Efficacy of Healing Ointment Containing Petrolatum and Anti-Inflammatory Ingredients in the Treatment of Mild-to-Moderate Chronic Hand Eczema

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Abstract

Chronic hand eczema is a common skin disease in Thailand. Due to its frequent relapse, long-term application of topical corticosteroid as a conventional therapy results in numerous adverse effects. In this study, the efficacy of healing ointment containing petrolatum and anti-inflammatory ingredients in the treatment of mild-to-moderate chronic hand eczema is determined by various parameters for assessment of disease severity, skin moisture, and also the quality of life of the patients. Intervention in this study is applying the healing ointment on the affected area of the hand twice daily for twenty-eight days. This study uses hand eczema severity index (HECSI), trans-epidermal water loss (TEWL), stratum corneum hydration (SCH), hemoglobin index from special 3D camera, dermatology life quality index (DLQI) and visual analogue scale for the intensity of itching (VAS) as the assessment tools at baseline and two as well as four weeks after treatment. The study results show that this healing ointment yields a significant improvement in HECSI, TEWL, SCH, hemoglobin index, DLQI, and VAS compared with baseline. No adverse events have been reported after a 4-week treatment with this ointment.

Keywords: *Bisabolol, Hand dermatitis, Hand eczema, Healing ointment, Moisturizer, Petrolatum*

1. Introduction

Chronic hand eczema is an important and common occupation-related dermatologic disease in many developing countries, including Thailand. This disease usually has a very prolonged course with frequent relapse (Lodén et al., 2010). It is proposed that this disease was mainly mediated by the inflammatory process; therefore, topical corticosteroids are usually considered as the first-line treatment (English et al., 2009). This treatment modality yielded the desirable outcomes; however, long-term application of topical corticosteroids, especially high-potency preparations, may induce numerous adverse events. Reported side effects included skin atrophy, telangiectasia, striae and also hypothalamic-pituitary axis suppression (Coondoo et al., 2014). Several studies had been done to identify the novel treatment modalities for chronic hand eczema which have good efficacy and less adverse effects. However, there is only a small number of well-designed studies about this treatment.

Impaired skin barrier function had been proposed to be an important risk factor for the development and relapsing of both allergic and irritant contact dermatitis of the hands (Fölster-Holst, Jensen, and Proksch, 2006). When the skin barrier has been damaged, the repairing process can occur only if the loss of moisture is retarded. Hence, a moisturizer plays an important role in a variety of dermatologic diseases which are aggravated by dryness, including chronic hand eczema (Purnamawati et al., 2017).

Generally, moisturizing ingredients can be classified into three main groups including occlusive, humectant and emollient ingredients. A healing ointment containing petrolatum and anti-inflammatory ingredients composes of three main groups of moisturizing ingredients. The main ingredients of this healing ointment include petrolatum (occlusive), panthenol as well as glycerin (humectant), and lanolin alcohol (emollient). Moreover, this healing ointment contains anti-inflammatory ingredients including bisabolol and panthenol. Previous studies showed that this healing ointment had been shown to provide a significant improvement after skin damaged by laser resurfacing on the face and forearm area (Rizer, Trookman, and Weber, 2011; Sarnoff, 2011). For these reasons, the application of this healing ointment should be an effective

treatment for chronic hand eczema. Consequently, this study is designed to demonstrate the efficacy and safety of this healing ointment in the treatment of mild-to-moderate chronic hand eczema.

2. Objectives

1. To determine the efficacy of healing ointment containing petrolatum and anti-inflammatory ingredients by applying twice daily for 28 days in the treatment of mild-to-moderate chronic hand eczema in term of anti-inflammatory effect determined by HECSI
2. To determine the efficacy of healing ointment containing petrolatum and anti-inflammatory ingredients by applying twice daily for 28 days in the treatment of mild-to-moderate chronic hand eczema in term of trans-epidermal water loss (TEWL), stratum corneum hydration (SCH), hemoglobin index from special 3D camera, dermatology life quality index (DLQI) and visual analogue scale for the intensity of itching (VAS)
3. To study the adverse effects of healing ointment containing petrolatum and anti-inflammatory ingredients after twice-daily application for 4 weeks

