DOI: 10.7860/JCDR/2014/9092.4878

Original Article

Pharmacology Section

Comparative Study of Efficacy of Oral Ivermectin Versus Some Topical Antiscabies Drugs in the Treatment of Scabies

PRAMOD KUMAR MANJHI[1], RANI INDIRA SINHA[2], MANISH KUMAR[3], KUMARI INDU SINHA[4]

ABSTRACT

Background: The conventionally used topical antiscabetics have poor compliance. Ivermectin, an oral antiparasitic drug, has been shown to be an effective scabicide and could be a useful substitute. This study was designed to compare efficacy of oral ivermectin with commonly used topical antiscabies drugs.

Materials and Methods: This study was conducted on four groups including 60 patients in each group by simple random sampling. Treatment given in each group was: Group 1: Ivermectin (200 µg/kg body weight) oral in a single dose, Group 2: Topical Permethrin 5% cream single application, Group 3: Topical gamma benzene hexachloride (GBHC) lotion 1% single application and Group 4: Topical Benzyl benzoate (BB) lotion 25% single application. All of the patients were followed for improvement in terms of severity of disease and severity of pruritus at the end of 1st wk and 6th wk.

Results: Efficacy of ivermectin, permethrin, GBHC and BB lotion considering improvement in severity of pruritus as parameter were 85%, 90%, 75% and 68.33% respectively at 2nd follow-up. Similarly considering improvement in severity of lesion as parameter, results were 80%, 88.33%, 71.66% and 65% respectively at 2nd follow up. Topical Permethrin (5%) was more effective as compared to topical BB lotion and topical GBHC lotion ($p<0.05$, significant) but statistical difference between efficacy of topical Permethrin and oral Ivermectin was non-significant ($p>0.05$).

Conclusion: The results suggested that oral Ivermectin and topical Permethrin (5%) were equally efficacious. Oral Ivermectin is well tolerated, non irritant to skin, does not show central nervous system side effects because it does not cross blood brain barrier. So, the good therapeutic response with few side effects seen with oral Ivermectin can be useful in those patients for whom topical treatment is potentially irritant and less well-tolerated.

Keywords: Benzyl benzoate lotion, Gamma benzene hexachloride lotion, Ivermectin, Permethrin, Scabies

INTRODUCTION

Scabies is a contagious skin infestation affecting humans and animals. Sarcoptes scabiei (human itch mite) is a tiny and usually not directly visible obligate parasite, an arthropod of the order Acarina which burrows under the host's skin, causing intense allergic itching. It infest some 300 million persons each year, is one of the most common causes of itching dermatoses.

Scabies is a neglected parasitic disease that is a major public health problem in many resource-poor regions. Scabies occurs in both sexes, at all ages, in all ethnic groups, and at all socio-economic levels. High prevalence is associated with crowded living condition [1]. Infestation occurs when female mites burrow under the skin and lay small number of eggs each day for several weeks. Symptoms are caused by allergic reactions of host's body to mite proteins found in eggs laid by female mites, gut proteins and mite faeces. The allergic symptoms (itching) continue for some days, and even several weeks, after all mites are killed [2]. Scabies is characterized by papular or vesicular eruption with intense itching made worse by warmth and experienced due to fewer distractions, especially at night. Acropustulosis or blisters and pustules on palms and soles of feet are characteristically seen in infants affected with scabies [3].

The disease may be transmitted from objects i.e. shared beddings, towels, clothings but is most often transmitted by direct skin-to-skin contact, with a higher risk after prolonged contact with an infected person. Initial infections require four to six weeks to become symptomatic. Re-infection, however, may manifest symptoms within as little as 24 h.

Current recommendation for disease control requires treatment of the affected individual and all people came in contact with patients regardless of whether symptoms are present or not, to reduce rate of recurrence [2].

Options to improve itchiness include antihistamines. Antibiotics are needed for superimposed bacterial infection. Treatment is often hampered by inappropriate or delayed diagnosis, poor treatment compliance or uptake and improper use of topical compounds such as permethrin, lindane or benzyl benzoate.

The practicality of topical treatment for community management of endemic scabies is questionable; the key barrier encountered being poor participation, inconvenience and unpleasantness of treatment. Therefore, the need for evidence based appropriate effective, acceptable and feasible treatment option is recognized. Oral Ivermectin is an alternative that has been tried successfully in community control programmes and in those who cannot tolerate topical therapy [1]. A safe, effective acceptable therapy option is needed to resolve the problem of low treatment participation. To realise a significant and sustained reduction in disease burden, treatment of scabies needs to be an integrated programme, with efforts to improve environmental and socio-economic conditions and education to create awareness and also to reduce stigma.

