ORIGINAL PROF-1400

SCABIES;
ORAL IVERMECTIN AS THE TREATMENT

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ABSTRACT... All the conventional scabicidal drugs are used topically and have poor compliance. In several reports and studies, ivermectin, an oral antiparasitic drug, has been shown to be an effective scabicide without any major side effect. **Objective:** To evaluate the efficacy and safety of oral ivermectin in the treatment of scabies. **Design:** An open, randomized clinical trial (convenience sampling). **Settings:** Dermatology Department, Divisional Headquarters (DHQ) and Allied Hospitals, Punjab Medical College, Faisalabad, Pakistan, from 1st September 2002 to 28th February 2003. **Material and methods:** The study comprised of 100 outdoor patients of scabies, 5-60 years of age, diagnosed on history, clinical examination and light microscopy. They and their affected family members were given a single oral dose of ivermectin 200 mg /kg body weight. Patients were followed up at intervals of 1, 2, 4 and 8 weeks. **Results:** Fifty-seven patients (57%) had complete recovery at 2 weeks whereas 93 patients (93%) had complete recovery at 4 weeks. Seven (7%) failure cases were given a second dose all of which had complete recovery at 8 weeks. No patient developed any major adverse effect. Blood, urine examinations and liver function tests did not show any significant abnormality. **Conclusion:** Oral ivermectin, in a single dose of 200 mg/kg body weight, was effective and safe in the treatment of scabies and could be a useful substitute to conventional topical antiscabietics. However further large scale studies are required to further evaluate its safety.

Key words: Scabies, antiscabietics, ivermectin

INTRODUCTION

Scabies is caused by a mite, Sarcoptes scabiei var. hominis[1-4]. It is still a major public health problem in developing countries[5-8]. Global estimates account for about 300 million cases of scabies (about 5% of the world's population) towards the end of the 20th century[9].

All the conventional scabicidal drugs are used topically[1,10]. Resistance, recurrence and allergic side effects to some of these drugs have been reported[11,12]. They have to be applied all over the body and left for at least 8-12 hours (hrs) before being washed off. This causes poor compliance in patients and their family contacts, making community control of scabies difficult[5,13]. Ivermectin is an antiparasitic agent effective against a variety of endoparasites and ectoparasites[14,15]. Initial reports have highlighted the utility of oral ivermectin in the treatment of scabies[16,17]. When used orally the drug is well tolerated without any major side

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effect[9,15]. All these reports and studies are from foreign countries. So it was considered worthwhile to evaluate the human use of oral ivermectin in the treatment of scabies in Pakistan.

OBJECTIVE OF STUDY

To evaluate the efficacy and safety of oral ivermectin in the treatment of scabies in Pakistan.

MATERIAL AND METHODS

This was an open, randomized clinical trial. A total of 100 patients suffering from scabies, diagnosed according to criteria mentioned below were enrolled randomly (convenience sampling) from 1st September 2002 to 28th February 2003 at the outdoor clinics of Dermatology Departments of Allied and DHQ Hospitals, Faisalabad, affiliated with Punjab Medical College Faisalabad.

DIAGNOSIS

Diagnosis of scabies was made by demonstration of mite, larvae or eggs by light microscopy of the scrapings from burrows mounted with 10% KOH, or by the presence of at least three of the following criteria[16].

1- Demonstration of burrows
2- Presence of lesions of scabies at the classical sites
3- Nocturnal pruritus
4- History of similar illness in the family

The patients were evaluated for the severity, duration, sites of lesions, types of lesions and family history of scabies on the first day before starting oral treatment with ivermectin. The weight of the patients was noted for dose determination. The patients including their family members were given ivermectin as a single supervised oral dose of 200 µg/kg body weight. Patients were advised not to apply any medicine for this disease during the study period. All members of the household were treated at the same time. Children under 5 years of age and pregnant women in the family contacts were treated with 5-10 % sulphur ointment.

