STUDIES

ORAL COLCHICINE IN CHRONIC PLAQUE PSORIASIS

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Colchicine is well known for its antimitotic and antiinflammatory effects. This study was designed to evaluate the role of oral colchicine in chronic plaque psoriasis. Fifty adults with chronic plaque psoriasis were randomly allocated into 2 groups of 25 patients each. Group A received oral colchicine 2 mg/day in 2 divided doses, while Group B patients were given placebo tablets. Patients were evaluated every week and the final result compiled after 8 weeks. 90% patients in Group A had gastrointestinal intolerance necessitating a reduction in dose of colchicine to 1 mg/day. After 8 weeks the lesions improved significantly in Group-A patients, compared to Group B ($t=2.815$, $p<0.01$). Apart from gastrointestinal intolerance and nephrotic syndrome, no other significant side effects were encountered. It may be worthwhile trying this drug in chronic plaque psoriasis recalcitrant to conventional topical treatment.

Key Words : Psoriasis, Colchicine

Introduction

Colchicum was first utilized by Baron von Störck of Vienna in 1763 for the treatment of acute gout.[1] Later the alkaloid colchicine was isolated from the plant autumn crocus (colchicum autumnale) in 1820.[2] Since then, Colchicine has been tried in a variety of dermatologic disorders.[1] Psoriasis was one of the first dermatosis treated with oral colchicine.[3]

There are remarkably few studies advocating the therapeutic efficacy of oral colchicine in chronic plaque psoriasis.[3,4] We report here a prospective single-blind, randomized clinical trial designed to evaluate the efficacy of the drug in the Indian context.

Meterial and Methods

Fifty adults diagnosed clinically as chronic plaque psoriasis were selected and randomly allocated into 2 groups (A and B), of 25 patients each. Baseline investigations included a routine haemogram and urine analysis. Excluded from the study were pregnant females, persons working under direct sunlight and those with a history of remission during autumn/winter- which was the period of trial. None were on any form of oral or topical medication for at least 4 weeks prior to the study.

Group A included 20 males and females in the age group 20-45 years. They received oral colchicine 2 mg/day in 2 divided doses after food. Group B patients included 17 males and 8 females in the age range 25-40 years, who were given multivitamin tablets twice daily as a placebo. Patients in both groups were instructed to liberally apply coconut oil twice daily on the lesions as an emollient. Patients were evaluated every week and the parameters erythema, scaling, induration and pruritus recorded on a 0 to 3 scale.

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The total duration of the study was 8 weeks and the baseline investigations were repeated at the end of each month

Results

In Group A, 1 patient defaulted after the 1st week of therapy and was dropped (Table I). Another patient developed

Table I. Correlation between groups A and B after 8 weeks

	A	B
Number	25	25
Age	20-45	23-40
Sex	M-20, F-5	M-17, F-8
No. withdrawn	1	0
No. defaulted	1	2
Score (E+S+I)		
Σx	799	850
$\bar{x}$	31.96	36.80
S	6.53	5.59
t = 2.815,	P<0.01.	

colchicine induced nephrotic syndrome after 2 weeks of therapy. Colchicine was withdrawn and the patient recovered with systemic steroids. This patient was also not included in the subsequent analysis. Of the remaining 23 patients, 20 (86.9%) developed gastrointestinal (GI) intolerance during the 1st week of therapy in the form of abdominal fullness, flatulence and diarrhoea and the dose of colchicine had to be reduced from the second week onwards to 1 mg/day. This dose was well tolerated and apart from occasional mild crampy abdominal pain and nausea, there were no significant GI upsets.

Clinical improvement of the psoriatic plaques was discernable in Group A only after the second week (Fig. 1). Scaling became appreciably less from the 3rd week and there was considerable reduction of induration at the end of the

