Journal of Population Therapeutics & Clinical Pharmacology

ORIGINAL ARTICLE
DOI: 10.47750/jptcp.2022.845

Comparison of the effects of ivermectin, permethrin, and gamma benzene hexachloride alone and with that of combination therapy for the management of scabies

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Submitted: 13 December 2021; Accepted: 28 January 2022; Published: 15 March 2022

ABSTRACT

The present study compared three scabicidal agents alone or with combination, the currently considered medicine of choice permethrin, oral ivermectin, and gamma benzene hexachloride in the local population of India. A total of 120 patients were studied. They were randomly divided into four groups –Group A, Group B, Group C, and Group D. Group A received topical 5% permethrin and oral placebo. Group B was given topical placebo cream and oral ivermectin in two dose regimen. Group C received topical 1% gamma benzene hexachloride with oral placebo, and Group D was given topical 5% permethrin and oral ivermectin. The improvement of lesions and pruritus were assessed in the next three follow-ups, i.e., on the 7th day, 14th day, and 28th day along with any adverse drug reactions (ADRs). It was found that Group A had 83%, 90%, 97%, and Group B had 70%, 81%, and 91% improvement of lesions in the three follow-ups respectively. Group C showed 57%, 70%, 86%, and Group D had 82%, 90%, 97% efficiency to decrease lesion count ($p>0.05$) respectively. Again, Group A observed 77%, 88%, and 94% improvement in pruritus in subsequent follow-ups, while for Group B it was 63%, 76%, and 86%. Group C had 55%, 71%, 85% efficiency, and Group D had recorded 77%, 88%, and 94% improvement to decrease pruritus ($p>0.05$). The

incidence of adverse effects was found to be less in Group B, Group C, and Group D when compared to Group A.

Conclusion: Group D or a combination therapy was a better choice for scabies in comparison to other monotherapy due to its better efficacy and safety profile.

Keywords: *gamma benzene hexachloride, ivermectin, permethrin, scabies*

INTRODUCTION

Scabies is an ectoparasitic infestation of the skin caused by the human itch mite, Sarcoptes scabiei var. hominis. Primary scabies infections typically cause intensely itchy rashes that worsens at night, and a highly contagious skin infection. But, long-term scabies acts as a gateway for secondary sequelae, and complications with high morbidity, social stigmatization and ongoing healthcare expenses. An ideal scabicide should be effective against adult mite and eggs, easily applicable or orally administered, non-sensitizing, non-irritating, non-toxic, economical, quick and high cure rate, and should be safe for all age groups.[1]

The mainstay of therapy in the present era is topical, and it includes benzyl benzoate, malathion, mono-sulfiram, crotamiton, gamma benzene hexachloride, and permethrin. But, this requires prolonged and repeated application. Resistance to some of these drugs has also been reported. In addition to it, the oral anti-parasitic agent ivermectin has been found to be an effective scabicidal agent. Gamma benzene hexachloride is an organochloride chemical that had been used both as an agricultural insecticide and as a pharmaceutical treatment for lice and scabies. Since gamma benzene hexachloride has limitations for use in children and pregnant women, and there were several reports of central nervous system toxicity, convulsions, and even death following accidental ingestion, overuse; even a single application of gamma benzene hexachloride may be noxious.[2,3] Permethrin cream (5%) was introduced in 1989 as an effective scabicidal agent, and seems to be a good substitute for the drug topical gamma benzene hexachloride. It has been approved by the FDA for the treatment of scabies.[4]

In India, where the disease is largely prevalent in the lower socio-economic strata, permethrin is considered an expensive option. Resistance has been reported with permethrin[5] Due to its higher cost, the use of permethrin (topical) for mass treatment is limited when compared to other topical anti scabies options. Ivermectin is an anti-parasitic agent with a broad spectrum of activity against nematodes and ectoparasites in animals and humans against Sarcoptes scabiei.[6] Ivermectin is administered orally and has the advantage of being cheaper, thus improving the compliance.

The Indian population being commonly affected by scabies, masses have poor affordability for the most efficacious and safe anti-scabetic. Hence, it was decided to study and the compare three available scabicidal agents alone or with combination – the currently considered medicine of choice – permethrin, oral ivermectin, and gamma benzene hexachloride in the local population of Hapur, Uttar Pradesh, India.

