



A COMPARATIVE CLINICAL STUDY OF EFFICACY AND SAFETY OF ORAL IVERMECTIN VERSUS TOPICAL PERMETHRIN IN THE TREATMENT OF SCABIES

Pharmacology

Dr Ankur Sharma*	III-year Post graduate, Department of pharmacology, S.P. Medical college & Hospital, Bikaner, Rajasthan. *Corresponding Author
Dr. Sumita Tanwar	Associate Professor, Department of pharmacology, S.P. Medical college & Hospital, Bikaner, Rajasthan.
Dr. Sonia Rana	II-year Post graduate, Department of pharmacology, S.P. Medical college & Hospital, Bikaner, Rajasthan, India.

ABSTRACT

Background and Aims: 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. This study aimed at comparing the efficacy of oral ivermectin with topical permethrin in treating scabies. **Materials and methods:** A total of 360 patients clinically diagnosed as scabies attending the department of Dermatology, Venereology and Leprology in hospital attached to S.P.M.C. Bikaner. Patients belonging to either sex and from 12 to 60 years of age were randomly allocated for each of the two regimens consisting of 180 patients in each group by following simple random sampling procedure. 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. Treatment was evaluated at intervals of 2 and 4 week. **Results:** Permethrin showed marginal better efficacy (90 %) in completely clearing scabietic lesions at fourth week of therapy as compared to ivermectin (85 %), the difference was insignificant ($P=0.202$). thirty-four patients in ivermectin group had side effects as headache, increase in itching and secondary bacterial infections as compared to permethrin group in which sixteen patients had erythema ($P=0.010$). **Conclusion:** 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.

KEYWORDS

Scabies, permethrin, ivermectin.

INTRODUCTION

Scabies is an infectious disease contagious in nature and caused by *sarcoptes scabiei* (it has got another name *acarus*) and characterized by papular or vesicular eruption with intense itching specially at night. Scabies is a neglected parasitic disease that is a major public health problem in many resource-poor regions. It causes substantial morbidity from secondary infections and post-infective complications such as acute post-streptococcal glomerulonephritis. Disease control requires treatment of the affected individual and all people they have been in contact with, but is often hampered by inappropriate or delayed diagnosis, poor treatment compliance and improper use of topical compounds such as permethrin, lindane or benzyl benzoate. In addition to concerns over toxicity with such compounds, parasite resistance seems to be increasing, oral ivermectin is an alternative that has been used successfully in community control programmes. The disease is strongly associated with poverty and overcrowding, and the associated stigma can ostracise affected individuals. Treatment of scabies in poor countries needs to be integrated drug treatment programmes, with efforts to improve the socioeconomic conditions and education programmes to reduce stigma.

The Aim of our study is the first to compare the efficacy and safety of oral ivermectin to commonly used topical antiscabies drug Permethrin.

METHODOLOGY

This is a prospective, randomized, parallel, non-crossover, comparative, controlled clinical study. In this study total 360 patients diagnosed with scabies were approached and enrolled from Department of Dermatology, PBM Hospital Bikaner. These patients should match with inclusion and exclusion criteria of the study. Permission was taken from institutional ethical committee. Written informed consent was taken from all patients before subjecting them for study. Patient's history including family and personal history with socio demographic data was obtained and filled in specially designed proforma and used for compiling the data. Selected patients were assigned randomly with the help of computer to either group A or group B. Both groups were having equal number of patients (180). Group A (180 patients) were given ivermectin 200 mcg / kg body weight orally. Group B (180 patients) were given permethrin 5% cream topically.