3. Materials and Methods

3.1 Patients: Twenty-six patients with hand eczema for longer than three months or more than two times recurrence per year and aged between 18 to 60 years were enrolled in this prospective, interventional study. Given verbal and written information, all patients signed the inform consent forms before enrollment. Exclusion criteria were patients who were pregnant or lactating, known allergy to ingredients of study products, treated with systemic immunosuppressive drugs, systemic corticosteroids as well as phototherapy on hands within the preceding 4 weeks, treated with topical corticosteroid, calcineurin inhibitors, or any topical products on the hands within the preceding 2 weeks, and those with psoriasis, pustular disease or skin infection of the involved skin areas.

3.2 Intervention: All patients were assigned to apply healing ointment containing petrolatum and anti-inflammatory ingredients twice daily on the hands. Other topical products on the involved skin area were prohibited during the study.

3.3 Evaluation: All patients were evaluated on the baseline (before active treatment, day 0) and additional 2 follow-up visits including day 14, and day 28. The assessment included questionnaires about quality of life (dermatology quality of life index: DLQI), 10-cm visual analogue scale (VAS) for the intensity of itch, hand examination by a dermatologist (hand eczema severity index: HECSI), evaluation of skin moisture in the term of Trans-epidermal water loss (TEWL) by Tewameter TM 300 (Courage + Khazaka electronic GmbH, Germany) as well as stratum corneum hydration (SCH) by Corneometer® CM 825 (Courage + Khazaka electronic GmbH, Germany), and evaluation of skin erythema in the term of hemoglobin index by Antera 3D® (Miravex Limited, Ireland). Before the evaluation of skin moisture, all patients were stayed in the controlled room (the temperature at 20-22 degrees Celsius and humidity 40-60%) for at least 20 minutes. All patients were marked in the areas which had the most disease severity on the hand by a plastic wrap to define the measurement site for all additional follow-up visits.

4. Results and Discussion

4.1 Results

Demographic data

Twenty-six patients (23 females, and 3 males) with the mean ± SD age of 50.04 ± 9.63 years (range from 27 to 60 years) were enrolled and completed the study. Occupations of the patients in this study included healthcare providers (23.1%), office clerks (23.1%), maids (15.4%), food providers (15.4%), factory labors (11.5%) and housewives (11.5%). For clinical subtypes, patients were hyperkeratotic (84.6%), interdigital (7.7%) and recurrent vesicular (7.7%). 84.6% and 15.4% of patients in this study were mild and moderate severity according to physician global assessment (PGA) at the beginning of this study.

Adverse effects:

Four (15.40%) of twenty-six patients reported stickiness and heaviness feelings from the healing ointment at the first follow-up visit. After the first follow-up visit, there was no reported of these feelings. Erythema, tenderness, pruritus or other complaints were not reported by the patients.

