

## RESEARCH ARTICLE

### Efficacy and cost-effective analysis of benzyl benzoate, permethrin, and ivermectin in the treatment of scabies and azithromycin versus doxycycline in the treatment of acne vulgaris

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#### ABSTRACT

**Background:** Acne and scabies are significant skin diseases and treatment of which carries major economic burden in Indian scenario. We planned study to compare safety, efficacy, and economy of treatment modalities of scabies for permethrin, benzyl benzoate, and ivermectin and acne for doxycycline and azithromycin. Hence, we can provide better treatment option for acne and scabies based on cost-effectiveness, efficacy, and safety. **Aims and Objectives:** This study aims to study therapeutic efficacy and cost-effective analysis of treatment in acne vulgaris and scabies. **Materials and Methods:** A multicentric, prospective observational study was carried out with patients attending the outpatient department of 32 health-care centers of Wardha district. One hundred and forty-eight patients of acne and 124 patients were screened, of which 108 patients of acne and 120 patients of scabies were analyzed for therapeutic efficacy. Of 120 scabies patients, 52 patients took benzyl benzoate lotion, 48 patients received permethrin cream, and 20 patients received tablet ivermectin. In acne, 60 patients received tablet azithromycin and 48 patients received tablet doxycycline. Cost-effective analysis was done. **Results:** In scabies, efficacy was near 93% for all therapeutic agents, but benzyl benzoate (INR 15.01 per case) and ivermectin (INR 16.07 per case) are more cost effective than permethrin (INR 21.55 per case). In acne, azithromycin (62.2%) and doxycycline (60%) showed similar efficacy, but doxycycline (INR 112 per case) is more cost effective than azithromycin (INR 216 per case). **Conclusion:** Therapeutic efficacy was similar for all therapeutic agents in both acne and scabies. Benzyl benzoate and ivermectin are more cost effective than permethrin in scabies. In acne, doxycycline is more cost effective than azithromycin.

**KEY WORDS:** Efficacy; Cost-effective Analysis; Acne Vulgaris; Scabies

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#### INTRODUCTION

Acne vulgaris and scabies are the major dermatological disorder in Indian population. In clinical practice, patient's life of dermatological disorders such as acne and scabies is impacted by most appropriate treatment for that patient.<sup>[1]</sup> It is commonly observed that drug prescription is inappropriate

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and ineffective in health-care system and, hence, increases cost of treatment and increases morbidity and mortality.

Acne vulgaris is a multifactorial chronic disease of pilosebaceous unit affecting primarily adolescent. Main factors for pathogenesis of acne vulgaris are increase of sebum production, proliferation of *Propionibacterium acnes* in skin microbial flora, inflammation, and increase in keratinocytes of pilosebaceous follicle.<sup>[2]</sup> Mild acne is treated using topical agents such as topical antibiotics or retinoids. Bacterial activity on skin is one of the main contributory factors. *P. acnes* and *Staphylococcus epidermidis* are mainly isolated from acne lesions.<sup>[3]</sup> Systemic antibiotics such as doxycycline and azithromycin are used in the treatment of moderate to severe acne.<sup>[4]</sup>

Scabies caused by *Sarcoptes scabiei* is of greater importance in India as it's more common in economically marginalized and immunocompromised hosts.<sup>[5]</sup> Treatment options include either topical or oral medication. The current treatment of scabies topical option includes permethrin 5% and benzyl benzoate 25% while oral option includes ivermectin only.

The rational prescription becomes effective to the patient in relation to the clinical needs, individual requirements, for an adequate period of time and at the lowest cost, but the irrational prescription of drugs is related to adverse drug events and the appearance of drug resistance.<sup>[6]</sup> Prescribing drugs are an essential skill, which is required to be continuously assessed and refined accordingly. Prescription audits and studies are applicable for prescription in dermatological disorders by informing the patient about the quality of drugs used in the health facility.<sup>[7]</sup> In clinical practice, irrational prescription of drugs is commonly seen.<sup>[8]</sup> For improving utilization patterns, collection of data is an effective tool at hospital outpatient level.<sup>[9]</sup>

In health-care delivery system, medical audit is used to oversee, monitor, and analyze the medical treatment and suggest modification in prescribing practices of medical professionals which is useful in medical care.<sup>[10]</sup> Cost-effective analysis is key tool to provide better and improved treatment option for acne and scabies in rural population for government system.