The treatment was given to both patients group and their close family members and they asked not to use any antipruritic drug or any other

topical medication. The data of this study was collected from Department of Dermatology, PBM and Associated group of hospital, Bikaner. Patients assessment will be done at day 0 by senior dermatologist. The proforma was filled with all information's about the patients. Total two follow ups were done. Patients were assessed at end of week 2 and week 4 after the first treatment. At each assessment, the sites and number of lesions on body and other complaints (Adverse Drug reaction) was recorded. Patients were clinically examined and evaluated based on previously-defined criteria. To collect required information from eligible patients a pre-structured pre-tested proforma was used. For data analysis Microsoft Excel and statistical software SPSS was used and data was analyzed with the help of frequencies, figures, proportions, measures of central tendency and appropriate statistical test.

RESULTS

The following results were obtained during the study and the data was analyzed using statistical software Microsoft excel and SPSS 22 for windows. Both the groups, the ivermectin group (group A) and the permethrin 5% group (group B) were comparable and statically non-significant with regards to the demographic profile i.e. age, sex, and education as well as the marital status and the prevalence of scabies is more in rural patients compare to urban patients and statistical comparison significant between two groups. (table 1).

Table 1: Demographic profile

	Group A, n (%)		Group B, n (%)		P value
	Mean	SD	Mean	SD	
Age (Years)	32.23	13.51	33.43	13.80	0.383
Education					0.691
Graduate	58(32.22)		51(28.33)		
Illiterate	3(1.66)		4(2.22)		
Under graduate	119(66.11)		125(69.44)		
Marital status					0.425
Married	120(66.66)		128(71.11)		
Unmarried	60(33.34)		52(28.89)		
Prevalence of scabies					
RURAL	133(73.88)		109(60.55)		0.324

URBAN	47(26.11)	71(39.44)	
Sex			
Male	122 (67.77)	107 (59.44)	0.125
Female	58 (32.23)	73 (40.55)	

The statistical comparison of Severity of infestation between two groups is non-significant.

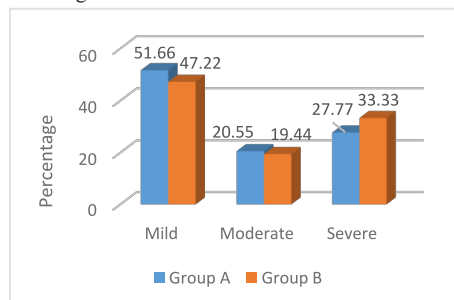


Figure 1: Severity of infestation.

Table 2,3 shows that statistical comparison of treatment efficacy at two weeks and 4 weeks follow up between two groups is non-significant.

Table: 2 Treatment efficacies at 2 weeks follow up between two groups.

	Group A		Group B	
Effective	139	77.22	148	82.22
Not Effective	41	22.78	32	17.77
Total	180	100	180	100.00
Result (p value)	0.294 (NS)			

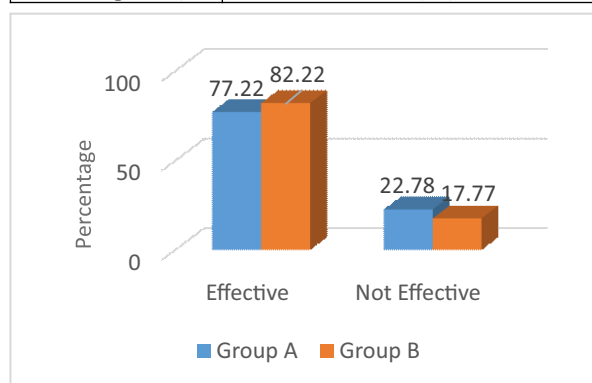


Figure:2 Treatment Efficacy at 2 weeks follow-up

Table: 3 Treatment efficacies at 4 weeks follow up between two groups.