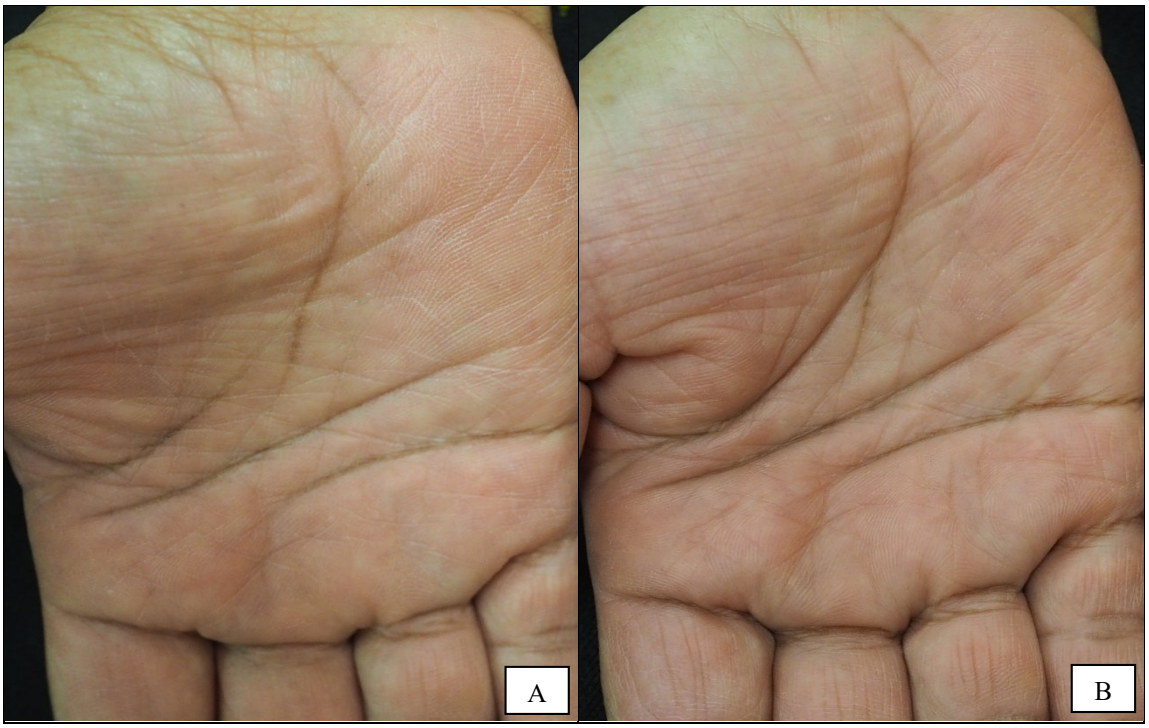

Figure 1 A photograph of the hand area after treatment with the healing ointmentat baseline (A), and 4th week (B)

Table 1 Demographic data from the patients in this study

Variable	Number	Percentages
Frequency of hand washing		
1-3 times/day	2	7.7
4-6 times/day	8	30.8
7-9 times/day	6	23.1
More than 9 times/day	10	38.5
Frequency of wet work activity (times per week)		
1-3 times/week	5	19.2
4-6 times/week	4	15.4
7-9 times/week	3	11.5
More than 9 times/week	14	53.8
Symptoms (Each patient can choose more than one symptoms)		
Itchy	7	26.9
Scaling	18	69.2
Erosion/burning sensation	5	19.2
Cosmetic concern	11	42.3
Previous treatment		
Topical corticosteroid with emollient	4	15.4
Emollient	10	38.5
No prior treatment	12	46.1

Table 2 Improvement of parameters from subjective evaluation after 2 and 4 weeks of treatment with this healing ointment compared with baseline; [a] Repeated ANOVA test; * denotes a statistically significant difference which is defined as p-value < 0.05; HECSI: Hand eczema severity index, DLQI: Dermatology life quality index, VAS: Visual analogue scale for itchy

Measurement	HECSI	DLQI	VAS
Baseline ± SD	38.54 ± 16.34	2.15 ± 0.83	3.81 ± 1.6
2nd week ± SD	29.654 ± 19.31	1.58 ± 0.7	2.19 ± 1.44
4th week ± SD	9.65 ± 12.23	0.96 ± 0.45	1.08 ± 0.63
Compared at 2nd week with baseline			
Mean change (95%CI)	-8.88 (-12.34, -5.43)	-0.58 (-0.84, -0.32)	-1.62 (-1.9, -1.33)
Mean change (95%CI) as percentages	-23.04% (-32.02%, -14.09%)	-26.98% (-39.07%, -14.88%)	-42.52% (-49.87%, -34.91%)
p-value[a]	<0.001*	<0.001*	<0.001*
Compared at 4th week with baseline			
Mean change (95%CI)	-28.88 (-33.38, - 24.39)	-1.19 (-1.57, -0.81)	-2.73 (-3.18, -2.28)
Mean change (95%CI) as percentages	-74.94% (-86.61%, -63.28%)	-55.35% (-73.02%, -37.67%)	-71.65% (-83.46%, -59.84%)
p-value[a]	<0.001*	<0.001*	<0.001*

