

Original papers

The efficacy of permethrin 5% vs. oral ivermectin for the treatment of scabies¹

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ABSTRACT. Human scabies is caused by an infestation of the skin by the human itch mite (*Sarcoptes scabiei* var. *hominis*). The aim of this study is to compare the efficacy and safety of permethrin 5% lotion with oral ivermectin for the treatment of scabies. In total, 60 patients with scabies were enrolled, and randomized into two groups: The first group and their family contacts received 5% permethrin cream twice with a one week interval, and the other received a single dose of oral ivermectin. Treatment was evaluated at intervals of 2 and 4 weeks. A single dose of ivermectin provided a cure rate of 62.4%, which increased to 92.8% with 2 doses at a 2-week interval. Treatment with two applications of permethrin with a one week interval was effective in 96.9% of patients. Permethrin-treated patients recovered earlier. Two applications of permethrin with a one week interval is more effective than a single dose of ivermectin. Two doses of ivermectin is as effective as a single application of permethrin.

Key words: scabies, permethrin 5%, oral ivermectin

Introduction

Scabies is a common condition found worldwide; it affects people of all races and social classes. Scabies can spread easily under crowded conditions where close body and skin contact is common. Institutions such as nursing homes, extended-care facilities, and prisons are often sites of scabies outbreaks [1–3]. Child care facilities also are a common site of scabies infestations.

Scabies frequently occurs in body crevasses such as those between the fingers and toes, the buttocks, the elbows, the waist area, the genital area, and under the breasts in women [4–6]. The face, neck, palms, soles and lips are usually not affected, except in infants or very young children. The most common symptoms of scabies, itching and a skin rash, are caused by sensitization, a type of “allergic” reaction, to the proteins and feces of the parasite. Severe itching (pruritus), especially at night, is the

earliest and most common symptom of scabies [7–9]. A pimple-like (papular) itchy (pruritic) “scabies rash” is also common.

Scabies treatment involves eliminating the infestation with medication [10–13]. Several creams and lotions are available. Patients usually apply the medication all over the body from the neck down, and leave the medication on for at least eight hours. A second treatment is needed if new burrows and rashes appear. All people in the household who have had close skin-to-skin contact with a scabies-affected person during the past month must be treated [14–16]. This usually includes everyone in the home, even if they don’t have symptoms: the symptoms can take 4 to 6 weeks to develop after a person is infested.

Scabies is most commonly treated with permethrin 5% dermal cream. Permethrin is an insecticide that kills the mites that cause scabies [17–19]. Permethrin should be washed off after

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8–14 hours and the application can be repeated 1–2 weeks later if live mites are seen [20–22]. The cream should be washed off in 8–9 hours in children less than 6 years but can be left on for up to 12–14 hours for older children. One dose is usually curative [23–25]. Ivermectin is an oral medication shown by many clinical studies to be effective in eradicating scabies, often in a single dose. It is the treatment of choice for crusted scabies and is often used in combination with a topical agent [26–28]. It has not been tested on infants and is not recommended for children under six years of age [29–30]. Topical ivermectin preparations have been found to be effective for scabies in adults and are attractive due to their low cost, ease of preparation, and low toxicity. They have also been useful for sarcoptic mange: the veterinary analog of human scabies [20,31–33].

The aim of this study was to compare the efficacy and safety of permethrin 5% lotion vs. oral ivermectin for the treatment of scabies.

Materials and Methods

Patient recruitment. A single-blind, randomized controlled trial was set up. Between April 2011 and April 2013, any patients with scabies who were older than 2 years of age and attending the Dermatology outpatient clinic, Tabriz and Teheran outpatient clinic were assessed for enrolment in the study. The exclusion criteria were an age younger than 2 years; pregnancy or lactation; history of seizures, severe systemic disorders, immunosuppressive disorders and presence of Norwegian scabies; and use of any topical or systemic acaricide treatment for 1 month before the study.

Before entry into the study, the patients were given a physical examination and their history of infestations, antibiotic treatment and other pertinent information was recorded. Age, gender, height and weight were recorded for demographic comparison, and photographs were taken for later clinical comparison. None of the patients had been treated with pediculicides, scabicides or other topical agents in the month preceding the trial.

The diagnosis of scabies was made primarily by the presence of the follow three criteria: presence of a burrow and/or typical scabietic lesions at the classic sites of infestation, a report of nocturnal pruritus and history of similar symptoms in the patient's families and/or close contacts. Infestation was confirmed by demonstration of eggs, larvae,

mites or fecal material under light microscopy.

The patients who satisfied the above criteria were randomly divided into two groups: group A were to receive ivermectin, and group B were to receive sulfur 10% ointment.

Randomization and treatment. In total, 68 patients were initially enrolled. Of these, 8 patients were not able to return after the first follow-up examination, and were therefore excluded from the study. The remaining 60 patients (42 male, 18 female; mean \pm SD age 44.16 \pm 10.78 years, range 4–72) constituted the final study population.

The first group received permethrin 5% cream twice with a one-week interval, and the second group received a single dose of 200 μ g/kg body weight oral ivermectin. The treatment was given to both patients and their close family members, and they were asked not to use any antipruritic drug or any other topical medication.

Evaluation. The post-treatment clinical evaluation was performed by experienced investigators who were blinded to the treatments received. Patients were assessed at 2 and 4 weeks after the first treatment. At each assessment, the investigators recorded the sites of lesions on body diagram sheets for each patient, and compared the lesions with those visible in the pre-treatment photograph. New lesions were also scraped for microscopic evaluation. The patients were clinically examined and evaluated based on the criteria given above in „Patient recruitment”.

