

A Comparative Study of Treatment Outcomes: Permethrin 5% VS Benzyl Benzoate 25% in Patients with Scabies

Permethrin 5%
VS Benzyl
Benzoate 25% in
Scabies

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ABSTRACT

Objective: To compare treatment outcomes, symptom improvement, and tolerability of topical permethrin 5% versus benzyl benzoate 25% in adults with classic scabies.

Study Design: Randomized comparative study

Place and Duration of Study: This study was conducted at the Dermatology unit, Lady Reading Hospital (LRH), Peshawar, Pakistan, from January 1 to December 31, 2024.

Methods: Adults (≥ 18 years) with classic scabies were enrolled through consecutive sampling and randomized 1:1 to permethrin 5% ($n=63$) or benzyl benzoate 25% ($n=63$). The primary outcome was clinical cure at Day 14 (absence of new lesions with clear clinical improvement). Secondary outcomes included pruritus severity (VAS 0–10), adverse effects, adherence, and recurrence/reinfestation by Day 28.

Results: Of 152 screened patients, 126 were randomized. Day-14 follow-up was completed for 60 (permethrin) and 58 (benzyl benzoate). Clinical cure at Day 14 was higher with permethrin than benzyl benzoate (52/63, 82.5% vs 41/63, 65.1%; $p=0.026$; $RR\approx 1.27$). Baseline pruritus VAS was similar (8.1 ± 1.3 vs 8.0 ± 1.4 ; $p=0.679$), while scores were lower with permethrin at Day 7 (3.6 ± 1.8 vs 4.4 ± 2.0 ; $p=0.020$) and Day 14 (2.1 ± 1.6 vs 3.0 ± 1.9 ; $p=0.005$). Burning/irritation was more frequent with benzyl benzoate (33.3% vs 14.3%; $p=0.012$).

Conclusion: Permethrin 5% achieved higher Day-14 cure rates, faster pruritus improvement, and better tolerability than benzyl benzoate 25% in adults with classic scabies.

Key Words: Scabies; Permethrin; Benzyl benzoate; Randomized trial; Pruritus; Treatment outcome.

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INTRODUCTION

Scabies, or *Sarcoptes Scabiei* var *hominis*, is a contagious, global, parasitic skin overrun that is mostly caused by the mite called *Sarcoptes scabiei* var *hominis*. It is a significant global public health issue due to its spread, which mostly occurs as a result of prolonged skin-to-skin contact^{1,2}. The disease burden is significant, and the signs of the condition include severe pruritus, insomnia, and a severe loss of quality of life. Secondary bacterial skin infection is a critical complication with potential to cause extreme sequelae such as rheumatic heart disease and post-streptococcal glomerulonephritis; and, such critical complication creates a disproportionate burden on vulnerable and resource-limited populations³.

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The individual case management with the use of scabidical agents is the key to the outbreak control. Topical permethrin 5% cream is usually suggested as first-line therapy by international guidelines because of its proven effectiveness and safety profile. Nevertheless, cost, availability and logistics of procurement often make permethrin unavailable in many low- and middle-income nations with the greatest scabies burden⁴. As a result, benzyl benzoate, most commonly as a 25% lotion or emulsion, is the most commonly used first line therapy in such endemic regions because it is cheaper and more widely available⁵.

Besides its practical and extensive application, benzyl benzoate is linked with significant practical issues. It may induce severe symptoms of skin irritation and burning when applied, which can undermine adherence to the treatment, which is one of the main predictors of effective treatment in clinical practice^{6,7}. Moreover, new issues are being raised around the world about treatment failure and possible acaricide resistance, making the management of scabies more difficult. Although the improper usage, reinfestation of the environment, and untreated contacts are identified as factors, there is no precise quantification of the performance and failure rates of benzyl benzoate used on a routine basis⁸.

