

AGGRAVATION OF PSORIASIS AND OCCURRENCE OF PSORIASIFORM CUTANEOUS ERUPTIONS INDUCED BY PRACTOLOL (ERALDIN®)

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Abstract. Twelve patients with cutaneous and/or eye symptoms caused by practolol have been studied. The morphological appearance of the skin eruptions was psoriasiform in 5, vesiculo-papular in one, and exfoliating dermatitis was seen in 2 patients. Keratoconjunctivitis sicca was the only adverse reaction to practolol in one and was present in 3 additional patients. Practolol was found to aggravate existing psoriasis in 3 patients and render it extremely refractory to therapy.

Key words: Psoriasiform eruption; Cyclic AMP; Practolol; Eraldin®; Side-effects

Beta-blocking agents are widely used for the treatment of cardiovascular diseases. They act on adrenergic isoproterenol-sensitive beta-receptors. Within the last year preliminary reports have appeared on cutaneous eruptions caused by practolol (Eraldin®-ICI) with a striking clinical similarity to those seen in psoriasis (3, 7, 8, 9, 11). Ocular damage and conjunctivitis was observed in several of these patients with or without concomitant skin manifestations (3, 5, 7, 9).

In this communication we present 12 patients with cutaneous and/or eye symptoms caused by practolol, and, furthermore, we report that practolol may aggravate psoriasis and make it very refractory to therapy.

MATERIAL AND METHODS

Twelve patients were studied, 8 women and 4 men. Their mean age was 61 years (43–72 years) (Table I). Ten patients were treated with practolol for angina pectoris and 2 for hypertension. The average daily dose was 300 mg in 8 patients and 200 mg in 4. Three of the 12 patients had

suffered from psoriasis for many years (20–41 years). The remaining 9 patients did not suffer from psoriasis and had no family history of the disease.

RESULTS

Clinical manifestations

One of the 12 patients (No. 11) developed eye symptoms but no cutaneous manifestations following practolol treatment, whereas the remaining 11 developed skin manifestations and 6 of these, furthermore, eye symptoms (Table I). No other side effects, including sclerosing peritonitis, otitis, etc., were recorded. The cutaneous symptoms appeared in 2 patients within one month after treatment with practolol and in 10, the symptoms appeared after 10–26 months of treatment (average 18 months). Three patients (Nos. 2, 3, 4) suffering from psoriasis, developed a resistance to the therapy for their condition. Five patients (Nos. 1, 5, 7, 9, 10) developed a psoriasiform, slightly itchy cutaneous eruption. This eruption was characterized by dry, erythematous, scaly, nummular elements or plaques on the extensor surfaces of the extremities and trunk (Fig. 1). Hyperkeratotic changes were present on the palms and soles in these 5 patients (Fig. 2). Two patients (Nos. 8, 12) developed exfoliating dermatitis and in one (No. 6) a generalized vesiculo-papular eruption was present. Nail changes, presenting as pitting and onycholysis were present in 3 patients besides the 3 patients with psoriasis. When treatment with practolol was stopped, the cutaneous manifestations waned within a few days and had completely disappeared after 3 weeks. Two of the 3 patients with

Table I. Clinical data

Patients	Sex	Age	Psoriasis previously (y.)	Practolol dosage (mg)	Duration of treatment at appearance of exanthema (mo.)	Time lapse from appearance of exanthema to cessation of treatment (mo.)	Nail changes	Subjective eye symptoms	Objective eye changes
1	♀	65	No	300	16	12	Yes	No	No
2	♂	55	41	300	26	9	Yes	Yes	Yes
3	♂	45	25	300	1	4	Yes	No	^a
4	♂	68	20	300	24	24	Yes	Yes	No
5	♀	61	No	300	24	5	No	No	No
6	♀	43	No	200	16	$\frac{1}{2}$	No	Yes	No
7	♀	72	No	300	14	5	No	Yes	^a
8	♀	70	No	200	18	3	Yes	No	^a
9	♀	72	No	300	12	6	No	No	No
10	♀	70	No	300	18	10	Yes	Yes	Yes
11	♂	55	No	200	(10)	(1)	No	Yes	Yes
12	♀	60	No	200	1	$\frac{1}{2}$	No	Yes	Yes

^a Not examined by ophthalmologist.

psoriasis (Nos. 2, 3) recovered shortly after treatment with practolol was stopped, and the condition improved considerably in the third (No. 4).

Seven patients complained of dryness and pain in the eyes, and kerato-conjunctivitis sicca was present in 4 of these (Nos. 2, 10, 11, 12), using Schirmer's test for evaluation. No corneal lesions were present.