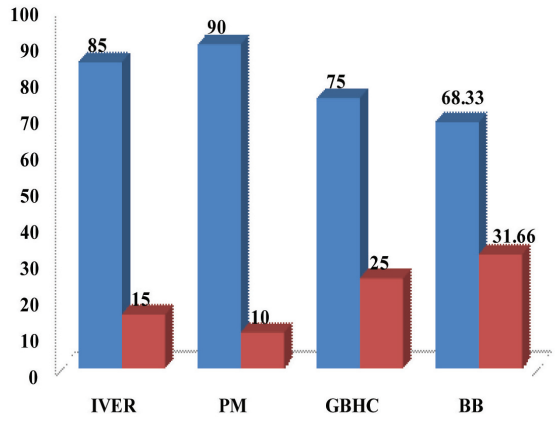
The main objective of the study is to know the efficacy and safety of Oral Ivermectin in comparison to commonly used topical antiscabies drugs such as Permethrin, Gama benzene hexa chloride and benzyl benzoate.

MATERIALS AND METHODS

Out of 741 diagnosed patients of scabies, 240 patients were included in this study, those attended OPDs of Department of Dermatology, Venereology and Leprology of Patna Medical College

Improvement seen with severity of pruritus as parameter		
	At 1st follow-up No.of cases (%)	At 2nd follow-up No.of cases (%)
Oral Ivermectin single dose 200µg/kg body wt.	31 (51.66%)	20 (33.34%)
Topical Permethrin 5% cream single application	38 (63.34%)	16 (26.66%)
Topical GBHC 1% lotion single application	26 (43.33%)	19 (31.66%)
Topical BB 25% lotion single application	30 (50.00%)	11 (18.33%)

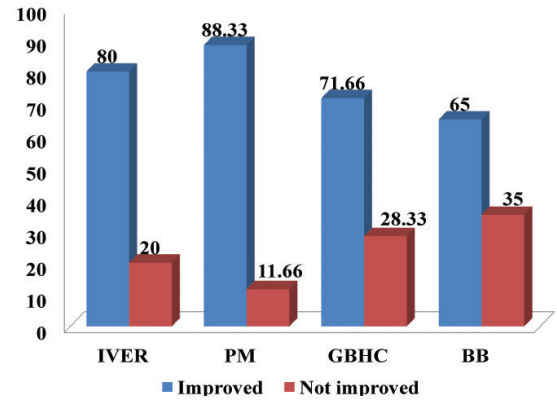
[Table/Fig-1]: Response to treatment in various groups



[Table/Fig-2]: Assessments of severity of pruritus at 2nd follow up (end of 6th week)

Improvement seen with severity of lesions as parameter		
	At 1st follow-up No.of cases (%)	At 2nd follow-up No.of cases (%)
Oral Ivermectin single dose 200µg/kg body wt.	32 (53.34%)	16 (26.60%)
Topical Permethrin 5% cream single application	43 (71.66%)	10 (16.66%)
Topical GBHC 1% lotion single application	28 (46.66%)	15 (25.00%)
Topical BB 25% lotion single application	29 (48.33%)	10 (16.66%)

[Table/Fig-3]: Improvement seen with severity of lesions as parameter



[Table/Fig-4]: Assessments of severity of lesions at 2nd follow up (end of 6th week)

Hospital, Patna, from 1st April 2011 to 31st March 2012. This study protocol was approved by Institutional Ethics Committee of Patna Medical College, Patna. Written informed consent was taken from patients during their enrolment for study. The patient related data, medical history, diagnosis, laboratory values and given treatment was noted in a case record form.

Inclusion criteria

1) Patients of above 5 years and below 60 years of age.
2) Patients of both sexes.

