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Acitretin as a Therapeutic Option for Chronic Hand Eczema

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Dear Editor:

The long-term treatment options for chronic hand eczema (CHE) refractory to topical corticosteroids are currently limited. In search of a safer therapy, oral alitretinoin (9-*cis* retinoic acid) was developed and approved for CHE, but its economic burden limits its broader use. Acitretin, a synthetic retinoid, is an alternative treatment for hand eczema that is more cost-effectiveness than alitretinoin[1,2]. This study describes the efficacy and safety of low-dose acitretin in patients with various subtypes of hand eczema. The study protocol was approved by the Institutional Review Board of Pusan National University Hospital, Busan, Korea (IRB no. E-2016013).

A total of 28 patients diagnosed with CHE (≥3 months) and were refractory to high potency topical corticosteroid (clobetasol propionate 0.5 mg or diflucortolone valerate 3 mg) for more than 3 months were screened in this prospective open-label study. Of them, 25 patients (89.2%) finished the protocol and 3 patients (10.7%) were withdrawn before completion. Patients were administered 10 mg acitretin twice daily for 8 weeks. A dose reduction to 10 mg once daily was allowed after 2 to 4 weeks according to therapeutic response. The use of systemic corticosteroids, other immunosuppressive agents, antibiotics, or other therapeutic strategies that could change the course of hand eczema was prohibited. The efficacy parameters were evaluated using the hand eczema severity index (HECSI) and 5-grade physician global assessment (PGA) at baseline and at weeks 2, 4, and 8. Clinical response was defined as a PGA assessment of clear or almost clear. Safety was evaluated by recorded adverse events and safety parameters such as complete blood count, lipid profile, liver and renal function measured every two weeks during this study.

The mean age at disease onset was 54 years (range, 33～77 years). The mean duration of disease at diagnosis was 22.8 months. Hand eczema was classified into 5 categories with dominant component, even though there can be overlap: hyperkeratotic (52.0%), pompholyx type (28.4%), fissured (20.0%), nummular (0%), and fingertip (0%) hand eczema[3].

The HECSI scores were reduced from 21.9 at baseline to 9.2 at week 8 with an overall reduction rate of 57.9% ($p<0.001$) and hyperkeratotic hand eczema was subtype showing the most significant improvement (68.3%, $p=0.004$). The clinical responses were seen in patients with pompholyx type (n=4/7, 57.1%) as well as hyperkeratotic type (n=4/13, 30.8%) or fissured type (n=1/5, 20.0%) (Table 1). The PGA score at baseline indicated that most cases of hand eczema were severe (n=14, 56.0%) or moderate (n=10, 40.0%) and that 1 patient (4.0%) had mild eczema. However, 9 patients (36.0%) showed a clinical response at weeks 8 (Fig. 1). No severe adverse events were reported, and acitretin was generally well tolerated, with a good safety profile throughout the study period. Two patients reported cheilitis and 1 patient, abdominal discomfort.

Current treatment strategies for hand eczema vary from

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Table 1. Clinical response and comparison of hand eczema severity index (HECSI) from baseline to week 8

Type	No. of patients	Clinical response at week 8 (%)	HECSI			
			Baseline	Week 8	Reduction rate (%)	*p*-value
Hyperkeratotic	13	30.8	25.0	7.9	68.3	0.004
Pompholyx	7	42.9	21.6	13.3	38.4	0.08
Fissured	5	20.0	14.4	7.0	51.4	0.87
Total	25	36.0	21.9	9.2	57.9	<0.001

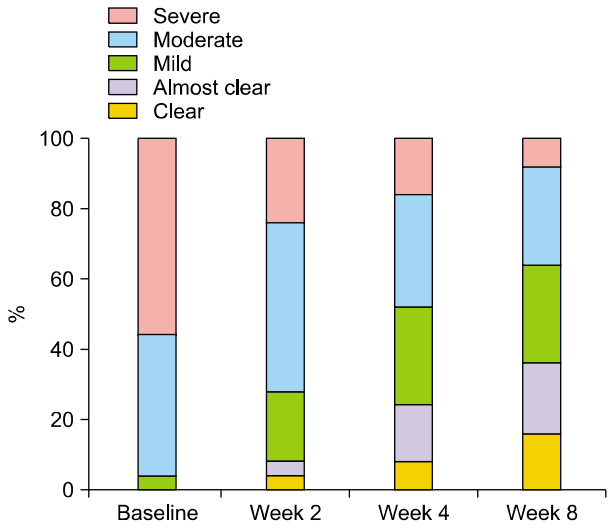

Fig. 1. Change in physician global assessment during the 8-week period.

