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Original Research Article

Prospective, randomized, and comparative study of efficacy of ivermectin, benzyl benzoate 25%, permethrin 5% and gamma benzene hexachloride 1% in the treatment of uncomplicated scabies

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ABSTRACT

Background: Scabies is an infectious and contagious human skin disease. The aim of the study was to study the efficacy and safety of four different treatment modalities in clinically diagnosed cases of scabies of single dose of oral ivermectin and commonly used topical scabicide agent's benzyl benzoate 25% (BB), permethrin 5% and gamma benzene hexachloride 1% (GBHC).

Methods: This study was carried out in the Department of Dermatology, Andhra Medical College, Visakhapatnam. 200 patients diagnosed of scabies were included in the study during the period from August 2013 to July 2014. The percentage of improvement was compared between four groups. Intergroup comparison between two groups was done Chi square test.

Results: In the present study a greater number of patients were students (54.5%). Subsidence of lesion and itching with oral ivermectin given as a single dose (200 µg/kg body weight) was 45 (90%) and 44 (88%), with topical permethrin 5% lotion single application 48 (96%), 47 (94%), with topical GBHC 1% lotion 40 (80%) patients, 38 (76%). Topical application of BB lotion 25% was 38 (76%), and 36 (72%) at fourth week.

Conclusions: In the present study permethrin 5% cream was found to be more effective among topical agents. Both BB and GBHC 1% lotion are being inexpensive and they can be used as an alternative treatment in developing country like India.

Keywords: Scabies, Ivermectin, Benzyl benzoate, Permethrin and gamma benzene hexa chloride

INTRODUCTION

Scabies is an infectious and contagious human skin disease caused by the mite *Sarcoptes scabiei* var. *hominis*. It is characterized by papular or vesicular eruption with intense itching especially at night. Scabies is transmitted readily, often throughout an entire household, by prolonged skin-to-skin contact with an infected person. Scabies affects people of all countries, particularly children of the developing nations. The

highest incidence is in countries with hot, tropical climates, where infestation is endemic especially in communities where overcrowding and poverty coexists.¹ Rate of scabies occurrence vary from 0.3% to 46% as per the recent literature.² In 2010 it was estimated that the direct effects of scabies infestation on the skin alone led to more than 1.5 million YLDS (years lived with disability), and the indirect effects of complications on renal and cardiovascular functions are far greater.¹ Scabies infestation is frequently complicated by bacterial skin

infections such as impetigo, cellulitis and abscess due to *Streptococcus pyogenes* and *Staphylococcus aureus*. Such bacterial skin infections predispose to serious suppurative and non suppurative sequelae. There are about three hundred million cases of scabies in the world each year. With the launch of International Alliance for the Control of Scabies (IACS) in 2012, which is recently formed group from across the globe to advance the agenda of scabies control, shows the current epidemiological situation for scabies across the world. Scabies recently included in the WHO NTD (neglected tropical disease) list is an important step towards greater recognition of this pathogen as a cause of considerable global morbidity and mortality.³

A meta-analysis reported that, there is no conclusive evidence that oral Ivermectin is superior to topical preparations for treating common scabies in the community setting.⁴ Therefore this type of research study is done with an aim to determine an easy, safe, effective and better patient compliance drug which can be an ideal anti-scabietic drug in future.

METHODS

This study was a prospective, randomized, and comparative clinical trial carried out in the Department of Dermatology in patients of uncomplicated scabies, King George Hospital, attached to Andhra Medical College, Visakhapatnam during August 2013 to July 2014. 200 patients diagnosed of scabies were allocated for each of four groups by following simple random sampling procedure using lottery method. Ethical clearance was obtained from Institutional ethics committee of Andhra Medical College, Visakhapatnam. Detailed informed consent form was signed by all adult patients or by parents of the children enrolled in the trial after a detailed explanation and clarification of doubts regarding the study. Basing on the inclusion criteria, newly diagnosed patients of scabies of either gender belonging to the age group between 5 to 60 years who are willing to participate for either topical therapy or oral therapy, complaint of nocturnal itching and presence of typical scabietic lesions like papule, vesicle, nodules-uncomplicated scabies.