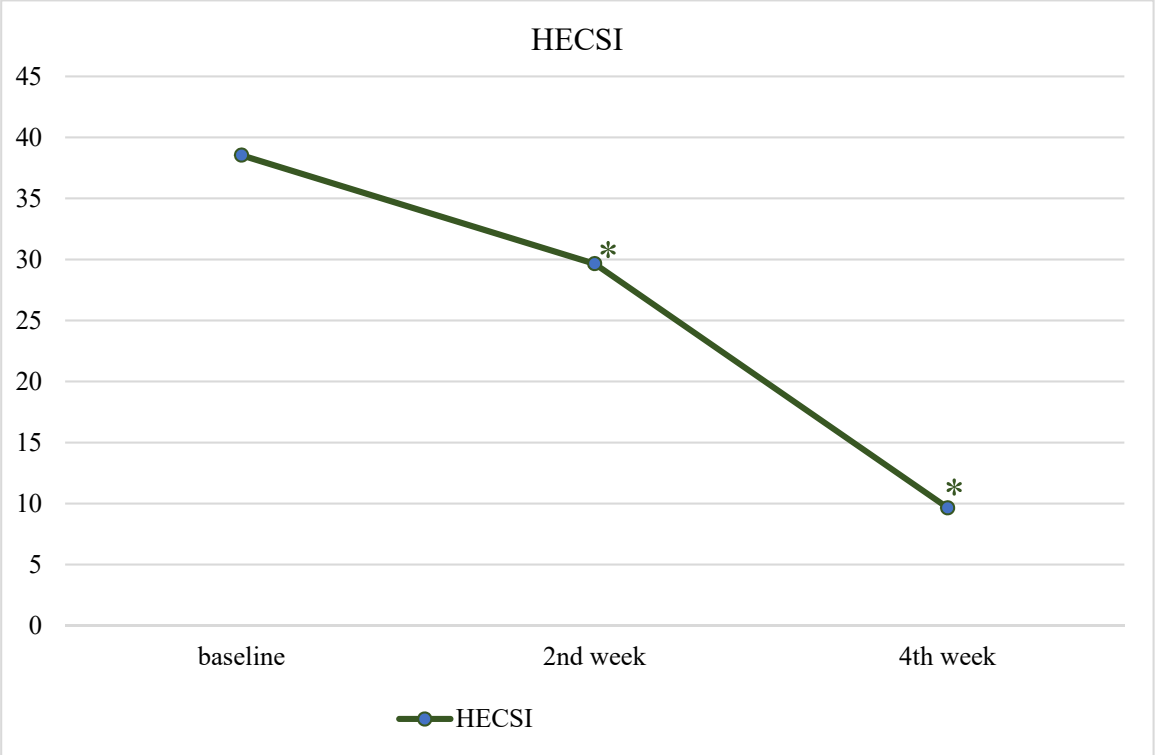

Figure 2 Hand eczema severity index (HECSI) at baseline, 2nd week, and 4th week
*denotes a statistically significant improvement when compared with baseline

Table 3 Improvement of parameters from objective evaluation after 2 and 4 weeks of treatment with this healing ointment compared with baseline; [a] Repeated ANOVA test; * denotes a statistically significant difference which is defined as p-value < 0.05; TEWL: Trans-epidermal water loss, SCH: Stratum corneum hydration

Measurement	TEWL	SCH	Hemoglobin index
Baseline ± SD	31.27 ± 7.07	22.53 ± 5.98	1.83 ± 0.26
2nd week ± SD	29.12 ± 9.47	22.78 ± 6.42	1.77 ± 0.24
4th week ± SD	24.19 ± 10.17	26.75 ± 8.12	1.71 ± 0.25
Compared at 2nd week with baseline			
Mean change (95%CI)	-2.15 (-5.64, 1.35)	0.25 (-0.88, 1.38)	-0.06 (-0.12, -0.01)
Mean change (95%CI) as percentages	-6.88% (-18.04%, 4.32%)	1.11% (-3.91%, 6.48%)	-3.28% (-6.56%, -0.55%)
p-value[a]	0.217	0.664	0.024*
Compared at 4th week with baseline			
Mean change (95%CI)	-7.08 (-11.14, -3.02)	4.22 (1.85, 6.59)	-0.13 (-0.18, -0.07)
Mean change (95%CI) as percentages	-22.64% (-35.63%, -9.66%)	18.73% (8.21%, 29.25%)	-7.10% (-9.84%, -3.83%)
p-value[a]	0.001*	0.001*	<0.001*

