Treatment of Psoriatic Arthropathy with Etretinate: A Two-year Follow-up

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In psoriatic arthropathy the data obtained after two years of etretinate treatment in 20 adult male patients, are reported. The beneficial effects of the drug on the objective symptoms are accompanied by an improvement in the biohumoral parameters evaluated. The dose was 1 mg/kg/day for one month, with subsequent adjustments in relation to the results obtained with a maintenance dose of 25 mg/day, or where possible, 10 mg/day, or on alternate days, for a maximum period of 25 months. The side effects appeared to be of an acceptable degree of severity. The authors consider etretinate one of the drugs of first choice in the treatment of psoriatic arthropathy. *Key words: Neutrophil chemotaxis: Side-effects.* (Received June 8, 1985.)

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Psoriatic arthropathy has been defined as a seronegative inflammatory arthritis associated with psoriasis (1), which may precede, accompany or, more often, follow the skin manifestations. The aetiology and pathogenesis both of cutaneous and joint lesions have still largely to be clarified, and this aetiopathogenic uncertainty is the reason of the failure of many forms of therapy and of their frequent inadequacy. Similarly, the mechanisms of action of a number of drugs of varying degrees of efficacy are known only approximately. Numerous substances have been used and are still used in the treatment of psoriatic arthropathy. Among these we mention: anti-inflammatory nonsteroid drugs (1, 2, 3, 4), gold salts (5), antimalarial agents (6), corticosteroids (7), antimitotic agents (8), penicillamine (9), dialysis (10) and zinc sulphate (11). Some of these therapies have led to a real improvement in the clinical picture and prognosis. However, the price paid for this has sometimes been the occurrence of fairly severe side effects and/or exacerbation of the skin manifestations.

MATERIAL AND METHODS

Numerous reports have appeared in the literature over the past few years regarding the beneficial effects obtained in the treatment of psoriatic arthropathy with a new class of drugs, the retinoids (12, 13, 14, 15, 16, 17). The most commonly used drug of this group is an aromatic ester of the retinoid acid known as etretinate. We used etretinate in the treatment of patients suffering from active seronegative psoriatic arthropathy. In most of the 20 subjects included in this trial the artropathy affected one or very few joints, mainly of distal interphalangeal localization. Nine cases also showed psoriatic onychopathy and 3 of them had palmo-plantar pustular psoriasis too. The patients, all adult males, ranging in age from 24 to 56 years, were selected on the basis of two criteria: substantial impaired function of the affected joints and poor or no response to previous therapy.

The drug (Fig. 1) was administered at a dose of 1 mg/kg/day (maximum dose 75 mg/day) during the first month, with subsequent adjustments in relation to the results obtained with a maintenance dose of 25 mg/day or where possible, 10 mg/day or on alternate days for a maximum period of 25 months. Seventeen months after the beginning of the trial, in early summer, the treatment was discontinued in 7 patients taking the minimum maintenance dose, in order to evaluate the stability of the improve-

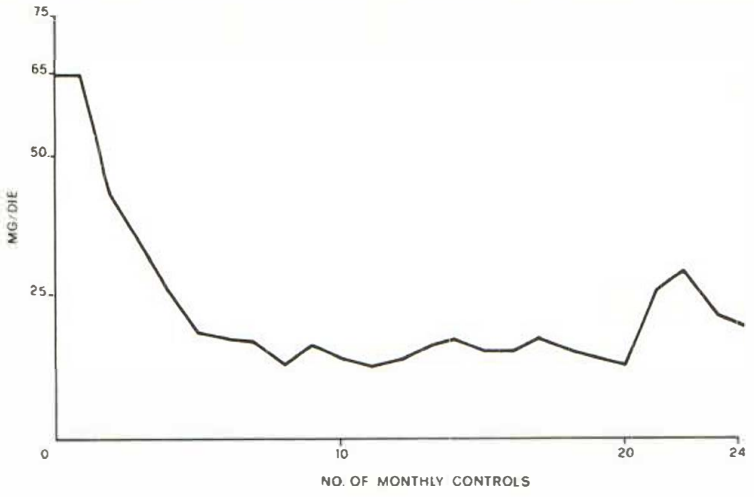


Fig. 1. Mean posology value.

ments obtained; relapse of symptoms occurred in all cases after 3 to 5 months and it was therefore necessary to resume treatment, though at doses lower than those given initially.

Laboratory tests (complete blood count, cholesterol, triglycerides, transaminases, rheumatic tests, ESR, serum uric acid, serum glucose, BUN, electrophoresis, immuno-electrophoresis, neutrophil chemotaxis, serum complement) were carried out before the start of therapy and thereafter at monthly intervals. X-rays of the joints were taken at the start of therapy and approximately every six months.

