

Original papers

Treatment of scabies: The topical ivermectin vs. permethrin 2.5% cream

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ABSTRACT. Human scabies is caused by an infestation of the skin by the human itch mite (*Sarcoptes scabiei* var. *hominis*). It is commonly treated with topical insecticides, but the treatment of choice is still controversial. The aim of this study is to compare the efficacy of topical ivermectin vs. permethrin 2.5% cream for the treatment of scabies. In total, 380 patients with scabies were enrolled, and randomized into two groups: the first group received 1% ivermectin applied topically to the affected skin at a dose of 400 microg/kg, repeated once the following week, while the second group received permethrin 2.5% cream and were told to apply this twice at one week intervals. Treatment was evaluated at intervals of 2 and 4 weeks, and if there was treatment failure at the 2-week follow-up, treatment was repeated. Two applications of topical ivermectin provided a cure rate of 63.1% at the 2-week follow-up, which increased to 84.2% at the 4-week follow-up after repeating the treatment. Treatment with two applications of permethrin 2.5% cream with a 1-week interval between them was effective in 65.8% of patients at the 2-week follow-up, which increased to 89.5% at the 4-week follow-up after this treatment was repeated. Two application of ivermectin was as effective as two applications of permethrin 2.5% cream at the 2-week follow-up. After repeating the treatment, ivermectin was as effective as permethrin 2.5% cream at the 4-week follow up.

Key words: scabies, topical ivermectin, Permethrin 2.5% cream

Introduction

Scabies is an itchy skin condition caused by the microscopic mite *Sarcoptes scabiei*. It is common all over the world, and it affects people of all races and social classes [1–3]. Scabies spreads quickly in crowded conditions where there is frequent skin-to-skin contact between people [4–6]. Hospitals, child-care centers and nursing homes are examples. Scabies can easily infect sex partners and other household members [7–9]. Sharing clothes, towels and bedding can also spread scabies. Mites can live for about 2 to 3 days in clothing, bedding, or dust, making it possible to catch scabies from people who share the same infected bed, linens, or towels [10–12].

Scabies is very easy to misdiagnose because early subtle infestation may look like small pimples or mosquito bites [13–15]. Those affected may

believe they have another condition, such as bedbug bites or other kinds of rashes [16,17]. Over a few weeks, however, mistakes like this become evident as patients feel worse and worse with symptoms they can't ignore. It is important to remember that the first time a person gets scabies they usually have no symptoms during the first 2 to 6 weeks they are infested; however they can still spread scabies during this time [18–20]. Most cases of scabies can be cured without any long-term problems. A severe case with a lot of scaling or crusting may be a sign that the person has a disease such as HIV [21–23]. In addition to the infested person, treatment also is recommended for household members and sexual contacts, particularly those who have had prolonged direct skin-to-skin contact with the infested person; both sexual partners and close personal contacts who have had such contact with an infected person within the preceding month should be examined and

treated [24–26]. All persons involved should be treated at the same time to prevent re-infestation.

Permethrin is the most effective treatment for scabies and the treatment of choice. It is applied from the neck down usually before bedtime and left on for about eight to fourteen hours, then showered off in the morning. One application is normally sufficient for mild infections. For moderate to severe cases, another dose is applied seven to fourteen days later [27,28].

Ivermectin, an oral medication, is an antiparasitic medication that has also been shown to be an effective scabicide, although it is not approved by the FDA for this use. Previous studies recommend taking this drug at a dosage of 200 micrograms per kilogram body weight as a single dose, followed by a repeat dose two weeks later [29,30]. This study is aimed at comparing the efficacy of topical ivermectin vs. permethrin 2.5% cream in the treatment of scabies.

Materials and Methods

This study was approved by the local Ethics Committee. Informed consent was obtained from the patients or their parents.

Patient recruitment

This was a single-blind, randomized controlled trial. Between April 2008 and October 2012, any patients with scabies who were older than 2 years of age and attending the Dermatology outpatient clinic, Tabriz and Teheran special clinic were assessed for enrolment in the study. Exclusion criteria were age younger than 2 years; existing 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 one month before the study.

Before entry into the study, 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, 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. Patients who satisfied the above criteria were randomly divided into two groups: group A were to receive ivermectin, and group B were to receive permethrin 2.5% cream.

Randomization and treatment

In total, 420 patients were initially enrolled. Of these, 40 patients were not able to return after the first follow-up examination, and were therefore excluded from the study. The remaining 380 patients (220 male, 160 female; mean \pm SD age 46.57 ± 13.67 years, range 4–72) constituted the final study population.