All the patients were followed up at regular intervals of 1,2,4 and 8 weeks and thoroughly examined clinically.

Improvement was graded as mild, if there was less than 50% reduction in number of lesions and pruritus, as moderate if there was more than 50% reduction, and as good if complete clearance occurred. Treatment was considered effective if, at the end of 4 weeks, there was relief in pruritus and clinical improvement in skin lesions with no new lesions, and inability to isolate mites or their products microscopically.

Treatment was considered a failure if by the end of 4 weeks, there was no improvement in pruritus and skin lesions, appearance of new lesions or presence of mites or their products on microscopy[16].

The following laboratory tests of patients were carried out before the start of treatment and at every subsequent visit:

1. Complete blood examination
2. Complete urine examination
3. Liver function tests
4. Scraping for mite

Inclusion Criteria

1- Diagnosed cases of scabies
2- Patients between 5 and 60 years of age
3- Informed consent of the patient or patient's guardian

Exclusion Criteria

1- Pregnancy
2- Lactation
3- Bacterial or fungal infections of the skin
4- Receiving treatment for a systemic infection
5- Taking steroids
6- Treated for scabies within last four weeks
7- Patients having crusted scabies

DATA ANALYSIS

All data was entered, retrieved and utilized using the Microsoft excel programme.

RESULTS

A total of 100 patients, 5-60 years of age were studied. The mean age of patients was 22.80 ± 14.69 years. The mean age of males was 23.89 ± 14.05 years and that of females was 21.83 ± 15.31 years. The largest age group of 11-20 years constituted 33 patients (33%), followed by 5-10years age group constituting 25 patients (25%). The smallest age group of 31-40 years constituted 11 patients (11%) (Table I). Forty-six patients (46%) were males and 54 (54%) females (Fig.1). Most of the patients i.e. 85 (85%) were from Faisalabad city and its suburbs whereas 15 (15%) were from rural areas of Gojra, Toba Tek Singh, Tandianwala and Jhang.

No patient was excluded, dropped out, or lost at any point in the study.

The family history of scabies was positive in 99 patients (99%) (Fig.2I).

The mean duration of scabies was 8.24 ± 9.12 weeks (Table II).

Nocturnal pruritus was present in 99 patients (99 %).

Severity of disease was recorded as mild (10 or fewer lesions), moderate (11-49 lesions), and severe (50 or more lesions). 17 The severity of disease was mild in 4 patients (4%), moderate in 58 patients (58%) and severe in 38 patients (38%) (Fig.3).

Fig-1. Sex distribution (n=100)

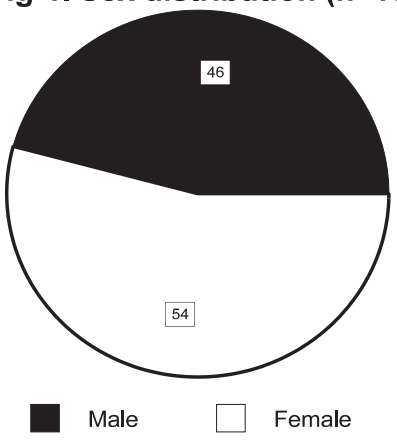


Fig-2. Family history of scabies (n=100)

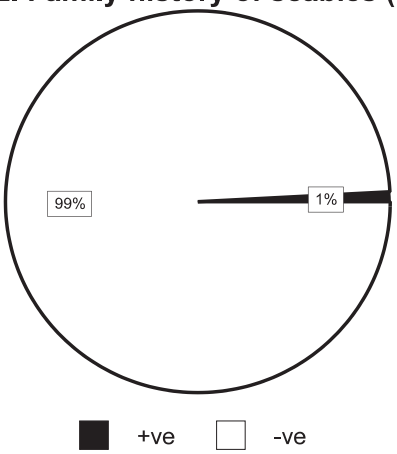
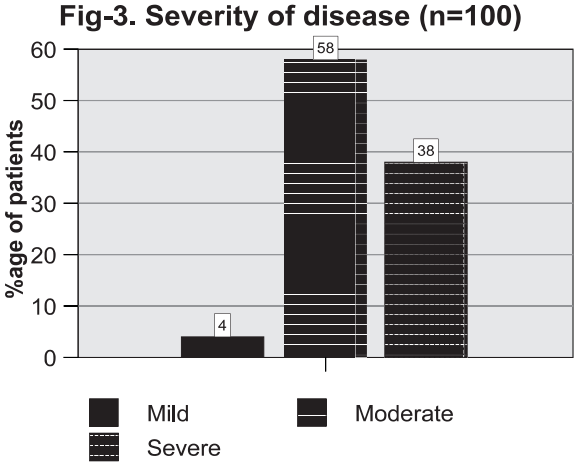


