

## COMPARISON OF IN-VITRO SUSCEPTIBILITY OF SARCOPTIES SCABIEIVAR HOMINIS TO 5% PERMETHRIN AND 1 % LINDANE

Muhammad Irfan Anwar, Syed Dilawar Abbas Rizvi\*, Mansoor Dilnawaz\*\*, Afsheen Ijaz\*\*\*, Tahira Muqaddas\*\*\*\*, Nazia Parveen\*\*\*\*

Pakistan Field Hospital 6 Sudan, \*Military Hospital Rawalpindi, \*\*Combined Military Hospital Kohat, \*\*\*Combined Military Hospital Multan, \*\*\*\*Lahore General Hospital Lahore

### ABSTRACT

**Objective:** To measure in-vitro susceptibility of Sarcoptes Scabieivar Hominis to 5% permethrin and 1 % lindane.

**Study Design:** Randomized controlled trials.

**Place and Duration of Study:** Study was carried out at Dermatology Department, Military Hospital, Rawalpindi from January 2012 to June 2012.

**Material and Methods:** A total of 60 mites from 60 patients were taken for assay. Mites from every patient were randomly allocated to two groups i.e. group A (5% permethrin) and group B (1% lindane). Permethrin and lindane were applied in a thin film over a glass slide. Live mites were then gently transferred to the glass slide and covered with a lid. Mites were inspected for leg movements at time interval of 1hr, 2hrs, 3hrs, 4hrs and 5hrs. Death was declared once all leg movements had ceased. All mites which died within 5 hours had been declared as susceptible to drugs, while mites having active leg movements even after 5 hours of drug application were considered as non-susceptible.

**Results:** A total of 93.33% (n=28) of mites in group-A died within 5 hours of application of permethrin (susceptible) and 6.67% (n=2) of mites in group-A were alive after 5 hours of drug application (resistant). While 53.33 % (n=16) of mites in group-B died within 5 hours of application of lindane (susceptible) and 46.67% (n=14) of mites in group-B did not die after 5 hours (non-susceptible). ( $p$  value < 0.001).

**Conclusion:** Permethrin is more effective as compared to lindane against Sarcoptes Scabei in terms of in-vitro susceptibility.

**Keywords:** Lindane, Permethrin, Scabies.

### INTRODUCTION

Scabies is an intensely itchy parasitic infection of the skin caused by the Sarcoptes scabiei mite. It is a common public health problem with an estimated global prevalence of 300 million cases<sup>1</sup>. In poor communities worldwide the prevalence of scabies is 10%. The infestation occurs at all ages, but particularly in children<sup>2</sup>.

Permethrin is widely used as an insecticide, acaricide and insect repellent. It belongs to the family of synthetic chemicals called pyrethroids and functions as a neurotoxin, affecting neuron membranes by prolonging sodium channel activation. Permethrin has been the most effective treatment for scabies, and the treatment of choice<sup>6</sup>.

Lindane, also known as gamma-hexachloride is a neurotoxin that interferes with GABA neurotransmitter function by interacting with the GABA receptor - chloride channel. Lindane is effective for treating scabies; however, after its initial use as a first-line therapy, there have been several reports of its neurotoxicity, especially among infants and young children. Literature review reveals that the risk of its neurotoxicity is minimal if used properly and strictly according to the prescribed recommendations. However, following availability of other safer and equally efficacious alternatives, it is now being regarded as a second-line therapy for scabies.

The study was designed to measure the susceptibility of sarcoptes scabiei mite to commonly used topical permethrin and lindane with a rationale to determine the efficacy of these drugs in vitro and to see any deviation in the susceptibility pattern. By making a comparison, we will be able to opt for the better treatment modality which will be further

**Correspondence:** Dr Muhammad Irfan Anwar, E-150/B-1, New Supper Town, Lahore, Pakistan  
Email: doctorirfananwar@gmail.com

Received: 11 Feb 2014; Accepted: 08 May 2014

helpful for treatment and management protocol.

### MATERIAL AND METHODS

Randomized controlled trials were carried out at Dermatology Department Military Hospital Rawalpindi from January 2012 to June 2012. Patients of scabies of all ages and both genders, in which diagnosis was made by extruding live mites from the lesions of scabies and later on confirmed by light microscopy were included in the study and previously treated patients of scabies within last two months were excluded. Sample size was calculated by using WHO sample size calculator, taking level of significance 5%, power of test 90%, anticipated population proportion P1 is 84.6%<sup>3</sup> and anticipated population proportion P2 is 48.6%<sup>3</sup>. So, there were 30 mites in each group making a total of 60 mites.