Patients were excluded who are less than 5 years and elderly patients more than 60 years, pregnant women, lactating women, women of child bearing age planning for conception in near future, who were not willing for follow up, taking any concurrent medication for other illness, with any other associated skin diseases which may alter the picture of scabies, Any serious systemic illness particularly CNS disorders, known/suspected immunocompromised individual, who have taken any anti-scabietic treatment in the previous week. Routine blood tests were done. Severity of lesions and site of lesions and grading of itching recorded for each patient.

Interventions

Group A patients received tablet ivermectin (oral)- 200 µg/kg to be consumed as single dose on empty stomach. Available as 6 mg/12 mg. Group B patients received permethrin 5% cream to be applied once to the whole body below neck and left overnight for 8 hours. Group C patients was treated with benzyl benzoate 25% lotion to be applied to the whole body below neck and left for 24 hours. Group D patients was advised GBHC- 1% lotion to be applied to the whole body below neck and left overnight for 8 hours.

Participants on intervention B, C, D group were advised to bath with warm water before application of medication and scrub bath was taken 12 hours later. The participants were recalled after one week and again at fourth week for follow up evaluation. During the follow up patients were observed for cure rate and adverse drug reaction (ADR) monitoring. The demographic data of the participants were collected in the case record form (CRF) by the principle investigator. At each follow up the participants were examined by two doctors, the dermatologist and the principle investigator. Patients were advised not to use or mix with any other treatment including antipruritic or antihistaminic medicines. All participants were issued Benzyl benzoate lotion 25% for topical application for their family members and close contacts, as per the standard treatment guidelines to check the re-infestation of the participants. Participants were reinforced with the importance of treatment of family members and other close contacts during each visit.

At the initial visit the baseline itching and clinical grading score was done. All the details were recorded and the efficacy was assessed on the basis of two parameters.

Clinical grading score

The primary efficacy parameter was total number of lesions. Severity of lesions was clinically graded on a scale of 0 to 3 arranged as follows, 0=free of lesion (no lesion), 1≤10 lesions (mild), 2=11-49 lesions (moderate) and 3≥50 lesions (severe).⁵

Itching grading score

The secondary efficacy parameter was assessment of reduction in severity of pruritus, considering the pruritus at first visit as 100%. The patient was asked for reduction in intensity of pruritus on subsequent visits and on basis of that grading was done on the given scale by the observer.⁵

Pruritus grading scale

Pruritus is graded as follows, 0=0% (no pruritus); 1=(1-25%) (mild pruritus); 2=(26-50%) (moderate pruritus), 3= (51-75%) (severe pruritus); and 4=(76-100%) (very severe pruritus).⁵

Statistical analysis

The percentage of improvement was compared between four groups. Intergroup comparison between two groups was done Chi square test. For all statistical tests, p value <0.05 were considered to be statistically significant.

RESULTS

Patients who were included in study were divided into 4 groups of 50 patients each. In the present study most of the patients belonged to the age group of 11-20 years 75 (37.5%). The number of patients in age group of 21-30 years and 6-10 years were 53 (26.5%) and 31 (15.5%) respectively. Male constituted to the majority of patients. Male: female ratio is approximately 3:2.

Out of 200 patients, majority were students who constituted to 119 (54.5%) followed by housewives 37 (18.5%), coolie 14 (7%), agriculturists 13 (6.5%) and others 12 (6%), hotel workers 9 (4.5%), teachers 6 (3%).

Family history of scabies was positive in 169 (84.5%) patients. Scabies gets transmitted to close contacts at home. Therefore, close contacts are to be treated to be prevent re-infestation. In the present study nocturnal itching was present in all 200 patients i.e., 100% of patients.

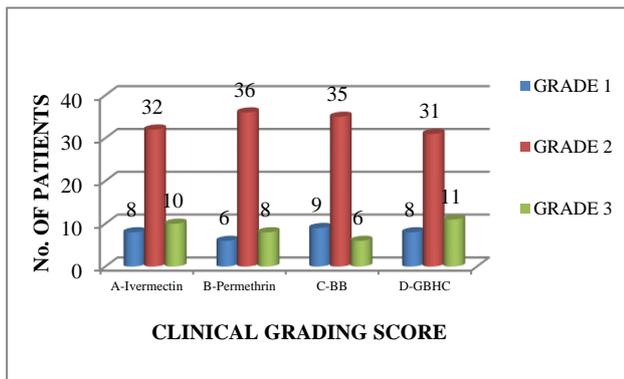


Figure 1: Represents clinical grading score.