The aim of the study was to evaluate the individual effects of topical permethrin 5% (single applicaton), topical gamma benzene hexachloride (double application) and oral ivermectin (200µg/kg/dose) in two dose regimen in scabies patients. It was also decided to compare the effects of monotherapy of three scabicidal agents with a combination therapy of ivermectin and permethrin.

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MATERIALS AND METHODS

This study was conducted in the Department of Pharmacology in collaboration with the Department of Dermatology, Saraswathi Institute of Medical Sciences, a tertiary care teaching hospital, Hapur, Uttar Pradesh, India. It was an open labelled, prospective, randomized, comparative, parallel group clinical study, and the study was performed after the protocol approval by Institutional Ethical Committee.

The OPD patients of the dermatology department was evaluated for the clinical establishment of diagnosed scabies, followed by proper inclusion and exclusion criteria meant for the study. A total 120 patients were chosen for the study between January 2021 and July 2021, with their written informed consent. The patients were randomly divided into four treatment groups, and each group contained 30 patients.

In **Group A,** the patients received topical 5% permethrin cream on day 1, and placebo Vit-B complex on day 1 and 15. In **Group B**, the patients had applied topical placebo cream on the first day with oral ivermectin 200µg/kg/dose on 1st and 15th day. In **Group C**, the patients received topical 1% gamma benzene hexachloride lotion on day 1 and day 15, with a placebo tablet of Vitamin B complex. In **Group D**, the patients received topical 5% permethrin cream on day 1 with oral ivermectin 200µg/kg/dose and placebo Vitamin B complex on day 15.

The primary end point of the study was the complete cure of scabetic lesions, achieving a better drug-dose response, while secondary end point was the cure of pruritus and safety assessment in the patients receiving various drug regimen for a period of four weeks.

A detailed medical history including demographic data and symptoms were recorded, and physical examination and cutaneous examination was conducted by the investigators. Patients were evaluated for the clinical demonstration of burrow, presence of scabetic lesions at the classical sites of the body like papule, nodule, vesicle on finger web, wrist, periumblical region, breasts, etc., nocturnal pruritus, itching, and family history of similar illness. The severity of scabetic lesions were assessed by counting the number of lesions, and assigned as score of (0 – 3), graded as: 0 = Free of lesions (no scabies), 1 = 10 or fewer lesions (mild), 2 = 11–49 lesions (moderate), 3 = 50 or more lesions (severe).[7] The severity of the pruritus was evaluated by the patients graded on a scale of (0 to 3) on basis of severity; Grade 0 - no itching, Grade 1 - mild itching, Grade 2 - moderate itching, and Grade 3 - severe/intense itching. The objective assessment of pruritus was also done by the patients on a scale of 0-10 using visual analogue scale (VAS score), supported by the International Forum for the Study of Itch (IFSI).

The patients in all the groups were followed up at 1st, 2nd, and 4th week. At every visit, patients underwent clinical assessments, including decrease in count of the lesions and decrease in symptoms like pruritus both subjectively and objectively by the patient as described on the first visit. A complete clinical cure was defined as a reduction in both the number of lesions and symptoms by more than or equal to 50% (i.e., moderate and good improvement) and or negative microscopy. Improvement of the lesions was graded as: mild = less than 50% reduction in number of lesions and pruritus, moderate = more than or equal to 50% reduction in number of lesions and pruritus, good = complete clearance of the lesions and pruritus. The subjects were informed to contact the principal investigator if they experience any untoward effects during treatment.

Statistical analysis

The student's 't' test, one way ANOVA, and chi-square test were used to measure the differences among the drugs. The result is expressed in the form of P-value. Software used was SPSS Version 23.

RESULTS

A total 120 patients chosen for the study and grouped into four treatment groups showed variable

improvement and outcomes. The demographic data and baseline characteristics of the patients were recorded and compared as statistically non-significant (Table 1). The mean number of lesions in Group A were 47.20 ± 41.51, for Group B it was 44.63 ± 39.09, for Group C 52.57 ± 38.10, and for Group D it was 46.83 ± 38.31. The differences in between treatment groups regarding the number of lesions was non-significant (p>0.05) (Table 1). When the severity of lesions amongst all the four treatment groups at the baseline was compared, the severity grading of lesions as mild/ moderate/severe did not show any significant difference between the various treatment groups (p>0.05) (Table 1).

