

## Original Article

# Treatment of scabies simplified

Shahid Javaid Akhtar\*, Muhammad Arif Maan\*, Javaid Iqbal\*, Naseema Kapadia\*\*

\* Dermatology Department, Punjab Medical College, Faisalabad

\*\* Dermatology Department, Karachi Medical and Dental College, Karachi

**Abstract** *Background* Scabies is rampant in our community and conventional scabiecidal therapies are cumbersome, difficult to instruct and hard to implement. This often results in high failure rates because of noncompliance and/or re-infestations.

*Objective* We examined the efficacy of prolonged oral ivermectin administration in the eradication of scabies.

*Methods* Six doses of oral ivermectin, each amounting to 300 µg/kg, were given one week apart to 50 patients and all of their family members/close contacts. No other instructions like change of personal wears, bed sheaths, etc were given.

*Results* A compliance rate of 60% was observed. One and two months follow ups showed a cure rate of 80% and 96% respectively in the patients who completed the full course of the therapy.

*Conclusion* Oral ivermectin is an effective antiscabietic that is easy to administer in our busy hospital/clinical settings and has reasonable patient acceptability. Furthermore, physicians need not bother about the application ritual, frequency and time of application, and change of clothing that are mandatory with the conventional treatment. Re-infestation is a major problem in our combined family system and/or large family size and *extended* administration of this comparatively safe drug also has potential to address this key issue.

**Key words**

Scabies, ivermectin, poor compliance, re-infestation, extended therapy.

## Introduction

Scabies is an ectoparasite infestation, caused by the mite *Sarcoptes scabiei* var. *hominis* and transmitted mainly by person-to-person contact. The name *Sarcoptes scabiei* is derived from the Greek word “sarx” (flesh) and “koptein” (to smite or to cut) and the Latin word “scabere” (to scratch).<sup>1</sup> Scabies was first described more than 2500 years ago. It was referred to in the Old Testament

and by Aristotle but it was not until 1687 that the causative organism was identified by Bonomo and Cestoni using light microscopy.<sup>2</sup>

Although the infectious agent is ubiquitous, it is endemic in impoverished communities. The worldwide prevalence has been estimated at about 300 million cases yearly.<sup>3</sup> Scabies is a major public health problem in developing countries, where the bulk of the disease burden falls on children. Scabies predisposes patients to bacterial superinfection. In streptococcal skin disease there is also the potential for glomerulonephritis.<sup>4</sup> Scabies occurs in both

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**Address for correspondence**

Dr. Shahid Javaid Akhtar  
Associate Professor of Dermatology  
Punjab Medical College, Faisalabad  
Tel: 0300-8652277, 041-8782364  
E-mail: skin227@yahoo.com

sexes, at all ages, in all ethnic groups, and at all socioeconomic levels.

Common scabies infestations are caused by 10-20 parasites per individual.<sup>5</sup> Mites cannot fly or jump but crawl at the rate of 2.5 cm per minute on warm skin. They can survive for 24 to 36 hours at room temperature and average humidity and remain capable of infestation and epidermal burrowing for short while.<sup>6</sup> The predominant route of transmission, therefore, is direct skin-to-skin contact. Transmission by means of shared clothing or other indirect method is rare with classic scabies but may occur with crusted scabies (e.g. in immunocompromised hosts).

Many effective topical scabiecidal medicines are available with success rate of more than 90% but the important factor is management of such cases, especially in our busy OPDs of public hospitals. Topical preparation are often cumbersome, difficult to instruct and problematic to apply to patients and all the family members and/or contacts. This often results in high failure rates because of noncompliance. All the contacts/family members seldom use the topical preparation especially if they are asymptomatic. This frequently causes therapy failure because of re-infestations. That is perhaps why scabies is still very rampant in our community despite the availability of fairly good diagnostic skills and high index of suspicion even at the general practitioner's level and provision of reasonably effective therapeutic remedies.

Although still not licensed in our country, oral ivermectin has been widely used in scabies, both locally and abroad, with excellent clinical benefits and few reports of

drug-related problems.<sup>7</sup> We planned a therapeutic trial to examine the efficacy of *extended use* of this novel oral scabiecidal agent to address the issues of noncompliance and re-infestation.