Number of patients with respect to the clinical grade (lesions) in each treatment groups with respect to lesions on the first day. Ivermectin group- number of patients in grade 1 was 8 (16%) in grade 2 was 32 (64%) and in grade 3 was 10 (20%). Permethrin (B)- number of patients in grade 1 was 6 (12%) in grade 2 was 36 (72%) and in grade 3 was 8 (16%). BB (C)- number of patients in grade 1 was 9 (18%) in grade 2 was 35 (70 %) and in grade 3 was 6 (12%). GBHC (D)- number of patients in grade 1 was 8 (16%) in grade 2 was 31 (62%) and in grade 3 was 11 (22%).

Ivermectin (A)- during first follow up patients in higher grades improved to lower grades and patients in grade 1, 8 (16%) got cured and 27 (54%) in grade 2 got cured.

Totally 35% got cured for lesions in this group. Permethrin (B)- patients in grade 1, 6 (12%) got cured and 33 (66%) got cured in grade 2. Totally 39 (78%) got cured during first follow up. BB(C)- patients in grade 1, 9 (18%) got cured and 19 (38%) got cured in grade 2. Totally 28 (56%) got cured during first follow up in this group. GBHC (D)- patients in grade 1, 8 (16%) got cured and 22 (44%) got cured in grade 2. Totally 30 (60%) patients got cured during the first follow up. In all treatment groups there were no patients in grade 3.

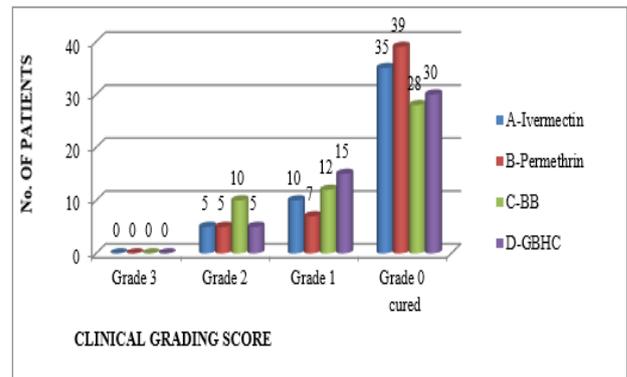


Figure 2: First follow up after first week lesion.

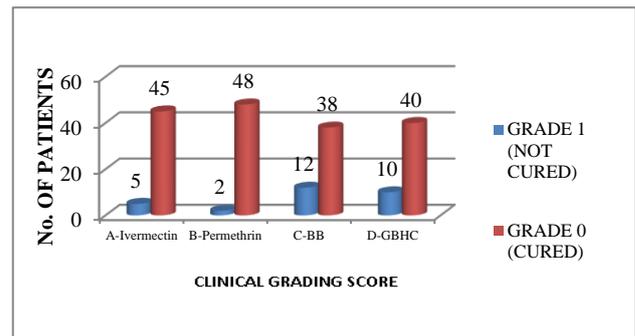


Figure 3: Second follow up in fourth week lesion.

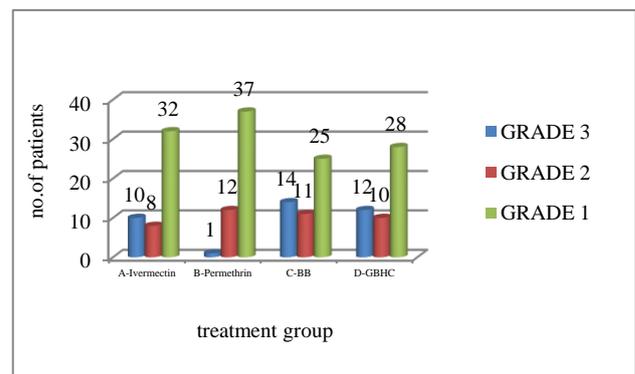


Figure 4: First follow up after first week itching.

