Journal of Pakistan Association of Dermatologists 2011; **21**: 87-92.

Original Article

Effectiveness of oral ivermectin for eradicating infesting mites in patients of scabies

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Abstract

Objective To evaluate the effectiveness of single and two doses of oral ivermectin in scabies by observing its effect on infesting *Sarcoptes scabiei*.

Patients and methods This quasi experimental study, after approval of the hospital ethical committee, was conducted at the Skin Centre, Military Hospital, Rawalpindi, from September 2009 to August 2010. Fifty patients with scabies of up to two month duration having at least ten burrows/papules/nodules each with a visible mite were included in the study. Patients with other concomitant illnesses, pregnancy, lactation and those who had been treated with antiscabies medicines in the previous two months were excluded. Patients with more than six household contacts were also excluded from the study. Patients were given oral ivermectin 200μg/kg (Mectis®). Patients were followed up after a week and previously identified lesions were explored for a living mite. If a living mite was extracted from a lesion, the patient was prescribed another dose of oral ivermectin. At second follow up after a week, demonstration of living mites was considered as treatment failure and the patient was prescribed 5% permethrin cream for topical application. Final review of patients was carried out at the end of fourth week.

Results Out of 50, in 22 (44%) patients, a living mite was isolated at one week follow up. At the end of second week, a living *Sarcoptes scabiei* was found in 11 (22%) patients. All of these 11 nonresponders were treated with topical application of 5% permethrin lotion. At the end of four weeks 49 patients reported for follow up without any identifiable living mite. One patient who had no mite at the end of first and second week did not report back after four weeks.

Conclusion Oral ivermectin is a convenient remedy for scabies with a cure rate of 56 % after a single dose and 78% after two doses, a week apart.

Key words
Scabies, ivermectin, *Sarcoptes scabiei*.

Introduction

Scabies is a commonly encountered parasitic infection in dermatology clinics. Patients usually present with itching leading to significant discomfort and at times, embarrassment. Its diagnosis is usually made clinically and medicines are prescribed accordingly. Topical antiscabies medicines have been the mainstay of therapy since ages and are still used as standard treatment. Patient is instructed to apply medicine from neck to toes and ensure it to remain there for the prescribed period ranging from eight hours to several days. Household contacts are advised to apply medicine simultaneously. Although it looks simple yet the most difficult aspect of management is adherence to instructions regarding application of medicines. Treatment failure, not uncommon, is often due to improper application of medicines or re-infestation by untreated contact.[1] Ensuring compliance to the prescribed treatment is, therefore, of prime importance and can logically be achieved by making treatment easy and simple.

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Oral ivermectin has practically resolved the issue of treatment compliance by curing the disease with single or two doses of medicine a week apart. Many studies have been carried out to determine its efficacy and compare it with other antiscabies treatment. Researchers have come out with variable results and its efficacy has been described from 70% to 100%. Most of the studies have determined its efficacy by the presence or absence of symptoms and lesions.[2,3] Extraction of mites from the lesions has seldom been used to evaluate efficacy of treatment. This study was carried out to evaluate the effectiveness of oral ivermectin for treating scabies by demonstrating the presence of living mites prior to and after treatment in patients of scabies.

Patients and methods

This quasi experimental study, after approval of the hospital ethical committee, was conducted at the Skin Centre, Military Hospital, Rawalpindi, from September, 2009 to August, 2010. Fifty patients of scabies of up to two months duration having at least ten burrows/papules/nodules each with a visible mite were included in the study. Patients with other concomitant illnesses, pregnancy, lactation and those who had been treated with antiscabies medicines in previous two months were excluded. Patients with more than six household contacts were also excluded from the study because of the difficulty of ensuring compliance in treating such a large number of household contacts simultaneously. After informed consent and thorough initial evaluation including history and physical examination, diagnosis was confirmed in all the patients by extracting a living *Sarcoptes scabiei*. A detailed examination of skin was then carried out and data regarding type and distribution of lesions showing unequivocal presence of mite were recorded on a body diagram. All patients were fully explained about the disease and were given tablet ivermectin in a dose of 200μg/kg. Their family members who were not included in the study were also prescribed treatment for scabies simultaneously with topical application of 5% permethrin lotion. Patients were followed up after one, two and four weeks and extraction of mite was attempted from the identified lesions.

The efficacy of ivermectin was defined as its ability to eradicate all living mites from the patient. Treatment was considered to be a failure if a living mite was isolated at follow up visit. At first follow up, one week after the first dose of medicine the lesions were carefully examined for the presence of mite. Those lesions showing mite clinically were explored one by one till a living mite was isolated. In case of treatment failure at the end of first week, dose of ivermectin was repeated. If the repeat treatment also failed, at the end of a further one week of follow-up, all remaining visible mites were removed for confirmation by microscopy and the patient was prescribed 5% permethrin cream for topical application. Final review of patients was carried out at the end of fourth week.