	Group A		Group B	
Effective	153	85.00	162	90.00
Not Effective	27	15.00	18	10.00
Total	180	100	180	100.00
Result (p value)	0.202 (NS)			

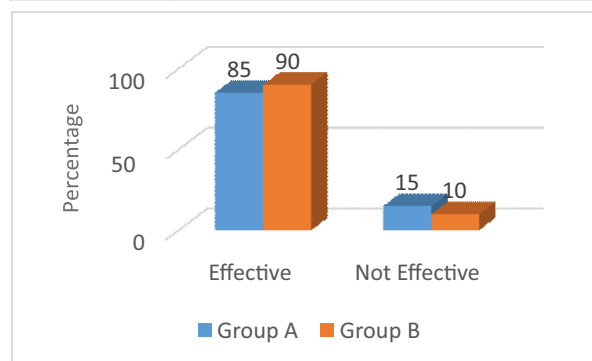


Figure 3: Treatment Efficacy at 4 weeks follow-up

Figure 2 shows that statistical comparison of adverse events between two groups is significant.

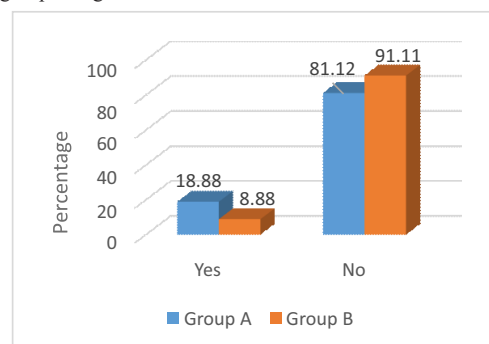


Figure 4: Adverse events seen in two groups.

DISCUSSION

The incidence of scabies was 11-13 % among all the patients in Bikaner. Nair et al⁵, in a population survey has observed an incidence of 6%. In the present study more patients (51.11 %) in Group A and (43.88%) in Group B belonged to the age group of 12– 30 years followed by 31 – 50 years who constituted to 36.66% in Group A 42.77% in Group B of scabies. Thus, scabies was found to be more common in children and young adults. Sehgal² found the disease to be more common in the age groups of upto 9 years, followed by the age group 10 – 19 years and 20 – 29 years. However, Gulati et al⁶, and Nair et al⁷ found the higher incidence in children. Schenon et al⁸, found the disease to be more common in the age group of 5– 15 years. Thus, the observations made in the present study are in agreement with the majority of the observations. In the present study males constituted to 67.77% in group A and 59.44% in group B whereas female constituted to 32.23 % in group A and 40.55 % in group B. Nair et al⁴, have observed a male preponderance. Sehgal², found it to be 64.9% in males and 35.1% in females. The observations of the present study are in concurrence with majority of the studies. There were no significant differences in age or gender between the two groups. The prevalence of scabies in rural / urban were 73.88% in groups A, 60.55 % in group B for rural populations and 26.11% in group A, 39.44% in group B for urban populations and difference was statically significant in both the groups. (Table 1) In our study education and marital status in the two groups were statistically non-significant. In the study, no significant difference was seen between the groups with regard to the number of patients graded as having mild, moderate or severe infestation (Figure 1).

At the 2-week follow-up, the treatment was found to be effective in 139 (77.22%) patients in the ivermectin group A and 148 patients (82.22%) in the permethrin 5% group B, with no significant difference between the groups (P=0.294). The treatment was not repeated for the 41 patients in the ivermectin group and 32 in the permethrin 5% group) who still had infestation. At the second follow-up, at 4 weeks, only 27 (15%) patients in the ivermectin group still had severe itching and skin lesions, compared with 18 (10%) patients in the permethrin 5% group. Thus, the overall cure rate was 153/180 patients (85%) in the ivermectin group and 162 of 180 (90%) in the permethrin 5% group (Table 7,8). In our study Oral ivermectin given single dose (200µg/kg body weight). Glaziou et al⁹, have reported 70% improvement at 30 days after treatment with ivermectin 100 mg/kg body wt. Usha et al⁷, found that a single dose of ivermectin provided a cure rate of 70%, which increased to 95% with 2 doses at a 2 week interval. Meinking et al¹⁰, reported 100% clearance with single oral dose of ivermectin in 11 patients with uncomplicated scabies. Chouela et al¹¹, found the cure rate of scabies at 15th day, after treatment with ivermectin single dose of (150 - 200 µg/kg) to be 74%. Madan et al¹⁰, have found 82.6% improvement of scabies lesions after 4 weeks. Elmogy et al¹¹, found 88.1% cure after two weeks after the initiation of ivermectin. Thus the results of the present study are comparable with other studies which have a cure rate of 70 – 80%. Out of 180 patients treated with 5% permethrin lotion cure was seen in 148 (82.22%) at 2nd week and total number of patients cured at 4th week was 162 (90%). Zargari et al¹², showed 84.6% improvement after 2 weeks of therapy. Hegary et al¹³, found that permethrin to be effective and found cure rate of 84.9% with one treatment course and 98% cure rate after two treatments. Taplin et al¹⁴, have found a cure rate of 43% at 2 weeks and after 4 weeks 91% cure rate was seen with permethrin 5% cream. Usha et al⁷, showed a

