Treatment of Scabies: Comparison of Ivermectin *vs.* Lindane Lotion 1%

Alireza Mohebbipour[1], Parviz Saleh[2], Mohamad Goldust[3], Mehdi Amirnia[4], Yousef Javad Zadeh[5], Ramin Mir Mohamadi[4], Elham Rezaee[6]

[1]Department of Dermatology, Department of mathematics Ardebil Branch, Islamic Azad university, Tabriz, Iran, [2]Department of infections diseases, [3]Student Research Committee, [4]Department of Dermatology, [5]Department of Pharmaceutics, Tabriz University of Medical Sciences; Tabriz, Iran, [6]Department of Medical Chemistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding author:
Mohamad Goldust
Student Research Committee
Tabriz University of Medical Sciences
Tabriz
Iran
Drmgoldust@yahoo.com

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SUMMARY Topical antiscabietics have poor compliance. This study aimed at comparing the efficacy and safety of oral ivermectin with topical lindane in treating scabies. In this clinical trial, 248 patients from 2 to 86 years of age were divided into two groups. Oral ivermectin was given to group A in a single dose of 200 µg/kg body weight. Group B received application of lindane lotion 1% twice at one-week interval. When there was no cure in two weeks, 2nd treatment was given with either drug in the respective group. A single dose of ivermectin provided a cure rate of 58.6% at two-week follow up, which increased to 92.7% with 2 doses at the end of 4-week interval. The application of lindane lotion 1% twice at one-week interval was effective in 44.3% of patients at two-week follow up, which increased to 71.7% after repeating the treatment for another two weeks. Single dose application of oral ivermectin was as effective as twice application of lindane lotion 1% at one-week interval. Two doses of ivermectin proved superior to lindane lotion 1% after repeating the treatment at 4-week follow up.

KEY WORDS: scabies, lindane lotion 1%, oral ivermectin

INTRODUCTION

Scabies is a re-emerging infection of the new millennium, especially with the pandemic of HIV infection. It is still a major public health problem in developing countries (1). The prominent features include intense itching, burrows and widespread eruption of inflammatory papules. Itching is generally worse at night when the patient is warm (2). Despite its long existence, an effective way to prevent scabies from spreading is still not known. Various treatment options include the use of topical agents like sulfur, benzyl benzoate, malathion, crotamiton and monosulfiram (3). Available antiscabietics are mainly topical and require prolonged and repeated application. Resistance to some of these drugs has been reported. Accidental ingestion, especially by children, may be fatal (4). Currently, topical 5% permethrin cream is considered as the drug of choice in the management of scabies, although recurrence and allergic side effects have been documented. Permethrin is costly and is applied all over the body for at least 8 hours. This causes poor compliance in patients and family contacts, making community control of scabies difficult (5). Lindane, γ-benzene hexachloride, is an organochloride insecticide that causes neurotransmitter inhibition and respiratory and muscular paralysis in the insect. It is contraindicated in pregnant and

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lactating women and children less than 2 years of age, due to its central nervous system toxicity (6,7). Resistance to lindane is increasing throughout the world and in 2002 it was forbidden in California State due to environmental pollution (8). Because of its potent toxicity, low efficacy, increased resistance and environment contamination, lindane is inferior to permethrin in the treatment of scabies. Ivermectin is a new drug structurally similar to macrolide antibiotics (9). Since its discovery in 1975, it has been approved for the treatment of strongyloidiasis and onchocerciasis (10). It is currently also being used for the treatment of scabies (11,12). The effective dose is 150-200 µg/kg body weight once or may be repeated at two-week interval (13). The advantages include single dose and better compliance in refractory infestations and in circumstances where head to toe topical application is logistically difficult, e.g., in large institutional outbreaks or mentally retarded patients (14). In the present study, we compared the efficacy and safety of oral ivermectin with topical lindane 1% lotion in the treatment of scabies.