Oral provocation tests

Five patients (Nos. 1, 2, 3, 4, 6) volunteered to have an oral provocation test performed. The patients with exfoliating dermatitis (Nos. 8, 12) were not tested and neither were the patients with eye symptoms tested after having realized that these symptoms might not be reversible (3, 13). All 5 patients orally tested redeveloped cutaneous symptoms within $\frac{1}{2}$ –3 days. Three were patients with psoriasis and they complained of burning and itching sensations in existing psoriasis plaques and in 2 of them new guttate elements of typical psoriasis developed within about one week.

Cutaneous tests

Intracutaneous tests were performed in 10 patients with cutaneous symptoms using practolol 0.1 ml, 0.5–5% w/w in saline. Four patients developed a positive reaction. Patient No. 3 with psoriasis complained of pain and tenderness and increased redness, and swelling of his psoriatic elements was observed 24 hours later. Patient No. 4 with psoriasis and patient No. 5 developed several papular

psoriasiform elements on the arms within an area of 10 cm from the site of injection within 2–3 days. Patient No. 9 developed redness, edema and itch in areas of the skin previously affected during treatment with practolol and this reaction occurred within 24 hours.

Epicutaneous tests were performed in the same 10 patients using 5–50% w/w of practolol in vaseline. These tests were negative in each case.

For control purposes, similarly performed epicutaneous and intracutaneous tests were carried out in 6 patients without psoriasis, not previously treated with beta-blocking agents. These tests all proved negative.

Histology

Biopsies obtained from new elements of 2 patients with psoriasis (Nos. 2, 4) were typical of psoriasis. The histological picture from the psoriasiform cutaneous lesions in patients 1, 5, 7, 9 was fairly uniform, with slight epidermal hyperplasia, acanthosis, hyperkeratosis, patchy parakeratosis and edema of the epidermis. Several polymorphonuclear leukocytes were present in the epidermis, occasionally forming Munroe-like microabscesses (Fig. 3). In the upper part of the dermis, a moderate infiltrate of mononuclear cells was present, mainly located perivascularly. The dermal papillae were slightly elongated, with dilated capillaries. Thus, the histological picture had features resembling to some degree those seen in early psoriatic lesions.



Fig. 1. Psoriasiform skin lesions.

DISCUSSION

Psoriasiform cutaneous eruption is now becoming a well recognized side effect in patients treated with practolol and the results of the present study confirm these previous observations. The prompt disappearance of the cutaneous eruption after treatment with practolol was stopped, and its reappearance within 3 days in patients re-exposed to the drug, makes the differential diagnosis from psoriasis possible. The clinical appearance—a psoriasis-like picture—in our patients was similar to previous observations (3). However, a careful clinical examination usually enables a distinction to be made between psoriasis and practolol-induced eruptions. Itch was a pronounced symptom in our patients, and the 3 patients with psoriasis also complained of itching during the periods of treatment with practolol. Even the histological picture that we obtained in non-psoriatic patients revealed features to some degree resembling those seen in psoriasis. However, the histological changes may also resemble lichen planus as in the two biopsies described by Felix et al. (3).

It has previously been suggested that practolol

causes a rash in patients with psoriasis similar to that seen in non-psoriatics (11). However, in our 3 patients with psoriasis, the condition during treatment and re-exposure to practolol was quite different from the usual cutaneous eruption seen in the non-psoriatics. Their psoriasis was aggravated, with the appearance of new typical psoriatic lesions and, furthermore, their psoriasis became extremely refractory to conventional anti-psoriatic therapy until treatment with practolol was stopped. Patients Nos. 2 and 4 were even ineffectually treated with an increased dose of methotrexate in an attempt to control their disease. Thus, these observations indicate that psoriasis may be aggravated by treatment with this beta-blocking agent.

Various pathogenetic mechanisms have been suggested to explain the cutaneous eruption, including immunological mechanisms (3) and beta-blockade per se (8). The results of our various cutaneous tests failed to support the view that a type I or type IV reaction could be held responsible for the development of the cutaneous eruption. Similar negative results were obtained by Felix et al. (3). The appearance of new elements and re-occurrence of psoriasis