A critical gap between actual practice in high-burden settings and recommended guidelines in treatment exists, which poses a significant gap in evidence. Although the effectiveness of benzyl benzoate is determined in the controlled trial setting, there is no strong evidence on its actual performance and the practical issues that influence its results in endemic, resource-deprived populations⁹. The absence of this hinders the formulation of optimal, context-sensitive treatment guidelines.

Hence, the research proposal will assess the practical outcomes of benzyl benzoate therapy of scabies in a high-endemic community with resources. In particular, we will evaluate its clinical efficacy, determine the perceived treatment failure rates and causes, and record the tolerability profile and adherence issues faced by the patients. The results will help provide the necessary evidence to make local treatment policies, patient education strategies, and help improve scabies control in the population where this agent is the most practical therapeutic option.

METHODS

This comparative study was carried out at the Department of Dermatology, Lady Reading Hospital (LRH), Peshawar, Pakistan, between January 1, 2024, and December 31, 2024. All the patients who came to the Dermatology OPD with symptoms suggestive of scabies were screened. Eligible respondents were recruited using consecutive sampling until the necessary sample was obtained and assigned in a 1:1 proportion to either topical permethrin 5% or benzyl benzoate 25%.

Adults (at least 18 years old) of any sex with classic scabies were recruited. The diagnosis was made according to the standardized clinical criteria (typical pruritus, characteristic lesions/distribution, and the presence of the contact history), which corresponds to the 2020 International Alliance against Scabies (IACS) framework¹⁰. When the diagnosis was not clear or when skin scraping or dermoscopy was available, the diagnosis was made. Critical exclusion criteria were crustal scabies, non-standard scabies and needs alternative / combination therapy, use of any scabicide treatment in the previous 4 weeks, known hypersensitivity to study medications, pregnancy or lactation, severe secondary bacterial infection that needs systemic treatment, and secondary bacterial infection that would confound the study.

The sample size was determined to compare two independent proportions ($p_1=0.73$ with permethrin and $p_2=0.475$ with benzyl benzoate as the expected cure rates), 95% confidence and 80% power and produced 57 participants per group. To allow 10% loss to follow-up/non-adherence, the final sample size was raised to 63 per group (total 126). The randomization was done through a computer-generated sequence. To guarantee allocation concealment, sealed and opaque envelopes

numbered in sequence were opened after a written consent.

Group A used permethrin 5% on the entire body (neck to nails) including skin folds and under nails, leaving it on the skin and under nails 814 hours and washing it off; it was recommended that the same be repeated after 7 days. Group B used the same technique (benzyl benzoate 25% but not in the case of head/neck, unless necessary), but left overnight (812 hours), repeated after 24 hours, and repeated after 1 week (three applications). Every participant was provided with standardized advice on how to treat close household contacts and hygiene/decontamination to minimize reinfestation and was informed that post-scabietic pruritus can be persistent.

The main endpoint was clinical cure (no new lesions) and evident clinical improvement on examination), Day 14, which was not viewed as a failure in persistent itch. Secondary outcomes were the change in the severity of pruritus by VAS (0-10), the presence of adverse effects (burning, erythema, irritant dermatitis), the adherence, and recurrence/reinfestation by Day 28. They were followed up at Day 1, 7, 14 and 28.

Data analysis was done with SPSS 25.0. The Chi-square /Fisher exact test was used to compare categorical variables and independent t-test /Mann-Whitney U test was used to compare continuous variables. Effect estimates were presented in the form of RR/OR and 95% confidence interval and a p-value of ≤ 0.05 was deemed significant. The Hospital Ethics Committee approved the study (Ref # 249) and all subjects were given written informed consent.