The sampling technique was non-probability consecutive sampling. Patients from Dermatology outpatient department (OPD) at Military Hospital Rawalpindi, fulfilling the

examination of all the patients was recorded. Mites were explored and collected from the lesions manually with the help of a sterilized paper pin. Extruded mites from every patient were randomly allocated to two groups i.e group A (5% permethrin) and group B (1% lindane) using random numbers table. Permethrin and lindane were applied in a thin film over a glass slide with a central shallow pit in it. Live mites were then gently transferred to the glass slide with avoidance of any physical damage and covered with a lid and maintained at room temperature. The vitality of mites was confirmed before assay. Mites were inspected for leg movements at time interval of 1 hr, 2 hrs, 3 hrs, 4 hrs and 5hrs. Death was declared once all leg movements had ceased. All mites which died within 5 hours had been declared as susceptible to drugs, while mites having leg movements even after 5 hours of drug application were considered as non-susceptible keeping maximum killing time in previous in-vitro studies in view<sup>9</sup>.

Data was analyzed by computer software SPSS version 13.0. Descriptive statistics were

**Table-1: Comparison of killing time between the two groups.**

Killing time (in hours)	Group-A(n=30)		Group-B (n=30)	
	No. of patients	%	No. of patients	%
0-2	2	6.67	0	0
After 2-3	14	46.67	2	6.67
After 3-4	8	26.67	4	13.33
After 4-5	4	13.33	10	33.33
Live Mites after 5 hrs	2	6.67	14	46.67
<i>p</i> value	< 0.001			

**Table-2: Comparison in-vitro susceptibility of sarcoptiesscabieivar Hominis between the two groups.**

Susceptibility of mites	Group-A (n=30)		Group-B (n=30)	
	No. of patients	%	No. of patients	%
Yes	28	93.33	16	53.33
No	2	6.67	14	46.67
<i>p</i> -value	< 0.001			

inclusion criteria were selected after informed written consent and permission from Hospital Ethical Committee. OPD registration number, name, age and gender were noted for each patient. A relevant history and physical

used to describe the data. The two groups were compared for effectiveness using Chi-Square test. A *p* value <0.05 was considered significant.

## RESULTS

A total number of 60 mites from 60 patients were exposed to both permethrin and lindane and continuously observed for 5 hours. Results of the killing time of permethrin and lindane is presented in table-1. Killing time was significantly higher in group B as compared to group A ( $p < 0.001$ ). In vitro susceptibility of mites in both groups is presented in table-2. In vitro susceptibility of mites was significantly higher in group A as compared to group B ( $p < 0.001$ ).

## DISCUSSION

Permethrin has been a drug of choice and a gold standard in the treatment of scabies for the last many decades<sup>4</sup>. Permethrin acts by blocking the sodium channels, resulting in delayed repolarization of the nerves leading to paralysis, and death of the parasite<sup>5</sup>. Usha et al demonstrated that a single application of permethrin was effective in 97.8% of patients<sup>6</sup>. To date, there is no confirmed report of in vivo resistance of scabies mite, but in vitro resistance had been demonstrated<sup>7</sup>. This in vitro resistance had raised concerns about in vivo mite resistance, as it has recently been described in some aboriginal communities in northern Australia<sup>8</sup>.

Passay et al observed that a proportion of scabies mites remained viable up to 5 h in vitro after continuous exposure to permethrin, thus probably showing permethrin resistance in this population of mites and also got evidence by mutation analysis in these pyrethroid resistant population, where single nucleotide polymorphism has been noticed in the genes of mites<sup>9</sup>.

In our clinics, many outdoor patients of scabies were harboring live mites even after 48 hours of application of permethrin, which prompted us to conduct this in vitro study. We believe that this assay represents a maximum exposure test of mites where they directly come in contact with the active drug without a skin barrier. Although 93.33% (n=28) of mites in permethrin group died within 5 hours of drug application, but 6.67% (n=2) were still viable. It is a possibility, that these two mites may be the

resistant mites, as observed by Passay et al and later on confirmed by mutational analysis<sup>9</sup>. If we translate the results of this in vitro assay to in vivo efficacy, where the mites may not be coming in direct contact with the desired concentration of drug as demonstrated in these in vitro assays, one can easily infer that the viable mites after 5 hours were probably, the resistant mites. Nevertheless, these two mites were having sluggish leg movements at 5 hours and it was also possible that they might have died in next few hours. But, at the moment, we cannot ignore this alarming finding which can depict an actual resistance in the community. At the same time, these findings need confirmation and call for further in vitro assays.

