A comparative study to assess the efficacy of permethrin (topical) and benzyl benzoate (topical) for the treatment of scabies patients

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ABSTRACT

Several attempts have been made to come up with the anti-scabies drugs that are more efficient and safer. In India, scabies is more prevalent in overcrowded communities with low socioeconomic conditions, due to which the best efficient anti scabies drugs or treatment are unaffordable to them. To comparatively assess the efficacy of permethrin (topical) and benzyl benzoate (topical) in scabies patients. Study subjects with a confirmed diagnosis of scabies were included in this study. After enrolling 178 study subjects, they were equally distributed to two study groups (A & B) using a computer-generated random allocation number and were given the desired respective therapeutic interventions. Subjects in Group A were given permethrin 5% cream. The Benzyl Benzoate 10% to 25% emulsion was allocated for Group B subjects. Efficacy of two groups of drugs was compared in terms of improvement in clinical grading of disease (%) & improvement in clinical grading of pruritus (%) during follow up visits at the end of 1, 2, 4 & 6 weeks. The mean age (± SD) for study subjects in the Group A was 18.18 ± 11.33 years, whereas, in Group B, it was 28.86 ± 12.39 years. The clinical cure rate of Permethrin and Benzyl benzoate was 72% and 34% at the end of the first week. It was 98% and 60% at the end of the second week. Data shows that permethrin is more efficacious than Benzyl benzoate. Comparatively, during consecutive visits, permethrin provided better and faster improvement in pruritis grade than benzyl benzoate. In the treatment of scabies permethrin (topical) was found to be more efficacious in comparison to benzyl benzoate (topical). The clinical cure rate of Permethrin and Benzyl benzoate was 72% and 34% at the end of the first week. Permethrin provided better and faster improvement in pruritis grade than benzyl benzoate.

INTRODUCTION

“Scabies” is a parasitic infection which is very frequently observed and is caused by an obligate human parasitic mite, i.e., “Sarcoptes scabiei var. hominis”. (Currie, 2015) The annual incidence of scabies remains high i.e., three million in the developing countries. (Jackson et al., 2007) Several attempts have been made to come up with the anti-scabies drugs that are more efficient and safer. In India, scabies is more prevalent in overcrowded communities with low socioeconomic conditions, due to which the best efficient anti scabies drugs or
treatment are unaffordable to them (Fitzgerald et al., 2014).

Topical benzyl benzoate (25% w/w) is applied from the neck to toe with a frequency of thrice a day with an optimal contact period of twenty-four hours and not to have a bath during a prescribed period. It causes neurotoxicity in mites. (Roos et al., 2001; Thomas et al., 2015) It is a drug of alternate choice due to its low cost in low-income countries with low socioeconomic conditions (Andersen et al., 2000; Thappa and Karthikeyan, 2002).

Medication with permethrin has shown very minimal toxicity to achieve effective outcomes against mites. Its mechanism of action is paralyzing and killing lice and their eggs (nits). Body metabolism of permethrin is easy and rapid via skin esterases and excretion in the urine. Topical Permethrin (5% w/w) are applied overnight to the whole-body including a head portion in case of infants with a frequency of once a week for the two weeks with optional contact period of eight hours (Hogan et al., 1991).

Resistance has been reported with permethrin. (Roth, 1991) Due to its higher cost, the use of permethrin (topical) for mass treatment is limited when compared to other topical anti-scarbies options. Keeping the above facts in mind, we conducted this study with the aim of comparing the two anti-scarbies drugs – one is the drug of choice at present permethrin (topical), and the other is the easily available and mostly used benzyl benzoate (topical).

MATERIALS AND METHODS

The present comparative study was conducted under the Department of Pharmacology, FH Medical College and Hospital, Tundla during February 2016 to 2018. Subjects visiting the outpatient department of dermatology during the study period for seeking care for scabies formed the study population. Study subjects with a confirmed diagnosis of scabies were included in this study.

Patients with a confirmed diagnosis of scabies, aged more than 5 years and those willing for follow-up up to six weeks were included in this study. Apart from this, the study subjects should have at least contact history with a patient having scabies, presents with increased itching at night hours, and a family history of scabies.

Patients with a confirmed diagnosis of scabies, aged more than 5 years and those willing for follow-up up to six weeks were included in this study. The study excluded subjects with a history of non-communicable diseases (NCD’s) such as diabetes mellitus, hypertension, or cardiovascular disease, neurological diseases, chronic infectious disorders, deranged liver and renal parameters, thyroid disorder, psychiatric disorders, eligible couples, and pregnant women or lactating mothers. Also, the subjects having substance abuse of any kind, including chewing or smoking tobacco, alcohol, and consuming therapeutic drugs for other ongoing illnesses, were not included in the present study. The study subjects were also excluded if they present with a related skin disorder, possibly hampering the scenario of scabies disease, having suspected/known immunocompromised status, uncommon scabies took other anti-scarbies drugs during an enrolled period and are unable to response in correct manner i.e., noncompliant.

The body of study subjects was clinically thoroughly examined to look for the classical burrows and typical scabies lesions presence i.e., nodules, papules, or vesicles.