single application was effective in 97.8%. The remaining 45 patients who were considered treatment failures in the study were retreated with open-label lindane lotion 1%, which cured the infestation in 2–3 weeks. In our study table 9 showed that the treatments were considered cosmetically acceptable by both patients and parents. None of the 360 participants experienced allergic reactions. The main adverse event was irritation, reported by 40 patients (34 in the ivermectin group and 16 in the permethrin 5% group), but this was not serious and did not affect compliance. None of the patients experienced worsening of the infestation during the study; even the treatment failures were improved compared with their pre-treatment status. Permethrin, 5% dermal cream, is a welcome addition to the available therapies for scabies. It is cosmetically elegant and easy to use, has no objectionable odor and does not stain clothing. Skin irritation, including itching, swelling and redness, may occur with scabies and temporarily worsen after treatment with permethrin, presumably due to absorption of dead parasite proteins. Mild burning or stinging may also occur. Ivermectin is an effective and cost-comparable alternative orally agents in the treatment of scabies infection. It may be particularly useful in the treatment of severely crusted scabies lesions in immune compromised patients or when other topical therapy has failed. In this study, ivermectin was seen to be as effective as permethrin at 2 weeks follow up in treating scabies, and this is in accordance with previous studies that have reported excellent cure rates with permethrin. In our patients, we found orally ivermectin to be as effective as topical permethrin when used twice over a period of 4 weeks. The data from the 4th week showed that ivermectin continued to decrease both the lesions and the degree of pruritus as compared to permethrin but this difference was not significant ($P > 0.05$). Patients on ivermectin showed less rapid symptomatic response (itching) and signs (papules). This could be because of the permethrin acts on all stages of mites (ovum, larva and adult) and also stem from its action on the voltage sensitive sodium channel of the parasite; as this channel is necessary for the generation of action potentials in excitable cells, its disruption causes paralysis of the mite and leads to its death. Since the 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, has not been proven to be ovicidal, and so a single application may be inadequate to eradicate all the stages of the parasite, and a second dose may be required within 1 to 2 weeks for a 100% cure. Usha et al⁷ report a higher number of patients showed clearance of lesions as compared to our results, and that both permethrin and ivermectin are effective in preventing recurrences of scabies over a period of 2 months. In a study carried out by Mumcuoglu et al¹⁵, a 100% cure was seen in both treatment groups, possibly because the study was carried on a smaller number of patients with a follow up of 2 weeks, or possibly that they were aged 12 years or above, when the activity of the sebaceous glands is greater. Permethrin is known to be significantly safer than ivermectin ($P < 0.05$). Ivermectin has been reported to cause rare serious side effects, which are seen when the drug is used in high doses, such as when it is accidentally ingested. However, in our study, we found it to be safe without significant adverse effects. 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. Although ivermectin was found to be as effective as permethrin, it has a few advantages over topical permethrin. Both drugs are cost-effective, but ivermectin has the advantage that treatment can be given to large numbers of patients with better compliance and with or without supervision. It can also be given safely in patients of scabies with secondary eczematization, erosions or ulcers where topical permethrin, can cause serious cutaneous and systemic side effects in addition to the problem of compliance.