RESULTS

By Day 14, follow-up was completed for 60 participants in the permethrin group and 58 in the benzyl benzoate group. Recurrence assessment at Day 28 was available for 58 and 56 participants, respectively. Baseline demographic and clinical characteristics were comparable between the two groups, including age, sex distribution, contact history, lesion distribution, severity grading, and baseline pruritus intensity. Table-1

At Day 14, the clinical cure rate was higher in the permethrin group compared with benzyl benzoate. By Day 28, recurrence/reinfestation was numerically lower in the permethrin group, though this difference was not statistically significant. Both groups demonstrated improvement in pruritus intensity over time, with lower mean VAS scores at Day 7 and Day 14 among permethrin-treated patients. Table-2

Adverse effects were more frequent in the benzyl benzoate group, particularly local burning/irritation. Due to small cell counts for contact dermatitis and discontinuation, Fisher's exact test was applied for those outcomes. Adherence was numerically higher in the permethrin arm, but the difference did not reach statistical significance. Table-3.

Table No.1: Baseline demographic and clinical characteristics

Variable	Permethrin 5% (n=63)	Benzyl benzoate 25% (n=63)	p-value
Age (years), mean \pm SD	26.9 \pm 8.7	27.4 \pm 9.1	0.753
Male, n (%)	35 (55.6%)	33 (52.4%)	0.721
Household crowding (\geq 3 persons/room), n (%)	41 (65.1%)	43 (68.3%)	0.705
Positive contact history, n (%)	46 (73.0%)	48 (76.2%)	0.682
Nocturnal pruritus, n (%)	58 (92.1%)	57 (90.5%)	0.752
Interdigital involvement, n (%)	52 (82.5%)	51 (81.0%)	0.818
Wrist involvement, n (%)	45 (71.4%)	44 (69.8%)	0.845
Axillae involvement, n (%)	21 (33.3%)	23 (36.5%)	0.709
Groin/genitals involvement, n (%)	29 (46.0%)	31 (49.2%)	0.721
Severity (mild/moderate/severe), n	18/34/11	17/36/10	0.936
Pruritus VAS (0–10), mean \pm SD	8.1 \pm 1.3	8.0 \pm 1.4	0.679

Note: p-values for continuous variables are based on independent t-test; categorical variables on Chi-square test.

Table No. 2. Treatment outcomes and pruritus scores

Outcome	Permethrin 5% (n=63)	Benzyl benzoate 25% (n=63)	p-value	Effect
Clinical cure at Day 14, n (%)	52 (82.5%)	41 (65.1%)	0.026	RR \approx 1.27
Not cured at Day 14, n (%)	11 (17.5%)	22 (34.9%)		
Recurrence/reinfestation at Day 28, n (%)	5 (7.9%)	9 (14.3%)	0.257	RR \approx 0.55
Pruritus VAS baseline, mean \pm SD	8.1 \pm 1.3	8.0 \pm 1.4	0.679	—
Pruritus VAS Day 7, mean \pm SD	3.6 \pm 1.8	4.4 \pm 2.0	0.020	—
Pruritus VAS Day 14, mean \pm SD	2.1 \pm 1.6	3.0 \pm 1.9	0.005	—

Note: RR = relative risk. VAS comparisons use independent t-test; categorical outcomes use Chi-square test.

Table No. 3: Adverse effects and adherence

Variable	Permethrin 5% (n=63)	Benzyl benzoate 25% (n=63)	Test	p-value
Burning/irritation	9 (14.3%)	21 (33.3%)	χ^2	0.012
Erythema	6 (9.5%)	13 (20.6%)	χ^2	0.081
Dryness	7 (11.1%)	15 (23.8%)	χ^2	0.060
Contact dermatitis	1 (1.6%)	5 (7.9%)	Fisher	0.210
Discontinued due to side effects	1 (1.6%)	3 (4.8%)	Fisher	0.620
Adherent to regimen	56 (88.9%)	50 (79.4%)	χ^2	0.144
Household contacts treated	44 (69.8%)	41 (65.1%)	χ^2	0.568
Decontamination done	49 (77.8%)	46 (73.0%)	χ^2	0.535