Results

Among 50 patients enrolled in the study 41 (82%) were males and 9 (18%) were females. Their ages ranged from 18 to 56 years with a mean of 28 years. In all patients a living mite was extracted during the initial visit to confirm the diagnosis.

At one week follow up, in 22 out of fifty (44%) patients a living mite was isolated whereas 28 (56%) patients were cured of scabies. At the end of second week mites were found in 11 (22%) patients and 39 (78%) were free of mite. All visible mites were removed from these patients and each one was found to be active. All of these 11 non-responders were

Table 1 Cutaneous lesions identified to contain a mite during initial and subsequent follow up visits.

Visit	*Burrows*	*Nodules*	*Papules*	*Total number of mites identified*
Initial visit	362	294	172	828
1st follow up visit (after a week)	72	112	15	199
2nd follow up visit (after two weeks)	16	31	1	48
3rd follow up visit (after four week)	0	0	0	0

treated with topical application of 5% permethrin lotion. At the end of four weeks 49 patients reported for review. No mite was observed in them. Detail of lesions containing a mite at the time of initial and subsequent examination is shown in **Table 1** and **2**. One patient who did not show mite at the end of first and second week did not report back after four weeks.

No side effects were observed in any patient.

Discussion

Many studies have been conducted to evaluate the effectiveness of oral ivermectin in scabies during the last twenty years with variable results. A cure rate ranging from 70% to 100% has been described in most of the studies.[2,3,4,5] These studies mostly relied upon the presence or absence of symptoms and lesions to assess the efficacy of the drug. The inherent drawback of this approach is that it is an indirect way of assessing efficacy of medicine. Ivermectin neither directly decreases itch nor it has any role in the resolution of lesion. It directly kills *S. scabiei* by binding selectively to specific neurotransmitter receptors that function in the peripheral motor synapses of parasites. More specifically it blocks chemical transmission across the nerve synapses that use glutamate-gated anion channels or γ-aminobutyric acid-gated chloride channels to paralyze the parasite.[6] Once the mites are eradicated, signs and symptoms of scabies gradually wane off. Therefore, to assess the efficacy of ivermectin, a researcher should concentrate on its effects on mites rather than presence or absence of signs and symptoms. This matter is further complicated by the fact that itch is a subjective symptom and stimulus of same intensity may produce different severity of itch in different people. Itch may persist for a variable period of time even after complete eradication of mites. Same is true for lesions of scabies like papules and nodules which may persist for weeks to months after effective treatment.[7] Therefore, using such a yardstick to assess the effectiveness of a scabicidal medicine seems unjustified.

Our study for assessing the efficacy of ivermectin in scabies is different from others in that we positively identified scabies mites in patients in the beginning and then observed the effect of medicine on already identified mites. Twenty eight (56%) patients were cured with a single dose of ivermectin and did not show any mite during follow-up period. This result is similar to what has previously been reported by Brooks and Grace in 2002.[8] They observed a cure rate of 56% after a single dose of ivermectin. The authors described cure as absence of skin lesions in patients followed up after three weeks and highlighted it as a major weakness of the study i.e. the primary outcome measure or cure of disease was measured in terms of skin lesions rather than live mites. These results are much lower as compared to what appeared in earlier studies. A study carried out in 1992-1993 showed 45% cure rate after two weeks and 100% after four weeks with a single dose of ivermectin in patients with uncomplicated scabies.[9] The authors considered patients as cured if they did not show pruritus, dermatologic evidence of scabies, and positive signs of infestation in skin scrapings. As the patients were not given second dose of ivermectin after two weeks, it may be assumed that scabies mites were

Table 2 Details of effect of ivermectin on mites of patients showing living *Sarcoptes scabiei* at the end of second week.

				Initial visit				*1st follow up visit*				*2nd follow up visit*			
Patient	*Age*	*Sex*	*Duration*	*Lesions showing mites*			*Total*	*Lesions showing mites*			*Total*	*Lesions showing mites*			*Total*
No	*years*		*weeks*	*burrow*	*nodules*	*papules*	*mites*	*burrow*	*nodule*	*papule*	*mites*	*burrow*	*nodule*	*papule*	*mites*
4	31	M	6	6	8	3	17	3	6	0	9	1	4	0	5
16	56	M	4	9	6	6	21	6	4	1	11	1	3	0	4
20	24	M	5	3	8	3	14	0	6	0	6	0	4	0	4
22	24	F	6	14	2	0	16	5	0	0	5	2	0	0	2
24	26	M	4	4	8	3	15	1	6	1	8	0	4	0	4
26	27	M	6	7	6	6	19	0	4	0	4	0	1	0	1
27	32	M	5	8	9	4	21	4	7	2	13	0	3	1	4
34	21	M	7	7	8	3	18	4	8	2	14	1	3	0	4
36	43	F	6	14	1	0	15	12	0	0	12	3	0	0	3
44	27	M	5	8	7	5	20	3	7	2	12	0	6	0	6
48	22	F	5	13	5	0	18	11	3	0	14	8	3	0	11
			Total	93	68	33	194	49	51	8	108	16	31	1	48