Group	No.of cases	Severity of pruritus at 6th week		Severity of lesion at 6th week	
		Improved No. (%)	Not improved No. (%)	Improved No. (%)	Not improved No. (%)
IVER	60	51(85)	9(15)	48(80)	12(20)
PM	60	54(90)	6(10)	53(88.33)	7(11.66)
GBHC	60	45(75)	15(25)	43(71.66)	17(28.33)
BB	60	41(68.33)	19(31.66)	39(65)	21(35)
Chi-Square Test		x^2 =10.54	p=0.01 p<.05,(S)	x^2 =10.19	p=0.02 p<.05,(S)
Degree of freedom (D.F.)		D.F.=3		D.F.=3	

Difference Between Groups (p-Values)						
	1-2	x^2 =0.80	D. F.= 1	p=0.37(NS)	x^2 =1.57	D. F.=1	p=0.21(NS)
	1-3	x^2 =1.88	D. F.= 1	p=0.17(NS)	x^2 =1.13	D. F.=1	p=0.29(NS)
	1-4	x^2 =4.66	D. F.= 1	p=0.03(S)	x^2 =4.38	D. F.=1	p=0.04(S)
	2-3	x^2 =4.68	D. F.= 1	p=0.03(S)	x^2 =5.21	D. F.=1	p=0.02(S)
	2-4	x^2 =8.02	D. F.= 1	p=0.005(S)	x^2 =9.13	D. F.=1	p=0.002(S)
	3-4	x^2 =0.66	D. F.= 1	p=0.42(NS)	x^2 =0.62	D. F.=1	p=0.43(NS)

[Table/Fig-5]: Comparison of results of various Groups at the end of 6 wks
x^2 =Chi-Square Test, p<0.05=Significant(S), D.F.=Degree of freedom, p>0.05= Not Significant (NS)

3) Patients willing for either topical or oral therapy.
4) Patients willing for follow-up at in the 1st wk and at 6th wk or if any complaints in between.

Exclusion criteria

1) Children below 5 y, elderly patients more than 60 y.
2) Pregnant and lactating women.
3) Patients who were not willing to come for follow-up.
4) Any serious systemic illness

MATERIALS AND METHODS

Two hundred and forty patients were randomly allocated to four Groups. Each group contained 60 patients and treatment given was as follows.

Group 1: Ivermectin 200 g/kg body weight (IVER) Oral single dose

Group 2: Permethrin 5% cream (PM) Topical single application

Group 3: Gamma benzene hexacloride1% (GBHC) lotion Topical single application

Group 4: Benzyl Benzoate 25% (BB) lotion Topical single application

In Group 2, 3 and 4 drug was applied topically below the jaw line after scrub bath and left overnight. All of the patients were followed up for improvement at the end of 1st wk and 6th wk.

Parameters used to compare the efficacy of the Groups by seeing improvement in

1) Severity of pruritus.
2) Severity of the disease.

1) Severity of pruritus is evaluated by Visual Analogues scale (VAS). VAS was defined as a 10 cm line, in which point 0 (zero) refers to existence of no pruritus and point 10 refers to the most severe pruritus. According to this scale, we scored pruritus of the patients.

   Point 1 to 3: Mild pruritus

   Point 4 to 6: Moderate pruritus

   Point 7 to 10: Severe pruritus

2) Severity of the disease is measured according to the number of lesions present. It can be graded as:

Mild: < 10 lesions.

Moderate : 11 – 49 lesions.

Severe : > 50 lesions.

A pre-structured proforma was used to collect the relevant information (patients data, clinical finding etc) at baseline, 1st wk and at 6th wk of follow-up or if any complaints in between.

Statistical analysis of the data was done by Chi-square test, degree of freedom and p-values.

RESULTS

Shown in [Table/Fig-1-5]

DISCUSSION

Response to treatment in various Groups

1) **Oral Ivermectin given single dose (200 µg/kg body weight):** In our study at the end of 2nd follow up complete improvement was seen in 85% and 80% when severity of pruritus and severity of lesion were taken as parameters respectively. Usha and Gopala [4] found that a single dose of Ivermectin provided a cure rate of 70%, which increased to 95% with 2 doses given at 2 wk interval. The lower efficacy of single dose Ivermectin could reflect the lack of ovicidal action of the drug. Thus, the results of the present study are comparable with other studies which have a cure rate of >80% [5-7].

2) **Topical Permethrin 5% cream single application:** Earliar studies [4,8-10] have reported cure rate >80% with Permethrin. Higher cure rates (98%) was reported after two applications. In our study cure rate with single application has been studied. At 1st follow up 63.34% showed cure rate which increased to 90% at 2nd follow up.

