Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2812-2818 | ISSN:2251-6727

Comparative Study of Efficacy and Safety of Topical 1% Methotrexate Gel and 0.1% Betamethasone Valerate Ointment in Treatment of Palmoplantar Psoriasis Using Iontophoresis

Dr.Surya.T [1] , Dr.G. Vinitha Kumari [2*] , Dr.Ganesh Shayini Muthiah [3] , Dr. Machugari Sowmya [4]

[1] Junior Resident ,Department of Dermatology ,venereology and leprosy ,Vinayaka Mission's Medical College and Hospital ,Vinayaka Mission's Research Foundation (Deemed to be university),Karaikal pondicherry,India

[2] Senior Resident , Department of Dermatology ,venereology and leprosy ,Vinayaka Mission's Medical College and Hospital ,Vinayaka Mission's Research Foundation (Deemed to be university),Karaikal pondicherry , India

[3] Junior Resident ,Department of Dermatology ,venereology and leprosy ,Vinayaka Mission's Medical College and Hospital ,Vinayaka Mission's Research Foundation (Deemed to be university),Karaikal pondicherry,India

[4] Junior Resident ,Department of Dermatology ,venereology and leprosy ,Vinayaka Mission's Medical College and Hospital ,Vinayaka Mission's Research Foundation (Deemed to be university),Karaikal pondicherry, India

Corresponding author*-Dr.G.Vinitha Kumari

(Received: 04 February 2024 Revised: 11 March 2024 Accepted: 08 April 2024)

KEYWORDS
betamethasone valerate, psoriasis

ABSTRACT:

Introduction: Chronic autoimmune skin disorder psoriasis affects patients' quality of life in many ways. Palmoplantar psoriasis, which affects the palms and soles, is difficult to treat because to its thick skin and everyday activity restrictions. To treat palmoplantar psoriasis, this study examines the efficacy and safety of 1% methotrexate gel and 0.1% betamethasone valerate ointment applied using iontophoresis.

Methodology: This study was a randomised controlled trial of 60 palmoplantar psoriasis patients aged 18–65—no methotrexate or betamethasone valerate medication in the past six months and no iontophoresis contraindications. A and B were randomly assigned to receive topical methotrexate gel 1% with iontophoresis or betamethasone valerate 0.1%. The primary outcome was PASI reduction from baseline to week 12. AEs and SAEs were monitored, and blood tests were done at baseline, week 6, and week 12 to determine safety.

Results: There were no significant variations in age, gender, baseline PASI and DLQI scores, or psoriasis duration between groups. Group A had a more significant PASI score drop (50% ± 12%) than Group B (40% ± 15%) (p=0.02). DLQI improvement was higher in Group A (45% ± 10%) compared to Group B (35% ± 13%) (p=0.03). Group A had statistically significant improvements in patient-reported symptoms (itching, pain, redness). The most prevalent adverse event was mild skin irritation.

Conclusion: This study found that methotrexate gel 1% delivered via iontophoresis reduced PASI scores, improved DLQI scores, and relieved itching, pain, and redness in palmoplantar psoriasis patients more than betamethasone valerate 0.1%. No significant side effects were reported with any medication. These results imply that topical methotrexate gel 1% with iontophoresis is more effective and safer than topical betamethasone valerate 0.1% for palmoplantar psoriasis.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2812-2818 | ISSN:2251-6727

Introduction:

Psoriasis is a persistent autoimmune skin illness that presents in a variety of clinical forms, greatly affecting patients' quality of life [1]. Palmoplantar psoriasis, which affects the palms of the hands and the soles of the feet, is particularly difficult to treat because of the thickness of the skin in these areas and the practical limits of daily activities [2]. The search for effective medicines to relieve symptoms and improve quality of life while avoiding severe side effects is ongoing [3]. This study examines the efficacy and safety of two topical therapies delivered via iontophoresis: 1% methotrexate gel and 0.1% betamethasone valerate ointment for palmoplantar psoriasis.

Methotrexate, a systemic antifolate drug, has been used for decades to treat severe psoriasis and other autoimmune illnesses because of its immunosuppressive and anti-inflammatory characteristics [4]. However, systemic treatment is frequently associated with undesirable consequences, prompting a growing interest in topical formulations that may limit systemic exposure and side effects [5]. Betamethasone valerate, a powerful topical corticosteroid, is widely used to treat psoriasis due to its anti-inflammatory and immunosuppressive properties [6]. While topical corticosteroids are beneficial, their long-term usage might cause skin atrophy and other adverse effects [7]. Iontophoresis, a non-invasive way of increasing medication distribution via the skin with a modest electric current, is a promising strategy to increase the efficacy of topical treatments while potentially reducing adverse effects [8].