„Cure” was defined as the absence of new lesions and healing of all old lesions, regardless of the presence of postscabetic nodules. „Treatment failure” was defined as the presence of microscopically-confirmed new lesions at the 2-week follow-up. In such cases, the treatment was repeated at the end of week 2 and patients were evaluated again at week 4. „Re-infestation” was defined as a cure at 2 weeks but development of new lesions with positive microscopic findings at 1 month. Any patients with signs of scabies, whether as a result of treatment failure or re-infestation, would then be treated with lindane lotion 1%.

Statistical analysis. The χ^2 test or the Fisher exact test was used as appropriate to examine the difference between groups, and $P < 0.05$ was considered significant. SPSS software (version 16; SPSS Inc., Chicago, IL, USA) was used for all analyses.

Table 1. Demographic characteristics of the study population

	Permethrin	Ivermectin
	(n=30)	(n=30)
Age	42.56±16.56	46.76±14.45
Sex		
Male	22	20
Female	8	10
Height (cm)	172±27	174±34
Weight (kg)	76±18	73±16

Results

A total of 68 patients were studied. Eight patients (4 from group A and 4 from group B) were not able to return after the first follow-up examination and were therefore excluded from the study. The remaining 60 patients continued the study. The demographic profiles of the two treatment groups showed no major differences (Table 1). The ages of the subjects ranged from 4 to 72 years (mean age 44.16±10.78). The mean age of those treated with permethrin 5% was 42.56±16.56, while those in the ivermectin group had a mean age of 46.76±14.45. On entry into the study, the number of patients in each treatment group who were graded as having mild, moderate or severe infestation was not significantly different (Table 2).

On follow-up, with a single dose, 14 patients (46.6%) in the ivermectin group and 24 patients (80%) in the permethrin group demonstrated symptomatic improvement by the first week. By the second week, 22 patients (73.3%) in the ivermectin group and 28 patients (93.3%) in the permethrin group had demonstrated symptomatic improvement. The nonresponders, 8 and 2 in each group,

Table 2. Severity of infestation pretreatment of all patients

Lesions	Permethrin	Ivermectin	Total subjects
Mild<50	4	6	10
Moderate 50-100	8	7	15
Severe> 100	18	17	35
	n=30	n=30	60

respectively, received repeat therapy. By the fourth week, 28 (93.3%) patients given ivermectin had shown a symptomatic improvement, whereas all the patients given permethrin were cured.

Two (3.1%) patients did not respond to 2 doses of ivermectin. They were given two applications of lindane lotion 1% with a one-week interval, and were cured after the second application. None of the 60 participants experienced significant irritation, allergic or other adverse reactions to the products. Permethrin was considered cosmetically elegant and well accepted by patients and parents. None of the patients deteriorated during the study.

Discussion

A number of medications are effective in treating scabies; however, treatment must often involve the entire household or community to prevent re-infection. The use of antihistamines represents one option to improve itchiness [21,34]. Permethrin, 5% dermal cream, is a welcome addition to the available therapies for scabies. It is cosmetically elegant and easy to use, has no objectionable odor, and does not stain clothing. Skin irritation, including itching, swelling, and redness, may occur with scabies and temporarily worsen after treatment with permethrin, presumably due to the absorption of dead parasite proteins. Mild burning or stinging may also occur [35]. Oral ivermectin is an effective and cost-comparable alternative to topical agents in the treatment of scabies infection. It has been used extensively and safely in the treatment of other parasitic infections, however, the U.S. Food and Drug Administration has not approved the drug for the treatment of scabies infection. The safety of oral ivermectin in pregnant and lactating women and young children has yet to be established [36,37].

In this study, two applications of permethrin with a 1-week interval was found to be more effective than a single application of malathion after 2 weeks. ($P<0.05$) After four weeks, considered the definitive point for evaluating the efficacy of treatments, topical permethrin was found to be as effective as ivermectin in treating scabies. This was in accordance with Taplin et al. [38].

The lack of efficacy of a single dose of ivermectin in some patients may be due to the lack of ovicidal action of ivermectin. Ivermectin, because of its specific site of action, may not be effective against the younger stages of the parasite inside the egg because the nervous system has not

yet developed [39,40]. The concentration achieved in the skin may also be variable because ivermectin is orally administered. These factors could also explain the temporal delay in complete recovery observed in the ivermectin group. Because ivermectin has not been proven to be ovicidal, a single dose of 200 µg/kg body weight may be inadequate for eradicating all the different stages of the parasite, and a higher dose or a second dose may be required within 1 to 2 weeks to achieve higher cure rates [41,42].

Although the persistence of pruritus in scabies for several weeks after cure is not uncommon and is not necessarily predictive of treatment failure, since it is the primary symptom of scabies, a drug with a more rapid effect on relieving pruritus is much more acceptable to patients. A study carried out by Usha et al. [43] reports a higher number of patients showing clearance of lesions compared to our results. This could be explained due to the longer follow up. In a study carried out by Khan et al. [44], a 100% cure rate was seen in both treatment groups, possibly because the study was carried out on a smaller number of patients with a follow up of 2 weeks, and their ages were 12 years or above, when the activity of sebaceous glands is higher. Regarding side effects, malathion was found to be significantly safer than permethrin ($P < 0.05$).

Conclusions

Although ivermectin was found to be as effective as permethrin, it offers a few outweighing advantages over topical permethrin. It is cost-effective and can be administered on a large scale with better compliance, with or without supervision. It can also be given safely in patients of scabies with secondary eczematization, erosions or ulcers where topical therapies such as permethrin, lindane and benzyl benzoate can cause serious cutaneous and systemic side effects, in addition to the problem of compliance.

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