Assessment of the lesions

There was improvement of lesions in various groups in scabies patients in the next three follow-ups, i.e., on the 7th day, 14th day, and 28th day (Figure 1). The 7th day follow-up visit showed an 83% improvement with lesions with Group A, while it was 70% with Group B. The improvement was 57% with Group C and 82% with Group D. The degree of improvement among all groups was statistically non-significant (p>0.05). At the 14th day visit, 90% improvement in lesions was found in Group A and Group D, 81% improvement in Group B and 70% improvement with Group C. But, the improvement was not statistically significant (p>0.05).

At the 28th day, Group A and Group D had 97% improvement in lesions, while Group B had 91% improvement, and Group C had 86% improvement in lesions. The improvement was not statistically significant (p>0.05) (Table 2). At the base line, 31.67% patients were presented with mild pruritus, 42.5% patients were presented with moderate pruritus, and 25.83% patients had severe pruritus.

When we compared the severity of pruritus amongst all the treatment groups at the baseline as mild, moderate, and severe, the pruritus grading in all the treatment groups did not show any significant difference of grading among these groups (p>0.05).

Assessment of pruritus: There was improvement in pruritus in various treatment groups in scabies patients in the next three follow-ups, i.e., at the 7th day, 14th day, and 28th day (Figure 2).

The 7th day follow-up visit showed a 77% improvement in itching in Group A patients, 63% improvement in pruritus with Group B patients, 55% patients improvement in Group C, and 77%

TABLE 1. Baseline characteristics of the patients in the 4 treatment groups

Parameters	Group-A	Group-B	Group-C	Group-D	p value
Mean age (years)	33.1 ± 14.03	37.7 ± 16.40	30.43 ± 12.69	33.96 ± 15.20	0.291 (NS)
Sex (male/female)	12/18	14/16	10/20	16/14	0.437 (NS)
Socio-economic status (lower middle/upper lower/lower) %	(50/33.3/16.7)	(33.3/33.3/33.3)	(50/23.3/26.7)	(40/33.3/26.7)	0.709 (NS)
Mean number of lesions	47.20 ± 41.51	44.63 ± 39.09	52.57 ± 38.10	46.83 ± 38.31	0.882 (NS)
Mean duration of illness	57.50 ± 29.19	63.47 ± 31.90	58.83 ± 27.30	66.40 ± 30.32	0.631 (NS)
Nocturnal pruritus (%)	73.3%	83.3%	93.3%	33.3%	0.144 (NS)
Family history of pruritus (%)	76.6%	93%	83.3%	73.3%	0.373 (NS)
Pruritus grading (mild/moderate/ severe)	9/15/6	7/13/10	13/8/9	9/15/6	0.399 (NS)
Severity of Disease (mild/ moderate/severe)	9/11/10	10/10/10	6/11/13	9/11/10	0.940 (NS)
Positive microscopy (%)	10	23.3	20	16.6	0.777 (NS)

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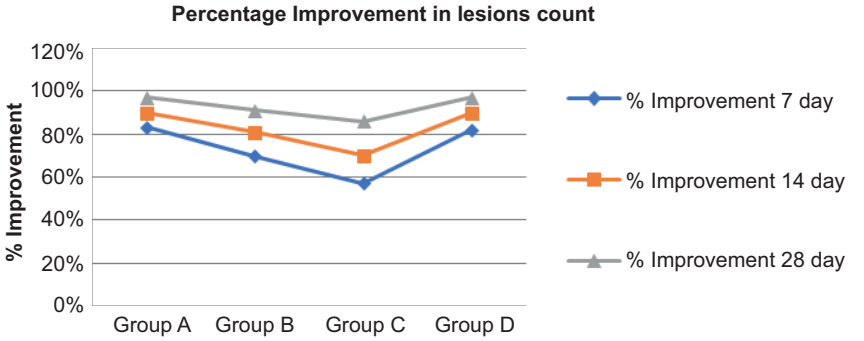