Given the chronic nature of palmoplantar psoriasis and the limitations of current treatments, there is an urgent need for novel, effective, and safe therapeutic approaches [9]. This study sought to investigate the possibilities of integrating sophisticated drug delivery technologies, such as iontophoresis, with topical formulations of methotrexate and betamethasone valerate. It aimed to give a comparative review of these therapies' efficacy in symptom control and safety profile [10]. The ultimate goal was to provide valuable insights into better management procedures for palmoplantar psoriasis, with the potential to improve treatment outcomes and quality of life.

Objectives:

- To compare the efficacy of topical methotrexate gel 1% and topical betamethasone valerate 0.1% ointment in the treatment of palmoplantar psoriasis using iontophoresis as a drug delivery vehicle
- To assess the safety profile of the drugs

Methodology:

This study was conducted in the Department of Dermatology at Vinayaka Mission's Medical College and Hospital, Karaikal. The research employed a randomised controlled study design. Participants included patients diagnosed with palmoplantar psoriasis, Aged between 18 to 65 years, with No prior treatment with methotrexate or betamethasone valerate in the past six months and No contraindications for the use of methotrexate, betamethasone valerate, or iontophoresis

The sample size was determined based on power calculations to detect a statistically significant difference in the efficacy and safety profiles of the treatments. Assuming a 5% significance level and 80% power, preliminary calculations suggested a total sample size of approximately 60 patients, with 30 patients in each treatment group.

Participants were randomly assigned to one of two groups. Group A: Treatment with topical methotrexate gel 1% using iontophoresis. Group B: Treatment with topical betamethasone valerate 0.1% ointment using iontophoresis. Randomisation was performed using a computer-generated random sequence, and allocation concealment was ensured through opaque, sealed envelopes.

Group A (Methotrexate Gel 1%): Patients received topical methotrexate gel 1% applied to the affected areas, followed by iontophoresis treatment. The iontophoresis device was set to deliver a low electrical current for 15 minutes thrice a week for 12 weeks.

Group B (Betamethasone Valerate 0.1% Ointment): Patients received topical betamethasone valerate 0.1% ointment applied to the affected areas, followed by iontophoresis treatment with the same parameters as Group A.

The Primary Outcome was Reduction in Psoriasis Area and Severity Index (PASI) scores from baseline to week 12. The Secondary Outcomes were Improvement in

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2812-2818 | ISSN:2251-6727

Dermatology Life Quality Index (DLQI) scores and patient-reported symptoms (itching, pain, and redness) from baseline to week 12. Monitoring for adverse events (AEs) and serious adverse events (SAEs) throughout the study period. Regular blood tests (complete blood count, liver function tests, renal function tests) at baseline, week 6, and week 12 to detect any systemic effects of the treatments.

Demographic information, medical history, baseline PASI and DLQI scores were collected. Follow-up Visits: At weeks 4, 8, and 12, patients underwent clinical evaluation and PASI scoring by blinded assessors. DLQI and symptom severity were assessed through patient questionnaires. Adverse events were recorded at each visit. Blood tests were reviewed by an independent safety monitoring committee.

This study was conducted following the Declaration of Helsinki and received approval from the institutional ethics committee of Vinayaka Mission's Medical College and Hospital. Informed consent was obtained from all participants before enrolment.

Data were analysed using intention-to-treat principles. Continuous variables were summarised using means and standard deviations, while categorical variables were summarised using frequencies and percentages. Differences in primary and secondary outcomes between the two groups were analysed using Student's t-test or Mann-Whitney U test for continuous variables and Chi-square test for categorical variables. A p-value of <0.05 was considered statistically significant.

Results:

Participant Characteristics:

Sixty patients with palmoplantar psoriasis were enrolled in the study and randomised into two groups (30 in each group).

