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Original Research Article

A comparative study on therapeutic efficacy between methotrexate iontophoresis and topical methotrexate 1% gel in palmoplantar psoriasis

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ABSTRACT

Introduction: Palmoplantar psoriasis is a disease which often leads to disfigurement and disability. It is resistant to conventional therapy where systematic therapy mostly with methotrexate is indicated. To overcome systemic toxicity of the drug, topical delivery methods has been tried recently with unsatisfactory results because of its poor penetration. Iontophoresis may help to increase its absorption and thereby efficacy.

Materials and Methods: Our study included a total of 60 patients fulfilling the selection criteria. They were randomly divided into two groups, group A & group B; comprising 30 patients in each. The patients in Group A received topical methotrexate 1% gel twice daily treatment for 8 weeks on all days. The patients in Group B underwent methotrexate iontophoresis once in a week for 4 weeks followed by every two weeks. A total of six session of iontophoresis was done and both groups were followed up for another 3 months. Evaluation of therapeutic efficacy was done by assessing the lesions for erythema, scaling and fissuring during each visit and follow up period.

Results: Overall improvement in group A and group B were 82.4% and 95.3% respectively. Recurrence rates were nearly similar in both groups.

Conclusion: There was highly statistical significant improvement and clearance rates with group B at the end of 8 weeks of therapy and after follow up period compared to group A (p value < 0.01).

1. Background

Palmoplantar psoriasis is a genetically predisposed and immunologically mediated inflammatory dermatosis. Even though it relatively affects lesser body surface area, it usually interferes with day-to-day activities of patients and affects the quality of life.[1,2] Topical therapies are the mainstay of treatment. But it is often resistant to conventional topical therapy. In these situations, systemic therapy is indicated. Drugs like methotrexate, retinoids, cyclosporin and biologicals can be used systemically. But these drugs have their own potential risks and side effects in systemic route. Methotrexate is the most commonly used and FDA approved drug in the treatment of psoriasis. But methotrexate can cause many serious adverse effects like hepatitis, hematological abnormalities and interstitial pneumonitis when given in systemic route.[3] To overcome systemic toxicity of methotrexate, topical delivery methods has been tried recently. But results are not satisfactory because of poor drug penetration by passive diffusion into the skin over palms and soles. Iontophoresis may help us to increase its absorption and efficacy. It is the application of a direct electric current to aid transdermal drug delivery

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by improving ionic substance penetration into the body for therapeutic purposes. It is a noninvasive, targeted, and convenient way to deliver ionised medications to the skin.[4] It also allows for larger medication concentrations to be given to a smaller area, resulting in less systemic side effects.[5] Drug is applied under the same charge electrode and the opposite charge return electrode is placed on the body surface at a neutral site. It works on the principle that like charges repel each other and that of opposite charges attract.[6] Methotrexate iontophoresis for transdermal drug delivery was evaluated by Alvarez-Figueroa et al. through boars' skin in 2001. He recommended that iontophoresis may increase the influence of local methotrexate in psoriasis.[7]

This study aims to determine the therapeutic efficacy and safety of methotrexate iontophoresis in comparison with topical methotrexate 1% gel in treatment of Palmoplantar psoriasis.

2. Materials and Methods

This is a Randomized controlled trial conducted at the Dermatology Out-Patient Department of a tertiary care institution for a period of eighteen months after obtaining approval from Institutional Ethical Committee.

A total of 60 patients of either sex aged 18 years to 60 years with palmoplantar psoriasis which affected more than 30% of the areas of palms and /or soles, were included in the study. Exclusion criteria were patients with psoriasis with more than 5% involvement of other body parts, Patients on topical or systemic medications for psoriasis other than bland emollients for the last one month, patients who were pregnant or planning for pregnancy, lactating women, patients with any hematological or liver disorders and patients who had implanted cardiac pacemakers. Patients of either sex in both groups were advised contraception and to avoid pregnancy during and for at least 3 months following the treatment.

Patients who fulfilled the selection criteria were included in the study after obtaining the written informed consent. Then they were randomly divided into two groups.

Group A (n = 30): These patients received topical methotrexate 1% gel twice daily treatment for 8 weeks on all days on both side palms and/or soles.

Group B (n = 30): Patients underwent methotrexate iontophoresis once a week in first 4 weeks and then every 2 weeks, comprising totally of 6 sittings on both side palms and/or soles.

