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Original Research Article

Comparative study of oral ivermectin, topical permethrin and benzyl benzoate in the treatment of scabies

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ABSTRACT

Background: Efficacy of these modalities as shown by various investigations are inconsistent and ambiguous. Thus, evidence based effective treatment option is warranted. Aim of the study was to compare the efficacy of oral ivermectin, topical permethrin and benzyl benzoate in the treatment of uncomplicated scabies.
Methods: Patients with confirmed diagnosis of scabies were included in this study. One hundred and ninety-five subjects were included in this investigation as per inclusion and exclusion criteria laid down. Equal numbers of patients were randomly allocated to one of the three treatment groups. Efficacy of three groups [oral ivermectin (Group A), topical permethrin (Group B) and benzyl benzoate (Group C)] of drugs was compared in terms of improvement in clinical grading of disease (%) and improvement in clinical grading of pruritus (%) during follow up visits.
Results: Those subjects receiving topical permethrin, at 1st follow up 56.9% showed cure rate which increased to 89.2% at 2nd follow up with respect to clinical improvement in pruritus. Maximum relief in severity of pruritus at the end of 6th week was reported by 58(89.2%) patients receiving group B treatment modality followed by 52 patients (80%) in arm A. Regarding efficacy of three treatment groups in terms of improvement in severity of lesion at the end of 6 weeks, maximum number of patients 57(87.7%), receiving group B treatment reported improvement which is better than other two treatment groups.
Conclusions: maximum number of patients receiving topical Permethrin treatment reported improvement better than other Oral Ivermectin therapy and topical benzyl benzoate. Oral ivermectin may serve a good alternative for managing scabies under certain conditions like poor compliance to topical scabicides.

Keywords: Benzyl benzoate, Efficacy, Ivermectin, Scabies, Permethrin

INTRODUCTION

Scabies is a skin infestation and clinical condition frequently encountered by health care providers in India. It is caused by a mite i.e. ecto-parasite of skin namely *Sarcoptes scabiei var*. hominis.[1] Characteristic feature of scabies is intense itching reported by the infected patients as it burrows under the subject's skin. Scabies affects more than three million people in India. Condition is characterized by papular or vesicular eruption with pruritis which is aggravated by warmth and more intense at nighttime.[2] Acropustulosis or blisters and pustules on palms and soles of feet are characteristically seen in infants affected with scabies.[3]

Scabies is a disease frequently seen among residents of lower socio-economic strata. Current recommendations direct the physicians not to treat only the affected individual but all those people who are in contact with the patient.[4] Treatment is often hindered by inappropriate or delayed diagnosis, poor treatment compliance or uptake and improper use of topical compounds such as

permethrin, lindane or benzyl benzoate. Antihistaminic are used to control itching.[5]

Various treatment options for scabies consist of topical anti-scabietics such as benzyl benzoate, crotamiton, lindane, and permethrin. Topical treatment for community management of endemic scabies is not warranted due to a variety of reasons. Efficacy of these modalities as shown by various investigations are inconsistent and ambiguous.[6-9] Thus evidence based effective treatment option is warranted. Keeping above facts in mind, author planned this study with the aim of comparing the three anti-scabetics-oral ivermectin, topical permethrin and benzyl benzoate in the treatment of uncomplicated scabies.

METHODS

This study was conducted at the department of Pharmacology in collaboration with the department of Dermatology, Venereology and Leprology of FH Medical College and Hospital, Tundla during February 2016 to December 2017. Study population included those visiting the outpatient department of dermatology for seeking care for scabies during the study period. Only those subjects, who were diagnosed with scabies, were included in this study.

Inclusion criteria

Patients of above 5 years and below 60 years of age, patients of both sexes, patients willing for either topical or oral therapy were included in this study.

Exclusion criteria

Included participants with systemic disorders, and psychiatric illnesses; pregnant or lactating women; women of childbearing age or planning for conception in near future. Subjects with any other associated skin disease, that may influence scabies; immunocompromised individuals, having scabies with atypical presentations like crusted scabies were also excluded.

In this quasi experimental study, three anti-scabietics oral ivermectin, topical permethrin and benzyl benzoate were given to study subjects in controlled environment. They were also provided with pamphlets in the local language. Any participant who did not answer correctly, were termed as non-compliant. Patients were clinically examined for presence of burrows underneath the skin. Classical lesions seen in scabies patients viz nodules, papule or vesicles were also searched for. Pruritis was managed symptomatically by oral hydroxyzine 10 mg or 25 mg twice daily to affected persons.

If any participant was found with signs of secondary infection, experienced physician treated him, then such subject was allowed to enter the study. Baseline information in the form of socio-demographic and economic data was captured in a structured sheet. During study period, a total of 488 subjects diagnosed with scabies, 195 were included in this investigation as per inclusion and exclusion criteria laid down. Equal numbers of patients (n=65) were randomly allocated to one of the three treatment groups as per random allocation number generated through computer. Finally, each treatment group served 65 subjects. Patients were instructed not to use or mix any other drug or medicines.