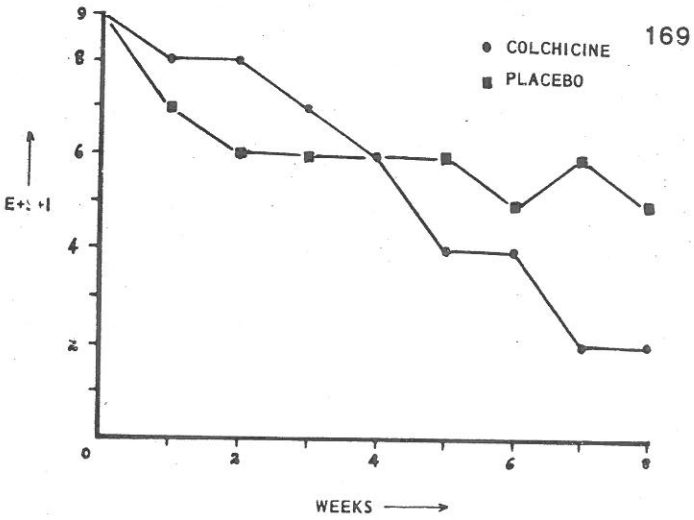

Fig. 1. Comparison of therapeutic response between oral colchicine and placebo in chronic plaque psoriasis

4th week. At 8 weeks, lesions were barely palpable though there was no complete remission in any of the patients. Reduction in erythema score was observed over 8 weeks though mild to moderate erythema of the lesions persisted even at the end of the trial. The grading of pruritus was difficult owing to the purely subjective nature of this parameter. While the majority of patients (69.6%) reported an increase in pruritus during the 1st 4 weeks, subsequentiy it decreased in intensity but nevertheless persisted throughout the trial. However the grading of pruritus was left out of the statistical analysis to avoid subjective bias. There was no difference in the ultimate clinical outcome between those who received colchicine in the dose of 1 mg/day and the 3 patients who were able to continue colchicine at 2 mg/day.

The results in group B was less than satisfactory. Though a reduction in scaling over the first 2 weeks was seen, there was no appreciable change in the erythema, induration or pruritus during the study period.

The erythema, sealing, induration (ESI) scores in group A and B were

compared by student 't' test and a significant improvement in group A was shown, $p<0.01$ (Table 1)

Comments

One of the characteristic histologic features of psoriatic lesions is the infiltration of the epidermis by numerous neutrophils.[5] Furthermore, it has been shown that the migration of neurtophils into the upper dermis is the earliest histological change, preceding the usual signs of epidermal hyperproliferation.[6] Psoriatic scale contains leukotactic substances that appear to be products of compliment activation.[7] Psoriatic plaque epidermis contains a greater amount of proteinase which induces the accumulation of neutrophils by activating compliment in contrast to uninvolved epidermis.[8] Thus the migration of activated neutrophils into the skin could play an important role in the pathogenesis of psoriatic lesions.[9]

Colchicine, a microtubule disruptive agent, is effective in inhibiting the chemotactic migration of neutrophils both in vivo[10] and in vitro.[11] The potent antimitotic activity of the drug is due to failure of spindle formation and arrest of cell division in metaphase.[12] This drug has been extensively used in the prophylactic treatment of gouty arthritis[13] and familial Mediterranean fever.[14] At the low dosage in which it is used in the above mentioned condition, colchicine therapy is considered to be safe even when administered over long periods of time.

Colchicine is extremely toxic: the most common toxic effects of this drug are nausea, vomiting, abdominal pain and diarrhoea. Gastrointestinal disturbances occur in about 80% of patients.[1] The incidence of such toxicity in our series was 86.9%. Malkinson and Lynfield[3] recommends 2-3 mg/day of oral colchicine in psoriasis and we initially chose the lower figure for our patients. But even with the lower dose advocated, the drug was poorly tolerated by our patients. Wahba and Cohen,[4] however, were more specific in titrating the dose. They recommended 0.02 mg/kg/day. Thus an average 50 kg adult would require 1 mg/day which was the modified dose we used and was well tolerated. Other reported toxicities of oral colchicine include bone marrow depression, alopecia, hepatic failure, mental depression, seizures, ascending paralysis, respiratory depression and death.[14] Apart from nephrotic syndrome, we did not encounter any of the above problems. We do not share the observations by Malkinson and Lynfield[3] that oral colchicine results in a remarkable improvement of psoriasis but are in agreement with Wahba and Cohen,[4] who noted that thin plaques responded better than chronic, stable, thick plaque lesions although decreased scaliness, erythema and infiltration and marked diminition of pruritus was observed in all cases. At best, we would venture to comment that oral colchicine is better than a placebo, though no complete remission is to be expected. Perhaps it may be worth a try with oral colchicine in recalcitrant chronic plaque psoriasis prior to considering other potentially harmful antimitotic drugs.

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