FIGURE 1. Comparative improvement of the lesions in the four treatment groups

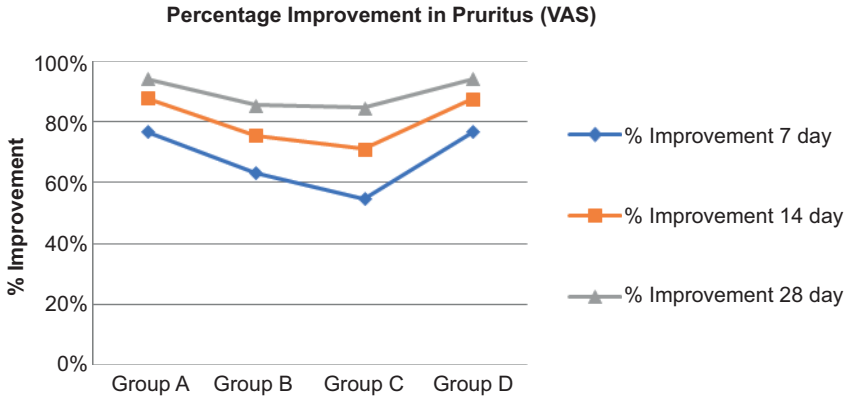

FIGURE 2. Comparative improvement of the pruritus in the four treatment groups.

improvement in itching in Group D patients. On the 14th day, the follow-up visit showed an 88% improvement in pruritus in Group A and Group D, 76% improvement in Group B, and 71% improvement in Group D. On the 28th day, Group A and Group D showed 94% improvement with pruritus. Group B showed 86% improvement, and Group C showed 85% improvement in pruritus. The degree of improvement among all groups at all visits was not statistically significant ($p>0.05$) (Table 3).

In the present study, permethrin treated Group A had more adverse drug reactions than Group D. Group A patients had 8 adverse drug reactions (ADRs) as burning sensation (2), skin irritation (2), nausea (2), headache (1), urticaria; while Group D patients had 2 ADRs like burning sensation (1) and gastritis (1). Group C and Group D had 2 ADRs in both groups.

DISCUSSION

In the present study, all the four treatment modalities revealed various efficacy at the end of 4 weeks. But topical permethrin and combination therapy was equally efficacious. In the present study, the clinical cure rate of oral ivermectin was 70% at the end of first week. It differs from other studies as the clinical cure rate observed was 79.3%, 50%, and 55.56%, respectively.[8,9,10] The clinical cure rate for oral ivermectin with 2 doses was 81% at the end of second week, while other studies had a cure rate of 74%, 70%, and 79 %.[11,12,13] Clinical cure rate for oral ivermectin at 4th week was 91%. Several studies reported 95% cure rate with oral ivermectin at the end of 4 weeks with two doses of oral ivermectin.[10,14] However, topical 5% permethrin showed

TABLE 2. Comparative improvement of lesions in the four treatment groups in the three follow-ups

Groups	Improvement %	Day 7	
		Chi-square value	p-value Result
Group A	83	6.11	0.1063 significant
Group B	70		
Group C	57		
Group D	82		
Groups	**Improvement %**	**Day 14**	
		Chi-square value	**p-value Result**
Group A	90	3.272	0.351 not significant
Group B	81		
Group C	70		
Group D	90		
Groups	**Improvement %**	**Day 28**	
		Chi-square value	**p-value Result**
Group A	97	0.914	0.822 not significant
Group B	91		
Group C	86		
Group D	97		

TABLE 3. Comparative improvement of pruritus in the 4 treatment groups in the three follow-ups

Groups	Improvement %	Day 7	
		Chi-square value	p-value Result
Group A	77	5.235	0.1553 significant
Group B	63		
Group C	55		
Group D	77		
Groups	**Improvement %**	**Day 14**	
		Chi-square value	**p-value Result**
Group A	88	2.759	0.430 not significant
Group B	76		
Group C	71		
Group D	88		
Groups	**Improvement %**	**Day 28**	
		Chi-square value	**p-value Result**
Group A	94	0.811	0.8468 not significant
Group B	86		
Group C	85		
Group D	94		

faster improvement at the first week follow-up, i.e., 81%. Usha et al.[9] also observed a superior efficacy with 5% permethrin as compared to single dose ivermectin (84.3% vs 50%) in an open label study. In a study by Madan[15] 82.6% of the patients improved with ivermectin after 4 weeks, whereas only 44.44% of their patients in the gamma benzene hexachloride group showed a similar response. Ivermectin induced an early and effective improvement in signs and symptoms such as pruritus.[15] Ivermectin has several clinical advantages that makes it superior to topical treatment. It is safe, inexpensive, simple to administer, and easily supervised. It treats the entire skin surface, is better tolerated in lesions with excoriations or open ulcerations, preferably better for mass treatment, and can be used in epidemics.

