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Original Article

Role of oral colchicine in plaque type psoriasis. A randomized clinical trial comparing with oral methotrexate

Mohammed Saiful Islam Bhuiyan, Md. Akramullah Sikder, Muhammad Munir Rashid*, Farzana Rabin**

* Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka Bangladesh
** Department of Psychiatry, Holy Family Red-Crescent Medical College, Dhaka, Bangladesh

Abstract

Background Patients with moderate to severe psoriasis generally require phototherapy, photochemotherapy or systemic agents to control their disease adequately. The potential toxic effects of long term use of the classic antipsoriatics, prolonged continuous therapy, higher cost and low socio-economic conditions of patients obligate us to consider some cheaper older alternatives like colchicine.

Patients and methods A prospective, randomized controlled clinical trial was carried out on two groups of patient of psoriasis, group A (Case, n=30) was treated with 2.1 mg per day oral colchicine, in two divided doses and group B (Control, n= 30) was treated with 7.5 mg of oral methotrexate once weekly for 8 weeks. No topical agent except bland emollients was applied during the trial period. Psoriasis area severity index (PASI) was calculated as main outcome measure at entry level and follow up after one month and two months.

Results The mean percentage reduction of PASI was statistically significant (p=0.001) at both first and second follow up with oral colchicine. PASI-50 was achieved in 23.3% of respondent in colchicine group and 53.3% in methotrexate group (p<0.05).

Conclusion Oral colchicine is an effective therapy for chronic plaque psoriasis but it is less effective than methotrexate, the gold standard antipsoriatic therapy (p<0.05).

Key words
Plaque psoriasis, colchicine, methotrexate

Introduction

Psoriasis is a common, chronic, disfiguring, inflammatory and proliferative condition of the skin, in which both genetic and environmental influences have a critical role.[1] Currently there is no cure for psoriasis and treatment options produce variable response, in part, because disease pathogenesis is not completely understood. Largely, traditional therapeutic agents target abnormal keratinocyte proliferation and differentiation or induced general immunosuppression, thereby producing temporary improvement, partial response, or serious adverse effects.[2] In general, classic antipsoriatics have proven to be highly effective in the treatment of psoriasis. However, potentially serious toxicities can limit their long-

Address for correspondence
Dr. Mohammed Saiful Islam Bhuiyan,
Flat no: C/2, Park reverie,
22/A Monipuri Para, Sangsad Avenue, Farmgate, Dhaka, Bangladesh.
Phone: 0088-01716-259319, 0088-02-8158708
email: drsaifulib@yahoo.com

term use. The benefits and risks of phototherapy, photochemotherapy and systemic therapy must be weighed carefully for each patient of psoriasis, and treatment should be individualized accordingly.[3] These limitations necessitate search for newer safer drugs.

Colchicine is an ancient drug, widely used in the treatment of gout.[4] It is a useful and well-tolerated medication. Occasionally patients experience gastrointestinal upset, but this is usually obviated by eating before taking the drug.[5] There is growing evidence that the anti-inflammatory effect of colchicine is multifaceted.[6] Logic dictates that colchicine, with its polymorphonuclear leukocytes (PML) suppression and antimitotic activity, would be beneficial in treating psoriasis and palmoplantar pustulosis.[5]

There are very few studies advocating the therapeutic efficacy of oral colchicine in chronic plaque psoriasis. In a prospective single-blind, randomized clinical trial by Bassak and Chatterjee,[7] it was demonstrated that oral colchicine (2 mg/day for 8 weeks) is effective for chronic plaque psoriasis, which supported the earlier study by Wahba and Cohen.[8] They recommended oral colchicine in recalcitrant chronic plaque psoriasis prior to considering other potentially harmful antimitotic drugs.[7,8] The current study was designed to see the efficacy and safety of oral colchicine in the treatment of plaque psoriasis comparing with methotrexate.

Patients and methods

It was a prospective, open, randomized controlled clinical trial, carried out in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period of July 2007 to October 2008. Out of 60 patients of plaque type psoriasis, thirty patients each were treated with oral colchicine (case group) and oral methotrexate (control). Simple random sampling method was followed. Only stable, chronic plaque type psoriasis patients diagnosed by consultant dermatologists with psoriasis area and severity index (PASI) >8 and age ≥18 years were included in the study. Exclusion criteria used were: pregnant and lactating females, hypersensitivity to colchicine, any form of topical or oral medication for at least 4 weeks prior to the study, impaired renal, hepatic, cardiovascular, gastrointestinal disorders and blood dyscrasias.

All patients were given an explanation of the study including the potential risks and obtainable benefits and were included in the trial after taking their informed consent.

