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Original Article

Comparison of efficacy and safety of oral ivermectin with topical permethrin in treatment of scabies

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Abstract

Background Scabies is an ectoparasitic, highly contagious skin disease caused by a mite called *Sarcoptes scabiei.* Topical permethrin and oral ivermectin are currently being used and considered to be safe and effective than the previously used agents.

Objective To compare the efficacy and safety of oral ivermectin with topical permethrin in treating scabies.

Patients and methods It was an interventional (quasi-experimental) study, conducted in out-patient clinic of Dermatology Department, Unit II, Mayo Hospital, Lahore. Hundred patients belonging to either sex and from 2 to 60 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 was given single application of topical permethrin 5% cream at night on whole body for 12 hours. When there was no cure in two weeks, a 2nd treatment was given with either drug in their respective group. Investigations were carried out at presentation and at 2nd week while patients were followed up at 2nd and 4th weeks.

Results Permethrin showed marginal better efficacy (88.1%) in completely clearing scabietic lesions at fourth week of therapy as compared to ivermectin (79.5%), the difference was insignificant (p=0.15). Seven patients in ivermectin group had side effects as headache, increase in itching and secondary bacterial infections as compared to permethrin group in which one patient had erythema (p<0.05).

Conclusion Ivermectin is as effective as permethrin in the treatment of scabies when used in two doses over a period of 4 weeks.

Key words
Scabies, permethrin, ivermectin.

Introduction

Scabies is a common ectoparasitic infection caused by a mite, *Sarcoptes scabiei* var. *hominis*. The arthropod causes an intensely pruritic and highly contagious skin infestation, which affects both sexes of all socioeconomic status and ethnic groups.[1,2] 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 sulphur, benzyl benzoate, malathion, crotamiton, monosulfiram, and lindane.[3,4]

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Topical permethrin is used nowadays for being safer and more effective than the previously used agents.[5,6]

Ivermectin is a new drug structurally similar to macrolide antibiotics. Since its discovery in 1975, it has been approved for the treatment of strongyloidiasis and onchocerciasis. It is currently also being used for the treatment of scabies. The effective dose is 150-200 µg/kg body weight once or may be repeated at two weeks interval. 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.[7-13] Reported side effects include fever, arthralgia, myalgia, dizziness, headache, hypotension, tachycardia, and lymphadenopathy. Prolonged prothrombin time, transient ECG and liver enzyme changes have also been observed.[8]

In the present study we compared the efficacy and safety of oral ivermectin with topical permethrin in the treatment of scabies.

Patients and methods

Patient selection

It was an interventional (quasi-experimental) study carried out in outpatient section of Dermatology Department, Unit II, Mayo Hospital, Lahore. Total duration of study was six months. The study included 100 patients presenting with scabies belonging to either sex between two and sixty years of age. Immunocompromised patients, pregnant and lactating females, patients having bacterial, fungal or viral infections of skin, patients receiving any treatment for systemic disorders or patients who received treatment of scabies in last four weeks were excluded from study.

A preformed pro forma was completed for all patients. An informed consent was obtained from the patients or parents in case of children.

All patients diagnosed of having scabies on history and examination were divided by using random number table into group A and group B. Scraping for mite was performed in cases of doubt.

Oral ivermectin was given to group A in a single dose of 200 µg/kg body weight. Group B was given single application of topical permethrin 5% cream at night on whole body for 12 hours. Those patients not responding to first treatment were given second dose at 2nd week in their respective groups.

Evaluation

Examination for burrows and papules was performed on 2nd week and 4th week of follow up. Scraping for mite and investigations like total leukocyte count, eosinophils, alanine aminotransferase and prothrombin time were carried out at baseline and 2nd week of follow up, as these changes are transient and their levels return to normal beyond two weeks. In patients where indicated these investigations were also performed at 4th week. Patients were considered as having mild (lesion count <10), moderate (lesion count of 11-50) and severe (lesions >50). Pruritus was graded as mild, moderate and severe on the basis of sleep disturbance.

The efficacy was ascertained by the disappearance of itching, clearance of skin lesions and absence of mites on microscopy of skin lesions. The safety was determined by the absence of headache, arthralgia, myalgia, hypotension, tachycardia, lymphadenopathy and normal investigations for oral ivermectin; and erythema, stinging and burning for topical permethrin. Those patients not responding to

first treatment were given second dose at 2nd week in their respective groups. Photographs were taken at the beginning and at 4th week.

Results

Of 100 patients, 44 patients in group A (ivermectin) and 42 patients in group B (permethrin) completed the study while 14 patients were lost to follow up. Age, sex distribution, family history and disease characteristics in two groups are shown in **Table 1**.

Two weeks after the first dose of respective treatments, 24 (54.5%) subjects in the ivermectin group and 20 (47.6%) subjects in topical permethrin group were cured of disease, p=0.5.

All patients with persistent lesions were given a second dose of both treatments at week 2. Two weeks after the second treatment, greater number of subjects had persistent lesions in the ivermectin group compared with subjects in the permethrin group. Similarly, greater percentage of patients in ivermectin group still complained of nocturnal pruritus at fourth week of treatment, as compared to only one patient in the permethrin group though the difference was insignificant (**Table 1**). At fourth week of follow-up, 35 (79.5%) patients in ivermectin group and 37 (88.1%) patients in permethrin group were cured of scabies, p=0.157.