Table-I. Age groups

Age group (Years)	N	Mean	S.D
5-10	25	7.80	1.50
11-20	33	16.06	2.77
21-30	18	26.33	3.61
31-40	11	37.73	2.33
41-60	13	51.23	6.37

Table-II. Scabies duration in different age groups (Wk)

Age group (Years)	N	Mean (weeks)	S.D
5-10	25	7.88	7.36
11-20	33	8.76	10.74
21-30	18	8.11	7.15
31-40	11	9.55	13.46
41-60	13	6.69	6.45
5-60	100 (All)	8.24	9.12



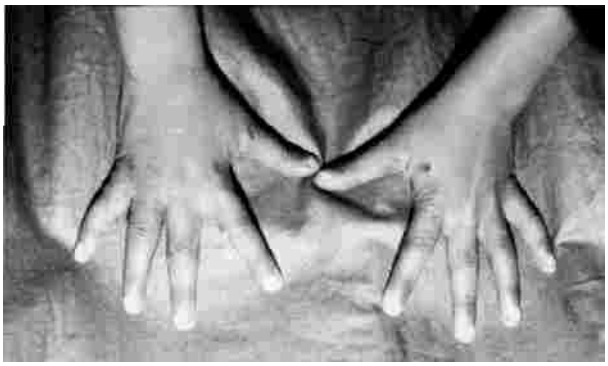


Fig-4 Burrows and papules of scabies in the interdigital clefts.

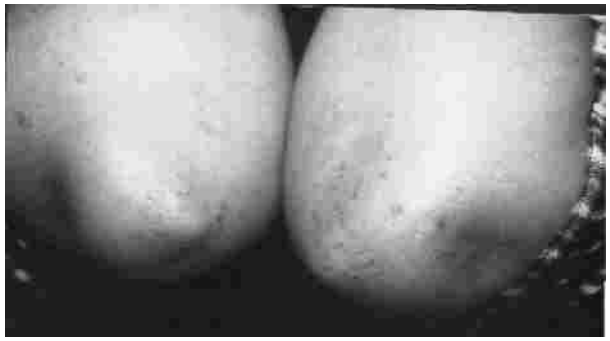


Fig-5. Burrows and papules of scabies on the elbows

Burrows (Fig.4 & 5) were found in 66 patients (66%) (Fig. VI), whereas skin scraping yielded mites or their products in 56 patients (56%) (Fig. 7).

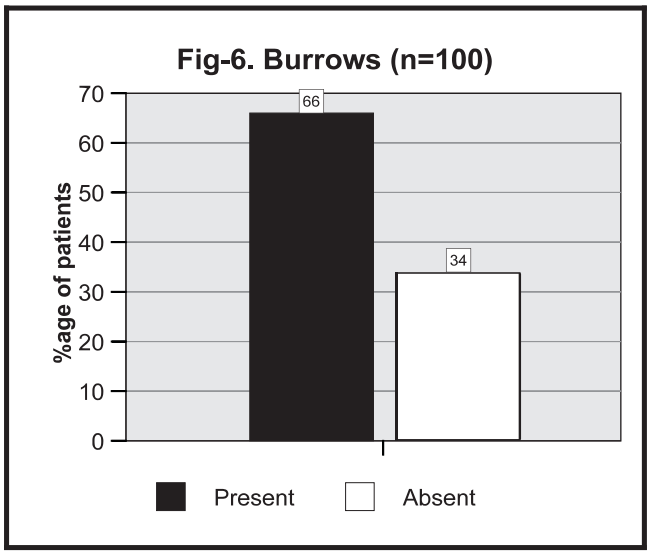
On follow-up, with a single dose, by the first week 36 patients (36 %) had mild improvement and 64 patients (64 %) had moderate improvement but no patient had complete recovery.

