Research Article

INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230-8407 [LINKING]

Comparative assessment of the efficacy of topical 1% methotrexate gel to methotrexate iontophoresis in subjects with palmoplantar psoriasis

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How to cite: Lahiri AK. Evaluation of the effectiveness of topical 1% methotrexate gel versus methotrexate iontophoresis in individuals with palmoplantar psoriasis in comparison. International Research Journal of Pharmacy. 2017;8:3:38-42.
Doi:10.7897/2230-8407.080333

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ABSTRACT

Background: Systemic medication, mostly methotrexate, is recommended for palmoplantar psoriasis, a condition that results in deformity and impairment and is resistant to traditional treatment. Topical methotrexate administration techniques have been attempted to combat systemic toxicity, however the outcomes have been disappointing. Its effectiveness and absorption can be improved using iontophoresis. However, there is a lack of data in the literature.

Aim: The objective is to evaluate the effectiveness of topical 1% methotrexate gel in comparison to methotrexate iontophoresis in individuals with palmoplantar psoriasis.

Methods: 120 participants were randomly assigned to one of two groups of 60 participants each. Group I participants received 1% topical methotrexate gel twice a day for eight weeks, every day of the week**.** For four weeks and then every two weeks after that, Group II individuals received methotrexate iontophoresis once a week. There were six iontophoresis sessions. For three months, both groups were monitored. During every visit and follow-up, the effectiveness of the treatment was evaluated by looking for signs of fissuring, scaling, or edema in the lesion.

Results: The study's findings indicated that both Groups I and II had improved overall. Subjects from Groups I and II showed improvements in 82.4% and 95.3% of cases, respectively. In terms of recurrence rates, both Groups I and II had rates that were quite similar.

Conclusion: The current study reveals that, after 8 weeks of therapy, participants receiving methotrexate iontophoresis for palmoplantar psoriasis show significantly higher clearance rates and improvements than those receiving 1% methotrexate gel.

Keywords: Iontophoresis, methotrexate, methotrexate gel, Palmoplantar psoriasis, psoriasis

INTRODUCTION

Immunologically caused inflammatory psoriasis is known as palmoplantar psoriasis, and it is a genetically predisposed skin disorder. Even if it affects a smaller portion of the body, it often has an impact on the daily activities and quality of life of those who are affected. The most popular method of treating palmoplantar psoriasis is still topical therapy. It typically resists traditional topical treatment, though. Systemic treatment is utilized in these situations. Systemically utilized medications include biologicals, retinoids, cyclosporins, and methotrexate. These medications do, however, have some dangers and potential adverse effects when used systemically. The most widely used medication with FDA approval for treating psoriasis is methotrexate.[1]

Although methotrexate has been authorized for the treatment of intestinal pneumonitis, hematological abnormalities, and other significant adverse effects like hepatitis when given via a systemic route. To overcome the systemic toxicity of methotrexate,

Recently, strategies for delivering methotrexate topically have been tested. However, because of the drug's limited passive diffusion penetration into the epidermis over the palms and soles, the results are not sufficient.2

Iontophoresis can improve methotrexate's effectiveness and absorption. The method of using direct electric current to aid in transdermal medication delivery and enhance the body's ability to absorb ionic compounds for therapeutic purposes is known as iontophoresis. Iontophoresis is a quick, precise, and non-invasive way to apply ionized drugs to the skin. It makes it possible to apply higher medication concentrations in smaller locations, which reduces systemic effects. The opposing charge return electrode is maintained on the body surface at the neutral position while the medication is administered beneath the same charged electrode.

The idea that opposing charges attract one another in the same way that they repel one another is the basis for iontophoresis. It was suggested that iontophoresis might enhance the effects of local methotrexate in psoriasis patients when it was originally evaluated in 2001 in boar's skin as a transdermal drug delivery method.Four In relation to methotrexate iontophoresis, the current study sought to evaluate the safety and effectiveness of topical 1% methotrexate gel in individuals with palmoplantar psoriasis.

The goal of the current randomized controlled clinical trial was to evaluate the safety and effectiveness of topical 1% methotrexate gel in comparison to methotrexate iontophoresis in individuals with palmoplantar psoriasis. The Institute's Department of Dermatology conducted the study. Prior to research participation, informed permission was obtained from each participant both verbally and in writing.

MATERIALS AND METHODS

A total of 120 participants, both male and female, between the ages of 18 and 60, who were willing to participate in the study and had palmoplantar psoriasis affecting more than 30% of the sole and/or palm regions, were included in the study. The study excluded participants who had a cardiac pacemaker implanted, had liver disease, hematological disorders, were lactating, pregnant, or planning to become pregnant, had been taking systemic or topical psoriasis medications other than bland emollients for the previous month, had less than 5% involvement of other body parts, or had not given their consent to participate. During and for at least three months after treatment, both male and female subjects were counseled to use contraception and refrain from getting pregnant.