3) **Topical GBHC 1% lotion:** Earlier studies [8,11-13] have reported <75% cure rate with 1% topical GBHC lotion. Nag et al.,[13] have reported a cure rate of 68% only with 2% GBHC 2 applications in a day. In our study single application of Topical GBHC 1% lotion has shown a cure rate of 75% at 2nd follow up.

4) **Topical application of B.B. lotion 25%:** Our study has been done with BB lotion 25% single application. At 2nd follow up 68.33% reported improvement in pruritus and 64.99% reported cure in severity of lesion. Earlier studies [12,14] by different researchers have been done with 10-20% of BB lotion. Sampaio [15] showed 57% of patients improved after treating with benzyl benzoate. Brooks and Grace [16] found improvement in 51% patients at the end of 3 wks.

Comparison of statistical significance among four Groups

[Table/Fig-5] shows comparison of results among four Groups at the end of 6 wks considering severity of pruritus and severity of the disease as a parameter of efficacy. Difference in efficacy of Group 1 (Ivermectin) therapy was statistically non-significant with Group 2 (Permethrin) and 3 (Gamabenzene hexachloride), but statistically significant with Group 4 (Benzyl bezoate). This shows that efficacy of Group 1 therapy was comparable to Group 2 and Group 3 therapy but more efficacious than Group 4 therapy.

Group 2 therapy was more efficacious than Group 3 and 4 because difference in efficacy was statistically significant. Difference in efficacy of Group 3 and 4 therapies was statistically non-significant.

Thus the finding of present study has statistical validation between groups.

Although topical agents carried certain drawbacks, our study reported that single application of Permethrin 5% gave maximum response when severity of pruritus and severity of lesion were taken as parameters to compare efficacy of different Groups thus making it the most effective treatment and therefore suitable to be the treatment of choice.

Response to single oral dose of Ivermectin 200 µg/kg body wt. was slightly low when compared to Topical Permethrin but higher when compared to response obtained with either topical GBHC or topical Benzyl Benzoate. Though the results obtained with single oral dose of Ivermectin (200 µg/kg body wt) (i.e. patients belonging to Group 1 were slightly low compared to Permethrin, patient acceptance was very good especially among students living in hostels, where inadequate facilities for bathing and taking a good scrub bath were the major hurdle in topical application.

Despite the need for further exploration, oral ivermectin could be a viable alternative for management of scabies especially where compliance to topical scabicides is improbable or impractical.

Higher cost and lower efficacy of single dose oral Ivermectin as compared to topical Permethrin supports consideration of initial therapy with Permethrin wherever possible. However, Oral Ivermectin can be used where topical scabicides fail.

Further study with combined oral and topical agents, repeated administration and use of softening agents to treat hyperkeratosis and increase efficacy of topical scabicides needs to be done for this benign but transmissible condition.

A significant reduction in disease burden is possible only when along with appropriate scabicides, treatment of all contacts and clothings are done simultaneously and the underlying environmental and social conditions that promote infectious skin diseases are addressed.

Improvement in literacy and economic status along with awareness about personal hygiene can definitely bring down the prevalence of this disease.

CONCLUSION

The results suggested that oral Ivermectin and topical Permethrin (5%) were equally efficacious and therefore suitable to be the treatment of choice. Oral Ivermectin is well tolerated, non irritant to skin, does not show central nervous system side effects because it does not cross blood brain barrier. So the good therapeutic response with few side effects seen with oral Ivermectin can be useful in those patients for whom topical treatment is potentially irritant and less well tolerated. Oral Ivermectin could be a valuable drug in mass community treatment in managing epidemics, in treating complicated cases, where topical scabicides fail, where Permethrin resistance is encountered or where non compliance is a problem with topical agents.

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PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Pharmacology, IGIMS, Sheikhpura, Patna, Bihar, India.
2. Associate Professor, Department of Pharmacology & Therapeutics, Patna Medical College & Hospital, Bihar, India.
3. Senior Resident, Department of Pharmacology, IGIMS, Sheikhpura, Patna, Bihar, India.
4. Professor and HOD, Department of Pharmacology & Therapeutics, Patna Medical College & Hospital, Patna, Bihar, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Pramod Kumar Manjhi,
Senior Resident, Department of Pharmacology,
Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna-800014, Bihar, India.
Phone : 09835659978, E-mail : drpramod02.pmch@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Feb 27, 2014**
Date of Peer Review: **Jun 14, 2014**
Date of Acceptance: **Jul 11, 2014**
Date of Publishing: **Sep 20, 2014**