CONCLUSION

Though scabies is a simple disease, it is very difficult to reduce its incidence as the socio-economic factors are very important in the transmission of the disease. Improvement in literacy and economic status can definitely bring down the prevalence of the disease, as the scabies appears to be parameters for the socio-economic status. Awareness about personal hygiene in addition to treatment is also very much required. One of the oldest diseases, scabies still continues to be a problem to treat as there is no effective drug which can give rise to 100% results in all situations. The newer topical medications and the oral ivermectin are found to be comparatively effective. Permethrin

was found to be more effective among the topical agents. Though the results obtained with oral ivermectin were slightly low compared to permethrin the patient compliance was very good especially among students living in hostels, where there are inadequate facilities for bathing and as they are young, they may not be able to take good scrub bath. Ivermectin can be a very useful weapon in patients who do not show compliance with topical therapy and for bedridden patients.

REFERENCES

1. Barish LC, Witkowski JA, Millikan LE. Scabies in the extended care facility.
2. Schgal VN. Scabies – epidemiology and ecology. *Indian J Dermatol Venereol Leprol* 1997;43:266-269.
3. Gulati PV, Sachder TR, Varma RK. Scabies - An epidemiological study in a resettlement colony. *Indian J Dermatol Venereol Leprol* 1981;47(6):299-302.
4. Nair BKH, Joseph A, Narayan. Epidemiology of scabies. *Indian J Dermatol Venereol Leprol* 1973;39:101-105.
5. Schenon H, Falah F, Gato M, Palomin H, Roj M, Roja A. *Rev Chil Pediatr* 1971;42:561-566.
6. Glaziou P, Cartel JL, Alzieu P, Briot C, Mouliat JP, Martin PM. Comparison of ivermectin and benzyl benzoate for treatment of scabies. *Trop Med Parasitol* 1993;4:331-332.
7. Usha V, Gopala Krishnan Nair TV. A comparative study of oral ivermectin and topical permethrin cream in the treatment of scabies. *J Am Acad Dermatol* 2000;4:1521-1524.
8. Meinking TL, Taplin D, Hermida JL, Pardo R, Kerdel FA. The treatment with Ivermectin. *N Engl J Med* 1995;333:26-30.
9. Chouela EN, Abeldano AM, Pellerano G, Laforghan, pable RM, Garsd A. Equivalent therapeutic efficacy and safety of Ivermectin and Lindane in the treatment of human scabies. *Arch Dermatol* 1999;135:651-655.
10. Madan V, Jaskiran K, Gupta U, Gupta DK. Oral Ivermectin comparison with 1% topical lindane lotion. *Int J Dermatol* 2001;28:481-484.
11. Elmoghy M, Fayed H, Marzok H, Rashad A. Oral ivermectin in the treatment of scabies. *Int J Dermatol* 1999;38:926-930.
12. Zargori O, Golchali J, Sobhani A, Dehpour AR, Sadr-Ashkevari S, Alizadeh N. Comparison of the efficacy of topical 1% lindane Vs 5% permethrin in scabies : A randomized, Double-blind study. *Indian J Dermatol Venereol Leprol* 2006;72(1):33-36.
13. Hegazy AA, Darwish NM, Ibrahim A, Hamid A, Hammad SM. Epidemiology and control of scabies in a Egyptian village. *Int J Dermatol* 1999;38:291-295.
14. Taplin D, Meinking TL, Porcelain SL, Castillero PM, Chen JA. Permethrin 5% dermalcream: A new treatment for scabies. *J Am Acad Dermatol* 1986;15:991-1001.
15. Mumcuoglu K.Y., Gilead L. 2008. Treatment of scabies infestations. *Parasite* 15: 248-251.
16. Khan I, Yasmin R. Ivermectin in the treatment of scabies. *J Pak Assoc Dermatol* 2007; 17: 78-83.