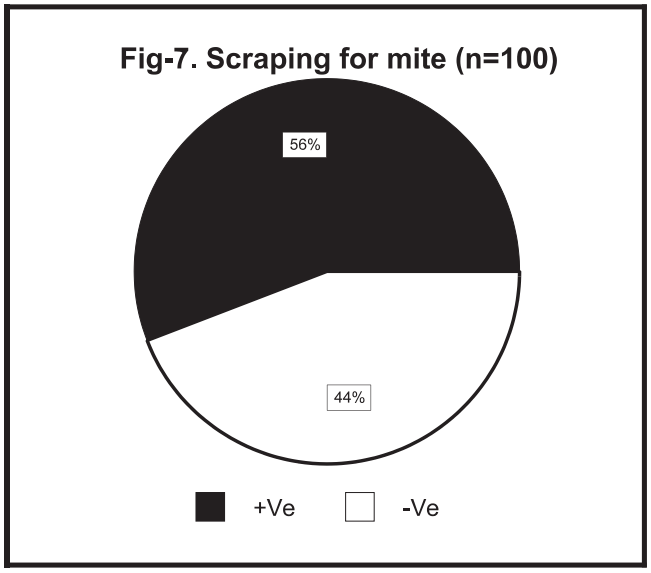
By the second week, 9 patients (9%) had mild improvement, 34 patients (34%) had moderate improvement and 57 patients (57%) had complete recovery.

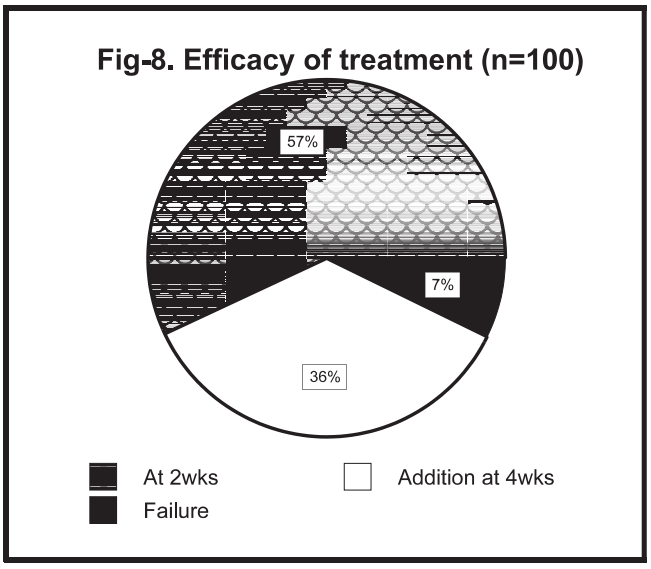
The patients were followed-up and by the fourth week 93 patients (93 %) had complete recovery (Fig. 8), whereas 7 (7 %) non-responders received a repeat dose and they were completely cured by the eighth week.

No patient, followed up to 8 weeks, had recurrence of disease.

No major clinical side effects were seen in any patient. One patient complained of mild to moderate headache on the first day of therapy, which subsided on the same day without any medication. No significant changes in laboratory investigations were noted.







DISCUSSION

Ivermectin, a synthetic macrolide, has been used successfully in many diseases such as strongyloidiasis, onchocerciasis, filariasis, larva migrans, head lice and scabies. It acts through glutamate-gated chloride channels causing excessive release of neurotransmitter (GABA) in the peripheral nervous system of parasite leading to its death. Ivermectin has been used for human scabies by different researchers since early 1990's.