Lindane is being used for the treatment of scabies since 1948. It is a neurotoxin that interferes with GABA neurotransmitter function by interacting with the GABA receptor - chloride channel. An overnight single application of lindane resulted in 44% efficacy after four weeks<sup>10</sup>. Hernandez-Perez first reported lindane resistance in patients of scabies even when used twice in 48 hours<sup>11</sup>. In recent years lindane resistance seems to be rising and there are several reports of lindane resistant scabies worldwide<sup>12,13</sup>. This study clearly showed increased survival timings of mites in lindane group. A total of 53.33% (n=16) mites died within 5 hours of application of lindane and 46.67% (n=14) mites did not die after 5 hours. These findings were consistent with previous in vitro studies with lindane<sup>14,15</sup>.

This study clearly showed that permethrin is far better than lindane when it comes to in vitro sensitivity, as 93.33% efficacy was seen in permethrin population as compared to 55.33% in lindane population. This difference is statistically significant as p-value is less than 0.05%. Also, chances of resistance are far higher in lindane treated group as compared to the permethrin treated group, as 46.67% (n=14) of mites were not susceptible to lindane. Mean killing time of permethrin is shorter than lindane, 2-3 hours and 4-5 hours, respectively.

Keeping the above mentioned results in view, we believe that the reasons of treatment failure in our patients might be multifactorial,

including the inadequate treatment guidance by the physicians, lack of compliance to guidance at patient's end and re-infestations from other family members if not treated simultaneously. But at the same, the possibility of a true drug resistance cannot be ruled out.

### CONCLUSION

Permethrin (5%) is more effective as compared to lindane against *Sarcoptes Scabiei Varhominis* in terms of in-vitro susceptibility. Mean killing time of permethrin is shorter than lindane. Permethrin (5%) should continue to be prescribed as the treatment of first choice in scabies. Detailed verbal and written instructions for the use of permethrin should be provided by the treating physicians, as lack of proper communication can lead to improper eradication of mite thus resulting in treatment failure. Simultaneously treating all family members, whether affected or not, would help prevent treatment failure, as re-infestation from family members is an important cause of treatment failure.

### CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

### REFERENCES

1. Hengge UR, Currie BJ, Jager G, Lupi O, Schwartz RA. Scabies: a ubiquitous neglected skin disease. *Lancet Infect Dis.* 2006; 6:769-79
2. Jackson A, Heukelbach J, Feldmeier H. Transmission of scabies in a rural community. *Braz J Inf Dis.* 2007; 11: 386-7
3. Strong M, Johnstone PW. Interventions for treating scabies. *Cochrane Database Syst Rev.* 2007; 3:143-6
4. Elgart ML. A risk benefit assessment of agents used in the treatment of scabies. *Drug safety.* 1996; 14: 386-93.
5. Scabies—clinical presentation and treatment. Focus on permethrin. Bombay: Croslands Research Laboratories; 1993.
6. Usha V, Gopalakrishnan Nair DNB, Gopalakrishnan Nair TV. A comparative study of oral ivermectin and topical permethrin cream in the treatment of scabies. *J Am Acad Dermatol.* 2000;42:236-40.
7. Walton SF, Myerscough MR, Currie BJ. Studies in vitro on the relative efficacy of current acaricides for *Sarcoptes scabiei* var. *hominis*. *Trans R Soc Trop Med Hyg.* 2000; 94(1): 92-96.
8. Mounsey KE, Holt DC, McCarthy J, Currie BJ, Walton SF. Scabies: molecular perspectives and therapeutic implications in the face of emerging drug resistance. *Future Microbiol.* 2008; 3(1): 57-66.
9. Passay C, Arlian L, Morgan M, Moher DV, Rose AD, Watson S, McCarthy JK. High-resolution melt analysis for the detection of mutation associated with permethrin resistance in a population of scabies mites. *Med Vet Entomol.* 2008; 22: 82-8.
10. Madan V, Jaskiran K, Gupta U, Gupta DK. Oral ivermectin in scabies patients: a comparison with 1% topical lindane lotion. *J Dermatol.* 2001; 28: 481-4.
11. Hernandez-Perez E. Resistance to antiscabietic drugs. *J Am Acad Dermatol.* 1983; 8: 121-3.
12. Taplin D, Meinking TL, Porcelain SL, Castillero PM, Chen JA. Permethrin 5% dermal cream: a new treatment for scabies. *J Am Acad Dermatol.* 1986; 15: 995-1001
13. Purvis RS, Tyring SK. An outbreak of lindane-resistant scabies treated successfully with permethrin 5% cream. *J Am Acad Dermatol* 1991; 25:1015-6.
14. Chosidow O. Scabies and pediculosis. *Lancet.* 2000; 355:819-26.
15. Fraser J. Permethrin: a Top End viewpoint and experience. *Med J Aust.* 1994; 160: 806.