### **Patients and methods**

The present study was an open trial undertaken simultaneously at the out-patient departments of Allied and DHQ Hospitals (affiliated with the Department of Dermatology, Punjab Medical College, Faisalabad), Abassi Shaheed Hospital, Karachi (attached with Karachi Medical and Dental College, Karachi), and at one of the authors (Akhtar SJ) private clinic between January, 2007 and April, 2007.

It was performed after review committee's approval and all patients gave their informed consent. Fifty consecutive patients of scabies were enrolled in this trial. Exclusion criteria were treatment for scabies within the previous one month, pregnancy, lactation, major intercurrent illnesses, or a history of meningitis or neurological illness, and unreliable patients.

The diagnosis of scabies was made mainly on clinical grounds by a consultant dermatologist or by the demonstration of eggs, larvae, mites, or fecal pellets by light microscopy in doubtful cases. For clinical purposes, presence of at least three of the four criteria (**Table 1**) was taken as a confirmative diagnosis of scabies.<sup>8</sup>

A detailed systemic and dermatologic examination was made, and weight was recorded to determine the dose of the ivermectin. The intensity of pruritus was

**Table 1** Clinical diagnostic criteria.

1. Demonstration of burrow
2. Presence of lesions at the classical sites
3. Nocturnal pruritus
4. Family history of similar illness

recorded with the visual analogue scale (VAS) and scored from one to ten. The severity and type of skin lesions were also recorded. Scrapings from skin lesions were taken in doubtful cases from multiple sites for demonstration of mites or their products.

Ivermectin was given in a dose of 300 µg/kg weekly for six weeks to the patients and all of their family members and contacts. Topical scabiecidal (mainly permethrin) was prescribed to the family members/contacts who were pregnant, lactating, or below two years of age. Ivermectin was given free of cost to all the patients and their family members by courtesy of one of local philanthropist. Pruritus, secondary infection, and eczematization, if present, were treated with cetirizine, appropriate antibiotics (systemic and/or topical), and topical steroids plus antibiotics combination or topical steroids alone.

All the patients were followed up monthly for two months after the completion of the therapy period (i.e. six weeks) and were thoroughly examined clinically. Improvement in pruritus was assessed by the VAS. A patient was declared cured if there were no active skin lesions (primary or secondary) and more than 80% improvement in pruritus as defined by VAS.

## Results

The demographic features and the baseline clinical features of the patients enrolled in

**Table 2** Demographic data and clinical features in the study population (n=50).

Age (years)	23.17±10.28
Sex (male/female)	19/31
Socioeconomic group upper/middle/lower	0/17/33
Marital status married/unmarried	37/13
Duration of illness (wk)	9.5 ± 4.70
Burrow (%)	66
Typical distribution (%)	80
Nocturnal pruritus (%)	82
Family history (%)	46
Secondary infection (%)	86
Severity of lesions mild/moderate/severe (%)	10.5/57/32.5
Severity of pruritus (VAS) (%)	7.8 ± 2.2

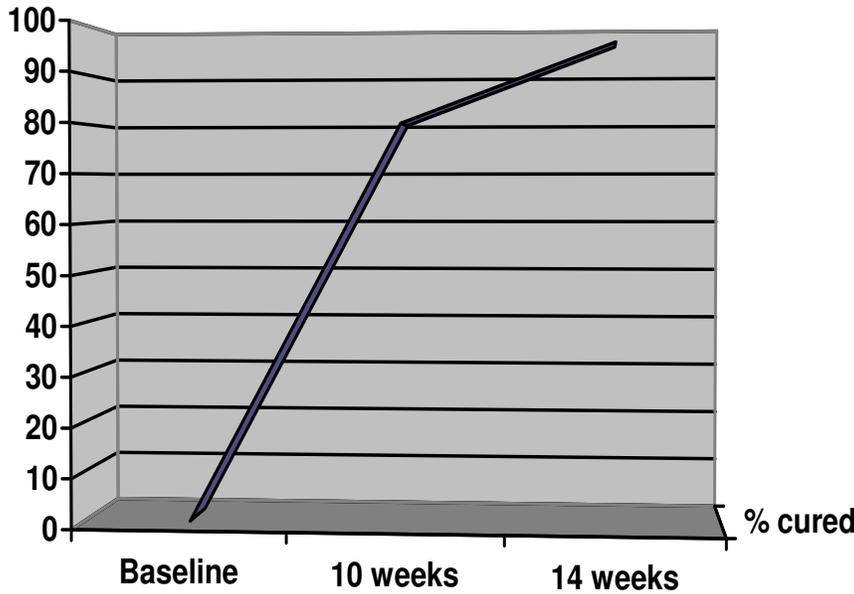
**Table 4** Side effects of the therapy noted (n=30)

