

Original papers

Ivermectin vs. lindane in the treatment of scabies

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ABSTRACT. Scabies is commonly treated with acaricides but the treatment of choice is still controversial. This study aimed at comparing the efficacy of oral ivermectin vs. lindane lotion 1% for the treatment of scabies. Four hundred fourty patients with scabies were enrolled, and randomized into two groups: the first group received a single dose of oral ivermectin 200 μg/kg body weight, and the second group were treated with two applications of topical lindane lotion 1%, with a 1-week interval. 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. Single dose of oral ivermectin provided a cure rate of 63.6% at the 2-week follow-up, which increased to 81.8% at the 4-week follow-up after repeating the treatment. Treatment with two applications of lindane lotion 1%, with a 1-week interval between them, was effective in 45.4% of patients at the 2-week follow-up, which increased to 63.6% at the 4-week follow-up after this treatment was repeated. Single dose ivermectin was as effective as two applications of lindane lotion 1% at the 2-week follow-up. After repeating the treatment, ivermectin was superior to lindane lotion 1% at the 4-week follow up.

Key words: scabies, oral ivermectin, Lindane lotion

Introduction

Scabies known colloquially as the seven-year itch, is a contagious skin infection that occurs among humans and other animals. It has been classified by the WHO as a water-related disease. It is caused by a tiny and usually not directly visible parasite, the mite *Sarcoptes scabiei*, which burrows under the host's skin, causing intense allergic itching [13]. Its signs and symptoms include: itching, often severe and usually worse at night, Thin, irregular burrow tracks made up of tiny blisters on the skin. The burrows or tracks typically appear in folds of the skin. Though almost any part of the body may be involved [4–6]. It affect everyone regardless of age, gender, race, social class, or personal-hygiene habits. However, a major risk factor is being a household member or sexual partner of an affected individual [7,8]. With today's treatments, scabies need only cause short-term distress [9,10]. Scabies may be diagnosed clinically in geographical areas where it is common when diffuse itching presents along with either lesions in two typical spots or there is itchiness of another household member. Curing scabies is rather easy with the administration of prescription scabicide drugs [11,12]. Most creams or lotions are applied to the entire body from the neck down. On infants, the medicine is also applied to the scalp, face, and neck, taking care to avoid the area around the mouth and eyes [13,14].

Lindane is available as a cream, lotion and shampoo. This medication isn't safe for children younger than age 2 years, women who are pregnant or nursing, or people with weakened immune systems. Lindane is effective; however, concerns over potential neurotoxicity has limited its availability in many countries. It is approved in the United States for use as a second-line treatment [15,16].

Oral 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 topical therapy has failed. Oral dosing may be more convenient in institutional outbreaks and in the treatment of mentally impaired patients [17,18].

This study aimed at comparing the efficacy of topical ivermectin vs. lindane lotion 1% 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 November 2008 and November 2012, any patients with scabies who were older than 2 years of age and attending the dermatology outpatient clinic in Tabriz were assessed for enrolment in the study. Exclusion criteria were 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 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 lindane lotion 1%.

Table 1. Demographic characteristics of the study population

	Ivermectin	**Lindane**
	(n=220)	(n=220)
Age	44.45±13.64	40.76±11.87
Sex		
Male	125	115
Female	95	105
Height (cm)	173±27	175±36
Weight (kg)	73±25	79±24

Randomization and treatment. In total, 500 patients were initially enrolled. Of these, 60 patients were not able to return after the first follow-up examination, and were therefore excluded from the study. The remaining 440 patients (240 male, 200 female; mean±SD age 42.18±12.86 years, range 4–72) constituted the final study population and were divided in to two groups with simple randomization. The first group received a single dose of 200 μg/kg body weight oral ivermectin and the second group received lindane lotion 1% and were told to apply this twice with 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 pre-treatment photograph. New lesions were also scraped for microscopic evaluation. Patients were clinically examined and evaluated based on the 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 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 permethrin.

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

Results

There were no significant differences in age or gender between the two groups (Table 1). On entry into the study, the number of patients in each treatment group who were graded as having mild, moderate or severe infestation was also not significantly different (Table 2). At the 2-week follow-up, the treatment was effective in 140 (63.6%) patients in the ivermectin group and 100 patients (45.4%) in the lindane lotion 1% group, with no significant difference between the groups (P=0.46). The treatment was repeated for the 200 patients (120 male, 80 female; 80 in the ivermectin group and 120 in the lindane lotion 1% group) who still had infestation.

At the second follow-up, at 4 weeks, only 40 of the 80 patients in the ivermectin group still had severe itching and skin lesions, compared with 80 of the 120 patients in the lindane lotion 1% group. Thus, the overall cure rate was 180/220 patients (81.8%) in the ivermectin group and 140 of 220 (63.6%) in the lindane lotion 1% group (P<0.05).

The remaining 120 patients who were considered treatment failures in the study were retreated with open-label permethrin cream, which cured the infestation in 2–3 weeks.

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 lindane lotion 1% 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.

Table 2. Severity of infestation pretreatment of all patients

Lesions	Ivermectin	Lindane	Total subjects
Mild < 50	30	35	65
Moderate 50–100	50	60	110
Severe > 100	140	125	265
	n=220	n=220	440

Discussion

For the past 50 years, lindane has been the preferred therapy for scabies. This product has become the most widely used antiscabietic drug in many countries, including Iran. Lindane (1%) in shampoo and lotion formulations became available in Iran more than 20 years ago. This agent needs to be used on successive nights to ensure that the eggs and live mites are adequately exposed to treatment [19]. Seizures secondary to this medication have been reported, particularly when this medication was applied to wet skin or to skin altered by inflammatory changes that cause easy absorption [20]. During recent years, resistance to lindane seems to be rising and there are reports of several clusters of patients with lindane-resistant scabies worldwide [21]. As far as resistance is concerned, therefore, it seems reasonable to conclude that a potential for adverse reactions from application of lindane preparations therapeutically does exist, if the preparations are not used properly. The risk of adverse reactions in their use, however, appears minimal when the preparations are used properly and according to directions [22–24].

Ivermectin is a novel antiparasitic agent effective against a variety of endoparasites and ectoparasites [25]. Evidence suggests that ivermectin may be a safe and effective treatment for scabies; however, ivermectin is not FDA-approved for this use [26,27].

In this study, two application of lindane with one week interval was as effective as a single apilication of ivermectin by 2 weeks (P=0.46). The lack of efficacy of a single application of ivermectin in some patients may be due to the lack of ovicidal action of ivermectin. This factor could explain the temporal delay in complete recovery observed in the ivermectin group [28,29]. In our patients we found that topical ivermectin was superior to lindane lotion 1% after repeating the medication 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 lindane lotion 1% (P<0.05). In the study carried out by Goldust et al. [13] the efficacy of oral ivermectin was as effective as topical permethrin that is the treatment of choice for the treatment of scabies. In accordance to current study, in the Chhaiya et al. trial [30], at the end of second week, cure rate was 63% in oral ivermectin group. At the end of third week, 99% cure rate was observed in oral

ivermectin group. In accordance to our study in Madan et al trial, after a period of four weeks, 82.6% of the patients in the ivermectin group showed marked improvement; only 44.44% of the patients in the lindane group showed a similar response (P<0.05) [31]. Regarding side effects, lindane lotion was found to be significantly more safe than ivermectin (P<0.05).

Conclusions

Ivermectin is a cost-effective and as treatment can be given to masses 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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