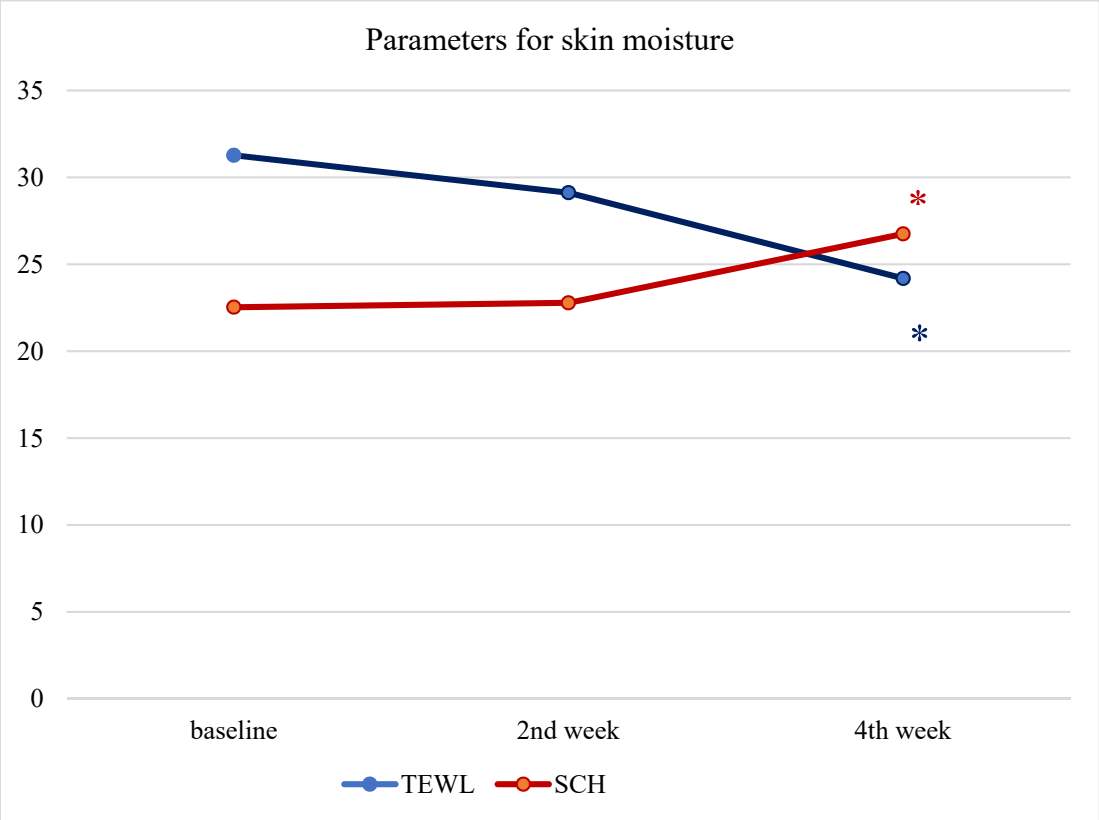

Figure 3 Parameters for skin moisture after treatment with the healing ointment
*denotes a statistically significant difference when compared with baseline
TEWL: trans-epidermal water loss, SCH: Stratum corneum hydration

4.2 Discussion

In our study, the experimental healing ointment containing petrolatum and anti-inflammatory ingredients provides the efficacy to improve chronic hand eczema demonstrated by a statistically significant improvement of HECSI, TEWL, SCH, DLQI, VAS, and hemoglobin index after 4 weeks application.

Previous studies conducted in patients with mild-to-moderate chronic hand eczema showed that 81.38% and 75.91% reduction of mean HECSI had been demonstrated after using a 4-week application of 0.1% betamethasone ointment and an 8-week application of 0.25% desoximetasone ointment, respectively (Agarwal & Besarwal, 2013; Juntongjin & Pongprasert, 2019). HECSI results from their studies were straightforwardly explained by the action of high potency topical corticosteroid for the reduction of skin inflammation. Compared with our study, the healing ointment showed a 74.94% reduction of mean HECSI compared with baseline after using a 4-week application. HECSI results from our study may be explained by three main mechanisms. Firstly, healing ointment improves the skin moisture resulting in the restoration of the natural skin barrier repair process. Secondly, a healing ointment containing bisabolol and panthenol, that can reduce skin inflammation by modulation of inflammatory cytokine (Jacob & Russell, 2010). Lastly, healing ointment can decrease the itchy by filling the defect gap in nerve ending resulting in decrease itch-scratch cycle.