Study subjects with present secondary infection were first given treatment as per clinical decision from the senior dermatologist team with the oral Azithromycin once per day for 3 days (Dosage 500mg) or oral Ampicillin four times per day for 5 days (Dosage 500 mg) and after getting cured, they were further enrolled in the study.

Principal investigator collected data in case of record form (CRF). The data included demographic details of study subjects like age, sex, educational status, working status, and marital status. After enrolling 178 study subjects, they were equally distributed to two study groups (A & B) using a computer-generated random allocation number and were given the desired respective therapeutic interventions. The principal investigator and dermatologist examined the study subjects on their respective follow-up visits. On each visit, the study subjects were given proper instructions regarding to avoid the use or mix of different drugs, which also included antihistaminic or antipruritic drugs. The subjects with complaints and symptoms of pruritis were treated by giving oral hydroxyzine twice daily (dosage 10 mg or 25 mg).

Subjects in Group A

The intervention permethrin dermal cream (5% w/w) was provided by the “Shalaks Pharmaceutical Ltd., New Delhi.” Along with the intervention, the study subjects were also provided with subject information sheets printed in their local vernacular language. The instructions given to study subjects included that the overnight topical application
of intervention from neck to toe, with optimum contact of minimum eight hours, and to take a bath with warm water after the required contact period is achieved.

**Subjects in Group B**

Topical benzyl benzoate emulsion (10 to 25% w/w) is applied from the neck to toe with a frequency of thrice a day with an optimal contact period of twenty-four hours and not to have a bath during a prescribed period. After the desired contact period is over subject shall take a bath with soap and warm water.

Prior to enrollment, the informed consent was obtained each subject. The study protocol was presented to the Institutional Ethical Committee (IEC) and was approved as the study was in accordance with the Declaration of Helsinki for human research. All proformas were checked for correctness and then coded for computer entry. Data collected in the proforma was entered in the excel sheet. The data was analyzed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp. Armonk, NY, USA).

Efficacy of two groups of drugs was compared in terms of improvement in clinical grading of disease (%) & improvement in clinical grading of pruritus (%) during follow up visits at the end of 1, 2, 4 & 6 weeks. Results were expressed after applying appropriate statistical tests and drawing conclusions.

**RESULTS AND DISCUSSION**

In this study, data of 178 subjects (89 in Group A & 89 in Group B) was included and analyzed. Basal characteristics of the study subjects of the two treatment groups are tabulated below. Both the study groups were comparable. As Table 1 shows the mean age (± SD) for study subjects in Group I was 18.18 ± 11.33 years, whereas, in Group II, it was 28.86 ± 12.39 years. The mean weight (± SD) for study subjects in Group I was 44.91 ± 18.41 Kg, whereas, in Group II, it was 61.48 ± 14.21 Kg. In Table 1, as such, no statistically significant difference was observed between the study groups with respect to age and weight.

Improvement in a clinical grade of scabies was assessed at the scheduled follow-up visits each time in both the treatment groups. In Table 2, the clinically observed cure rate among two groups i.e., Permethrin and Benzyl Benzoate at the end of the first and second week were 72% & 34%; and 98% & 60% respectively; and these observations was statistically significant (P < 0.05). In Table 2, data shows that permethrin (topical) was found to be highly efficacious than benzyl benzoate (topical) in improving the clinical grade of scabies, but as such no statistically significant difference between two groups was observed at the end of four and six weeks (P>0.05).

In Table 3, Improvement in clinical grade of pruritis was assessed at the scheduled follow-up visits each time in both the treatment groups, and it was found that permethrin provided better and fast improvement in pruritis grade than benzyl benzoate, and these observations was statistically significant (P < 0.05), but as such no statistically significant difference between two groups was observed at the end of four and six weeks (P>0.05).

An individual with generalized pruritis, which is intense and intractable in nature, shall raise the concern about Scabies disease. As scabies affects plenty of people and is also frequently associated with complications, it is being considered as “public health problem” of significant importance in developing countries, and it contributes to a significant number of cases in the daily out-patient department of (OPD) of urban and rural primary health care (PHC) centers.

The Sarcoptes scabiei causes hypersensitivity reactions, which are mixed in nature, namely Type I and Type IV. There also occur cross-reactions due to different mites like Sarcoptes scabiei and house dust mites. In individuals with scabies infection, the Interleukin-6 (IL-6) and Vascular Endothelial Growth Factor (VEGF) are markedly raised, and this raised level of Interleukin-6 (IL-6) further activates the lymphocytes (Th1 CD4+) which will, in turn, enhances the secretion of Interleukin-2 (IL-2). The raised Interleukin-2 (IL-2) enhances the differentiation and proliferation of lymphocytes. For effective transmission of itch mite, only fifteen to twenty minutes of direct dermal to dermal contact is sufficient. Usually, the average count of mite ranges between five to twelve on an individual, but there are plenty of mites are being shedded by the patient with crusted scabies.

In present study the clinically observed cure rate among two groups i.e., Permethrin and Benzyl Benzoate at the end of first and second week were 72% & 34%; and 98% & 60% respectively; and permethrin (topical) was found to be highly efficacious than benzyl benzoate (topical) in improving the clinical grade of scabies.

