Comparison of Fumaric Acid 5% Cream versus Triamcinolone 0.1% Cream in the Treatment of Hand Eczema

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Abstract- Hand eczema is a common distressing skin problem. It is an immune reaction to haptens. Thus, substances that inhibit Immune system can be effective in the treatment of hand eczema. In this study, topical fumaric acid 5% cream is compared with topical steroid in the treatment of hand eczema. Patients with hand eczema were randomly divided into two groups. One group received fumaric acid 5% in a cream base, and the other received triamcinolone 0.1% in the same cream base. Both groups used creams twice daily for one month. Patients were checked for erythema, excoriation, population and lichenification, EASI score, and pruritus before and after treatment. In both groups, the mean of all signs of the disease and EASI score decreased after one month of treatment. There was no significant difference between the two treatments in decreasing erythema, but excoriation, population, lichenification, EASI score and itching were all decreased more in triamcinolone 0.1 % group. Although fumaric acid can inhibit the immune system; it was less effective for the treatment of all signs of hand eczema except erythema in comparison to triamcinolone. These results may be justified for two reasons: low penetration of topical fumaric acid through the skin or a low concentration used in this study.

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Keywords: Hand eczema; Fumaric acid; Triamcinolone; Immune System

Introduction

Hand eczema is a common and distressing disorder that comprises up to 30% of occupational diseases visited in clinics (1). Nearly 50% of patients dealing with hand eczema are seeking treatment, and approximately 5% quit work because of this problem (2). Occupational hand eczema is the most common occupational disease in most countries (3).

In most studies, the prevalence was higher in the female gender. Recent researches have shown that female predominance was because of environmental factors and not the genetics (4).

Hand eczema has different etiologies. The most common causes are irritant contact dermatitis, allergic contact dermatitis, and atopic dermatitis. Other less common forms include nummular eczema, hyperkeratotic eczema, and dyshydrotic eczema (1).

Treatment of hand eczema is difficult and includes lifestyle changes and preventive measures, topical treatments and systemic agents (5).

Topical steroids are the mainstay of topical treatments in hand eczema. Long-term use of topical steroids has several side effects such as skin atrophy (1). As hand eczema is usually a chronic and recurrent problem, finding an alternative therapy to topical steroids could be of great value.

Topical fumaric acid is a documented treatment in psoriasis. It suppresses the immune system through several pathways (6,7). Since this decrease in the immune milieu of eczema could be of great therapeutic potential, and fumaric acid has minor reported side effects it could be a novel treatment in hand eczema. In a previous study of ours, *Fumaria parviflora L.* extract was effective in the

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treatment of chronic hand eczema. *Fumaria parviflora L.* (FP), also known as Shahtareh, is a plant frequently used in Persian folk medicine, and fumaric acid is one of its biological active components (8).

In this double-blind randomized clinical trial, we compared the efficacy of topical fumaric acid 5% cream and triamcinolone 0.1% cream in the treatment of hand eczema.

Materials and Methods

This study was a controlled, randomly selected, double blind-study, conducted at teaching dermatology clinics of the Shiraz University of Medical Sciences. A total of 92 consecutive patients including those who referred to teaching dermatology clinics of Shiraz University of Medical Sciences with the clinical diagnosis of hand eczema were enrolled in the current study. Exclusion criteria were: pregnancy, lactation, use of any topical or systemic immunosuppressant drugs during the last month, and patients under 12 years of age. Any patients who develop side effects during the study were also excluded. Psoriasis was excluded pathologically in clinically probable cases. We had two groups, in one of them patients used topical fumaric acid 5% cream while in the other triamcinolone 0.1% cream was used. A list of randomized coded groups was given to the study investigator, and as patients consecutively were enrolled in the study, they were assigned to the next available randomized group on the list.

Patients were required to discontinue any other topical preparations for two weeks before entering the study and during it. Patients were asked to use both drugs twice a day for a period of 1 month. Also, patients were asked to decrease their environmental exposures to as little as possible. Patients <12 years old, pregnant and lactating women, those who were on topical treatments during the last 2 weeks or systemic therapies in the last one month were excluded from the study.

Signs of the disease including erythema, excoriation, population, lichenification and disease score based on EASI score (Eczema Area and Severity Index) (9) were observed and recorded before and after four weeks of treatment. Degree of pruritus before and after therapy was also questioned and recorded.

Each of the four signs and pruritus was scored based on the severity from 0 to 3 (0=none, 1=mild, 2=moderate, 3=severe). EASI score was the sum of the scores of the aforementioned four signs.