Group A participants (Oral Ivermectin single dose 200 µg/kg body wt.)

Participants in this treatment arm were given tablet ivermectin orally in the dose of 200 µg/kg body wt.) as a single dose to be self-administered along with printed information sheet in the local vernacular language.

Group B participants (Topical Permethrin 5% cream single application)

Patients were instructed to apply the cream to whole body covering neck to toe. They were explained that the cream must remain in contact with the skin for at least 8 hours. They were advised to take bath with warm water not earlier than 8 hours after application.

Group C participants (Topical Benzyl benzoate 25% lotion single application)

In this group, patients were instructed to apply Benzyl Benzoate 25% emulsion below the neck, with 3 applications during a 24-hour period. Subjects were asked to apply enough medicine to cover the entire skin surface from the neck down, including the soles of your feet, and rub in well. They were also advised to allow the medicine to remain on the body for 24 hours. Then, thoroughly washing the body with warm water and soap was advised.

Follow up was done twice at the end of 1st week and 6th week to find out the improvement in the following two important parameters to look into efficacy of treatment modalities under question.

Severity of pruritus

Visual Analogues Scale (VAS) was utilized for its assessment. Scale was graded from 0 to 10.

Point 0 (zero) signifies no pruritus and point 10 signifies the most severe form of pruritus. According to this scale, Author scored pruritus of the patients. Point 0: No pruritus, point 1 to 3: Mild pruritus, point 4 to 6: Moderate pruritus and Point 7 to 10: Severe pruritus.

Severity of the disease

Severity of the disease was equated with number of lesions. Grading of the lesions was done in the following

manner: Mild: <10 lesions, Moderate: 11-49 lesions and Severe: >50 lesions.

Institutional Ethical Committee approved the study. Data collection was done only after taking consent. The study adhered to the tenets of the Declaration of Helsinki for research in humans. Data collected in the structured proforma was entered in the excel sheet. Analysis was done by Statistical Package for Social Sciences (SPSS), version 20 (IBM, Chicago, USA). Results were expressed after applying appropriate statistical tests like Chi-square test. p value <0.05 was considered statistically significant.

RESULTS

In this study, out of total 488 subjects diagnosed with scabies, 195 were included in this investigation. Equal numbers of patients (n=65) were randomly allocated to one of the three treatment groups. Finally, each treatment group served 65 subjects. Baseline parameters of the study participants of the three groups were comparable. Mean age of subjects in Group A, B and C was found to be 26.18±9.04 years, 29.85±8.66 years and 27.12±10.28 years respectively. Mean weight of patients in Group A, B and C was 55.06±12.61 kg, 60.94±11.46 kg and 58.04±9.22 kg respectively.

Out of total 65 subjects allocated to treatment arm Group B, most patients 37(56.9%) reported clinical relief in pruritus as compared to 33(50.8%) subjects in Group A and 28(43.1%) patients in group C; at the end of 1st week i.e. first follow up visit. In the same manner, highest number of patients, 21(32.3%) receiving group B treatment arm, reported relief in severity of pruritus; at the end of 6th week i.e. at 2nd follow up visit. 40(61.5%) revealed clinical relief in severity of lesions as compared to 28(43.1%) subjects in Group A and 25(38.5%) patients in group C; at the end of 1st week i.e. first follow up visit. Maximum relief in severity of pruritus at the end of 6th week was reported by 21(32.3%) patients receiving group A treatment modality (Table 1).

Table 1: comparison of response to treatment modalities in terms of clinical improvement in during follow up visits.

Treatment modalities/groups	Clinical improvement in severity of pruritus		Clinical improvement in severity of lesions	
	At the end of 1st week	At the end of 6th week	At the end of 1st week	At the end of 6th week
Group A	33(50.8%)	19(29.2%)	28(43.1%)	21(32.3%)
Group B	37(56.9%)	21(32.3%)	40(61.5%)	17(26.2%)
Group C	28(43.1%)	18(27.7%)	25(38.5%)	18(27.7%)
Group A= Ivermectin, Group B= Permethrin, Group C= Benzyl benzoate				

Efficacy of three treatment arms was noted down in terms of improvement in severity of pruritus at the end of 6 weeks. Maximum relief in severity of pruritus at the end of 6th week was reported by 58(89.2%) patients receiving group B treatment modality followed by 52 patients (80%) in arm A. Regarding efficacy of three treatment groups in terms of improvement in severity of lesion at the end of 6 weeks, maximum number of patients 57(87.7%), receiving group B treatment reported improvement which is better than other two treatment groups (Table 2). Difference in efficacy of Group A (Ivermectin) therapy was statistically non-significant with Group B (Permethrin) and C (Benzyl benzoate). But difference in efficacy of Group B (Permethrin) therapy was statistically significant with Group C (Benzyl benzoate) (Table 2).

Table 2: Comparison of efficacy of three groups of drugs in terms of improvement in severity of pruritus at the end of 6 weeks.