eradicated in all patients by the end of second week and it took another two weeks for the signs and symptoms of scabies to disappear. Hundred percent cure rate has also been reported in other studies published in 1998 and 1999. All these studies were carried out on a small number of patients, 11, 19 and 6, respectively.[9,10,11] Larger controlled studies on the other hand documented much lower response rate.

Decreasing efficacy of medicine over a period of time has raised concerns about the emergence of ivermectin resistance. *In vivo* and *in vitro* resistance of *S. scabiei* to ivermectin was first reported in 1994 from Australia in patients who had previously received many doses of oral ivermectin for recurrent crusted scabies.[12] With extensive use of the drug the chances of drug resistance are likely to increase. *In vitro* sensitivity of mites to ivermectin has already been reported to decrease significantly. Mites exposed to ivermectin *in vitro* survived about twice as long in 2006 as compared to 1997. This matter becomes more serious with the observation that sensitivity of mites to drug can decrease very rapidly and ivermectin tolerant mites have reportedly been collected from a patient after 8 days and 3 doses of ivermectin.[13] Such tolerance of mite to the drug tends to persist and carries the potential of spreading drug resistance.[13]

In our study treatment failure was observed in twenty two patients after one week of single dose of ivermectin. Second dose of ivermectin did eradicate mites in half of them but mites were still seen in eleven patients after two weeks. All remaining mites were removed and were recognized as adult females under microscope. Isolation of living mites one week after a dose of oral ivermectin is not an unusual thing and the researchers attribute it to lack of its effect on ova. These ova hatch over a period of three to four days and explain the presence of young nymphs a week after the dose of ivermectin.[7] The second dose of medicine after a week interval should theoretically eliminate all the mites. The presence of adult mites a week after the second dose of drug, as was the finding in our study, can most likely be explained due to primary ivermectin resistance. It was the most unexpected finding of our study. The detail of lesions of all eleven patients who had living mites despite two doses of ivermectin are shown in **Table 2**. It is evident from this table that 48 out of 193 (25%) mites initially observed in these patients were alive after two doses of ivermectin. Another interesting finding was that mites surmounting the nodules were less affected by the medicine and 31 out of 68 (45.5%) survived even after two weeks in contrast to those seen in the burrows (16 out of 93-17%) or over the papules (1 out of 33 [3%]).

Ivermectin has been marketed in Pakistan for treating human scabies since 2009. Its free availability will naturally result in a change in the prescription pattern of dermatologists as well as other doctors, as the conventional treatment of scabies with topical application of scabicidal medicines is quiet difficult to carry out in practice. It may not be much difficult for a young person to apply medicine on the whole body after taking a bath and then keep the drug on body for prescribed period, however, it is really a nuisance for a family to perform the same ritual simultaneously. Chances of treatment failure are therefore high, mostly because of lack of treatment compliance. Oral ivermectin has practically solved the issue of noncompliance. It is safe, simple to administer, and treats the entire skin surface without neglected areas. It should be the logical drug of choice for patients having comorbid conditions like blistering disorders, where erosions and crusts may pose a hindrance to topical applications. Similarly, patients with crusted scabies are other ideal

candidates for oral ivermectin. However, in view of the resistance of mites observed in our study, its indiscriminate use to treat every patient of scabies cannot be recommended. Such a practice will only contribute towards the emergence of ivermectin resistant cases of scabies just like MDR tuberculosis or chloroquine resistant malaria. A safe practice may be simultaneous use of oral ivermectin and topical scabicidals in order to ensure eradication of mite from the patient. It is a very effective scabicidal medicine in the armamentarium of dermatologists and should be used intelligently to achieve its maximum benefit.

Conclusion

Oral ivermectin is an effective and convenient treatment for scabies in otherwise healthy patients with a cure rate of 56% with a single dose and 78% with two doses at a weekly interval. Primary drug resistance is already there and its indiscriminate use to treat common cases of scabies will add up to the existing problem in all likelihood. The drug should therefore be used judiciously to prevent this catastrophe.

Acknowledgement

Tablet ivermectin (Mectis®) was supplied for this study by Incepta Pharma, Pakistan Limited.

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