The study was approved by committee of ethics in medical research, the Shiraz University of Medical Sciences.

Statistical analysis was performed with the SPSS 15.0 statistical package, using paired T. test. The criterion for statistical significance was at P-value<0.05. A total of 58 patients participated in the study and came for a follow-up visit.

Results

Thirty of 58 participants of the study were in the fumaric acid group, and the remaining was in the triamcinolone group. Four of our patients developed side effects and was excluded from the study. Mean age in group one (fumaric acid) was 28.7 yrs and in group two was 31 yrs. Age difference was not statistically significant between the two groups (P=0.373). Group one comprised of 30 patients, 21(70%) female. Group two comprised of 19 (68.9%) female. Using chi- square test, no significant difference was between the two groups (P=0.86).

The average duration of the disease was 39.7 months in group 1 and 42.82 months in group 2 (not significantly different, P=0.808).

The mean score of all four signs of the disease, pruritus and EASI score was significantly reduced after therapy in group 1(fumaric acid) (Table 1).

Table1. Comparison of the symptoms and EASI score in group 1(fumaric acid 5%) before and after therapy

Clinical Symptoms	Mean before therapy	Mean after therapy	*P*-value
Erythema	83.1	93.0	001.0
Excoriation	86.0	7.0	025.0
Lichenification	6.0	46.0	046.0
Population	13.1	9.0	020.0
Itching	9.1	3.1	004.0
EASI score	43.4	3	001.0

Likewise, the mean score of all four signs of the disease, pruritus and EASI score was significantly reduced after therapy in group 2 (triamcinolone) (Table 2).

Table 2. Comparison of the symptoms and EASI score in group 2 (triamcinolone 0.1%) before and after therapy

Clinical Symptoms	Mean before therapy	Mean after therapy	*P*-value
Erythema	6.1	42.0	001.0
Excoriation	14.1	67.0	001.0
Lichenification	92.0	64.0	014.0
Population	07.1	42.0	001.0
Itching	92.1	57.0	001.0
EASI score	75.4	1.2	001.0

No significant difference was between the two groups according to the decrease in erythema (P=0.145), but triamcinolone was superior to fumaric acid in decreasing excoriation, pruritus, papulation, lichenification and EASI score P=0.023, 0.002, 0.005, 0.001, 0.006, respectively) (Figures 1-6).

Determining the efficacy of either drug according to age, sex, or duration of the disease was not feasible because of the limited number of the patients.

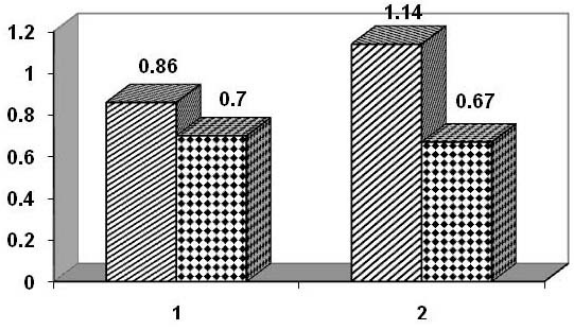

Figure 1. Comparison of the degree of erythema before and after therapy in group 1 and 2

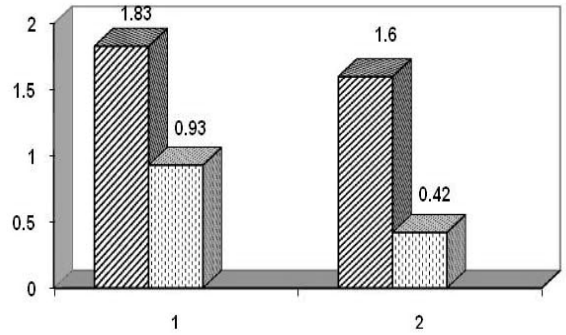

Figure 2. Comparison of the degree of excoriation before and after therapy in group 1 and 2

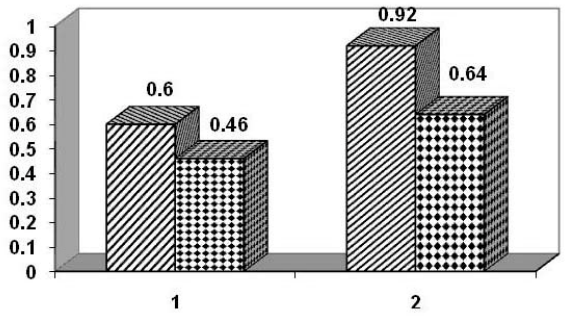

Figure 3. Comparison of the degree of lichenification before and after therapy in group 1 and 2