MATERIALS AND METHODS

In this clinical trial, 248 patients aged 2 to 86 (mean 44±12.24) years with the diagnosis of scabies participated from April 2008 to April 2011. All patients younger than 2 years of age, pregnant and lactating women, patients with a past history of seizures, severe systemic disorders, immunosuppression and Norwegian scabies were excluded. Patients had not received any topical or systemic acaricide therapy for 1 month prior to the study. Informed consents were obtained from patients. The treatment team members who applied medications took no part in pretreatment scoring of the severity and extent of the infestations and played no role in subsequent evaluations. During the initial visit, medical history was taken following thorough physical examination. Previous concomitant medication use was recorded. Detailed dermatologic examination was then carried out and recorded, including description of the lesions and their distribution on a body diagram. Compatible lesions were scarified only on the initial visit and the resulting specimens were examined microscopically for evidence of *Sarcoptes scabiei* (adult forms), their eggs, or their fecal pellets. Results were considered positive if any of these were identified. A positive result of the scarification was considered an ancillary indicator for the diagnosis. A negative result had to be evaluated together with the presence of other signs and symptoms to determine infestation and cure. Patients who satisfied the above criteria were divided into two groups randomly. One group and their family contacts received a single dose of 200 µg/kg body weight oral ivermectin (group A), and the other received 1% topical lindane lotion 1% (group B) in a double-blind manner. Patients were treated with the scabicides and then followed up at intervals of 2 and 4 weeks. Pretreatment clinical photographs were taken of the body site most affected, and additional photographs were taken at the 1-month evaluation. Clinical evaluations after treatment were made by experienced investigators without knowledge of the treatments. At all evaluation times, they recorded the sites of lesions on body diagram sheets. The notations of their appearance and whether or not they were new or residuals of original lesions were determined by comparison with the pretreatment photograph. New lesions were also scraped for microscopic examination. Cure was defined as the absence of new lesions and all old lesions healed. Treatment failure was defined as a patient with microscopically confirmed new lesions at 1 month and who was not considered cured at 2 weeks. The term reinfestation was applied to the patients who were completely clear at 2 weeks and developed new lesions with positive microscopic findings at 1 month. In case of treatment failure, another dose of the same treatment was repeated. If the repeat treatment also failed, at the end of another 2 weeks of follow-up (fourth week after randomization), the treatment was crossed over to the other group. Data were analyzed using SPSS 16 (χ^2-test and exact Fisher test). *P* values less than 0.05 were considered significant.

RESULTS

A total of 272 patients were studied, however, 24 patients (8 from group A and 16 from group B) were not able to return after the first follow-up examination and were therefore excluded from the study. The remaining 248 patients continued the study. The remaining 248 patients included 132 (53.2%) male and 116 (46.8%) female patients, age range 4 to 76 (mean 40.4±12.6) years. Demography of the two treatment groups showed no significant difference (Table 1). Of these 248 patients, 124 were treated with ivermectin and the others with lindane. 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 by the first week, 52 (41.9%) patients in the ivermectin group and 36 (29.3%) patients in the lindane group were cured. At 2 weeks post-treatment, cure was observed in 72 (58.6%) patients of the ivermectin group and 55 (44.3%) patients in the lindane group (Table 3). This difference was not significant (*P*=0.24) and the nonre-

Table 1. Baseline characteristics of patients			
Clinical parameter	**Ivermectin**	**Lindane 1%**	**P value**
Age distribution (yrs)	42.28±12.66	46.36±12.82	0.064
Sex distribution, M/F (%)	62/38	78.4/21.6	0.424
Duration (wk)	7.8±6.32	8.32±6.4	0.542
Nocturnal pruritus (%)	8	96.2	0.649
Family history (%)	84.2	72.1	0.032
Secondary infection (%)	24	32	0.438
Severity of pruritus (%)	72.64±8.6	71.3±7.6	0.559
Microscopy (%)	78	76.4	0.376

Table 2. Severity of pretreatment infestation in all study patients			
Lesions	**Ivermectin**	**Lindane 1%**	**All subjects**
Mild <50	24	32	56
Moderate 50-100	42	26	68
Severe >100	56	68	124
	n = 124	n = 124	248

Table 2. Severity of pretreatment infestation in all study patients			
	Ivermectin (%)	**Lindane 1%(%)**	**P**
	N=124	**N=124**	
1 week	52(41.9)	36 (29.3)	0.32
2 week	72 (58.6)	55 (44.3)	0.24
After repeating treatment			
4 week	115(92.7)	89 (71.7)	0.042

sponders (52 and 69, respectively) received a repeat therapy. By the fourth week, 115 (92.7%) patients were cured with ivermectin, whereas 89 (71.7%) patients were cured with lindane. This difference was statistically significant (P=0.048). Nine (7.3%) patients from ivermectin group and 35 patients from lindane group did not respond to the extra doses of medication. They were crossed over to the other group and were cured after a single application. None of the 248 participants experienced irritation, allergic reactions, or other adverse reactions to the products, which were considered cosmetically elegant and were well accepted by the patients and parents. None of the patients worsened during the study. All of the treatment failures were improved compared with their pretreatment status, and none had more than fifty new lesions.