	n (%)
Increased pruritus	8 (26.7)
Abdominal pain	5 (16.7)
Nausea	2 (6.6)

the study are depicted in **Table 2**. Thirty (60%) of the initially enrolled 50 patients completed the follow up. One and two months follow-ups after the completion of six weeks therapy showed a cure rate of 80% and 96%, respectively (**Figure 1**) in these patients (n=30). No serious adverse reaction was noted with the treatment prescribed. **Table 3** summarizes the side-effects encountered.

## Discussion

Scabies is also known as the "Seven Year Itch" because classically its incidence runs in cycles.<sup>3,9</sup> But in many under-developed countries, like ours, it remains hyperendemic. Documented estimations of its incidence in overcrowded areas in India ranges from 24% to 40% of the population<sup>10</sup> and similar, or even worse, is the situation in our country. These infestations carry substantial morbidity and upset finances of



**Figure 1** Patients cured at one and two months of post-therapy follow ups.

the already resource-poor affected population. Pyoderma caused by *Streptococcus pyogenes* and *S aureus* is a major complication of scabies that indeed affects rate of post-streptococcal glomerulonephritis in a community.<sup>11-18</sup> In fact, scabies is a major health problem in our area.

Many reasonably effective topical scabiecidals are currently available<sup>19,20</sup> but have low compliance because of the need of application to the whole body and to all family members/contacts. Subungual regions and difficult-to-apply areas are often missed.<sup>21-23</sup> Topical treatments may also be poorly tolerated by some patients (e.g. they are messy and may cause burning or stinging, especially when the skin is excoriated or eczematous, and potential percutaneous absorption may pose a risk). An alternative approach is the use of oral ivermectin, an agent that has been used extensively for several parasitic infections,

including onchocerciasis, lymphatic filariasis, and other nematode-related infestations.<sup>24</sup> Ivermectin is a synthetic derivative of the antiparasitic class of avermectins. Ivermectin is used against a wide range of endoparasites (e.g. nematodes) and ectoparasites (e.g. insects, *S. scabiei*, *Pediculus humanus*, *Demodex folliculorum*, and *Cheyletiella* spp).<sup>25</sup>

Ivermectin is thought to interrupt glutamate-induced and  $\gamma$ -amino butyric acid-induced neurotransmission in parasites, leading to their paralysis and death. Humans are immune to this effect as in them this sort of neurotransmission occurs only in central nervous system and ivermectin does not cross the blood-brain barrier. Ivermectin shows good bioavailability, is metabolized in the liver, and excreted in the faeces by more than 98% of intake. Peak concentrations are reached around 5 hours post-dosing. Minimal concentrations have been

observed in human milk. No genotoxicity or teratogenicity has been observed. Pharmacologically, the half-life of ivermectin in the blood is 16 hours. The drug is lipophilic and may have some affinity for retention with epidermal cells.<sup>25</sup>

Ivermectin is cheap and has repeatedly been shown to be an effective and safe treatment for scabies both in randomized trials and in community-based studies.<sup>26,27</sup> Most comparative studies have shown that in common scabies oral ivermectin is equivalent to the conventional topical scabiecidal treatments (benzyl benzoate, lindane, and permethrin) following one or two oral doses of 200µg/kg.<sup>28-30</sup>

Although initially many observers found that one dose of ivermectin at 200µg/kg was curative, many have altered their dosing pattern. Indeed, there is uncertainty whether optimal therapy for scabies is 200 to 250µg/kg given on day 1 and day 8 or whether it is simply a one-dose treatment at 400µg/kg.<sup>25</sup> Because ivermectin is not very effective ovicidal, a second dose after 7-12 days may seem more logical for scabies and pediculosis.