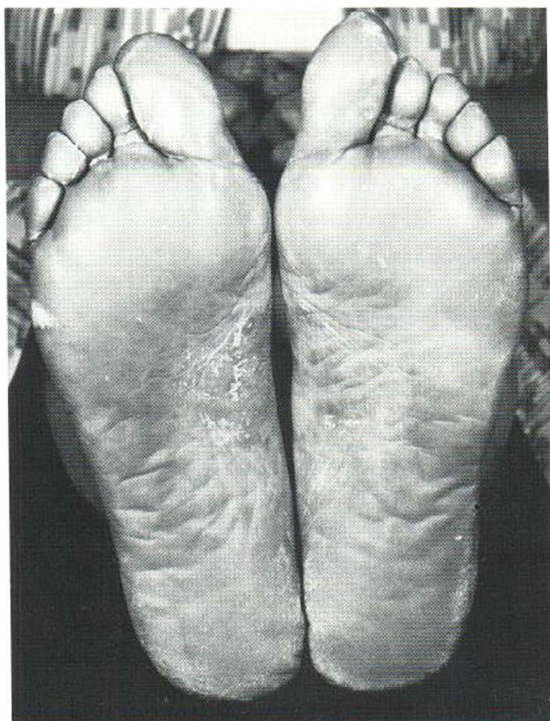


Fig. 2. Hyperkeratotic psoriasiform changes on sole.

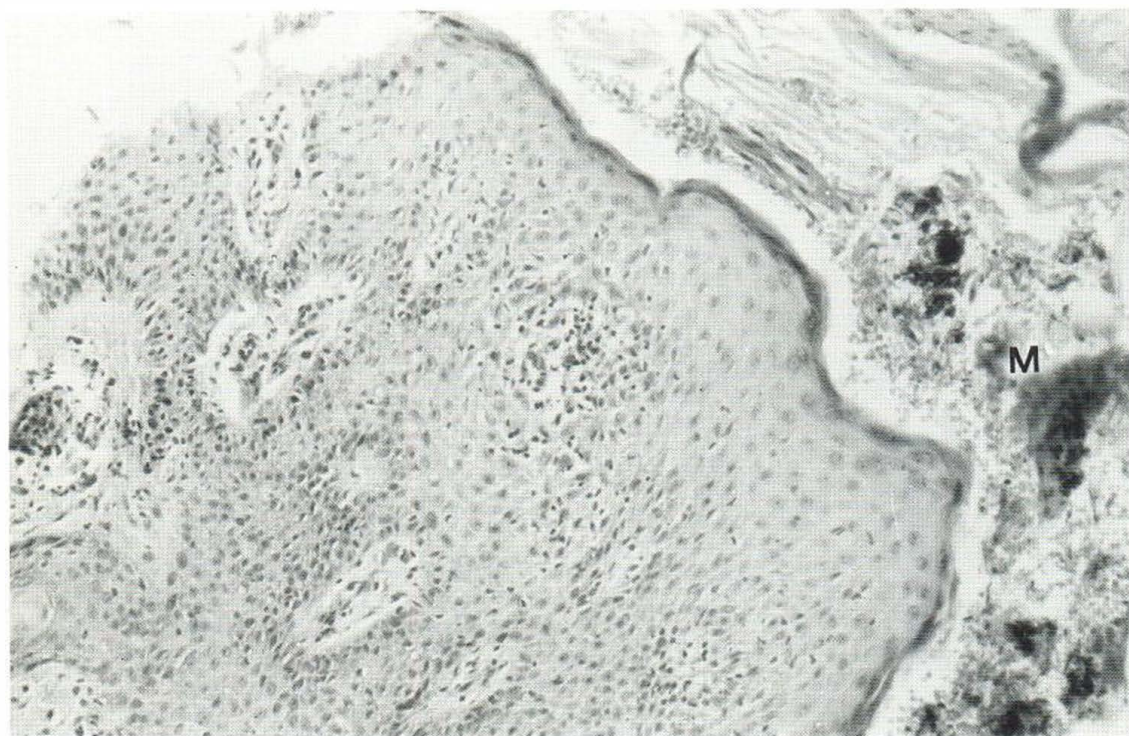


Fig. 3. Light microscopic micrograph from patient 1, showing epidermal hyperplasia, acanthosis, hyperkeratosis, patchy parakeratosis and edema of the

epidermis. Several polymorphonuclear leukocytes are present, forming "Munroe-like" microabscess (M).

in previously affected areas of the skin in the vicinity of the intracutaneous injections is of interest, but seems unrelated to a type I reaction, since the reaction occurred after a latent period of more than 12 hours and not exactly at the sites of practolol-injection. As a working hypothesis we have previously suggested that blockade of the epidermal beta-receptors might lead to a reduced intracellular concentration of cyclic AMP (8). In psoriasis, cyclic AMP is low (12). Work is in progress to elucidate this possibility.

Practolol has now been withdrawn from the market in most countries, except for acute treatment of certain well-defined conditions and substitution by other beta-blocking agents has been recommended. However, since other beta-blocking agents, including propranolol (1, 2, 4, 6, 10) may cause similar side-effects as those described after practolol, the clinician should be alert and the dermatologist should even reconsider this possibility in patients with recalcitrant psoriasis treated with beta-blocking agents.

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