This study was carried out in rural as well as urban population of Wardha district. There is little knowledge of efficacy of drugs used in acne and scabies in rural population. Cost-effectiveness analysis is economic analysis comparing the relative costs and outcomes (effects) of various treatment modalities. Indian populations have poor affordability for the most efficacious drugs. Hence, this study was carried out to compare efficacy and cost-effectiveness of the treatment of scabies and acne vulgaris to suggest the best treatment for cure and for finding most economical therapy.

## Aims

This study aims to suggest better and improved treatment option for scabies and acne based on cost-effectiveness, efficacy, and safety profile.

## Objectives

The objectives of this study were as follows:

- To study the different available treatment options in scabies and acne
- To compare efficacy and cost-effectiveness of three treatment lines for scabies and two antimicrobial drug treatment modalities for acne and also suggest the best intervention for cure and to find most economical therapy.

## MATERIALS AND METHODS

A multicentric, prospective observational study was carried out with patients attending the outpatient department of 32 health-care centers of Wardha district.

### Study Design

This was a multicentric, prospective observational study.

### Locus of Study

Thirty-two health-care centers of Wardha district are as follows:

1. Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe) and Acharya Vinoba Bhave Grameen Rugnalaya Seloo (2 health-care centers)
2. Grameen Aarogya Kendra, Deoli, Shaskiya Grameen Rugnalaya, Seloo, Grameen Rugnalaya, Samudrapur, and Grameen Rugnalaya, Karanja (4 health-care centers)
3. Pratham Aarogya Kendra, Deoli, Mandgaon, Nandori, Zads, Salai (Kala), Anji (Mothi), Kharangana (Morangana), Talegao, Allipur, Kangaon, Giroli, Gaul, Vijaygopal, Nachangaon, Rohana, Wayfad, Jalgaon, Aashti, Sahur, Girad, Burkoni, Kannamwargram, Kharangana (Gode), Hamadpur, Dahegaon, and Sindi (Railway) (26 health-care centers).

### Methodology

One hundred and forty-eight patients of acne and 124 patients of scabies age above 12 years in the primary health-care centers and rural hospital of Wardha district were seen. Of these, 108 patients of acne and 120 patients of scabies were analyzed for therapeutic efficacy. Of 120 scabies patients, 52 patients took benzyl benzoate lotion, 48 patients received permethrin cream, and 20 patients received tablet ivermectin. In acne, 60 patients received tablet azithromycin and 48 patients received tablet doxycycline. Cost-effective

analysis was done using cost of drugs as per medguideindia.com lowest cost.

The research protocol was approved by institutional ethics committee. After explaining the aim and objectives of the study, the written consent was obtained from the patients.

1. Interview of patients suffering from acne and scabies
2. Monitoring and evaluation: The study included the following aspects:
  - I. Treatment modules
  - II. Response to prescribed therapy
  - III. Final outcome
  - IV. Alteration in initially prescribed drug (if any) with reason
  - V. Duration of treatment.
3. Treatment
  - i. Scabies: 25% benzyl benzoate lotion to be applied and left overnight to the whole body below neck for two consecutive nights. Permethrin 5% cream was applied once to the whole body below neck and left overnight. Oral tablet ivermectin (200 mcg/Kg) 12 mg was given as a single dose. Patients are followed up for 2 weeks.
  - ii. Acne: Tablet azithromycin 250 mg daily and tablet doxycycline 100 mg were administered daily oral and followed up for 16 weeks.
4. Cost-effectiveness analysis: Cost-effectiveness was calculated on the basis of total amount requires for medicines at the end of 2 weeks for scabies and 16 weeks for acne in INR and cure rate in percentage. All these treatments were compared on the basis of expenditure needed to treat one case successfully in INR.