Intervention Group A patients were treated with oral colchicine at a dose of 2.1 mg daily, in two divided doses and group B patients were treated with 7.5 mg of oral methotrexate once weekly, along with folic acid 5 mg daily on rest of week days. Total duration of treatment was eight weeks. No other systemic drug except antihistamines or topical drugs except bland emollient were allowed. Patient's history, general physical examination and follow-up investigations (complete blood count, platelets, SGPT, serum creatinine and urinalysis) for assessing adverse effects, were done after one week, four weeks (one month) and finally after eight weeks (two months) of treatment.

Outcome measure PASI score was noted at baseline and after four weeks and eight weeks of treatment.

Data processing and analysis Data analysis was performed by Statistical Package for Social

Science (SPSS), version-12. Statistical analyses were done and level of significance were measured by using appropriate procedures like chi square test (χ^2), relative risk (RR) measurement, t-test, and proportion (d) test and others where applicable. Level of significance (*p* value) was set at 0.05 and confidence interval at 95%. Results were presented as text and tables.

Results

Mean PASI of group A (colchicine) and group B (MTX) at baseline was 14.66±3.86 and 16.32±3.27 respectively ($p>0.05$). After 1 month therapy, the mean PASI was 11.39±3.41 in group A and 12.71±2.85 in group B and the mean percent reduction of PASI, was 22.94±6.17 and 22.30±6.23 in group A and group B, respectively (**Table 1**).

The mean PASI at after 2 months therapy was 8.24±3.02 and 7.96±2.74 for group A and group B, respectively. The mean percent reduction of PASI at final follow up was 45.00±7.56 and 52.25±8.93 in group A and group B, respectively. The t test revealed a significant difference in term of percentage reduction of PASI from baseline to second follow up (**Table 1**).

Statistically significant improvement of psoriasis based on PASI reduction was observed at first follow up after one month of treatment ($p=0.001$) with both colchicine and MTX and also at final follow up after two months of treatment ($p=0.001$) [**Table 1**].

≥50% PASI reduction (PASI-50) was obtained in 23.3% of respondents of group A (colchicine) and 53.3% of group B (methotrexate) and <50% PASI reduction in 76.7% of group A and 46.7% of group B patients. So, colchicine had a significantly less response than MTX ($p<0.05$).

In colchicine group, gastrointestinal side effects were most commonly observed e.g. abdominal pain (46.7%), dyspepsia (43.3%), nausea/vomiting (36.7%) and diarrhea (30.0%) [**Table 2**].

Discussion

It is assumed that about 30% of psoriatics have at least moderate disease, often requiring systemic treatment in addition to topical treatment. About two-thirds of psoriasis patients have a chronic course with the need for continual control of disease activity.[9] Considering the potential toxicity of common classical anti-psoriatics and need for long term treatment, we intended to search for a relatively safer alternative therapy. Current study was conducted to evaluate the safety and efficacy of oral colchicine in the treatment of plaque psoriasis, comparing with MTX.

After one month therapy with colchicine, mean percent reduction of PASI was 22.94±6.17, and after two months therapy it was 45.00±7.56. The improvement of PASI was statistically significant ($p=0.001$) at both first and second follow up, so we consider oral colchicine as an effective therapy for chronic plaque type psoriasis (**Table 1**).

Efficacy of colchicine on chronic plaque type psoriasis was first noticed by Malkinson and Lynfield,[10] who reported three cases of widespread psoriasis involving more than 80% skin surface area, unresponsive to the usual therapeutic method. They treated with a dose of 2-3 mg oral colchicine daily with subsequent use of tar and salicylic acid ointments locally. After one to two months, moderate to significant improvement of skin lesions were noticed.[10] As they used other concomitant drugs we cannot conclude that the improvement was due to

Table 1 Distribution of the respondents by PASI score

PASI score		*Group*		*p value*
		Group-A (Colchicine) Mean ± SD	*Group-B (Methotrexate) Mean ± SD*	
PASI at baseline		14.66 ± 3.86	16.32 ± 3.27	0.078 NS
PASI at 1st follow up		11.39 ± 3.41	12.71 ± 2.85	0.109 NS
PASI at 2nd follow up		8.24 ± 3.02	7.96 ± 2.74	0.708 NS
Reduction of PASI at 1st follow up from baseline (%)		22.94 ± 6.17	22.30 ± 6.23	0.692 NS
Reduction of PASI at 2nd follow up from baseline		45.00 ± 7.56 (30.97-60.20)	52.25 ± 8.93 (38.73-69.23)	0.001**
Paired t value (*p*)	PASI for baseline to 1st follow up	19.698 (0.001**)	16.725 (0.001**)	
	PASI for baseline to 2nd follow up	27.055 (0.001**)	31.688 (0.001**)	

t test was done to measure the level of significance, * = Significant ($p < 0.05$), **= Highly significant, NS = Not significant