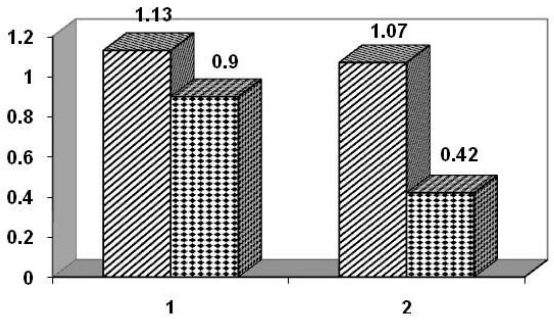

Figure 4. Comparison of the degree of population before and after therapy in group 1 and 2

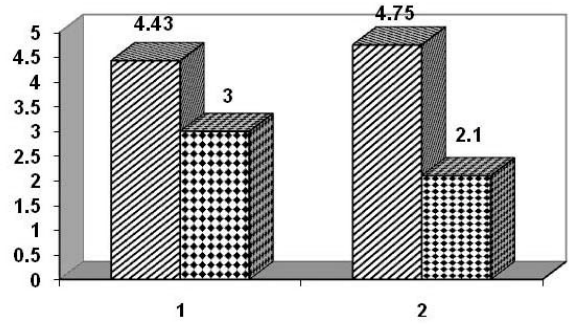

Figure 5. Comparison of the EASI Score before and after therapy in group 1 and 2

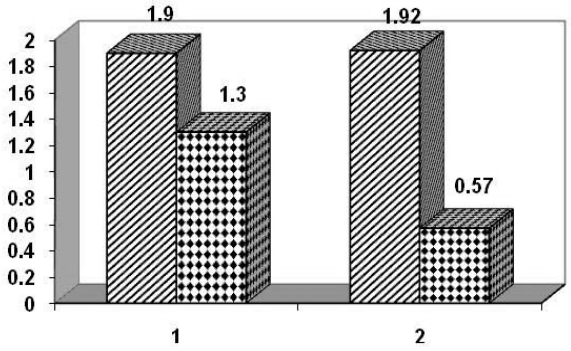

Figure 6. Comparison of the degree of itching before and after therapy in group 1 and 2

Discussion

Hand eczema has different etiologies. The most common causes are irritant contact dermatitis, allergic contact dermatitis, and atopic dermatitis. The interaction of the trigger factors, keratinocytes and T cells, are particularly important in most cases of eczema. In allergic or irritant contact dermatitis, the interaction with antigen-bearing DCs causes T-lymphocyte differentiation and secretion of different cytokines (1). These cytokines and chemokines trigger the entrance of T-cells to the

epidermis. Cellular damage is mainly caused by T-cells and cytokines, and this may be the final common pathway between most types of eczema.

Fumaric acid can be useful in treating hand eczema through several pathways: Increasing the production of IL-10, which has an anti-inflammatory effect (7), inhibiting the differentiation of dendritic cells and, as a result, decreasing antigen-presenting capability (7), suppressing the immune system (6,7), decreasing the production of IFN-gamma (10) and down-regulating production of type I cytokines by T helper lymphocytes (11).

In the present study, two individuals in both groups developed adverse effects manifested as erythema and severe pruritus. In previous studies with both fumaric acid (12,13) and topical corticosteroids (14) contact dermatitis was reported. Consistent with previous studies, the disease was more common in females.

In both groups, the severity of signs and symptoms decreased after treatment. Effectiveness of both medications was the same in decreasing erythema.

But the effectiveness of triamcinolone 0.1% was superior in decreasing excoriation, lichenification, population, and EASI score and itching.

According to findings of present study fumaric acid 5% can be effective in treating erythema of hand eczema. Although other signs and symptoms of the disease subsided after treatment with fumaric acid, but this is meaningfully lower in comparison to triamcinolone 0.1% which is the well known treatment of hand eczema.

As the effectiveness of fumaric acid is dependent on its concentration, (14) the lower effectiveness of this drug in this study could be due to its lower concentration in the skin .This may be caused by lower capability of fumaric acid for penetrating deep into the skin or may be caused by its low concentration in the cream.

Further studies are needed to evaluate the effectiveness of fumaric acid in the treatment of hand eczema with using higher concentrations of this drug or combining it with a penetration enhancer.

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