For skin moisture, Varothai et al. (2018) showed that four commercially available hand moisturizers can significantly improve stratum corneum hydration of the hand after a 4-week application. However, their study had failed to show a significant improvement of trans-epidermal water loss from any products. Compared with our study, the healing ointment showed significant improvement of both TEWL and SCH after a 4-week application. Significant TEWL improvement from our study may be explained by the action of active ingredients, especially petrolatum. Elias, Ghadially & Halkier-Sorensen (1992) showed that a 5% petrolatum can reduce TEWL by more than 99%. Unsurprisingly, the healing ointment containing about 40% of petrolatum can reduce TEWL significantly from baseline. Significant SCH improvement from our study may be explained by the combination of three main groups of moisturizing ingredients. Moreover, panthenol is the key precursor for the biosynthesis of coenzyme A, which is the essential cofactor involved in fatty acid metabolism (Jackowski & Leonardi, 2007). Replenishment of lipid structure in stratum corneum is the main reason that a moisturizer containing panthenol such as this healing ointment could significantly increase stratum corneum hydration.

For significant improvement of the hemoglobin index, this study is the very first study using hemoglobin index measurement on the hand area. Most studies using the hemoglobin index as the assessment tool for skin inflammation on the face area showed good clinical correlation with other parameters (Matias et al., 2015). Data from this study suggested that the reduction of skin redness on hand is also correlated with the reduction of clinical severity scales (HECSI) and the improvement of clinical photographs from the patients. However, no cut point for significant clinical improvement had been proposed right now. Thus, further studies may require to demonstrate the application of hemoglobin index measurement on hand.

For adverse events, there are many studies showed that long-term application of topical corticosteroid may result in numerous local and systemic adverse effects. Barnes, Kaya & Rollason (2015) showed that the amount of skin thinning was about 10-22% after 2-6 weeks of application of 0.05% clobetasol propionate. Moreover, a report of exogenous Cushing's syndrome due to topical corticosteroid application ensured that systemic side effects can occur after topical corticosteroid use (Tempark et al., 2010). When considering about natural history of chronic hand eczema, this disease usually has a prolonged clinical course with frequent relapse. Long-term application of high potency corticosteroid as a conventional therapy is likely to cause numerous adverse events. For these reasons, the healing ointment without topical corticosteroid ingredients should be the novel treatment for chronic hand eczema, especially in term of safety profile.

A previous study suggests that healing ointment containing petrolatum and anti-inflammatory ingredients can create a semi-occlusive environment allowing to facilitate wound healing after laser resurfacing on forearm area (Trookman, Rizer and Weber, 2011). Moreover, treatment with this healing ointment can show fast and effective improvement in wound healing after skin damaged by laser resurfacing at perioral area without significant adverse effects (Sarnoff, 2011). Likewise, the results from this study

showed that no serious adverse events had been reported after twice-daily application of this healing ointment on hand area for four weeks. Hence, this healing ointment showed a good safety profile for the treatment of chronic hand eczema.

Further study about the long-term efficacy of this healing ointment is recommended. Limitations of this study include a small sample size, a short period of follow up, and only the study in the middle-aged adult population. Thus, more sample size, more disease severity, younger or elder age group, and a longer study period are recommended to obtain more accurate information about treatment results of this ointment containing anti-inflammatory effect in the treatment of chronic hand eczema.

5. Conclusion

Healing ointment containing petrolatum and anti-inflammatory ingredients yields a desirable efficacy after 4 weeks of application in the treatment of mild-to-moderate chronic hand eczema. No serious adverse events have been reported. Thus, treatment with this healing ointment offers the possibility for alternative therapy for the long-term treatment of chronic hand eczema to avoid adverse effects from high potency corticosteroid and improve skin moisture.

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