## RESULTS

### Scabies

Of 120 patients with scabies, 52 patients took benzyl benzoate lotion, 48 patients received permethrin cream, and 20 patients received ivermectin. Cost of 25% benzyl benzoate lotion (INR 14), 5% permethrin cream (INR 20), and tablet ivermectin 12 mg (INR 15) was taken as per medguideindia.com lowest cost.

Fifty-two patients received 25% benzyl benzoate lotion to be applied and left overnight to the whole body below neck for two consecutive nights. Forty-eight patients received permethrin 5% cream to be applied once to the whole body below neck and left overnight. Twenty patients consumed tablet ivermectin (200 mcg/Kg) 12 mg as a single dose.

All patients were followed up for 2 weeks. After the initiation of treatment, patients were seen every week to assess their response. After 2 weeks, cured rate (efficacy) was evaluated by relief of symptoms and disappearance of lesions which

was near 93% for all therapeutic agents. [Table 1] Efficacy is similar, but cost-effective analysis shows that benzyl benzoate (INR 15.01 per case) and ivermectin (INR 16.07 per case) are more cost effective than permethrin (INR 21.55 per case) [Table 2].

### Acne

In acne, 60 patients received tablet azithromycin 250 mg daily and 48 patients received tablet doxycycline 100 mg daily. Cost of tablet azithromycin 250 mg (INR 1.2) and tablet doxycycline 100 mg (INR 0.6) was taken as per medguideindia.com lowest cost.

All patients were followed up for 16 weeks. After the initiation of treatment, patients were seen every fortnight to assess their response.

At the end of 16 weeks, 25 patients (62.2%) were cured those taking azithromycin and 12 patients (60%) were cured by doxycycline [Table 3]. Efficacy was evaluated by the relief of symptoms and disappearance of the lesion. Azithromycin and doxycycline showed similar efficacy, but cost-effective analysis shows that doxycycline (INR 112 per case) is more cost effective than azithromycin (INR 216 per case) [Table 4].

## DISCUSSION

In our study, benzyl benzoate, permethrin, and ivermectin were equally effective and safe treatment for scabies. At the end of 2 weeks, all the patients in this treatment recovered with complex healing of lesion. No significant side effects were noted on follow-up. Thus, in selection of treatment, only the cost-effectiveness played the decisive role. Benzyl benzoate and ivermectin are more cost effective than permethrin. Ivermectin paralyzes *S. scabiei* by intensifying gamma-aminobutyric acid-mediated transmission of signals in peripheral nerves. Permethrin causes neurological paralysis in *S. scabiei*, probably by delaying depolarization and benzyl benzoate is toxic to *S. scabiei*.<sup>[11]</sup>

The study by Brooks and Grace,<sup>[12]</sup> no significant differences in clinical cure rates were found between ivermectin and 10% benzyl benzoate similar to our study. Studies by Madan *et al.* and by Zargari *et al.* have been done to compare the efficacy of ivermectin with lindane and permethrin and it was found that there was no difference at the end of 4 weeks.<sup>[13,14]</sup>

In the study by Sule and Thacher in Nigeria patients, ivermectin had similar or better efficacy compared with the commonly used topical treatment of 25% benzyl benzoate lotion.<sup>[15]</sup> Buffet and Dupin found that there was no difference in efficacy comparing permethrin to benzyl benzoate.<sup>[16]</sup> Some studies have showed that permethrin is also superior to ivermectin in the treatment of scabies.<sup>[17]</sup> Usha and Nair

**Table 1: Cure rates (efficacy) in patients with scabies**

Therapeutic agents	Benzyl benzoate	Permethrin	Ivermectin
Number of patients	52	48	20
Number of patients attended the OPD for follow-up at the end of 2 weeks	30	28	15
Number of patient cured which attended OPD for follow-up at the end of 2 weeks	28	26	14
Efficacy (% of patient cured)	93.3	92.8	93.3

OPD: Outpatient department

**Table 2: Cost-effective analysis at the end of 2 weeks**

Parameter	Benzyl benzoate	Permethrin	Ivermectin
Cost in INR for 100 participants	14×100=1400	20×100=2000	15×100=1500
Cure rate (%) (effectiveness)	93.3	92.8	93.3
Cost-effectiveness	INR 1400 for 93.3 patients	INR 2000 for 92.8 patients	INR 1500 for 93.3 patients
Cost to treat one case (INR)	15.01	21.55	16.07

