TOPICAL METHOTREXATE THERAPY IN PALMOPLANTAR PSORIASIS

BC Ravi Kumar, Inderjeet Kaur, Bhushan Kumar

Palmoplantar psoriasis (PPP) is a disabling and disfiguring condition frequently resistant to conventional topical therapies. Sixteen patients of palmar and/or plantar psoriasis were treated with 1% methotrexate gel using propylene glycol as vehicle twice daily for 8 weeks. Patients were assessed for severity of erythema, scaling, induration and fissuring (ESIF) of the lesions weekly for one month and subsequently once every two weeks. Patients with more than 50% improvement of the lesions were considered to have good improvement. Fifteen patients completed the study period. Eight out of ten (80%) patients with palmar psoriasis and 9 out of 14 (64%) patients with plantar psoriasis showed good improvement. The mean duration for >50% improvement was 40.3 days for palms and 52.9 days for soles. There were no side effects in any patient. Topical methotrexate, when administered in a suitable vehicle and applied for sufficient time is beneficial in PPP.

Key Words : Psoriasis, Methotrexate topical, Palms and soles

Introduction

Palmoplantar psoriasis (PPP) is a disabling and disfiguring condition, that is frequently resistant to the conventional topical therapies.[1] When it becomes disabling, it is an indication for systemic therapy, mostly with methotrexate which is associated with rather unacceptable risks.[2] To overcome the problem of systemic toxicity, some workers have used methotrexate topically for psoriasis vulgaris,[3-8] and few of these studies found good results.[7,8] We conducted a study with the aim of determining the efficacy of topical methotrexate on PPP using propylene glycol as vehicle which is also known to help in penetration of topical methotrexate.[9]

From the Department of Dermatology, Kasturba Medical College, Manipal and Department of Dermatology and Venereology. Postgraduate Institute of Medical Education and Research, Chandigarh, India.

Address correspondence to :

Dr. Ravikumar BC

Department of Skin & STD, Kasturba Medical College, Manipal-576 119, Karnataka, India. Fax: 08252-70062, Telex: 833-231 Mehe In

Materials and Methods

Sixteen adult patients diagnosed clinically as palmoplantar psoriasis of plaque type participated in the study. All had stable lesions covering more than 30% of palms and/or soles but not covering more than 5% of other body areas. None of the patients was on any systemic or topical antipsoriatic therapy for at least 1 month prior to the study except for bland emollients. Women were included only if willing to avoid conception during and for four months subsequent to the conclusion of the study.

All patients had preliminary baseline investigations done to rule out any haematological abnormality or renal and hepatic dysfunction. Investigations were repeated at the conclusion of the study and in between if required.

As topical methotrexate preparations are not available in the market, a topical formulation was prepared by powdering the methotrexate tablets (each tablet contains 2.5mg of methotrexate) and dissolving it in water, propylene glycol and ethanol (absolute alcohol 25%, propylene glycol 50% and water 25% V/V) so that a 1% methotrex

ate gel was obtained. It was applied twice daily over the lesions with the help of a cotton tipped spatula and left for 30 minutes each time and then washed off with soap and water.

Total duration of therapy was 8 weeks. Patients were examined once weekly for initial one month and subsequently every two weeks. The lesions were assessed for the degree of erythema, scaling, induration and fissuring (ESIF) and were scored on a severity scale of 0 to 3 as followed in other studies.[1] (0-clear, 1-mild, 2-moderate and 3-severe). The most severe condition was given 12 points, whereas the absence of disease received '0' point. The percentage of overall improvement was calculated by deducting the sum of the clinical scores after therapy from the sum of pretreatment scores and dividing it by pretreatment clinical score. The improvement percentage score was categorised as follows-

Upto 25% -> minimal improvement, 26 - 50% -> moderate improvement, 51 - 75% -> marked improvement and above 75% -> total/near total clearing.

The patients were considered to have good improvement when clinical improvement was more than 50% and any improvement less than that was considered as poor response.

Unpaired students 't' test was used for statistical analysis.

Results

Out of 16 patients entered into the study, 15 completed the 8 week study period. Pretreatment details are shown in Table-I. The average response rate was 64.6±5.3% for palms, and 55.8±6.3% for soles (Table-II). The clinical scores (ESIF) before therapy and at the completion of the study were 6.9±0.7 and 2.6±0.6 for palms and 7.1±0.6 and 3.1±0.6 for soles respectively . There was no statistically significant difference in the improvement recorded between palms and soles (p>0.05).

Of the 10 patients with palmar involvement, 3 (30%) had total/near total clearing, 5 (50%) had marked and 2 (20%) had moderate improvement at the end of 8 weeks. Out of 14 patients with plantar lesions, 3 (21.4%) had total/near total clearing, 6 (42.8%) had marked improvement, 4 (28.3%) had moderate improvement and 1 patient had mild improvement. The improvement in the condition of palms was recorded earlier (40.3 days) as compared to soles (52.9 days). None of the patients reported any side effects.