Following their final inclusion in accordance with the inclusion criteria, the study participants were split into two groups of 60 at random. For eight weeks, 60 participants in Group I received 1% topical methotrexate gel twice a day on both the palms and/or soles. For the first four weeks, 60 individuals in Group II received iontophoresis with methotrexate once a week. After that, they had six sittings on both sides of their palms and/or soles every two weeks.

To reach a concentration of 1 mg/ml, 50 ml of distilled water was progressively mixed with an injectable methotrexate solution containing 50 mg/2 ml. The afflicted region on the palms and soles was covered with gauze that had been soaked in the prepared solution. The aluminum foil was then placed over this gauze.

The medicine was then delivered to the afflicted region for 20 minutes using a direct current of 5–10 mA that was transferred from the iontophoresis equipment via the solution. During the current passage from the iontophoresis device to the skin, the subjects experienced minor numbness and a tingling feeling in the palm and sole.

At 2-, 4-, 6-, and 8-week treatment visits, lesions were evaluated for fissuring, scaling, or erythema at each visit. Each parameter was rated on a scale of 0–3, where 0, 1, 2, and 3 represented clear, mild, moderate, and severe scores. This allowed for the evaluation of therapeutic effectiveness.

Clinical scores after therapy divided by pre-treatment clinical score X100 is the percentage of the whole sum of the clinical scores before to therapy minus the sum of improvement. where less than 25% indicated little to no improvement, 26–50% indicated moderate improvement, 51–75% indicated noticeable improvement, and more than 75% indicated complete or almost complete clearance.

The statistical analysis of the collected data was conducted using the chi-square test, one-way ANOVA (analysis of variance), Pearson correlation, and descriptive measures evaluation using SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk, NY, USA). The findings were presented as frequency, percentages, mean, and standard deviation. Statistical significance was defined as a p-value of less than 0.05.

RESULTS

In order to compare the safety and effectiveness of topical 1% methotrexate gel to methotrexate iontophoresis in patients with palmoplantar psoriasis, a randomized controlled clinical study was conducted. The study evaluated 120 participants who were split into two groups of 60 at random. Group I participants received 1% topical methotrexate gel twice a day, every day of the week, for eight weeks.

Group II subjects were given methotrexate iontophoresis once a week for 4 weeks and then every two weeks. There were six sessions of iontophoresis. The distribution of research participants' ages and genders was statistically comparable ($p<0.05$). In 13% of study participants, nail involvement manifested as subungual hyperkeratosis and nail pitting. Groups I and II experienced mean durations of 10.3 and 12.7 months from the time of illness start, respectively.

When the presence of erythema in two study groups was evaluated and compared after treatment, it was found that at the eighth week, 66.7% (n=40) of Group I subjects had no erythema in their lesions, and 33.3% (n=20) of Group I subjects had mild erythema. In contrast, Group II subjects had no erythema (n=58) and mild erythema (3.3%; n=2), respectively. Significantly higher erythema was seen in Group I using 1% gel compared to Group II with methotrexate iontophoresis with p=0.005 (Table 1).

Concerning the presence of scaling in two study groups following the treatment, it was seen that in the 8th week, no, mild, and moderate scaling was seen in 56.7% (n=34), 40% (n=24), and 3.33% (n=2) subjects respectively from Group I, whereas, none, mild, and moderate scaling was seen in 90% (n=54), 10% (n=6), and 0 study subjects respectively. Scaling was significantly higher in lesions from Group I using 1% gel compared to Group II with methotrexate iontophoresis with p=0.01 (Table 2).

It was seen that for assessment of fissuring in two study groups following the treatment, it was seen in at 8th week, none, and mild fissuring was seen in 20% (n=12) and 80% (n=48) study subjects respectively from Group I using 1% gel compared to none and mild fissuring in 80% (n=48) and 20% (n=12) subjects respectively from Group II using iontophoresis. The presence of fissuring was significantly higher in subjects from Group I compared to Group II with p=0.0004 (Table 3). The study results showed that for overall improvement percentage comparison in two groups of study subjects, the mean overall improvement was 82.2±15.2 in Group I subjects using 1% methotrexate gel compared to 95.1±7.8 in Group II subjects that underwent methotrexate iontophoresis.

Mean overall improvement was significantly higher in the methotrexate iontophoresis group compared to the 1% methotrexate gel group with p=0.0004 (table 4).

DISCUSSION

In order to compare the safety and effectiveness of topical 1% methotrexate gel to methotrexate iontophoresis in patients with palmoplantar psoriasis, a randomized controlled clinical study was conducted. The study evaluated 120 participants who were split into two groups of 60 at random. Group I participants received 1% topical methotrexate gel twice a day, every day of the week, for eight weeks.

