B., Tanenbaum, L. & Pathak, M. A.: Photochemotherapy of psoriasis with oral methoxalen and longwave ultraviolet light. N Engl J Med *291:* 1207, 1974.

Methotrexate in Psoriasis with and without Leucovorin: Effect of Different Dosage Schedules on Acute Liver Toxicity

Hugh Zachariae and Peter Bjerring

Department of Dermatology, Marselisborg Hospital, University of Aarhus, Denmark

Received February 1, 1982

Abstract. Studies on thirty-six psoriatics revealed no differences in acute liver toxicity of four different intermittent dosage schedules of methotrexate with or without addition of leucovorin, as judged by daily determinations of SGOT for one week. Three patients with psoriatic erythroderma receiving high-dosage methotrexate (100 mg i.v.) with leucovorin rescue responded extremely well to treatment and did not distinguish themselves from the other patients with regard to acute liver toxicity.

Key words: Methotrexate; Leucovorin rescue; Psoriasis; Liver toxicity

Methotrexate is one of the most useful drugs for controlling severe psoriasis, but the fact that the drug may inflict liver damage that will lead to fibrosis and cirrhosis in some patients has caused great concern (1, 5, 8). Data from an international cooperative study indicated clearly that daily oral therapy was associated with the greatest degree of hepatotoxicity (7), but which of various other dosage schedules is the less damaging to the liver is still under debate. We have tried to evaluate acute liver toxicity in various dosage schedules with and without leucovorin by determining GO-transaminases (SGOT) daily for 8 days following methotrexate administration.

Leucovorin, known also as citrovorum factor or folinic acid, is a useful antidote to methotrexate, but is also in current use as an active principal to improve the therapeutic index of methotrexate. It is this quality which allows the physician to increase methotrexate dosage without any significant increase in toxicity, which is named leucovorin rescue. Leucovorin, although commonly used in methotrexate cancer therapy (6), has received little attention in psoriasis (2, 3, 4).

MATERIAL AND METHODS

Thirty-six psoriatics with a disease severity that indicated use of methotrexate were treated with one of the following dosage schedules: I) a divided oral dose of 5 mg methotrexate three times at 12-hour intervals; II) a single oral dose of 25 mg methotrexate; III) a single intramuscular dose of 25 mg methotrexate; and IV) a divided oral dose of 5 mg methotrexate three times with 12-hour intervals followed by leucovorin 9 mg i.m. 36 hours later. 3 patients with psoriatic erythroderma received 100 mg methotrexate i.v. followed by leucovorin 9 mg i.m. 36 hours later. All patients had normal leukocyte- and thrombocyte counts, normal values of SGOT and alkaline phosphatases as well as a normal serum creatinine clearance prior to treatment. None of the patients were chronic abusers of alcohol. SGOT values were monitored daily for a week; the clinical response was evaluated after one week.