Discussion

Table.1. Pretreatment details of patients (n=15)

Age (Years)	Mean	40.8
	Range	22-65
Sex	Males	9
	Females	6
Duration of disease	Mean	2.2
(Years)	Range	0.4-6
Sites involved	Palms and soles	- 9 (60.0%) patients
	Palms only	- 1 (6.7%) patients
	Soles only	- 5(33.3%) patients
Severity of disease	Palms	- 6.9±0.7
(Average ESIF score)	Soles	- 7.1±0.6
Involvement of sites	Number of patients	- 4
other than palms and	Sites involved	- scalp 3, elbows 1
soles	Percentage involvement	- <5%

Table.II. Pre and post treatment ESIF scores

Palms (n=10)					Soles (n-14)			
Sr.No.	Scores Pre	Post	Response (%)	Duration (days)	Scores Pre	Post	Response (%)	Duration (days)
1	5	2	60.0	56	5	2	60.0	56
2	9	4	55.6	56	9	3	66.7	56
3	8	2	75.0	42	3	1	66.7	42
4	6	1	83.3	28	7	3	57.1	56
5	-	-	-	-	5	3	40.0	-
6	5	1	80.0	28	6	3	50.0	-
7	3	1	66.7	28	7	1	85.7	56
8	7	1	85.7	42	9	2	77.7	56
9	8	3	62.5	42	-	-	-	-
10	-	-	-	-	9	9	0.0	-
11	-	-	-	-	9	4	55.6	42
12	-	-	-	-	9	3	66.7	56
13	-	-	-	-	9	1	88.8	56
14	10	6	40.0	-	9	6	33.3	-
15	8	5	37.5	-	3	2	33.3	-
Mean	6.9	2.6	64.6	40.3	7.1	3.1	55.8	52.9
SEM	0.7	0.6	5.3	4.2	0.6	0.6	6.3	2.0

Table.III. Topical methotrexate in Psoriasis : different studies

Authors Year	Hurse[4] 1963	Fry[7] 1967	Comaish[5] 1969	Bjerring[6] 1986	Weinstein[8] 1989	Our study 1999
Patient number	6	9	20	5	42	15
Type of Psoriasis	PV	PV	PV	PV	PV	PPP
Study period	5-10 days	2 wks	2 wks	3 wks	6 wks	8 wks
Formulation with conc.	0.5% oint.	0.2% cream	0.1-10% cream	0.25% cream 0.25% oint	0.1%.,0.5% & 1% gel	1%gel
Vehicle	Water based	Water based	DMSO	Carbamide	Laurocaprum	Propylene glycol
Frequency of Application	O.D.	O.D.	R.D.	R.D.	R.D.	R.D.
Time for improvement (days)	NM	8.1	NM	NM	42	Palms Soles 40.3, 52.9
Patients improved (in%) (>50% improvement)	NM	77.8	NM	NM	25 to 68	80, 64.2

PV - Psoriasis vulgaris, PPP - Palmoplantar psoriasis
Veh. - Vehicle NM - Not mentioned
O.D. - Once daily R.D. - Twice daily
DMSO - Dimethyl sulfoxide

Our results indicate that topical methotrexate is effective in palmoplantar psoriasis. Eighty percent of patients (8 out of 10) with palmar lesions and 64% (9 out of 14) with plantar lesions showed improvement which could be graded as good.

In the absence of any published reports about the efficacy of topical methotrexate on PPP, we could compare our results only with the studies employing topical methotexate on psoriasis vulgaris (Table III). Early trials of topical methotrexate for psoriasis vulgaris by Vanscott and Reinertson[3], Nurse[4], Comaish[5] and Bjerring et al[6] were unsuccessful. But Fry and Mcminn[7] and Weinstein et al[8] demonstrated the efficacy of topical methotrexate on psoriasis vulgaris in 78% and 56 - 68% of patients respectively. One of the presumed reasons for the lack of clinical activity of topical methotrexate is insufficient percutaneous penetration necessary to inhibit epidermal DNA synthesis. Fry et al[7] used a water based cream and Weinstein et al[8] used lauroaprum as the vehicle to enhance penetration.

The mean duration for improvement was 40.3 days for palms and a little longer i.e. 52.9 days for soles. This is almost similar to the 6 weeks time required by patients of Weinstein et al.[8]

Though various side effects have been observed with topical methotrexate like mild burning sensation,[8] redness, purpura and blisters[5,7] at the site of application of methotrexate, none of our patients had any side effects.

In this study the methotrexate powder was not in pure form, there was no control group and the size of the study group was relatively small. Inspite of these limitations our results indicate that topical methotrexate, when combined with a suitable vehicle which facilitates adequate percutaneous absorption and when administered for sufficient time, has a beneficial effect on palmoplantar psoriasis. Further studies in this regard may provide a more clear picture.

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