DISCUSSION

This comparative study shows a pronounced disparity in therapeutic healing in two common scabicides in a limited resource, high-burden environment. The fact that topical permethrin 5% had a better cure rate at Day 14 (82.5) than benzyl benzoate 25% (65.1) is consistent with the accepted hierarchy of international treatment guidelines, where permethrin is preferred as first-line treatment over benzyl benzoate because of its powerful efficacy profile (11,12). This finding is in line with a number of comparative studies conducted in the recent past (13,14). As an example, a study by Hay et al (15)

in a comparable endemic area found that 14 days of permethrin had an 85% cure rate vs. 68% with benzyl benzoate because permethrin was ovicidal and had longer skin retention. The uniformity of the studies supports the validity of the biological plausibility of the higher efficacy of permethrin, which is presumably because of its insecticidal as well as acaricidal effects. Nevertheless, compared to the findings of Sonderkotter et al (16), the relative effectiveness of 65.1% is significantly less than that of benzyl benzoate we achieved in our study (65.1%). This inconsistency can be explained by the essential contextual variables that can affect the practical performance. An interesting

explanation is the much higher rates of local adverse effects, especially burning and irritation (33.3% vs. 14.3%), in the group of benzyl benzoate. One of the problems that have been documented to impede full and proper implementation is tolerability, which directly undermines therapeutic efficacy (17). This mechanism of the efficacy gap in our study is further supported by the observed tendency of lower adherence in the benzyl benzoate group (79.4% vs. 88.9%), though not significant. This highlights the fact that practical effectiveness of benzyl benzoate is extremely reliant on the regional tolerability and patient education, which might not be entirely reflected in controlled efficacy studies.

The considerably higher decrease in pruritus VAS scores in permethrin group on Day 7 and 14 is clinically significant in our study. This quicker symptomatic relieve is probably linked to quicker mite elimination and this could further enhance compliance. Although there are not many studies which directly compare the kinetics of pruritus resolution, our findings are consistent with the rule that the more efficient acaricide is the sooner the inflammatory and allergic response to mite antigens will reduce (18).

The numerically smaller rate of recurrence in the permethrin group in the Day 28 analysis (7.9% vs. 14.3%) is, logically, the logical product of a higher cure rate initially. A study by Thandanipon et al (19) also reflects this trend with results that initial treatment failure was the greatest predictor of early recurrence. The fact that household contact treatment and environmental decontamination were similar in both our groups is an indicator that the reinfestation pressure differences were reduced as much as possible which reinforces the internal validity of this result.

The overlying contradiction that this research elucidates is the contradiction between effectiveness and practical availability. Although it has shown excellent performance, permethrin is still costly, and in most primary care practices of low- and middle-income countries, using benzyl benzoate is a more feasible primary therapy (20). The possible effectiveness penalty of this practical decision, which is measured in our data, is about a 20% relative cure-rate loss. This fact is paramount to health policy. It does not call to quit using benzyl benzoate, but to use it wisely by providing structured patient education to enhance adherence and manage expectations to side effects and to recommend better access and subsidy schemes to permethrin in high-prevalence regions.

This study has certain limitations. Although it was pragmatic and in keeping with WHO recommendation regarding resource-limited setting, it might have led to inclusion bias, but IACS criteria standardized this procedure. The 28-day follow up time is sufficient to determine early curing and recurrence but fails to determine long term results. Moreover, the single-

center design can restrict the extrapolation to other populations that have varying healthcare habits or mite sensitivity patterns. The use of molecular methods to track the emergence of acaricide resistance, which has become a large concern in recent reviews, should be introduced into future research. Comparative cost-effectiveness studies of these agents in LMIC settings are also highly demanded to inform national treatment policy.

CONCLUSION

This study concludes that topical permethrin 5% is clinically superior to benzyl benzoate 25% for treating classic scabies in a resource-limited setting, demonstrating a significantly higher cure rate, faster symptomatic relief, and better tolerability. However, given the cost and accessibility constraints that often dictate therapeutic choices in such environments, benzyl benzoate remains a practical alternative, provided its use is supported by targeted patient education to improve adherence and manage its more frequent side effects, thereby helping to narrow the observed efficacy gap between the two treatments.

Author's Contribution:

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