Ivermectin (A)- during second follow up patients in higher grades improved to lower grades and out of patients in grade 1, 10 (20%) got cured. Totally 45 (90%) got cured for lesions in this group. Number of patients

not cured is 5 (10%). Permethrin (B)- out of patients in grade 1, 7 (12%) got cured and 2 (4%) got cured in grade 2. Totally 48 (96%) got cured during second follow up. Number of patients not cured is 2 (4%). BB (C)- out of patients in grade 1, 10 (20%) got cured. Totally 38 (76%) got cured during second follow up in this group. Number of patients not cured is 12 (24%). GBHC (D)- out of patients in grade 1-10 (20%) got cured. Totally 40 (80%) patients got cured during the second follow up. Number of patients not cured is 10 (20%). Baseline itching severity was considered very severe- (100%) in all 200 patients.

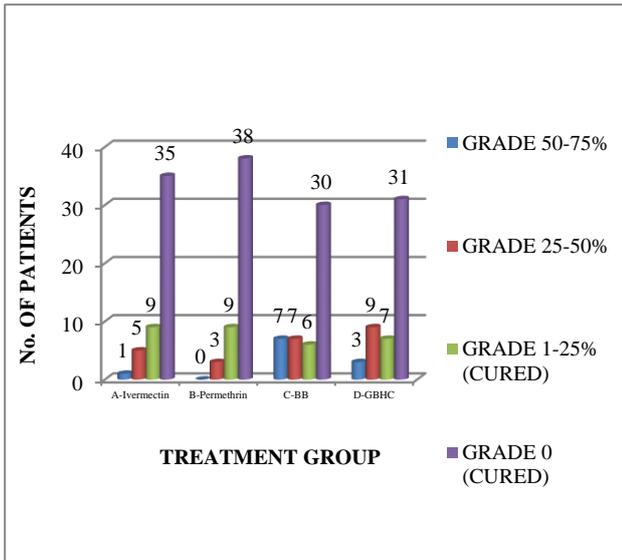


Figure 5: Second follow up in fourth week itching.

During first follow up at the end of first week, patients in all groups improved from grade 3 to grade 1. Ivermectin- (A) out of 50 patients, 10 (20%) grade came down to (50-75%) (grade 3), 8 (16%) came down to (25-50%) grade 2, and rest of the patients 32 (64%) got (1-25%) grade 1 for itching. Permethrin- B out of 50 patients, 1 (2%) grade came down to (50-75%) grade 3, 12 (24%) came down to (25-50%) grade 2, and rest of the patients 37 (74%) got (1-25%) grade 1 for itching. BB- (C) out of 50 patients, 14 (28%) grade came down to (50-75%) grade 3, 11 (22%), came down to (25-50%) grade 2, and rest of the patients 25 (50%) got (1-25%) grade 1 for itching.

GBHC- (D) out of 50 patients, 12 (24%) grade came down to (50-75%) grade 3, 10 (20%), came down to (25-50%) grade 2 and rest of the patients 28 (56%) got (1-25%) grade 1 for itching.

Ivermectin - (A) at first follow up 18 (36%) patients were not cured, out of them, 9 (18%) improved to grade 1-25% and 3 (6%) came down to grade 0 at 4th week. Both these grades were considered as cured. Total no of patients cured for itching is 44 (88%) Number of patients not cured is 6 (12%).

Permethrin- B at first follow up 13 (26%) patients were not cured, out of them, 9 (18%) improved to grade (1-25%) and 1 (2%) came down to grade 0 at 4th week. Both these grades are considered as cured. Total no of patients cured for itching is 47 (94%), number of patients not cured is 3 (6%).

BB- (C) at first follow up 25 (50%) patients were not cured, out of them, 6 (12%) improved to grade (1-25%) and 5 (10%) came down to grade 0 at 4th week. Both these grades were considered as cured. Total no of patients cured for itching is 36 (72%). Number of patients not cured is 14 (6%).