**Table 3: Cure rate in patients with acne**

Therapeutic agents	Azithromycin	Doxycycline
Number of patients	60	48
Number of patients attended the OPD for follow-up at the end of 16 weeks	40	20
Number of patient cured which attended OPD for follow-up at the end of 16 weeks	25	12
Efficacy (% of patient cured)	62.2	60

OPD: Outpatient department

**Table 4: Cost-effective analysis at the end of 16 weeks (112 days)**

Parameter	Azithromycin	Doxycycline
Cost in INR for 100 participants	1.2×112×100=13,440	0.6×112×100=6720
Cure rate (%) (effectiveness)	62.2	60
Cost-effectiveness	INR 13,440 for 62.2 patients	INR 6720 for 60 patients
Cost to treat one case (INR)	216	112

showed that both permethrin and ivermectin are effective in preventing recurrences of scabies over a period of 2 months.<sup>[17]</sup>

Ideal anti-scabietic is effective against adult and egg, non-sensitizing, non-irritating, non-toxic, easily applicable, and economical.<sup>[18]</sup> In the study by Bachewar *et al.*, benzyl benzoate and ivermectin are more cost effective similar to our study.<sup>[19]</sup> Abdel-Raheem *et al.* showed that benzyl benzoate was cheapest and cost effective drug similar to our study. Treatment choice will decide by the age, the general condition of cases, patient compliance, and the economic condition of the patient.<sup>[20]</sup>

In acne, the systemic treatment includes antibiotics, hormone therapy, isotretinoin, and corticosteroids. Antibiotics are an effective treatment for acne due to their anti-inflammatory and antimicrobial properties. Azithromycin prevents

bacterial protein synthesis by binding to the 50S ribosomal subunit and interferes with translocation step. Doxycycline prevents bacterial protein synthesis by binding to the 30S ribosomal subunit and blocks the binding of aminoacyl-tRNA to the acceptor site on the mRNA-ribosome complex.<sup>[21]</sup> In our study acne patients, a significant improvement was observed during the study period with azithromycin and doxycycline. The response to azithromycin was shown to be as effective as doxycycline in improving acne state. This result is similar to other studies.<sup>[22,23]</sup> Kus *et al.*<sup>[22]</sup> and Parsad *et al.*<sup>[23]</sup> found that azithromycin is as effective as doxycycline.

Plewig *et al.*<sup>[24]</sup> reported that patients had good to excellent response (50–75%) to doxycycline in acne vulgaris, which is comparable to our results (60%). Gruber *et al.*<sup>[25]</sup> showed that azithromycin and minocycline had satisfactory clinical response. In a study by Amatya *et al.* showed comparable results as our study that doxycycline can be used as an alternative drug for poor patients as it is less expensive than azithromycin, as both drugs have similar efficacy.<sup>[26]</sup> A meta-analysis by Kim *et al.* shows that oral azithromycin pulse therapy may be a good alternative to doxycycline in the management of acne for those unable to tolerate doxycycline.<sup>[27]</sup>

As this study was conducted in rural as well as urban population, it involves majority of population from society. Different government bodies purchase different brands of

drugs as per availability and rate contract. Hence, we have taken lowest rate for economic analysis. There should be little variability in cost of drugs in health-care system. The study does not involve children and patients from private skin specialists and general practitioners. Further study is necessary to involve population from all age groups and patients from private setup also.

## CONCLUSION

Therapeutic efficacy and safety of benzyl benzoate, permethrin, and ivermectin in scabies are equivalent. Benzyl benzoate and ivermectin are more cost effective than permethrin. Azithromycin and doxycycline have similar efficacy and safety in the treatment of acne vulgaris, but cost-effective analysis shows that doxycycline is more cost effective than azithromycin. Hence, in government setups, cost-effective analysis is a key factor to determine drug recommendation. Our recommendation in scabies patient should first apply benzyl benzoate topically and non-responders then advised ivermectin orally. Scabies with resistance cases and children permethrin should be given. In acne patient, doxycycline should be preferred over azithromycin for treatment.

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