The first group received 1% ivermectin in a solution of propylene glycol applied topically to the affected skin. The dose employed was 400 microg/kg, repeated once the following week, while the second group received permethrin 2.5% cream and were told to apply this twice with a one-week interval. 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 clinical evaluation after treatment was made 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 pretreatment photograph. New lesions were also scraped for microscopic evaluation. Patients were clinically examined and evaluated based on previously-defined criteria (see: Patient recruitment). „Cure” was defined as the absence of new lesions and healing of all old lesions, regardless of 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

at one month. Any patients with signs of scabies, whether as a result of treatment failure or re-infestation, would then be treated with 1% lindane lotion.

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.

Results

There were no significant differences in age or gender between the two groups (Table 1). On entry into the study, no significant difference was seen between the groups with regard to the number of patients graded as having mild, moderate or severe infestation (Table 2).

At the 2-week follow-up, the treatment was found to be effective in 120 (63.1%) patients in the

Table 1. Demographic characteristics of the study population

	Ivermectin (n=190)	Permethrin 2.5% (n=190)
Age	37.46±14.73	37.46±14.55
Sex		
Male	120	100
Female	70	90
Height (cm)	175±24	179±26
Weight (kg)	76±12	75±16

ivermectin group and 125 patients (65.8%) in the permethrin 2.5% group, with no significant difference between the groups ($P=0.68$). The treatment was repeated for the 135 patients (70 male, 65 female; 70 in the ivermectin group and 65 in the permethrin 2.5% group) who still had infestation.

At the second follow-up, at 4 weeks, only 30 of the 70 patients in the ivermectin group still had severe itching and skin lesions, compared with 20 of the 65 patients in the permethrin 2.5% group. Thus, the overall cure rate was 160/190 patients (84.2%) in the ivermectin group and 170 of 190 (89.5%) in the permethrin 2.5% group ($P=0.43$).

The remaining 50 patients who were considered treatment failures in the study were retreated with open-label lindane lotion 1%, which cured the infestation in 2–3 weeks.

Table 2. Severity of infestation pretreatment of all patients

Lesions	Ivermectin	Permethrin 2.5%	Total subjects
Mild <50	40	30	70
Moderate 50-100	50	50	100
Severe >100	100	110	210
	n=190	n=190	380

Adverse events

The treatments were considered cosmetically acceptable by both patients and parents. None of the 400 participants experienced allergic reactions. The main adverse event (AE) was irritation, reported by 50 patients (30 in the ivermectin group and 20 in the permethrin 2.5% group), but this was not serious and did not affect compliance. None of the patients experienced worsening of the infestation during the study; even the treatment failures were improved compared with their pre-treatment status, and none had > 50 new lesions.

Discussion

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 absorption of dead parasite proteins. Mild burning or stinging may also occur [31,32]. Ivermectin is an effective and cost-comparable alternative to topical agents in the treatment of scabies infection. It may be particularly useful in the treatment of severely crusted scabies lesions in immunocompromised patients or when other topical therapy has failed [33,34] In this study, ivermectin was seen to be as effective as permethrin at 2 weeks follow up in treating scabies, and this is in accordance with previous studies that have reported excellent cure rates with permethrin. In our patients, we found topical ivermectin to be as effective as topical permethrin when used twice over a period of 4 weeks. The data from the 4th week showed that ivermectin continued to decrease both the lesions and the degree of pruritus as compared to permethrin but this difference was not significant ($P > 0.05$). Patients on ivermectin showed less rapid

symptomatic response (itching) and signs (papules). This could be because of the permethrin acts on all stages of mites (ovum, larva and adult) and also stem from its action on the voltage sensitive sodium channel of the parasite; as this channel is necessary for the generation of action potentials in excitable cells, its disruption causes paralysis of the mite and leads to its death [35,36].

Since the prior dose of permethrin killed most of the mites, the improvement in pruritus can be due to decrease in the egg laying stages of the mite [37,38]. Ivermectin, though very effective on the adult stages of the mite, has not been proven to be ovicidal, and so a single application may be inadequate to eradicate all the stages of the parasite, and a second dose may be required within 1 to 2 weeks for a 100% cure [39,40]. Usha et al. report a higher number of patients showed clearance of lesions as compared to our results, and that both permethrin and ivermectin are effective in preventing recurrences of scabies over a period of 2 months [41]. In a study carried out by Mumcuoglu et al. [42], a 100% cure was seen in both treatment groups, possibly because the study was carried on a smaller number of patients with a follow up of 2 weeks, or possibly that they were aged 12 years or above, when the activity of the sebaceous glands is greater. Permethrin is known to be significantly safer than ivermectin ($P < 0.05$). Ivermectin has been reported to cause rare serious side effects, which are seen when the drug is used in high doses, such as when it is accidentally ingested. However, in our study, we found it to be safe without significant adverse effects.

Conclusions

Although ivermectin was found to be as effective as permethrin, it has a few advantages over topical permethrin. Both drugs are cost-effective, but ivermectin has the advantage that treatment can be given to large numbers of patients with better compliance and with or without supervision.

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