2.1. Procedure

Injectable methotrexate solution (50mg/2ml) was added to 50 ml of distilled water resulting in a concentration of 1mg/ml. Gauze was soaked in this solution and wrapped over the affected areas in the palms and soles. The gauze was then covered with an aluminum foil. A direct current (5-10 mA) was then passed from iontophoresis unit through the solution to deliver the drug to affected area for 20 minutes. Patients felt mild tingling sensation and numbness in the palm/sole during the passage of current from iontophoresis unit into the skin.

Therapeutic efficacy evaluation was done by assessing the lesions for erythema, scaling, and fissuring with each parameter scored on a scale of 0-3 during 2, 4, 6 and 8 weeks of treatment.

0 – clear, 1 – mild, 2 – moderate, 3 –severe

Percentage of overall Sum of the clinical scores before therapy – sum of improvement

$$= \frac{Clinical\ scores\ after\ therapy \times 100}{Pretreatment\ clinical\ score}$$

1. < 25% - minimal improvement
2. 26-50% - moderate improvement
3. 51-75%- marked improvement
4. >75% - total/ near total clearing.

3. Results

The collected data were analysed using IBM SPSS Statistics, Version 23.0. (Armonk, NY: IBM Corp). The probability value (p value) of 0.05 is considered as significant level.

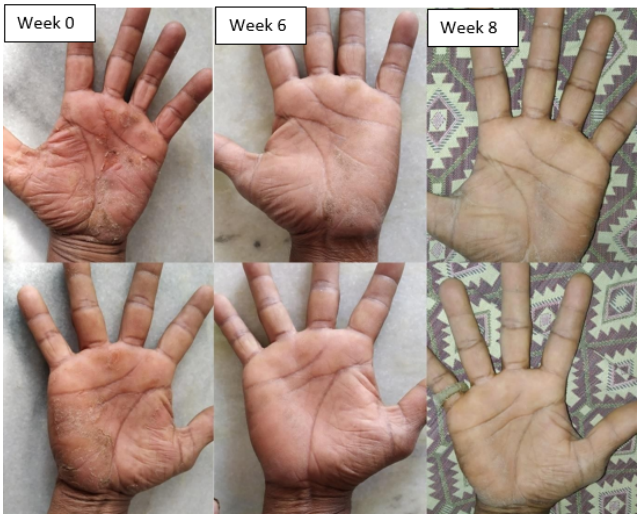

Figure 1: Methotrexate iontophoresis

There was no significant statistical association of age and gender distribution between the groups. A total of 13.3% had nail involvement, such as nail pitting and subungual hyperkeratosis. The mean duration from the time of onset of the disease was 10.1 months in group A and 12.9 months in group B.

The erythema between Groups at 8^{th} Week by Pearson's Chi-Square test were c^2=9.017, (p=0.006) which showed statistically significant association. (Table 1) The Scaling

Table 1: Comparison of erythema between Groups at 8th week

Erythema			Groups		Total	χ2 - value	p-value
			Gel	Iontophoresis			
8th Week	None	Count	20	29	49	9.017	0.006 **
		%	66.7%	96.7%	81.7%		
	Mild	Count	10	1	11		
		%	33.3%	3.3%	18.3%		
Total		Count	30	30	60		
		%	100.0%	100.0%	100.0%		

** Highly Statistical Significance at p < 0.01 level

Table 2: Comparison of scaling between Groups at 8th week

Scaling			Groups		Total	χ 2 - value	p-value
			Gel	Iontophoresis			
8th Week	None	Count	17	27	44	8.673	0.013 *
		%	56.7%	90.0%	73.3%		
	Mild	Count	12	3	15		
		%	40.0%	10.0%	25.0%		
	Moderate	Count	1	0	1		
		%	3.3%	0.0%	1.7%		
Total		Count	30	30	60		
		%	100.0%	100.0%	100.0%		

* Statistical Significance at p < 0.05 level

Table 3: Comparison of fissuring between Groups at 8th Week

Fissuring			Groups		Total	χ 2 - value	p-value
			Gel	Iontophoresis			
8th Week	None	Count	6	24	30	21.600	0.0005 **
		%	20.0%	80.0%	50.0%		
	Mild	Count	24	6	30		
		%	80.0%	20.0%	50.0%		
Total		Count	30	30	60		
		%	100.0%	100.0%	100.0%		

** Highly Statistical Significance at p < 0.01 level

Table 4: Comparison of overall improvement % between Groups by Unpaired t-test

Variables	Groups	N	Mean	SD	t-value	p-value
Overall improvement %	Gel	30	82.4	15.0	4.212	0.0005 **
	Iontophoresis	30	95.3	7.6		

** Highly Statistical Significance at p < 0.01 level

and Fissuring between Groups at 8^{th} Week by Pearson's Chi-Square test were c^2=8.673, (p=0.013) and c^2=21.600, (p=0.0005) respectively which also show statistically significant association. (Tables 2 and 3)

82.4% in group A and 95.3% in group B showed overall improvement (t-value=4.212, p=0.0005) which shows highly statistically significant difference. (Table 4)

Three patients in group A had irritation and 2 patients in group B had burns. The Side effects between Groups by Pearson's Chi-Square test were c^2=5.018, p=0.081>0.05 which shows no statistically significant association.