In 1995, Meinking et al reported 45% success at 2 weeks and 100% success at 4 weeks with a single oral dose of ivermectin in patients of scabies[17].

In this study our results showed 57 % recovery at 2 weeks and 93% recovery at 4 weeks with a single dose of oral ivermectin. These results are similar to the earlier reports of Madan et al[18], Leppard et al[19], Meinking et al[17] and Nnoruka et al[20].

We have consistently noted that it may take a month after any single scabies treatment for all cutaneous signs and symptoms to resolve which is in accordance with the studies of Madan et al[18] and Meinking et al[17]. This delay may well explain a significant number of treatment failures in the studies conducted by some other authors such as Usha et al who evaluated their patients at two weeks after treatment with ivermectin[16].

The complaint by one patient, of mild to moderate headache on the first day of therapy, subsiding on the same day without any medication, is a finding similar to that of others such as Madan et al[18].

Contrary to other studies such as that of Usha et al[16], none of our patients complained of aggravation of pruritus after taking the medicine.

The comparison with other studies is shown in (table III).

We did not include patients over 60 years of age though an increase in the death rate among old residents in a long-term care facility, after the use of ivermectin has remained unconfirmed[21].

Though ivermectin has not been used extensively in human scabies, its safety in humans has been evaluated in other diseases such as onchocerciasis. Ivermectin is the mainstay of treatment in the onchocerciasis control programme, with about 19 million doses distributed over the world without any major side effect. In the same control programme, 400 pregnant women inadvertently received the drug in the first trimester, but no significant increase in teratogenicity was observed[16].

Table-III. Comparison with other studies			
Study	N	Response	
		At 2wks	At 4wks
Present study Pakistan 2003	100	57%	93%
Nnoruka et al Nigeria 2000	29	-	93%
Leppard et al Tanzania 2000	1153	-	88%
Usha et al India 2000	40	70%	-
Meinking et al USA 1995	11	45%	100%

While a variety of therapies are available for scabies, it appears that ivermectin will play an important role in selected cases[22,23]. When used properly, it can avoid some concerns regarding the apparent development of lindane- or permethrin-resistant strains[24].

Ivermectin has the additional potential advantage of being a systemic medication[25]. Since a single oral dose of the drug can be administered under supervision at the time of diagnosis, it has the additional advantage of avoiding the problems of noncompliance, misuse, and inadequate application associated with topical therapy.

In previous attempts to control scabies in communities, nursing homes, or institutions, success has depended on treating all persons at risk at the same time, whether or not they show or admit signs or symptoms of scabies. Control programmes currently rely on neck-to-toe application of antiscabietic creams and lotions, with particular attention to body crevices and genital areas. Accomplishing this on a community basis, or in institutions, is difficult, since the treatments need to be administered simultaneously to large numbers of patients to avoid re-infestation. Some people may refuse to participate because they do not believe they have scabies—or are reluctant to admit it—or simply because they wish to avoid the embarrassment and fuss of topical treatment. An oral medication with an excellent safety record, such as ivermectin, offers important benefits in the control of scabies on a large scale, in addition to the benefits of treatment in individual cases and families[16].

The main limitation of the study was that ivermectin could not be given to children below 5 years of age (or < 15kg) and to pregnant or lactating women because there are concerns regarding its use in these conditions due to possibility of more drug penetrance of the immature blood-brain barrier[22]. However, the availability of an effective oral scabicidal agent opens a new era in the management of the oldest identified disease of man, making the possibility of even eradication of the disease.

CONCLUSIONS

- Oral ivermectin in a single dose of 200 µg/kg body weight is effective and safe for the treatment of scabies.
- It may be a convenient alternative to conventional topical scabicides.

However additional large-scale studies are required to further evaluate its adverse effects especially long-term side effects.

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