Table 2 Distribution of the respondents by percent reduction of PASI at final follow up

Percent reduction for final follow up	*Group-A (Colchicine) (n=30)*	*Group-B (Methotrexate) (n=30)*	*Total*
<50	23 (76.7%)	14 (46.7%)	37 (61.7%)
≥50	7 (23.3%)	16 (53.3%)	23 (38.3%)
Total	30 (100.0%)	30 (100.0%)	60 (100.0%)

Chi-Square test was done to measure the level of significance, Chi-Square value = 5.711, df = 1, p value = 0.017

Table 3 Combined side effects of both colchicine and methotrexate in the treatment of psoriasis

Side effects	*Group-A (Colchicine) (n=30)*	*Group-B (Methotrexate) (n=30)*	*p value*
Abdominal pain	14 (46.7%)	1 (3.3%)	0.001**
Dyspepsia	13 (43.3%)	5 (16.7%)	0.024*
Nausea/vomiting	11 (36.7%)	4 (13.3%)	0.037*
Diarrhea	9 (30.0%)	0 (0.0%)	
Mouth ulcers	2 (6.7%)	2 (6.7%)	0.999 NS
Muscle weakness	2 (6.7%)	0 (0.0%)	
Anemia	1 (3.3%)	5 (16.7%)	0.085 NS
Jaundice	1 (3.3%)	0 (0.0%)	

Chi-Square test was done to measure the level of significance, * = Significant ($p < 0.05$), **= Highly significant NS = Not significant

colchicine. Wahba and Cohen[8] with a more specific dose 0.02 mg/kg/day, for 2 to 4 months on 22 patients of chronic plaque psoriasis, found significant improvement, greater than 50% in 11 patients whose lesions were papules and plaques of small dimension. The response was not so satisfactory in the patients with thick and chronic lesions, which might be due to insufficient dose, though they had a longer duration of treatment (2-4 months).[8] Our study design and findings are much closer to the study carried out by Bassak and Chatterjee[7] in respect of study design, dosage, duration and results. The lesions did not disappear completely in any

of their patients and our study revealed maximum reduction of PASI (60.20%) in colchicine group. Bassak and Chatterjee followed up the cases weekly and clinical improvement of the psoriatic plaques was discernable only after the second week.

Wahba and Cohen[8] also found that low dose colchicine for long time (4-9 months) can successfully prevent significant recurrence, where Colchicine therapy was initiated after achieving complete clearing with another well-known modality. We, as well as Bassak and Chatterjee,[7] did not observe the long term suppressive role of colchicine. There are other reports of efficacy of colchicine on psoriasis. Kaidbey *et al*.[11] found topical colchicine beneficial for recalcitrant chronic plaque disease.

Mean percent of PASI reduction was 52.25±8.93 with a maximum 69.23% after 2 months of treatment with methotrexate. The improvement with methotrexate was statistically significant. In this study we found that both the drugs are effective in plaque type psoriasis. In colchicine group only 23.3% achieved PASI-50 whereas in methotrexate group 53.3% achieved PASI-50. Methotrexate may reduce the severity of psoriasis by at least 50% in more than 75% of patients.[12] Possible cause of lower achievement of PASI-50 with methotrexate in comparison to previous studies is lower therapeutic dose (7.5 mg weekly) and short duration (8 weeks) of treatment. As the onset of action of methotrexate is rather slow, therapeutic effects usually require 4 to 8 weeks to become evident.[12]

Here, colchicine therapy was significantly effective against psoriasis but less effective than the gold standard antipsoriatic methotrexate (p<0.05). As same type of case-control study comparing colchicine with methotrexate was not available, our finding could not be compared.

The main side effect of colchicine is gastrointestinal toxicity, which occurs in up to 80% of patients receiving a maximal dose.[5] Abdominal pain, dyspepsia, nausea/vomiting, diarrhea were common adverse effects in our study. Other observed adverse effects of colchicine reported in this study were anemia and jaundice. Adverse effects of methotrexate were found in at least 40% of patients which included anemia, dyspepsia, nausea, vomiting, mouth ulcers, muscle weakness and abdominal pain. None of these adverse effects of both drugs were serious. GIT adverse effects were significantly higher among colchicine group but other adverse effects were not significantly different between two drug groups. Changes of total count of WBC, platelet count, serum SGPT and serum creatinine were noted from baseline to final follow up after treatment with methotrexate, but these changes were within their individual normal level.

So, we conclude that oral colchicine is an effective and safe therapy for chronic plaque psoriasis.

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Dr. Ijaz Hussain

drijazhussain@gmail.com