We used ivermectin in a dose of 300µg/kg orally for extended period of six weeks primarily to address the issues of reinfestation. This *extended therapy* provided a cure rate of 96% two months after the completion of the therapy period (**Figure 1**). These results are slightly better than previously reported in the literature and are probably because of the repeated weekly attacks of ivermectin on the life cycle of the mite.

The safety of ivermectin has been well-documented in vast numbers of people with microfilarial diseases.<sup>31</sup> Indeed, more than 96 million doses of ivermectin have been administered in Africa, Latin America and the Middle East in the treatment of onchocerciasis. This includes millions of doses to children aged 5-15 years. In this setting, there have been no reports of serious toxicity. Only 1.8% of 150000 adverse reports caused by ivermectin were severe in nature.<sup>7,25</sup> Transient and mild adverse reactions included anorexia, asthenia, headache, arthralgia, myalgias, fever, eosinophilia, and maculopapular rashes. Our study also bears out good safety profile of this novel drug (**Table 3**). However, about 27% of patients complained of aggravation of pruritus for 2-3 days after intake of ivermectin. This effect is probably related to Mazzotti reaction and occurs because of release of antigens due to the death of the parasite.

Oral use makes the drug particularly useful for control measures in endemic communities. Ivermectin has many practical advantages over topical therapy. It is potentially the simplest method of treating large numbers of infected adults and children in addition to its value for clinically challenging infections such as crusted scabies. Furthermore, oral treatment with ivermectin could substitute for topically applied compounds, particularly in resource-poor communities where poly-parasitism is common.<sup>32</sup>

One of our main exclusion criteria in the current study was “unreliable patients” i.e. the patients who could not understand the nature, scope, and protocol of the study, who

seemed likely to be noncompliant with the treatment regime, and who could not visit for follow-ups. Despite this somewhat strict standard and free of cost provision of ivermectin, twenty patients (40%) either did not take the medicines as prescribed or not visited for follow-up examinations. Noncompliance, therefore, is not merely because of lack of counseling/understanding or due to economical constraints as many of us may speculate. It is a complex phenomenon and is probably also instinctive in our community.

The mite cannot move well at room temperature and must be transmitted by close personal contact, sexual contact, or mother-to-infant contact.<sup>33</sup> Classical studies by Mellanby showed that direct person-to-person body contact was generally necessary for transmission of scabies. Only four new cases (1.3%) resulted from 272 attempts to infest volunteers who climbed nude into warm beds just vacated by moderately infested patients (with less than 20 mites per person).<sup>34</sup> This finding suggested that clothing or mites shed on the floor were an unlikely means of infestation with the exception of patients with hyperinfestation (crusted or Norwegian scabies) who can shed thousands of mites daily.

Since the predominant route of transmission in classic scabies is direct skin-to-skin contact,<sup>35</sup> we gave no special instructions regarding the change, washing, fumigation, or disposal of personal clothing and/or fomites. The high cure rates seen in the present study substantiate that transmission by means of shared clothing or indirect methods is not important in the common scabies.

The main cause of failure of therapy in our setups is noncompliance of the family members and/or contacts.<sup>36,37</sup> Despite the repeated instructions/advice, they do not use the scabiecidal drugs especially if they are asymptomatic. Even when they use it, they use it incorrectly and haphazardly. This often results in re-infestations and "ping pong" scabies. Intrafamily transmission as the most common means of infestation and/or reinfestation is further supported by molecular studies showing the genotypes of mites from household members to be more homogeneous than those from separate households within a community.<sup>38</sup> The *extended* use of ivermectin specifically addresses this issue of re-infestation.

Scabies is hyperendemic in the numerous poor communities and is commonly associated with considerable morbidity and the country's weakening public-health system.<sup>39,40</sup> Poverty with its typical consequences - inadequate living conditions, overcrowding, and a low level of education - seems to be a major driving force for maintaining a high incidence and prevalence of the disease.<sup>41,42</sup> The best evidence for the predominant role of poverty in determining the occurrence of scabies in a community comes from Bangladesh.<sup>43</sup> Compared with households without scabies, families with scabies were significantly less likely to own their house, as well as being less likely to have constant electricity, and were more likely to live in a house constructed from waste material, and to have a lower monthly income.