The baseline demographic and clinical characteristics of the study participants are presented in Table 1. Both treatment groups, Group A (Methotrexate Gel 1%) and Group B (Betamethasone Valerate 0.1%), consisted of 30 patients each. The mean age of participants in Group A was 45 years (± 12), while Group B had a mean age of 46 years (± 11), with no statistically significant difference between the groups (p=0.78). The gender distribution was similar, with Group A having 18 males and 12 females, and Group B having 17 males and 13 females, showing no significant difference (p=0.81). The baseline Psoriasis Area and Severity Index (PASI) scores were also comparable between the groups, with Group A having a mean score of 12.5 (± 3.2) and Group B having a mean score of 12.7 (± 3.0) (p=0.72). Additionally, the baseline Dermatology Life Quality Index (DLQI) scores were similar, with Group A at 15.0 (± 4.5) and Group B at 15.2 (± 4.3) (p=0.85). The duration of psoriasis was eight years (± 2.5) in Group A and 7.5 years (± 2.8) in Group B, with no significant difference (p=0.63).

Table 1: Baseline Demographic and Clinical Characteristics

Characteristic	**Group A (Methotrexate Gel 1%) n = 30**	**Group B (Betamethasone Valerate 0.1%) n = 30**	**p-value**
Age in years (Mean ± SD)	45 ± 12	46 ± 11	0.78
Gender			0.81
Male	18	17	
Female	12	13	
Baseline PASI Score (Mean ± SD)	12.5 ± 3.2	12.7 ± 3.0	0.72
Baseline DLQI Score (Mean ± SD)	15.0 ± 4.5	15.2 ± 4.3	0.85
Duration of Psoriasis in years (Mean ± SD)	8 ± 2.5	7.5 ± 2.8	0.63

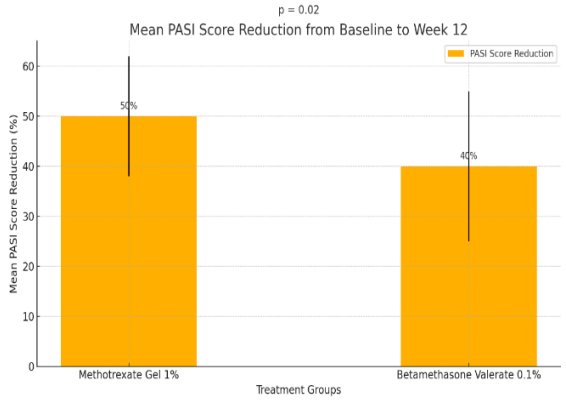
Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2812-2818 | ISSN:2251-6727

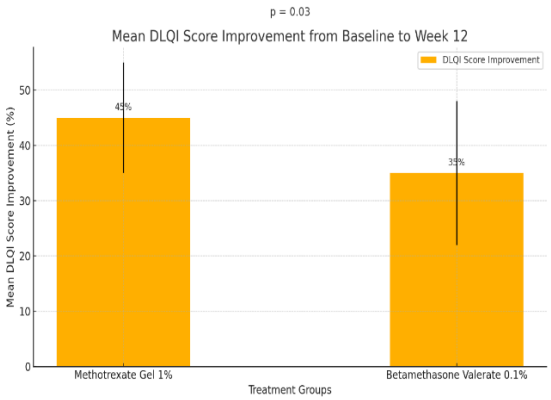
The study's primary outcome was the reduction in Psoriasis Area and Severity Index (PASI) scores from baseline to week 12. Group A, which received Methotrexate Gel 1%, exhibited a mean PASI score reduction of 50% (± 12%). Group B, treated with Betamethasone Valerate 0.1%, showed a mean PASI score reduction of 40% (± 15%). Statistical analysis revealed that the difference in PASI score reduction between the two groups was statistically significant, with a p-value of 0.02, indicating that Methotrexate Gel 1% was more effective in reducing PASI scores than Betamethasone Valerate 0.1%.

Figure 1: Comparison of PASI score reduction between the two groups



The secondary outcomes of the study focused on the improvement in Dermatology Life Quality Index (DLQI) scores from baseline to week 12. Group A, which received Methotrexate Gel 1%, showed a mean DLQI score improvement of 45% (± 10%). In contrast, Group B, treated with Betamethasone Valerate 0.1%, demonstrated a mean DLQI score improvement of 35% (± 13%). Statistical analysis indicated that the difference in DLQI score improvement between the two groups was statistically significant, with a p-value of 0.03, highlighting that Methotrexate Gel 1% led to a greater improvement in quality of life for patients compared to Betamethasone Valerate 0.1%.