Regarding the safety, only one patient in permethrin group had erythema and burning on second day of treatment whereas 4 (9.1%) patients in ivermectin group suffered from severe itching, 3 (6.8%) had secondary bacterial infections, while 1 patient (2.3%) complained of headache. Difference of side effects between two groups was statistically significant (p=0.05).

Discussion

In our patients we found that oral ivermectin is as effective as topical permethrin when used in two doses over a period of 4 weeks. These results are consistent with the international study by Usha *et al*.[11] There are minor variations when we compare the two studies. In our study, more subjects in the ivermectin group (54.5% vs. 47.6%) were cured of lesions by the second week of therapy, but the results were insignificant, while in the study by Usha *et al*.[11] first dose of permethrin was more effective in clearing lesions than ivermectin. One reason to account for this discrepancy could be that more patients in the ivermectin group had moderate and severe lesions as compared to permethrin group, although patients were divided into two groups using random number table. It may be assumed that increased efficacy of ivermectin is due to its effect on only adult stages of the mite, thereby improving severe scabies more than permethrin. It acts by causing excessive release of neurotransmitter γ-aminobutyric acid (GABA) in the peripheral nervous system of the parasite resulting in its death. Also, more patients in the permethrin group with mild to moderate scabies had clearance of lesions as compared to ivermectin, where improvement was seen more in patients with severe scabies.

The data from the 4th week showed that permethrin continued to decrease both the lesions and the degree of pruritus as compared to ivermectin. In this last follow-up, patients in ivermectin group showed less response regarding symptoms (itching) and signs (papules). This could be because of permethrin action on all stages (ova, larvae and adults) of mite and because of its action on the voltage-sensitive sodium channel of the parasite, which is necessary for the generation of action potentials in excitable cells, thus causing the

Table 1 Characteristics of patients at baseline, 1st week and 2nd week.

	Group A (Ivermectin) n (%)			*Group B (Permethrin) n (%)*		
Sex distribution						
Female	20 (45.5)			24 (54.5)		
Male	22 (52.4)			20 (47.6)		
Family History						
Present	42 (95.5)			38 (90.5)		
Absent	2 (4.5)			4 (9.5)		
Lesions at presentation	*1st week*	*2nd week*	*4th week*	*1st week*	*2nd week*	*4th week*
No lesion	0	24 (54.5)	11 (25)	0	20 (47.6)	17 (40.5)
Mild	0	10 (22.7)	9 (20.5)	1 (2.4)	17 (40.5)	5 (11.9)
Moderate	20 (45.5)	8 (18.2)	0	28 (66.7)	5 (11.9)	0
Severe	24 (55.5)	2 (4.5)	0	13 (31)	0	0
Nocturnal pruritus	*1st week*	*2nd week*		*1st week*	*2nd week*	
Mild	0	9 (20.5)	3 (6.8)	0	11 (26.2)	1 (2.4)
Moderate	16 (36)	16 (36.4)	0	18 (43)	7 (16.7)	0
Severe	28 (64)	1 (2.3)	0	24 (57)	0	0
Scraping for mite	*1st week*	*2nd week*		*1st week*	*2nd week*	
Not applicable	37 (84.1)	38 (86.4)	44 (100)	33 (78.6)	33 (78.6)	42 (100)
Positive	4 (9.1)	0	0	8 (19)	0	0
Negative	3 (6.8)	6 (13.6)	0	1 (2.4)	9 (21.4)	0

paralysis of mite and leading to its death.[12-15]

Since 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. Ivermectin, though very effective on the adult stages of the mite, is not ovicidal, thus explaining the comparatively decreasing efficacy in reducing the lesions and pruritus with the second dose of the drug.

Another possible explanation for relatively less efficacy of ivermectin is that being a lipophilic drug, it is secreted in higher concentration in sebum.[16,17] Areas where activity and number of sebaceous glands is less such as web spaces, palms and soles, sides of fingers may not be benefited by systemic ivermectin as compared to the topical permethrin.

In the study carried out by Usha *et al*.[11] higher number of patients showed clearance of lesions as compared to our results. This could be explained due to the longer follow up of their patients (eight weeks) as compared to 4 weeks in our study.

In the study carried out by Khan and Yasmeen,[16] 100% cure was seen in both treatment groups possibly because study was carried on 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. Also permethrin was applied twice with interval of one week whereas in our study it was applied once for 8-12 hours.

Regarding side effects, permethrin was found to be significantly more safe than ivermectin (p=0.05). Only one patient had mild superficial burning as compared to 7 patients in ivermectin group who had secondary bacterial infection, headache and increase in pruritus.

Ivermectin has been reported to cause serious side effects. It was found that such effects were seen when higher doses of the drug were accidentally ingested by the patients.[8] We have found it to be quite safe in our cases.

Bacterial infection seen in 3 of our patients has not been reported before. Though the number in which we observed this side effect was not significant but further studies on a larger number of patients may clarify the situation. More studies are needed with larger patient population at community level to assess the effects of ivermectin and permethrin separately in patients for better control of this communicable disease.

Although ivermectin was as effective as permethrin, it has few outweighing advantages over the topical permethrin. It is 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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