Group	No. of cases	Severity of pruritus at 6th week		Severity of lesion at 6th week	
		Improved N (%)	Not improved N (%)	Improved N (%)	Not improved N (%)
A	65	52(80%)	13(20%)	49(75.4%)	16(24.6%)
B	65	58(89.2%)	7(10.8%)	57(87.7%)	8(12.3%)
C	65	46(70.8%)	19(29.2%)	43(66.2%)	22(33.8%)
Inter-group comparison					
Difference between groups	A and b	Chi-square=2.12	p=0.14	Chi-square=3.2	p=0.07
	A and C	Chi-square=1.49	p=0.22	Chi-square=1.33	p=0.24
	B and C	Chi-square=6.92	P=0.008*	Chi-square=8.49	P=0.003*
Group A= Ivermectin, Group B= Permethrin, Group C= Benzyl benzoate; statistically significant at p<0.05					

DISCUSSION

In developing countries including India, its common to see scabies patients at health centers as well as at community level. Any person with intense itching should be suspected having infested with *Sarcoptes scabiei*. Scabies is a significant public health problem in developing regions in true sense. As per literature, direct skin-to-skin contact for a period not less than fifteen to twenty minutes is required for transfer of itch mite form one person to another. On an average, on infested individual harbors only five to twelve itch mites. But a person with crusted scabies can shed thousands of such mites.[10,11]

Immunologically, parasite causes a mixed type I/ type IV hypersensitivity reaction in the body of host. A sharp rise in interleukin-6 (IL-6) and vascular endothelial growth factor occurs during the period of infestation. IL-6 activates Th1 CD4+ lymphocytes to secrete IL-2. These lead to proliferation and differentiation of lymphocytes in the body of host.[12]

In this quasi-experimental trial, efficacy of three antiscabetics-oral ivermectin (Group A), topical permethrin (Group B) and benzyl benzoate (Group C) were evaluated in treating uncomplicated scabies.

In this study author found that patients receiving oral ivermectin (Group A), at the end of 6 weeks improvement was seen in 80% and 75% in severity of pruritus and lesion respectively. Other authors observed that a single dose of Ivermectin provided a cure rate of 70%, which increased to 95% with 2 doses given at 2 wk. interval.[13]

Regarding subjects receiving topical permethrin (Group B), At 1st follow up 56.9% showed cure rate which increased to 89.2% at 2nd follow up with respect to clinical improvement in pruritus. Earliar studies have reported cure rate >80% with Permethrin. Higher cure rates (98%) was reported after two applications.[14,15] Those who received benzyl benzoate (Group C); at the end of 6 weeks, 70.8% reported improvement in pruritus and 66.2% reported cure in severity of lesion. Another study observed that 57% of patients improved after treating with benzyl benzoate.[16] Other author noted improvement in 51% patients at the end of 3 wks.[17]

In this study, author observed that difference in efficacy of Group A (Ivermectin) therapy was statistically non-significant with Group B (Permethrin) and C (Benzyl bezoate). But difference in efficacy of Group B (Permethrin) therapy was statistically significant with Group C (Benzyl bezoate). This shows that efficacy of Group B treatment modality was comparable to Group A therapy but more efficacious than Group C modality.

Topical medications have its own drawbacks. Use of such medications for community management of endemic scabies remains doubtful. Reasons for such hindrance are poor participation, inconvenience and unpleasantness of treatment. Although topical agents carried certain drawbacks, this study reported that single application of Permethrin 5% gave maximum response with respect to clinical improvement in pruritus and severity of lesion. Therefore, this evidence makes Permethrin as most effective treatment and suit to be the treatment of choice.

In this study, author also observed that efficacy of oral Ivermectin was better than topical Benzyl benzoate but less than topical Permethrin. Such oral medication is more suitable to subset of people having inadequate facilities for bathing or water scarce areas. Its acceptance was very good especially among students living in hostels and taking a good scrub bath were the major hurdle in topical application.[18]

Therefor oral ivermectin may serve a good alternative for managing scabies under certain conditions like poor compliance to topical scabicides. Cost wise, oral Ivermectin is costly than other two medications in this study therefore higher cost and lower efficacy of single dose oral Ivermectin as compared to topical Permethrin provide us a base to consider as initial therapy with Permethrin if needed.

Additionally, from theory point of view, management of scabies appears quite easy but from practical point of view its extremely difficult task as success of the treatment of scabies depends on a variety of factors. Literacy, personal hygiene, socio-economic status, presence of co-infection etc. influence the course of disease. Thus, correct medication, correct dosing, correct duration of treatment, treatment of contacts along with other factors can being down the burden of disease.

CONCLUSION

This study observed that maximum number of patients receiving group B (topical Permethrin) treatment reported improvement better than other Group A (Oral Ivermectin) therapy and Group C (topical benzyl benzoate). Oral ivermectin may serve a good alternative for managing scabies under certain conditions like poor compliance to topical scabicides. Improvement in clinical grading of pruritus and severity of lesion during follow up visits shows that permethrin cause rapid improvement compared to other two medications. Further controlled trials should be rolled out to support authors findings.

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