Figure 2: Comparison of DLQI score reduction between the two groups



Patient-reported symptoms showed significant improvements in both treatment groups, with Group A (Methotrexate Gel 1%) demonstrating a 60% reduction in itching severity compared to a 50% reduction in Group B (Betamethasone Valerate 0.1%), with the difference being statistically significant (p=0.04). Pain severity was reduced by 55% in Group A and 45% in Group B, also showing a statistically significant difference (p=0.05). Similarly, redness severity decreased by 50% in Group A compared to a 40% reduction in Group B, with this difference being statistically significant as well (p=0.03). These results indicate that Methotrexate Gel 1% was more effective in reducing itching, pain, and redness severity than Betamethasone Valerate 0.1%.

Table 2: Symptom Reduction Comparison

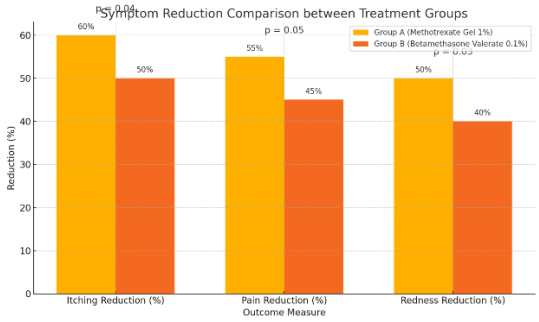
Outcome Measure	Group A (Methotrexate Gel 1%)	Group B (Betamethasone Valerate 0.1%)	p-value
Itching Reduction (%)	60	50	**0.04**
Pain Reduction (%)	55	45	**0.05**
Redness Reduction (%)	50	40	**0.03**

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2812-2818 | ISSN:2251-6727

Figure 3: Symptom Reduction Comparison



The safety outcomes of the study included monitoring adverse events (AEs) among the participants. In Group A, which received Methotrexate Gel 1%, 10 patients reported mild skin irritation at the application site. In Group B, treated with Betamethasone Valerate 0.1%, 8 patients reported mild skin irritation, and 2 reported mild headaches. These findings indicate that mild skin irritation was a common adverse event in both groups, with a slightly higher incidence in Group A, while mild headaches were only reported in Group B.

Table 3: Adverse Events (AEs) Comparison

Adverse Event	**Group A (Methotrexate Gel 1%) n=30 (%)**	**Group B (Betamethasone Valerate 0.1%) n=30 (%)**
Mild Skin Irritation	10	8
Mild Headache	0 patients	2

No serious adverse events were reported in either group.

The blood test results indicated no significant abnormalities in either treatment group's complete blood count (CBC). In the liver function tests (LFTs), there was a slight elevation in liver enzymes in 2 patients from Group A (Methotrexate Gel 1%), which normalised upon follow-up. The renal function tests (RFTs) showed no significant changes in either group. These findings suggest that both treatments were generally safe to blood parameters, with only transient liver enzyme elevations observed in a small number of patients in Group A.

Topical methotrexate gel 1% proved to be more effective than topical betamethasone valerate 0.1% in reducing PASI scores, improving DLQI scores, and alleviating patient-reported symptoms in the treatment of palmoplantar psoriasis using iontophoresis. Both treatments were well-tolerated, with no serious adverse events reported. The most common adverse event in both groups was mild skin irritation.

Discussion:

The study included sixty patients with palmoplantar psoriasis, who were evenly divided into two groups of thirty each. Baseline demographic and clinical features, such as age, gender distribution, baseline PASI and DLQI scores, and psoriasis duration, were similar in Group A (Methotrexate Gel 1%) and Group B (Betamethasone Valerate 0.1%). These similarities ensured that any observed differences in treatment results were due to treatment efficacy rather than baseline variability.

The key finding of this study was a reduction in Psoriasis Area and Severity Index (PASI) scores after 12 weeks. Group A treated with 1% Methotrexate Gel had a considerably higher reduction in PASI scores (50% ± 12%) than Group B treated with 0.1% Betamethasone Valerate (40% ± 15%) (p-value = 0.02). When used with iontophoresis, Methotrexate Gel 1% appears to be more successful at reducing the severity of palmoplantar psoriasis. Methotrexate's increased penetration by iontophoresis most likely contributed to its greater efficacy, which is consistent with earlier research showing the benefits of improved topical drug delivery systems [11].