Scabies is a major public health threat in our country and control of its epidemic can only be achieved by treatment of the entire

population at risk. Drug shortages do contribute to a high prevalence of infestation in the community.<sup>39</sup> Presumably also, existing treatment options (mainly benzyl benzoate, permethrin, and sulphur compounds) are responsible for poor adherence to treatment protocols. Mass treatment with topical drugs can be difficult since the whole body surface has to be covered with the compound.<sup>23</sup>

Oral treatment with ivermectin is more easily accepted and administration can be directly supervised by auxiliary personnel. Mass treatment with ivermectin can be considered in this setting. As a matter of fact, mass treatment with ivermectin was an effective and safe means of reducing the prevalence of most of the parasitic diseases endemic in a poor community in north-east Brazil<sup>44</sup> and, since the effects of treatment lasted for a prolonged time, mass treatment is probably the best option for reducing hyperendemicity of both ectoparasites and intestinal helminthiases - in conjunction with prevention and education programs. There is evidence that health education combined with improved diagnosis and improved drug supply will result in a greater reduction in scabies.

The best strategies against parasitic skin diseases need to be tailored to different scenarios.<sup>45</sup> In industrialized countries the patient is usually lightly infested with a single ectoparasite species, and there is no or little risk of reinfestation and good compliance can be anticipated. In such a case a topically applicable insecticide could be the treatment of choice for scabies, provided resistance is not a problem in the area. In developing countries population

groups are simultaneously infested with several ectoparasite species, the parasite burden and risk of reinfestation are high, and compliance for prolonged and/or repeated treatment is poor. Here, repeated oral treatment with a broad-spectrum antiparasitic such as ivermectin would be the ideal solution.

However, simple mass treatment with scabicides will produce little long-term effect.<sup>46</sup> Even after long-term surveillance and treatment programs, any interruption of vigilance or logistics will result in a significant increase in incidence. Few studies have addressed the problem of community-administered treatments for scabies,<sup>47</sup> despite the argument that without a community approach to therapy in many developing countries, the successful management of scabies in areas where it affects more than 5 to 6 percent of the population is doomed to failure.<sup>47,48</sup>

Economically disadvantaged people usually have restricted access to health care, which delays diagnosis and treatment, and thus increases the number of individuals spreading the infestation for a protracted period.<sup>49,50</sup> In an urban squatter settlement in Dhaka, for example, 375 (49%) of infested children were not treated for up to 44 weeks after the characteristic signs and symptoms had developed.<sup>43</sup> Even the provision of health care free of charge, as in Brazil, cannot guarantee that patients with scabies will be identified and treated appropriately. In a primary health-care setting in Northeast Brazil, clinically apparent scabies went unnoticed by doctors in 52% of patients.<sup>45</sup>

Controlling scabies at the community level in resource-poor settings has rarely been attempted.<sup>51-53</sup> A few successful examples show that prolonged reduction of prevalence can be achieved by *mass therapy* in combination with public health education and training of health-care providers. Parallel to the reduction of scabies, the occurrence and severity of streptococcal pyoderma, and even childhood glomerulonephritis decreased significantly.<sup>54,55,56</sup> Health education should also address the stigma attached to diseases such as scabies.

The *extended* use of ivermectin does successfully address the issues of noncompliance and re-infestation. We, however, are skeptical that a sustained reduction of scabies in our area can be achieved by this drug treatment alone. What is needed is an integrated approach that combines treatment with the amelioration of the socioeconomic situation of people at risk. Treatment of scabies needs to integrate drug treatment programs with efforts to improve the socioeconomic conditions and educational programs. This knowledge has to be applied in combination with environmental sanitation, health education, and culturally acceptable interventions that are affordable by our underprivileged socioeconomic setting.

### Conclusion

*Extended* oral administration of ivermectin has excellent clinical efficacy with reasonably good safety profile. It is especially suitable to address the issues of noncompliance and re-infestations which are very common in our setups. *Mass treatment*

with ivermectin may be considered to check the high prevalence of scabies current in our community but drug therapy alone is likely to fail without increasing the level of understanding/education, faith on health care delivery system, and living conditions of the people affected. Indeed, treatment of scabies may be simple but the eradication of this hyper-endemic ailment from our community is a very difficult task.

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