

will be carried out because long-term drug therapy could lead to changes not observed in early biopsies (10).

REFERENCES

1. Dahl, M., Gregory, M. & Scheuer, P.: Liver damage due to methotrexate in patients with psoriasis. *Br Med J*: 625, 1971.
2. Elliot, J.: The treatment of vitiligo with 8-methoxypsoralen. *South MJ* 49: 691-693, 1956.
3. Nyfors, A., Lee, J. & Maibach, H.: Light and electron microscopy of liver biopsies from long-term methotrexate treated psoriatics and controls. *Proc 19th Scand Congr Derm*, Oslo 1971.
4. Parrish, J.: Photochemotherapy of psoriasis. *Arch Dermatol* 112: 35-36, 1976.
5. Swanbeck, G., Thyresson-Hök, M., Bredberg, A. & Lambert, B.: Treatment of psoriasis with oral psoralen and long wave ultraviolet light. *Acta Dermatovener (Stockholm)* 55: 367-376, 1975.
6. Tucker, H.: Clinical and laboratory tolerance studies in volunteers given oral methoxalen. *J Invest Dermatol* 32: 277-280, 1959.
7. Weismann, K., Howitz, J. & Bro-Jørgensen, A.: Treatment of resistant psoriasis with oral 8-methoxypsoralen and long wave ultraviolet light (PUVA). *Acta Dermatovener (Stockholm)* 57: 73-76, 1977.
8. Wolff, K., Hönigsmann, H., Geschnait, F. & Konrad, K.: Photochemotherapie bei Psoriasis. *Deutsche Med Wschr* 100: 2471-2477, 1975.
9. Zachariae, H. & Søgaard, H.: Liver biopsy in psoriasis—a controlled study. *Dermatologica* 146: 149-155, 1973.
10. Zachariae, H., Grunnet, E. & Søgaard, H.: Liver biopsy in methotrexate treated psoriatics—a reevaluation. *Acta Dermatovener (Stockholm)* 55: 291-296, 1976.

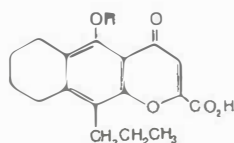
Clinical Trial of a New Chromone Compound for Systemic Treatment of Atopic Dermatitis

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Abstract. In a double-blind group comparative study, 14 adults with atopic dermatitis were treated systemically for 6 weeks with a new anti-allergic chromone compound (FPL 57787) 6 mg four times a day. A similar group of 13 adults was given placebo. Both groups improved during



FPL 57787

Fig. 1. Structural formula of FPL 57787.

the trial in all the clinical assessments without significant differences, but there was a tendency to a decreased use of local treatment (hydrocortisone butyrate) in the active group during the trial. There were no drug-related complaints, but one patient in the active group had transiently elevated liver enzyme levels. Further investigations are warranted.

Key words: Atopic dermatitis; Chromone-carboxylic acid; Systemic treatment; Double-blind trial

In a recently published study (2) 10% sodium chromoglycate in white soft paraffin was shown to be effective as a local treatment for atopic dermatitis in children. We have tried a new member of the chromone group for systemic treatment of atopic dermatitis in adults.

MATERIAL AND METHODS

The new drug is a chromone-2-carboxylic acid (FPL 57787) with the empirical formula $C_{17}H_{18}O_5$ (Fig. 1). The drug possesses anti-allergic activity following intravenous and intestinal administration using passive cutaneous anaphylaxis in the rat. In vitro, FPL 57787 inhibits antihuman IgE-induced histamine release from human basophil leukocytes (IC_{50} of 6×10^{-5} M). Sodium chromoglycate is inactive in this in vitro system and always when given by the intestinal route (1).

