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Original Article

Ivermectin in the treatment of scabies

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Abstract

Background Ivermectin is structurally similar to the macrolide antibiotics, but does not have antibacterial activity. It is, however, active against number of ecto- and endoparasites. It has been extensively employed in veterinary medicine, and in humans it is used to treat filarial diseases, principally onchocerciasis.

Objective A clinical trail was conducted for the first time in Pakistan to determine the efficacy of oral ivermectin in patients with scabies and its comparison with the most effective standard treatment available until now i.e. permethrin applied locally.

Patients and methods This non randomized, open-label comparison study was conducted in department of dermatology, Pakistan Institute of Medical Sciences, Islamabad, from January, 2007 to March, 2007. 30 patients, 12 years of age or older were enrolled in the study. Diagnosis was made on the basis of clinical features, including history and clinical examination with typical lesions and sites of involvement. 15 patients received orally administered ivermectin, two doses of 200 µg/kg body weight separated by one week. Remaining 15 patients received local treatment with permethrin 5%, according to the standard method, in which it is applied for 12 hours and was repeated after one week. Pre-treatment complete physical examination was done along with necessary laboratory investigations in all cases. They were repeated after 2 weeks at the end of treatment to note any abnormality developing. Groups were almost matched in terms of age, sex and weight. The efficacy was evaluated by the relief of symptoms and disappearance of the lesions.

Results All patients completed therapy without any complication. Patients recovered completely with relief of symptoms and complete healing of skin lesions. The cure rate was 100% in both groups, at the end of treatment period.

Conclusion Ivermectin seems to be a safe and effective alternative to permethrin. The striking advantage of ivermectin being its benefit of oral administration and low cost.

Key words
Scabies, ivermectin, permethrin

Introduction

Scabies is a skin disease caused by infestation with the mite *Sarcoptes scabiei*. Although it may infest any human in any climate, it is most common in children younger than two years and is endemic in the tropics.[1] The female mite, whose life expectancy is about 30 days, burrows into the epidermis to lay eggs. The eggs hatch into larvae in three to four days, and larvae mature into adults in 14 to 17 days.[2] Male adult mites are smaller than females, remain on the skin surface, and die shortly after mating. There is evidence that mites can live for up to three days without a human host, and a reported outbreak of scabies among

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laundry workers provides evidence that fomites may spread disease.[3] While animal strains of scabies exist and can infect humans, the mites cannot complete their life cycle or be passed to other hosts.[4]

Symptoms of scabies infestation include rash and intense pruritus that is often worse at night. The lesions begin as tiny erythematous papules and can progress to vesicles or pustules. Linear burrows are a classic feature but are not seen commonly. Excoriation and ulceration also may be present, and a more generalized hypersensitivity reaction, including urticaria, may occur. In severe cases and in immunocompromised hosts, large areas of crusting may be seen. Although outbreaks can occur almost anywhere, the axillae, web spaces between fingers, and flexor surfaces of the wrists are the most common areas. Male genitalia, female breasts, the gluteal crease, waistband, and antecubital fossae also are frequently affected. The face and scalp usually are spared except in infants.[5]

Typical distribution of lesions, intense pruritus, and patchy, discrete lesions with secondary excoriation signal scabies infection. The diagnosis usually is clinical but may be confirmed by skin scrapings near the newest and least disturbed skin lesions or under the fingernail edge.[6] Light microscopy of the scrapings may detect the female mite, eggs, and feces pellets. Topical sulfur treatments have been used for centuries to treat scabies infection. More recently, topical benzyl benzoate and lindane were mainstays of therapy. In 1990, a study[7] comparing lindane with topical permethrin showed improved efficacy of permethrin at 28 days, with a lower risk for neurotoxicity. Topical permethrin was subsequently compared favorably with 10 percent crotamiton[8] and has become a widely used treatment for scabies. In some studies, it has been shown to be more effective than a single dose of oral ivermectin, although it has equivalent efficacy when 2 doses of ivermectin are used at time zero and 2 weeks later. Scabiecides should be prescribed for patients, household members, and close personal contacts. Symptomatic treatment may require antihistamines. More severe symptoms may require a short course of topical or oral steroids. Secondary infections may require antibiotics

We undertook the present study to compare the efficacy and safety of oral ivermectin with topical permethrin 5% cream, the standard treatment of scabies.

Patients and methods

A randomized, open-label comparison of orally administered ivermectin and permethrin was carried out in dermatology department of Pakistan Institute of Medical Sciences, Islamabad, from January, 2007 to March, 2007. Patients were of either sex, aged 12 years or older. Informed consent was taken from the patients before starting treatment. Diagnosis was made on the basis of symptoms of itching all over the body, typically more at night and involving other family members or people in close contact along with widespread inflammatory papular, pustular or nodular eruption involving typical body sites like web spaces, periumbilical region and genital areas, with or without burrows. They did not have any other significant concomitant disease. They

had normal blood counts, liver and renal function tests before starting treatment. Patients who were pregnant or lactating were excluded from the study.

30 patients fulfilling the inclusion criteria were finally enrolled and were divided into two equal groups of 15 patients each, who were almost matched in terms of age, weight and duration of disease. Group A patients received ivermectin, two doses of 200 µg/kg body weight separated by one week. Remaining 15 patients received local treatment with permethrin 5%, according to the standard method, in which it is applied for 12 hours and is repeated once after one week. Pretreatment complete physical examination was done along with necessary laboratory investigations in all cases. Patients received medicine with meals. Patients were reviewed weekly for subjective adverse events. Blood samples were obtained in the beginning and at 2 weekly intervals at the end of treatment period for blood cell count, liver function tests, and renal function tests along with urine routine examination.

