
Benoxaprofen in Treatment of Systemic Sclerosis

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Ten patients with systemic sclerosis were treated with benoxaprofen, a potent lipoxygenase inhibitor, for a period of 6 months. In an attempt to evaluate the efficacy a number of physical disease parameters were followed during the trial. None of these parameters revealed any significant differences. There was, however, a trend for a change towards normalisation of a defect monocyte chemotaxis. In view of the slow and progressive nature of systemic sclerosis the present study leaves undetermined whether benoxaprofen exerts a beneficial effect on systemic sclerosis.

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Systemic sclerosis is a chronic connective tissue disease, often associated with Raynaud’s phenomenon. An early inflammatory stage, predominantly with mononuclear cells, is recognized (1).

Benoxaprofen is a non-steroidal anti-inflammatory agent (NSAID) with an action that differs from other NSAID’s. It inhibits the arachidonate lipoxygenase system (2), a system that leads to formation of leukotrienes (3). On the other hand benoxaprofen has a far less pronounced inhibitory effect on the cyclo-oxygenase pathway (4), which produces prostaglandins and prostacyclin. Benoxaprofen has also been shown to reduce mononuclear cell migration into sites of inflammation (5). In rheumatoid arthritis, another connective tissue disease, benoxaprofen therapy has led to significant improvement (6). Furthermore treatment of Raynaud’s phenomenon by intravenous infusion of prostacyclin (PGI2) has been reported to be useful (7). Therefore theoretically benoxaprofen could be effective in systemic sclerosis by diminishing the inflammatory response without interfering with Raynaud’s phenomenon. Our trial was performed before benoxaprofen finally was taken off the market, due to unacceptable side-effects (8, 9).

MATERIAL AND METHODS

Three males and 7 females, with mild to severe scleroderma, aged 22–65, were treated with 600 mg of oral benoxaprofen (a gift from Eli Lilly & Co) daily for a period of 6 months. The average duration of their disease was 6 years. One month before admission to the study the patients were instructed to
discontinue their present medication (penicillamine or prednisone). In an attempt to evaluate the
efficacy and safety of benoxaprofen the following parameters were investigated before and after
benoxaprofen therapy: rheumatic parameters (joint motion disorder), pulmonary function tests, skin
thickness and elasticity, central corneal thickness, monocyte chemotaxis, monocyte antibody-de­
pendent cell-mediated cytotoxicity (ADCC), changes in glycosaminoglycans and oesophageal condi­
tion by X-ray and manometry. Laboratory data, possible adverse effects and the patients own
subjective assessment were recorded.

RESULTS
To determine whether statistically significant changes occurred during benoxaprofen
therapy, the Wilcoxon test for pair differences was used. No statistically significant
differences were recorded. Nine patient felt no overall difference during benoxaprofen
therapy, while one had the feeling of mild progression. Four declared that benoxaprofen
improved parameters such as pain and stiffness. An equal percentage had abnormal
laboratory values before/after benoxaprofen treatment. Seven patients reported side­
effects from benoxaprofen (dry mouth 1, altered taste 1, dyspepsia 2, diarrhea 2, flushing
2, rash 2, itching 1, paresthesia 1, frail nails 1, SGOT elevated 1).

DISCUSSION
All 10 patients with systemic sclerosis had previously received penicillamine therapy. The
outcome of this treatment was not considered satisfactory by the patients in our selected
material.

None of the disease parameters revealed any statistically significant changes after 6
months of benoxaprofen therapy. However, when compared to healthy controls, patients
with systemic scleroderma had significant depressed monocyte chemotaxis and ADCC,
before benoxaprofen treatment was started. Since chemotactic activity of leukocytes in
scleroderma, to our knowledge, has not been investigated previously, it may be of interest
to mention that 3 patients with the most severe scleroderma had pronounced depressed
chemotactic responses. Depressed leukocyte chemotaxis has been found in other connec­
tive tissue diseases (10, 11). After benoxaprofen treatment there was no longer any
significant difference, when monocyte chemotaxis in patients with sclerosis were
compared to controls.

The present investigation leaves undetermined whether benoxaprofen exerts any benefi­
cial effect in systemic sclerosis. Due to the withdrawal of benoxaprofen from the market it
was not possible for us to continue the study.

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A Trial of 1% Minoxidil Used Topically for Severe Alopecia areata

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Fifty patients with extensive alopecia areata took part in a prolonged double blind trial to compare the effect of 1% minoxidil in unguentum merck with that of unguentum merck alone. There was no significant difference between the hair growth of patients treated with the placebo or with the active compound. (Received August 30, 1985.)

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The encouraging results obtained in early studies of the value of topical minoxidil in alopecia areata (1, 2) led to further trials, the results of which have been conflicting (3, 4). To clarify this issue we undertook a double blind, randomised study of the effect of a 1% minoxidil ointment in 50 patients with severe alopecia areata.

PATIENTS

Fifty patients (males-22; females-28) with longstanding (average duration-16 years; average age at onset-20 years) and severe alopecia areata agreed to take part in the trial. Their degree of alopecia was classified as follows: extensive alopecia areata affecting more than two thirds of the scalp (11 patients); ophiasiform (6 patients); totalis (10 patients); and universalis (23 patients).

METHODS

At their first visit patients were randomly allocated to treatment with 1% minoxidil in unguentum merck or with unguentum merck alone. They were asked to rub a measured lg of the ointment into the hairless areas at night and to wash it off the next morning. Patients were reviewed after eight weeks; if new hair had grown the same preparation was used for a further eight weeks. If not they were changed to the alternative preparation, still under double blind conditions. After 16 weeks without promising hair growth, the code was broken and 1% minoxidil was prescribed for the rest of the study. One patient defaulted from the trial, and one became pregnant and was withdrawn. The remaining 48 patients all completed at least 32 weeks of treatment, 46 continuing for 40 weeks, six for 52 weeks, eight for 60 weeks and three for 78 weeks.