The material consisted of 27 patients suffering from atopic dermatitis. All were above 18 years of age and selected in accordance with the criteria laid down by Hanifin & Lobitz (3). The study was performed double-blind and the two groups were comparable as to age, sex, severity and duration of their disease. Only women using effective contraceptives were accepted as participants. On admission each patient was allocated at random to one of two treatment groups. One group (14 patients) received tablets of 6 mg FPL 57787 four times a day for 6 weeks and the other group (13 patients) was given placebo. All patients received placebo for 2 weeks before and 2 weeks after this period. Previous treatment was stopped. The patients were seen once a week and each time were given 50 g of hydrocortisone butyrate 0.1% in cream (Locoid®, Gist-Brocades) and asked to use topical treatment only to relieve discomfort. Three regions were selected for evaluation of scaling, colour, lichenification, general assessment of the dermatitis and severity of itch.

The following laboratory investigations were performed

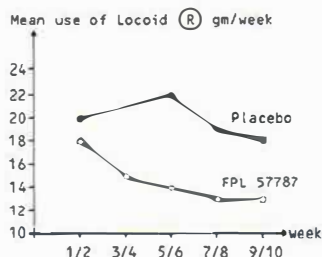


Fig. 2. Mean use of hydrocortisone butyrate topical in each 2-week period.

regularly during the trial: ESR, full blood count, haematocrit, MCV, MCH, MCHC, differential white cell count, platelets, sodium, potassium, calcium, albumin, urea, creatinine, acid phosphatase, basic phosphatase, SGOT, SGPT, LDH, phosphate, urate, total lipid, bilirubin, cholesterol, iron and prothrombin time. Urine was analysed for blood and protein.

Statistical testing was conducted at the two-tail 5% level using a Mann-Whitney U-Test on differences of clinicians' scores.

RESULTS

Both groups showed nearly identical recovery during the trial and there were no statistically significant differences in the clinicians' scores for any parameter. Only in estimating the amount of hydrocortisone butyrate used, was it possible to show that the patients of the placebo group did use more cream than those in the active group (Fig. 2). However, the difference failed to reach statistical significance.

No patients had any drug-related complaints. In one patient of the active group and in 2 patients of the placebo group there were slightly, but transiently, elevated liver enzyme levels. The other laboratory tests were within normal range.

DISCUSSION

In this investigation we were not able to prove the new chromone drug to be effective in systemic treatment of atopic dermatitis. Being the first group to use this drug in a large-scale investigation, we applied the minimum dose expected to show an effect. To avoid patients in the placebo group withdrawing from the trial because of exacerbation, all the patients were allowed to use hydrocortisone butyrate topically, which might have obscured an effect of the drug. The investigation took place in

the spring and summer months when most patients with atopic dermatitis are getting better, an effect which again would tend to obscure the expression of the drug to be investigated. One patient had transient slightly elevated liver enzymes which might have been produced by the drug. There were no drug-related complaints.

New investigations with this anti-allergic drug in the treatment of atopic dermatitis are warranted.

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REFERENCES

1. Augstein, J., Cairns, H., Hunter, D., Lee, T. B., Suschitzky, J., Altounyan, R. E. C., Jackson, D. M., Mann, J., Orr, T. S. C. & Sheard, P.: New orally effective chromone derivatives for the treatment of asthma. *Agents Actions* 7: 433, 1977.
2. Haider, S. A.: Treatment of atopic eczema in children: Clinical trial of 10% sodium chromoglycate ointment. *Br Med J* i: 1570, 1977.
3. Hanifin, J. M. & Lobitz, W. C.: Newer concepts of atopic dermatitis. *Arch Dermatol* 113: 663, 1977.

Peroral Aromatic Retinoid Treatment of Palmoplantar Pustulosis: Double-Blind Comparison of Ro 10-9359 and Placebo.

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Abstract. Nineteen patients with chronic, recalcitrant palmoplantar pustulosis took either placebo or aromatic retinoid ethyl ester (Ro 10-9359) during a 4-month therapeutic trial. The maximal dose of Ro 10-9359 varied between 25 and 100 mg per day, according to the individual patient's tolerance. An excellent or good therapeutic response was obtained in 6 out of 9 patients on the active medication and in 2 out of 10 patients on placebo. The difference in therapeutic response between the Ro 10-9359 group and the placebo group was statistically significant ($p < 0.05$). Drying and chapping of the lips