The findings of the present study were in coherence with the trails conducted in the past where the cure rate of more than 90% was reflected with the topical permethrin treatment (Thomas et al., 2015; Walker et al., 2000) but in one of the study, a recommendation was made that scabies patients should...
Table 1: Distribution of basal characteristics among study subjects in respective groups

| Group | Age Mean | Age SD | Weight Mean | Weight SD |
|-------|----------|--------|-------------|-----------|
| A     | 18.18    | 11.33  | 44.91       | 18.41     |
|       | 28.86    | 12.39  | 61.48       | 14.21     |

Group A=Permethrin, Group B= Benzyl benzoate.

Table 2: Comparison to assess the efficacy of two treatment group in terms of improvement in clinical grading of disease (%) during followup visits

| Variable | No lesions | Mild | Moderate | Severe | No lesions | Mild | Moderate | Severe |
|----------|------------|------|----------|--------|------------|------|----------|--------|
| Baseline | 4          | 42   | 34       | 16     | 4          | 38   | 36       | 18     |
| After 1st week | 72       | 18   | 8        | 0      | 34         | 32   | 28       | 0      |
| After 2 week  | 2         | 98   | 2        | 0      | 60         | 22   | 16       | 0      |
| After 4 week  | 4         | 100  | 0        | 0      | 98         | 0    | 0        | 0      |
| After 6 week  | 6         | 100  | 0        | 0      | 98         | 0    | 0        | 0      |

Group A=Permethrin, Group B= Benzyl benzoate.

Table 3: Comparison to assess the efficacy of two treatment group in terms of improvement in clinical grading of pruritus (%) during follow up visits

| Variable | Mild | Group A | Moderate | Severe | Group B | Moderate | Severe |
|----------|------|---------|----------|--------|---------|----------|--------|
| Baseline | 0    | 10      | 90       | 0      | 4       | 96       |
| After 1st week | 30   | 64      | 6        | 32     | 46      | 14       |
| After 2 week  | 2   | 44      | 8        | 0      | 48      | 12       | 2      |
| After 4 week  | 4   | 2       | 0        | 0      | 2       | 0        | 0      |
| After 6 week  | 6   | 0       | 0        | 0      | 0       | 0        | 0      |

Group A=Permethrin, Group B= Benzyl benzoate.

be given topical benzyl benzoate instead of permethrin. (Thawani et al., 2009) The cure rate with topical benzyl benzoate medication was around fifty percent in the studies done by Glaziou and Halima (Glaziou et al., 1993; Sule and Thacher, 2007).

The primary objective of scabies treatment is not just scabicide action, but it must also focus on relief from symptoms and prevention of secondary bacterial infections. The secondary bacterial infection occurs as a consequence of disintegration in the continuity of the dermal layer due to excessive and intensive itching. (Mimouni et al., 2003) Due to the scabicide action of anti-scabies drugs, dead Sarcoptes scabiei and their debris cause dermal reactions, which leads to dermal itching for several weeks even after the effective treatment. The side effects of topical anti scabies drugs includes itching of severe nature and allergic contact dermatitis, so keeping that in mind the scabies patient shall be provided proper instructions to avoid its excessive use and not to become habitual of it. (Karthikeyan, 2005) In the present study, improvement in the clinical grade of pruritus was assessed at the sched-
uled follow-up visits each time in both the treatment groups, and it was found that permethrin provided better and fast improvement in pruritis grade than benzyl benzoate.

From the theory point of view, the management of scabies appears quite easy, but from a practical point of view, it is extremely difficult task as the success of the treatment of scabies depends on a variety of factors. The most commonly observed causes for treatment failure, relapse and reinfection are that the topical anti-scabies drugs are not applied in adequate quantity and appropriate manner as prescribed like applying cream to the body part that is affected not to the whole body and physicians inability in providing the proper instruction to patients like avoid diluting the cream or emulsion and should be used as provided and it also includes missing the opportunity in treating the family members or contacts (Chosidow, 2000; O’donel and , 1984).

The resistance to anti scabies drugs means a patient is not getting cured even after ruling out other causes of treatment failure. There are several anti-scabies drugs for which resistance is seen like lindane resistance is being observed in countries like Peru, New Zealand, Panama, etc., but rarely there are any resistance is being observed or reported for permethrin (Roth, 1991; Hernandez-Perez, 1983; Meinking, 1999). In regions with such resistance to lindane, the combined therapy of lindane and benzyl benzoate or permethrin shall be prescribed.

CONCLUSIONS

On the basis of empirical findings of the present study, it concludes that the improvement in scabies clinical grade and itching grade for permethrin (topical) was found to be more efficacious in comparison to benzyl benzoate (topical). The clinically observed cure rate among two groups i.e., Permethrin and Ivermectin at the end of the first and second week were 72% and 34%, and 98% and 60%, respectively. Improvement in a clinical grade of pruritis was assessed at the scheduled follow-up visits each time in both the treatment groups, and it was found that permethrin provided better and fast improvement in pruritis grade than benzyl benzoate. Further controlled trials are warranted to support the findings of this study.

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