GBHC- (D) at first follow up 22 (50%) patients were not cured, out of them, 7 (14%) improved to grade (1-25%) and 6 (12%) came down to grade 0 at fourth week. Both these grades were considered as cured. Total number of patients cured for itching is 38 (76%). Number of patients not cured is 12 (24%).

In various regimens at the end of 4 weeks as depicted in the above Table 1; there was statistical significance with results obtained with topical permethrin 5% with BB lotion 25% with regards to parameter for both itching and severity of lesion. Similarly, there was statistical significance with results obtained by permethrin 5% cream with GBHC 1% lotion in consideration with both the parameters itching and severity of lesions. Oral Ivermectin shows statistical significance with BB lotion with parameter itching is considered. Oral ivermectin and permethrin results were not statistically significant for both parameters.

Table 1: Comparison of results of various regimens at fourth week.

Regimens	No. cases	Lesion at fourth week		Itching at fourth week	
		Cured N (%)	Not cured N (%)	Cured N (%)	Not cured N (%)
A-IV	50	45 (90)	5 (10)	44 (88)	6 (12)
B-PM	50	48 (96)	2 (4)	47 (94)	3 (6)
C-BB	50	38 (76)	12 (24)	36 (72)	14 (28)
D-GBHC	50	40 (80)	10 (20)	38 (76)	12 (24)

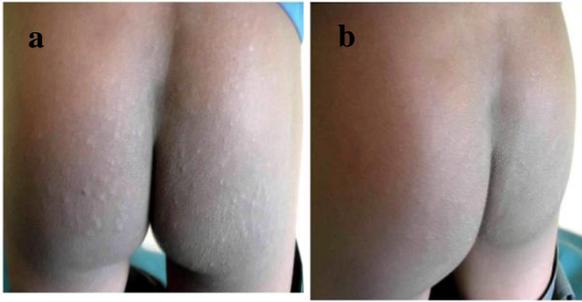


Figure 6: Response to oral ivermectin group (a) before treatment and (b) after treatment 4th week.

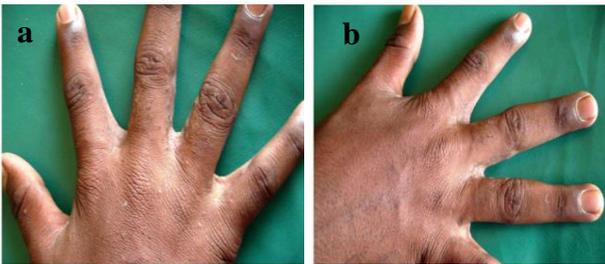


Figure 7: Response to permethrin 5% lotion (a) Before treatment and (b) after treatment 4th week.

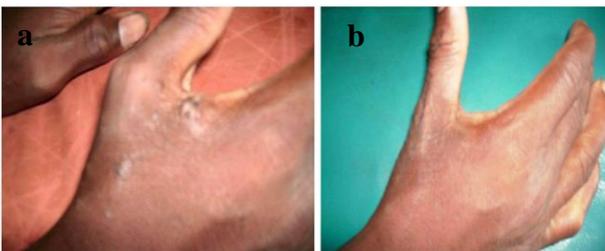


Figure 8: Response to benzyl benzoate 25% lotion (a) before treatment and (b) after treatment 4th week.

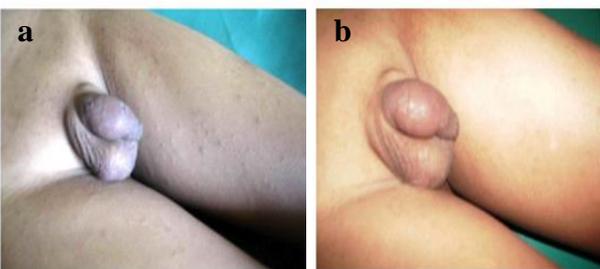


Figure 9: Response to GBHC 1% (a) before treatment and (b) after treatment 4th week.