During follow up, two patients from group A and one patient from group B showed recurrence of the lesion.

4. Discussion

In our study the age group spanned from 18 to 56 years, with a mean age of 30 years. This was consistent with the age incidence reported by Spuls et al.[8] which indicated a mean age of onset of 28 years. In addition, Sharma et al[9] and Lal et al[10] found that the second decade had the highest incidence. In our study males were more commonly affected than females.

In our study, 13.3% of patients had nail involvement, such as pitting and subungual hyperkeratosis, which was consistent with Yesim Ainar Kara's study, which found that between 15 to 69 percent of psoriasis patients have nail involvement. According to the Khandpur et al study,

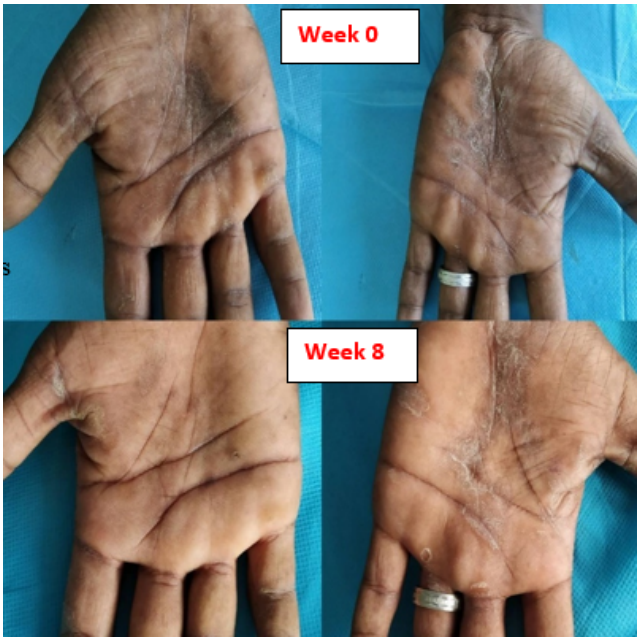

Figure 2: 1% Methotrexate gels

41% of individuals had nail involvement.[11] After the commencement of skin lesions, nail lesions usually take ten years to manifest. The lower percentage of nail involvement in our study may be because, many of the patients included in our study were within two years of the onset of the disease.

At the end of eight weeks, in group A, there was 66.7% patients had full resolution of erythema, 56.7% had full resolution of scaling and 20% had full resolution of fissuring. In group B, there was 96.7% patients had full resolution of erythema, 90% had full resolution of scaling and 80% of full resolution of fissuring. (Figures 1 and 2)

Group B patients who underwent methotrexate iontophoresis showed more compliance than group A patients who received topical methotrexate gel because the former group received directly observed treatment.

Overall improvement in group A is 82.4% and in group B is 95.3% which was comparable to a study done by Haseena et al. their study compared the efficacy of methotrexate iontophoresis versus coal tar application in palmoplantar psoriasis where they had an improvement of 63.94% in the group who underwent methotrexate iontophoresis and 47.66% improvement in coal tar group.[12] Group A who received topical 1% methotrexate gel for 8 weeks showed 82.4% overall improvement which was significantly high than the study done by Kumar et al who used 0.25% topical methotrexate gel for 12 weeks and showed no significant response.[13] Also Ravi et al stated that there was 51.4% improvement with use of 1% topical methotrexate gel for 8 weeks which is lower than our study.[14]

During treatment, three patients from group A developed irritation after using topical methotrexate gel and they were advised to use it along with emollients. Two patients from group B developed burns following the next day of iontophoresis in the dorsum of foot, which may be due to wrong placement of electrodes. The recurrence of the lesion may be a Koebner phenomenon which may be attributable to their occupation as manual labourers.[15]

5. Conclusion

Methotrexate iontophoresis is better than topical methotrexate 1% gel in palmoplantar psoriasis. Recurrence rates were nearly similar in both the groups.

6. Limitation

The major limitation of our study is the small sample size. So larger trials are required to quote the safety, efficacy and stability of response with the above modes of treatment in palmoplantar psoriasis.

7. Source of Funding

None.

8. Conflict of Interest

None.

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