RESULTS

Positive therapeutic effects were observed in all patients after as little as 4 to 6 weeks. Reduced oedema was observed together with a gradual reduction of the severity of the arthropathy to the minimum values of the Ritchie Index (Fig. 2). There were also an almost complete disappearance of spontaneous pain (with a drastic reduction, or withdrawal of anodyne drugs) and a remarkable improvement of the function of the affected joints.

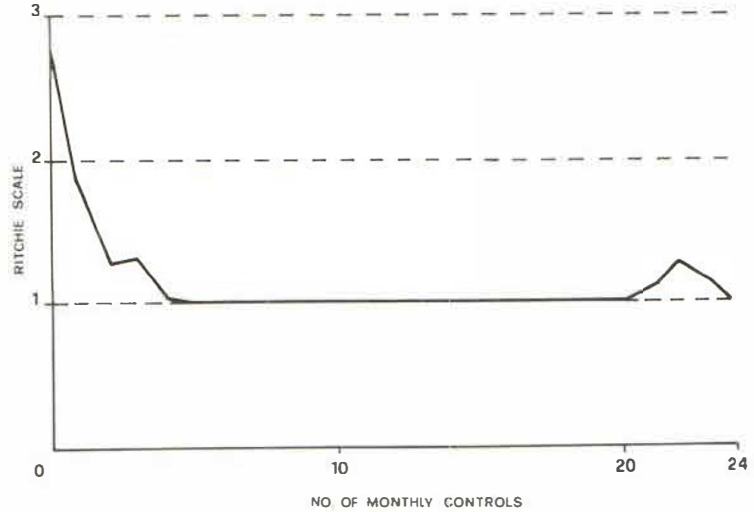
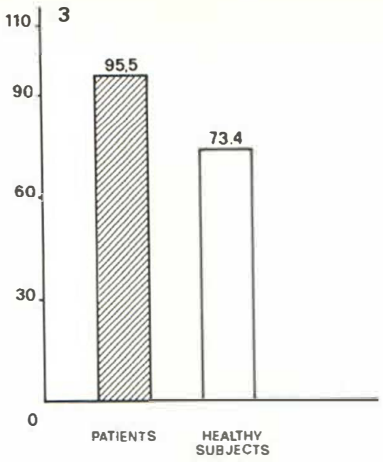


Fig. 2. Ritchie Joint index.



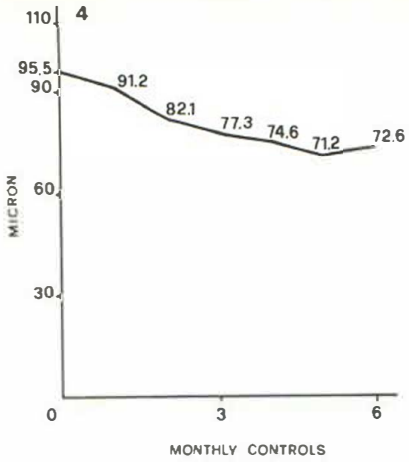


Fig. 3. Mean chemotaxis value before therapy.

Fig. 4. Mean chemotaxis value after six months of therapy.

The side effects observed in the trial group as a whole, many patients complained of more than one, were dose-related; the following were observed in order of frequency: cheilitis, dryness of the mucosae, slight hair loss, itching, fragility of the skin, nose-bleeding and conjunctivitis. None of the patients complained of the so-called "retinoid dermatitis" described by various authors (18).

As regards the blood tests performed, dose-related transient increases were noted in cholesterol (4 cases) and triglycerides (9 cases). Slightly increased activity of transaminases occurred in 3 cases, though these could not be related with certainty to the use of the drug. They disappeared despite continuation of the treatment. The inflammatory indexes showed initially increased values in 17 cases: ESR 15 cases, C Protein 7 cases (together 5 cases). The values normalized over varying periods of time: ESR two to six months, C Protein two to five months after the beginning of treatment. Neutrophil chemotaxis was assessed in all patients and 20 healthy subjects, before the start of therapy (Fig. 3) and thereafter at monthly intervals, using the Boyden modified chamber, according to the method proposed by Wilkinson (19). The chemotaxis values, constantly high initially in all patients, returned to normal level two to four months after the beginning of therapy (Fig. 4). As regards the serum complement, there was initially a slight increase of C_3 and C_4, in four patients, and in three a decrease of C_3. These values showed no significant changes during treatment. Periodic X-ray examination of the joints revealed no particular modifications.

DISCUSSION

The entire evaluation of the clinical and humoral trend in the patients treated over the two-year period confirms the usefulness of the above mentioned treatment, as already suggested by the preliminary data presented in Trieste (20).

The drug, with low toxicity, is capable of producing and maintaining beneficial long-term clinical and biohumoral effects at very low and well-tolerated maintenance doses on both the psoriatic arthropathy and the skin lesions. This justifies, in our opinion, the use of etretinate in psoriatic arthropathy with all due precautions.

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