DISCUSSION

In our study, majority of the patients (37.5%) belonged to the age group of 11-20 years followed by 21-30 years who constituted to 26.5% of scabies. Children between 6-10 years constituted to 15.5% and very few people belonged to 41 years and above. Thus, scabies was found

to be more common in children and young adults. Similar results were also found in others studies like Gulati et al.⁶ The higher incidence of scabies found in students is due to multiple causes like playing together in the school, living together in hostels and the habit of using the dresses and linen of the friends, which add to the transmission of the disease in them. In the present study males constituted 58% whereas female constituted 42% and thus the male to female ratio was approximately 3:2. The higher prevalence among the middle socio-economic group (71.5%) followed by the low-income group (22.5%). Bedi, Nair, Hati et al, Gulati et al, have observed higher prevalence of scabies in low and middle socio-economic groups.⁶⁻⁹

In the present study, nocturnal itching was present in all of the patients. Nair et al, found nocturnal itching in 100% of the patients.⁸ Thus, it may be a helpful information in making the diagnosis, especially in the absence of facilities for demonstrating the mite.

Response to treatment in various regimens

With oral ivermectin given as a single dose (200 µg/kg body weight), out of 50 patients considering the lesions as the parameter 35 (70) patients improved at the end of 1 week and 15 (20) at fourth week. Total number of patients showing after complete subsidence at fourth week was 50 (90%). Similarly considering severity of itching as the parameter in 50 patients, improvement was seen in 35 (70%) and 9 (18%) at fourth week. Total number of patients who showed improvement was 44 (88%). Usha et al and Chouela et al, found that a single dose of Ivermectin provided a cure rate of 70%, which increased to 95% with 2 doses at a 2 weeks interval.^{10,11}

With topical permethrin 5% lotion single application: out of 50 patients, cure of lesion was seen in 39 (78%) at the end of 1st week and 9 (18%) at fourth week respectively. Total number of patients cured at fourth week was 48 (96%). Considerably the severity of itching number of patients cured was 37 (74%) and 10 (20%) at the end of 1st week and fourth week respectively. Total number patients cured at fourth week were 47 (94%). Zargari et al, showed 84.6% improvement after 2 weeks of therapy.¹² In this study we observed that Permethrin decrease pruritus to 74% compared to 88% in ivermectin. This is comparable to Bachewar et al study.¹³

In present study permethrin scored over Ivermectin in providing statistically significant higher cure rates at 4 weeks post-treatment. This may have an important bearing in highly contagious disease like scabies where chain or risk of transmission of disease may curbed at a relatively early stage.

With topical GBHC 1% lotion: out of 50 patients in the present study with lesion as the parameter, improvement was seen in 30 (60%) and 10 (20%) of the patients at the

end of 1st week and between 1st to 4th weeks. Total improvement was seen in 40 (80%) patients.

Considering the severity of itching as the parameters, improvement was seen in 28 (56%) and 10 (20%) of patients at the end of 1st week and between 1st and 4th week. The total patients improved were seen in 38 (76%). Taplin et al, have found cure rate 65%, Zargari et al 48.9%.^{12,14}

With topical application of BB lotion 25%

In the present study out of 50 patients, considering the severity of lesion patients improved at the end of 1st week and between 1st to the 4th weeks was 28 (56%) and 10 (20%) respectively. At end 4th weeks total patients improved was 38 (76%).

Considering the severity of itching as the parameter, patients' improvement was seen in 25 (50%) and 11 (22%) at the end of 1st week and 1st-4th weeks respectively. Total number of patients improved at 4th weeks was 36 (72%). Glaziou et al conducted investigator-blind trial with oral Ivermectin versus topical BB lotion. After 30 days of treatment follow up showed a cumulative recovery cure rate of 70% and 48% with BB lotion.¹⁵

CONCLUSION

In the present study permethrin 5% cream was found to be more effective among topical agents. In present study permethrin scored over Ivermectin in providing statistically significant higher cure rates at 4 weeks post treatment. This may have an important bearing in highly contagious disease like scabies where chain or risk of transmission of disease may curbed at a relatively early stage. Though the results obtained with oral ivermectin were slightly low compared to permethrin, the patient compliance was very good. Permethrin was significantly more effective than benzyl benzoate and GBHC 1%. Both benzyl benzoate and GBHC 1% lotion are being inexpensive and they can be used as an alternative treatment in developing country like India.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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