DISCUSSION

Since the introduction of topical lindane for the treatment of scabies in 1948, 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 (15). The general consensus appears to be that the benefits to be derived from the continued use of lindane as a scabicide and pediculicide outweigh the associated risks. This would appear to be the view of van den Hoek *et al*. (16) and Page *et al*. (17). Current evidence weighs on the side of continued use of this very effective agent (15). Seizures secondary to this medication have been reported, particularly when this medication was applied to wet skin or to the skin altered by inflammatory changes

that cause easy absorption (18). In recent years, resistance to lindane seems to be rising and there are reports of several clusters of patients with lindane-resistant scabies worldwide (19). As far as resistance is concerned, therefore, it seems reasonable to conclude that a potential for adverse reactions from the application of lindane preparations therapeutically does exist, if the preparations are not used properly. The risk of adverse reactions with their use, however, appears minimal when the preparations are used properly and according to directions (20). Ivermectin is a novel antiparasitic agent effective against a variety of endoparasites and ectoparasites (9). In this study, ivermectin was as effective as lindane 1% at two-week follow up in treating scabies and this is in accordance with previous studies (21). In our patients, we found that oral ivermectin was superior to lindane 1% lotion when used in two doses over a period of 4 weeks. Data from the 4th week showed that ivermectin continued to decrease both the lesions and the degree of pruritus as compared to lindane 1% lotion, and this difference was statistically significant (P=0.042). Because ivermectin has not been proven to be ovicidal, a single dose of 200 µg/kg body weight may be inadequate to eradicate the different stages of the parasite, and a higher dose or a second dose may be required within 1 to 2 weeks for 100% cure (22). In the study carried out by Elgart *et al*., a higher number of patients showed clearance of lesions as compared to our results (23). This could be explained by the longer follow up. They showed that ivermectin was effective in preventing recurrences of scabies over a period of 2 months. In the study carried out by Walton (24), 100% cure was seen in the treatment with ivermectin, possibly because the study was carried in a smaller number of patients with follow up of 2 weeks and ages were 12 years or above, when the activity of sebaceous glands is more pronounced.

CONCLUSION

We found ivermectin to be more effective than lindane for the treatment of human scabies, allowing fast and safe cure of this condition through simple administration. The treatment of scabies with ivermectin then becomes an effective resource to control infestation in confined populations and, more generally, for medical plans to eradicate human scabies

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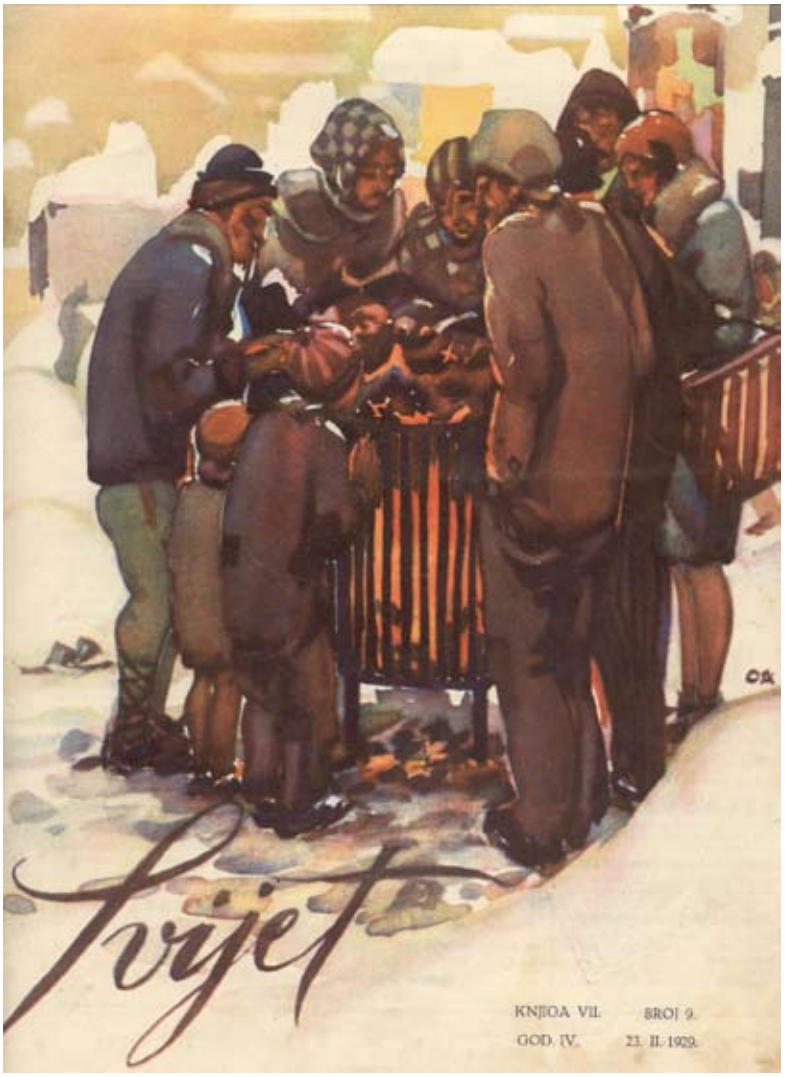

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