Group II subjects were given methotrexate iontophoresis once a week for 4 weeks and then every two weeks. There were six sessions of iontophoresis. The distribution of research participants' ages and genders was statistically comparable ($p<0.05$). In 13% of study participants, nail involvement manifested as subungual hyperkeratosis and nail pitting. Groups I and II experienced mean durations of 10.3 and 12.7 months from the time of illness start, respectively.

It was seen that on assessing and comparing the presence of erythema in two study groups following the treatment, it was seen that at 8th week, erythema was not seen in lesions of 66.7% (n=40) subjects from Group I and Mild erythema was seen in 33.3% (n=20) subjects in Group I, whereas, in Group II, no erythema was seen in 96.7% (n=58) subjects and mild erythema in 3.3% (n=2) subjects respectively. Significantly higher erythema was seen in Group I using 1% gel compared to Group II with methotrexate iontophoresis with p=0.005. These results were consistent with the findings of Kumar B et al[7] in 2002 and Haseena K et al[8] in 2017 where similar to the present study.

The study results showed that concerning the presence of scaling in two study groups following the treatment, it was seen that at the 8th week, no, mild, and moderate scaling was seen in 56.7% (n=34), 40% (n=24), and 3.33% (n=2) subjects respectively from Group I, whereas, none, mild, and moderate scaling was seen in 90% (n=54), 10% (n=6), and 0 study subjects respectively. Scaling was significantly higher in lesions from Group I using 1% gel compared to Group II with methotrexate iontophoresis with p=0.01. These findings were in agreement with the previous results of Mehta TK et al[9] in 1976 and Lal S

et al[10] in 1966 where authors suggested similar results with higher scaling in topical methotrexate psoriasis subjects compared to methotrexate iontophoresis.

It was also seen that for assessment of fissuring in two study groups following the treatment, it was seen that at the 8th week, none and mild fissuring was seen in 20% (n=12) and 80% (n=48) study subjects respectively from Group I using 1% gel compared to none and mild fissuring in 80% (n=48) and 20% (n=12) subjects respectively from Group II using iontophoresis. The presence of fissuring was significantly higher in subjects from Group I compared to Group II with p=0.0004. These results correlated to the findings of the previous studies of Kumar B et al[11] in 2004 and Kalia YN et al[12] in 2004 where similar to the present study.

Concerning the assessment of the overall improvement percentage comparison in two groups of study subjects, the mean overall improvement was 82.2±15.2 in Group I subjects using 1% methotrexate gel compared to 95.1±7.8 in Group II subjects that underwent methotrexate iontophoresis. Mean overall improvement was significantly higher in the methotrexate iontophoresis group compared to the 1% methotrexate gel group with p=0.0004. These findings were similar to the results reported by Law JH et al[13] in 2008 and Andanooru Chandrappa NK et al[14] in 2020 where overall better improvement was reported with methotrexate iontophoresis compared to topical methotrexate in subjects with psoriasis.

CONCLUSION

The current study reveals that, after 8 weeks of therapy, participants receiving methotrexate iontophoresis for palmoplantar psoriasis show significantly higher clearance rates and improvements than those receiving 1% methotrexate gel. Highly significant clearance rates and improvement are seen in subjects undergoing methotrexate iontophoresis for palmoplantar psoriasis compared to 1% methotrexate gel on 8 weeks of treatment. However, further multi-institutional studies in the future assessing subjects for longer duration and including a larger number of participants might further help in better clarity of the topic.

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TABLES

S. No	Erythema	Gel		Iontophoresis		Total		p-value
		n	%	n	%	n	%	
1.	8th week							0.005
a)	None	40	66.7	58	96.7	98	81.7	
b)	Mild	20	33.3	2	3.3	22	18.3	
2.	Total	60	100	60	100	120	100	

Table 1: Comparison of erythema in two groups of study subjects at 8th week

S. No	Scaling	Gel		Iontophoresis		Total		p-value
		n	%	n	%	n	%	
1.	8th week							0.01
a)	None	34	56.7	54	90	88	73.3	
b)	Mild	24	40	6	10	30	25	
c)	Moderate	2	3.33	0	0	2	1.7	
2.	Total	60	100	60	100	120	100	

Table 2: Comparison of scaling in two groups of study subjects in 8th week

S. No	Fissuring	Gel		Iontophoresis		Total		p-value
		n	%	n	%	n	%	
1.	8th week							0.0004
a)	None	12	20	48	80	60	50	
b)	Mild	48	80	12	20	60	50	
2.	Total	60	100	60	100	120	100	

Table 3: Comparison of scaling in two groups of study subjects in the 8th week

S. No	Variables and Groups	Number (n)	Mean ± S. D	p-value
1.	Overall improvement			
a)	Gel	60	82.2±15.2	0.0004
b)	Iontophoresis	60	95.1±7.8	

Table 4: Overall improvement percentage comparison in two groups of study subjects