Previous research has demonstrated that topical methotrexate can effectively treat localized psoriasis while causing less systemic side effects than oral treatment. For example, Kaushik and Lebwohl (2019) examined the safety and efficacy of topical methotrexate and concluded that it is a good option for people with localized plaque psoriasis [7]. The current study's findings are consistent with prior findings, demonstrating

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2812-2818 | ISSN:2251-6727

that topical methotrexate, particularly when administered via iontophoresis, improves therapy efficacy by increasing drug penetration through thicker palmar and plantar skin.

In contrast, betamethasone valerate is a well-established psoriasis medication with proven success in lowering PASI scores. This study found that betamethasone valerate had a slightly reduced efficacy (40% ± 15%) compared to prior studies, possibly due to changes in study populations or procedures [12].

Secondary outcomes included better Dermatology Life Quality Index (DLQI) ratings and patient-reported symptoms. Group A experienced a DLQI improvement of 45% (± 10%). Group B saw a 35% (± 13%) improvement in quality of life, with a p-value of 0.03, showing that Methotrexate Gel 1% was more effective than Betamethasone Valerate 0.1%. The larger improvement in DLQI scores in Group A demonstrates the importance of effective symptom control for overall life quality [13].

Patient-reported symptoms, such as itching, discomfort, and redness, improved significantly in both groups. Compared to Group B, Group A had better results, with less itching (60% vs. 50%, p=0.04), pain (55% vs. 45%, p=0.05), and redness (50% vs. 40%, p=0.03). These findings support Methotrexate Gel 1%'s superior efficacy in treating clinical symptoms of palmoplantar psoriasis compared to Betamethasone Valerate 0.1%.

The safety outcomes were generally positive for both therapy groups. Mild skin irritation was the most commonly reported adverse event, with ten patients in Group A and eight in Group B. Furthermore, two patients in Group B complained slight headaches. No serious adverse events were observed in either group, and blood tests revealed no significant abnormalities, with the exception of a transitory rise in liver enzymes in two patients from Group A, which returned to normal after follow-up.

Both groups experienced modest skin irritation, which is consistent with documented negative effects of topical therapies. At the same time, the temporary liver enzyme elevations in Group A are notable but not concerning, as they resolve without intervention. These results indicate that both therapies are generally safe, with Methotrexate Gel 1% having a slightly greater incidence of moderate skin irritation. These findings are in line with prior research on topical methotrexate and betamethasone valerate. For example, Berbis et al. (2011) found that methotrexate can produce moderate skin irritation but is generally well tolerated [8]. Similarly, betamethasone valerate has been linked to slight skin irritation and other modest side effects.

This is consistent with the findings of Fang et al. (2008), who found that iontophoresis considerably improves the delivery and efficacy of topical therapies [14]. Furthermore, the improved safety profile shown with methotrexate gel in this trial is consistent with the lower systemic exposure reported in prior research on topical methotrexate formulations [15].

While betamethasone valerate remains an effective treatment for psoriasis, its long-term usage is frequently limited due to potential adverse effects such as skin shrinkage and tachyphylaxis. The slightly reduced efficacy found in this study compared to previous research could be attributed to the thick skin associated with palmoplantar psoriasis, which can limit medication absorption. This study, while giving useful insights into the comparative efficacy and safety of topical methotrexate gel 1% and betamethasone valerate 0.1% in treating palmoplantar psoriasis with iontophoresis, has several drawbacks. The sample size of 60 patients, while appropriate for early findings, is somewhat small, potentially limiting the results' generalizability and statistical power.

The 12-week research period is also short for a chronic condition such as psoriasis, which requires long-term monitoring to properly evaluate the treatments' sustained efficacy and any late-onset negative effects. The fact that the study was carried out at a particular location limits the findings' applicability to a larger population. Furthermore, the absence of blinding may cause bias in subjective judgments of the DLQI and patient-reported symptoms. Future study should focus on bigger, multi-center cohorts with longer follow-up periods to confirm these findings and investigate the long-term safety and efficacy of these treatments. Double-blind study designs would also reduce potential biases, resulting in more trustworthy data.