Efficacy was evaluated by relief of symptoms and disappearance of lesions. Relapse was defined by signs and symptoms suggestive of scabies and appearing after an initial cure (1 month). Treatment failure was defined as either lack of initial cure or relapse, or appearance of new lesions. Chi-square test was used to compare response (categorical variables) while Mann-Whitney U test (non-parametric test for paired data) was used to evaluate the efficacy of the treatment.

Results

A total of 30 patients were enrolled in the study, which belonged to both sexes and aged over 12 years. Group A (ivermectin) had a mean and S.D. of age 35.93±23.53 years while group B (permethrin) had mean age of 37.80 with standard deviation of 22.79 years (**Table 1**). In group A (ivermectin), 9 (60%) patients were male and 6 (40%) patients were females while in group B (permethrin 5%), 10 (70%) patients were males and 5 (30%) were females. In group (A) 10 (66.6%) patients had inflammatory papular lesions, 4 (26.6%) patients had mixed eruption of papules and pustules and 1 (6.6%) had papular lesions with secondary eczematization. While in group (B) 7 (46.6%) of patients had inflammatory papular lesions, 6 (40%) patients had mixed eruption of papules and pustules, 2 (13.3%) had papular lesions with secondary eczematization. So in both groups majority of patients had inflammatory papular lesions.

In both the groups at the end of treatment, all patients were cured. This was based on the relief of symptoms with clinical resolution of the lesions. The cure rate at the end of one week was 60% and 46% in the ivermectin and permethrin groups, respectively while it increased to 100% in both groups at the end of second week (**Table 1**).

In both groups no major side effect was noted, except in group B in which 86% of patients had complaint of irritation after application of the drug. In group A four patients, while in group B six patients had

Table 1 Demographic characteristics and efficacy in two groups

	Group A (Ivermectin) (n=15)	*Group B (Permethrin 5%) (n=15)*
Mean age (years)	35.93±23.53	37.80±22.79
Male:female	9:6	10:5
Efficacy		
At end of one week	9 (60%)	7 (46.6%)
At end of therapy (2 weeks)	15 (100%)	15 (100%)

infected lesions for which cephradine was used orally for 7 days.

Discussion

Scabies is a common skin infection. Worldwide, the prevalence of scabies has been estimated at 300 million cases annually. It is seen frequently in the homeless populations but occurs episodically in other populations, as well. While scabies appears to be more common in the younger population, it certainly occurs in all ages, all ethnic groups, all socioeconomic levels, and in both sexes. It is not directly related to hygiene, but it is associated with poverty and crowding.

Treatment options include either topical or oral medication. Topical options include permethrin 5%, lindane 1%, benzyl benzoate 12.5-25%, crotamiton 10%, sulfur 3-10%, tea tree oil, oil of the leaves of *Lippia multiflora moldenke,* a shrub found growing in West Africa Savannah. Oral options include ivermectin. Ivermectin is an anthelminthic agent that has been a safe, effective treatment for onchocerciasis (river blindness) when given in a single oral dose of 150 to 200 µgm/kg body weight. Ivermectin is structurally similar to the macrolide antibiotics, but does not have antibacterial activity. Ivermectin selectively binds with glutamate-gated chloride ion channels in invertebrate nerve and muscle cells, causing cell death. Half-life is 16 h and it is metabolized in liver.

Side effects of ivermectin include fever, headache, chills, arthralgia, rash, eosinophilia, and anorexia.[15] Many of these symptoms are thought to result from the death of parasites rather than as a reaction to the drug. Ivermectin seems to be concentrated in the liver and fat tissue, with very low levels reaching the central nervous system.[19] No significant drug interactions have been reported.[20] A study of elderly nursing home patients treated for scabies infection showed an increased death rate among ivermectin-treated patients,[21] but this finding has not been confirmed in multiple subsequent trials.

Studies have been done to compare the efficacy of ivermectin with lindane and permethrin, and it was found that there was no difference at the end of four weeks.[22,23] Although there are several studies which favour the use of ivermectin as antiscabies, still people have doubts in their minds about the safety of the drug. This trial was planned for not only determining the efficacy of the drug but also the possible side effects.

Our present trial in immunocompetent patients, 12 years of age or older showed that oral ivermectin is effective and safe treatment for scabies. At the end of trial period, all the patients in this treatment

group recovered with complete healing of lesion. No side effect was noted in both groups. Significantly higher cure rates were seen in our trial. We compared ivermectin with conventional permethrin and found both of them to be equally effective.

Therapeutic agents may be compared with respect to efficacy, tolerance, convenience and cost of administration. Ivermectin is a very appealing therapy for use in chronic care facilities, where simultaneous oral dosing of residents and personnel can be used to treat scabies outbreaks that affect symptomatic persons as well as asymptomatic carriers. Oral ivermectin also appears to be effective in the treatment of crusted (Norwegian) scabies, especially in HIV-infected patients, which in some cases is impossible to eradicate by topical therapy alone. A combination of aggressive topical therapy combined with oral ivermectin may be the optimal management for crusted scabies.

Very high cure rate of 100% in our study clearly shows the efficacy of the drug and side effects profile also shows that it is well tolerated. Oral treatment with ivermectin is very easy to take as compared to the local treatments which are not only difficult to apply but also socially acceptable by many patients.

Conclusion

Ivermectin appears to be a safe and effective alternative to currently available therapies for scabies. Oral administration makes it easy to use. However, its safety in children should be well-documented before it can be recommended for this age group.

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