country to country based on clinical experiences, available drugs in the market, and special circumstances, such as insurance coverage. Although alitretinoin was covered by national health insurance from 2016 in Korea, the cost burden for the patients suffering hand eczema was approximately 10 times more in alitretinoin than acitretin. The socioeconomic burden on patients cannot be ignored and needs to be considered, especially because the disease can be chronic. Our selection of acitretin as an alternative treatment resulted in a satisfactory outcome at an acceptable cost in our patients.

Acitretin reduces T-helper (Th)1 and Th17 cell infiltration and downregulates cytokines[4]. In addition, it also inhibits the production of keratinocyte-derived vascular endothelial growth factor[5]. Consequently, acitretin normalizes epidermal cell proliferation, differentiation, and cornification. However, the exact mechanisms for the effect on eczema are not known. Acitretin may be preferred in the treatment of hyperkeratotic hand eczema owing to its modulating effect on keratinization. There are data suggesting that in patients with hyperkeratotic hand eczema, it can achieve results better than those achieved in the current study[6-8]. In our study, it was also useful in patients with pompholyx type eczema, even those without hyperkeratosis. However, there are few reports on the use of acitretin in the treatment of pompholyx type eczema.

When comparing the effectiveness of acitretin and alitretinoin, the main difference is that alitretinoin is not limited to the treatment of a distinct type of hand eczema. However, this may only be because acitretin has not yet been used to treat other types of hand eczema. An overall response was achieved in up to 48% of patients taking oral alitretinoin (10 mg or 30 mg) once daily, and 49%, 33%, and 44% of patients with hyperkeratotic, pompholyx, and finger tip hand eczema responded to 30mg alitretinoin, respectively[9]. Comparable results were achieved in our study using acitretin 20 mg daily, with a 57.85% overall HECSI score reduction and 36.0% of patients showing a clinical response.

There is slow but steady interest in acitretin, and our study will hopefully encourage physicians to take a second look at this familiar old drug in the pool of newer, fancier drugs. To our knowledge, this is the first study to show that low-dose of acitretin can induce clinical improvements in patients with various subtypes of hand eczema. Considering the cost-effectiveness of this drug, acitretin is an effective adjunctive non-immunosuppressive treatment modality in patients with persistent CHE, with less medical burden. However, the number of subjects was too small for a statistical analysis of each subtype, and treatment and follow-up duration was relatively short to evaluate recurrence.

A large, well-designed study is needed to overcome these limitations and improve our understanding of acitretin for the treatment of hand eczema.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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Fournier's Gangrene: A Rare Complication of Sweet's Syndrome

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Dear Editor:

A 31-year-old woman presented with 7 days history of pruritic multiple various sized erythematous plaques on whole body (Fig. 1A). Before the skin lesions appeared, she was prescribed some medicines at a private hospital. The patient had a fever (38.2°C) and the lab findings showed increased ESR (77, 0～20 mm/h) CRP (7.72, 0.0～0.3 mg/dl), and normal procalcitonin (0.125, 0～0.5 ng/ml). Based on her past history, clinical and lab findings, Sweet's syndrome (SS) was suspected, and she was treated with high dose steroids for 5 days (80 mg of intravenous methylprednisone every 12 hours, tapered to 20 mg). During hospitalization, edematous papillary demis and neutrophilic infiltrate with leukocytoclasis could be seen in the biopsy (Fig. 1B). Our patient showed 1) sudden onset of erythematous plaques, 2) neutrophilic dermal infiltrate (2 major criteria), 3) fever, 4) rapid response to steroid therapy (2 minor criteria)[1]. Consequently, on basis of clinical, histologic, lab findings, and criteria, we could diagnose as SS. Three days after discharge, she revisited us

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