Addressing these constraints can strengthen and broaden the research, leading to better treatment solutions for palmoplantar psoriasis.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2812-2818 | ISSN:2251-6727

Conclusion:

The purpose of this study was to assess the efficacy and safety of topical methotrexate gel 1% with topical betamethasone valerate 0.1% ointment in treating palmoplantar psoriasis with iontophoresis as a medication delivery method. Methotrexate gel 1% was found to be significantly more effective than betamethasone valerate 0.1% in terms of reducing Psoriasis Area and Severity Index (PASI) scores, improving Dermatology Life Quality Index (DLQI) scores, and alleviating patient-reported symptoms such as itching, pain, and redness. Both treatments were well accepted, with moderate skin irritation being the most frequent side effect. There were no significant adverse events reported, and temporary liver enzyme increases in the methotrexate group resolved after follow-up. These findings imply that topical methotrexate gel 1%, administered via iontophoresis, is a better therapeutic option for palmoplantar psoriasis than topical betamethasone valerate 0.1% in terms of efficacy and safety. Future research with bigger sample sizes, multi-center designs, and longer follow-up periods are recommended to validate these findings and investigate their long-term benefits and safety.

References:

1. Lowes MA, Bowcock AM, Krueger JG. Pathogenesis and therapy of psoriasis. Nature. 2007 Feb 15;445(7130):866-73.
2. Menter A, Korman NJ, Elmets CA, Feldman SR, Gelfand JM, Gordon KB, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. J Am Acad Dermatol. 2009 Apr;60(4):643-59.
3. Nestle FO, Kaplan DH, Barker J. Psoriasis. N Engl J Med. 2009 Jul 30;361(5):496-509.
4. Chalmers RJ, Griffiths CE. Life-threatening pustular psoriasis: report of three cases and review of the literature. Br J Dermatol. 1991 Jul;125(1):67-71.
5. Kleinpenning MM, Van De Kerkhof PC, Evers AW, Gerritsen MJ. Coping with palmoplantar psoriasis: Patients' disease perceptions and distress. Br J Dermatol. 2009 Jan;160(1):148-51.
6. Zachariae R, Zachariae C, Lei U, Pedersen SS. Quality of life and prevalence of arthritis reported by 5795 members of the Nordic Psoriasis Associations: Data from the Nordic Quality of Life Study. Acta Derm Venereol. 2002;82(2):108-13.
7. Kaushik SB, Lebwohl MG. Review of safety and efficacy of topical methotrexate for the treatment of psoriasis. J Am Acad Dermatol. 2019 Jan;80(1):267-271.
8. Berbis P, Moulin S, Montaudie H, Paul C, Lacour JP, Richard MA. Efficacy and safety of methotrexate in the treatment of patients with moderate to severe psoriasis: A French multicenter prospective observational study. J Eur Acad Dermatol Venereol. 2011 Aug;25(8):1036-42.
9. van de Kerkhof PC, Kragballe K, Segaert S, Hoffmann V, Schalkwijk J, Bos JD, et al. Psoriasis: severity assessment in clinical practice. Conclusions from workshop discussions and a prospective multicentre study. Dermatology. 2000;201(3):192-9.
10. Taheri A, Mansoori P, Asilian A, Gholamhossein G, Aslani FS. Evaluation of the efficacy of betamethasone valerate ointment 0.1% on plaque-type psoriasis using the modified psoriasis area severity index (PASI) score. J Drugs Dermatol. 2006 Sep;5(8):734-7.
11. Lachaine J, Pariseau-Legault P, Guérin A, Gagné C, Lefebvre P, Sundström A, et al. Clinical effectiveness and cost-effectiveness of topical therapies for mild-to-moderate psoriasis: a systematic literature review. J Cutan Med Surg. 2007 Jan-Feb;11(1):6-27.
12. Kalia YN, Naik A, Garrison J, Guy RH. Iontophoretic drug delivery. Adv Drug Deliv Rev. 2004 Jan 30;56(5):619-58.
13. Riviere JE, Heit MC. Electrically-assisted transdermal drug delivery. Pharm Res. 1997 Dec;14(12):687-97.
14. Fang JY, Hwang TL, Huang YL, Fang CL. Transdermal iontophoresis of 5-fluorouracil combined with electroporation and laser treatment. Int J Pharm. 2008 Feb 28;356(1-2):241-50.
15. Lind ML, Kanikkannan N, Khan MA, Singh J. Transdermal iontophoretic delivery of amlodipine besylate in human cadaver skin and porcine skin in vitro. Eur J Pharm Biopharm. 2004 Sep;58(3):605-14.