In 1986, Taplin et al., showed a cure rate of 91% for permethrin in comparison with 65% for gamma benzene hexachloride in treating scabies at 4 weeks post-treatment.[16] In another trial, Schultz et al., reported cure rates of 91% and 86.3% with permethrin and gamma benzene hexachloride respectively. Although this difference was not statistically significant, permethrin was significantly found to be more effective in reducing pruritus.[17] The results of the present study show that topical permethrin was superior to gamma benzene hexachloride in treating scabies, and is significantly ($p<0.05$) more effective.

As far as the relief from pruritus is concerned, at 3 weeks follow-up, 86% patients were free of pruritus in the oral ivermectin group compared

to 94%, 85%, 94% in permethrin, topical gamma benzene hexachloride, and the combination group respectively. It suggests that topical permethrin and the combination group rapidly cured the disease, and hence led to rapid improvement in pruritus as compared to the oral ivermectin and topical gamma benzene hexachloride group of patients. A previous study also showed that oral ivermectin was less effective in relieving pruritus as compared to permethrin.[18] A drug with a faster effect in relieving pruritus is also much more acceptable to patients. While oral ivermectin was found to be significantly less effective than the topical treatments such as permethrin, but superior than gamma benzene hexachloride. Permethrin alone or in combination would reduce the number of follow-up visits required, thus improving compliance and cost-effectiveness.

Although there have not been many documented cases of scabies resistant to permethrin, several controlled studies have revealed diminished sensitivity to this insecticide in developing countries like northern Australia and Africa.[19,20] Factors influencing the emergence of drug resistance include the biology and life cycle of the parasite,[21] and the genetic diversity of the parasite prior to drug selection. Increased diversity also increases the likelihood of resistance alleles existing in a population before selection. The molecular evidence suggests that ivermectin-resistance mechanisms are complex, multifactorial, and may differ between closely related organisms. The efficacy of ivermectin is due to its effect on only adult stages of the mite, thereby improving severe scabies more than permethrin. It acts by causing excessive release of neurotransmitter γ-aminobutyric acid (GABA) in the peripheral nervous system of the parasite, resulting in its death. While permethrin acts by disrupting the sodium channel current, resulting in delayed repolarization, paralysis, and death of the parasite by acting at all the stages of its life cycle. This is why permethrin-ivermectin combination therapy is now growing in use to prevent drug resistance, and also for rapid clearance of lesions and improvement in pruritus. But, it can increase the cost of the therapy, can increase its adverse effects, and thus should be used judiciously.[22,23]

In the present study, it was also found that though topical permethrin was equally efficacious as combination therapy to clinically cure patients, the studied group of patients had more adverse effects to it like skin irritations, headache, etc.

CONCLUSIONS

Recent developments leading to the expression and use of topical and oral drugs have been identified with potent treatment potential, and the current studies include the comparison of the efficacy and adverse effects of these drugs in individuals with active scabies. In the present study, we compared the efficacy of four drug groups, i.e., 5% topical permethrin, oral ivermectin, topical gamma benzene hexachloride 1%, oral ivermectin, and 5% topical permethrin combination group. In the study, gamma benzene hexachloride or Group C was the least efficacious in terms of reduced number of lesions and improvement in pruritus, followed by Group B or (oral ivermectin). Topical 5% permethrin showed effective results as combination groups of oral ivermectin and topical 5% permethrin to clear up lesions and to improve pruritus in patients with uncomplicated scabies. But, the topical 5% permethrin group showed more adverse effects among its patients in comparison to the combination group. Thus, Group D was considered more superior than Group A. That is why, Group D, i.e., oral ivermectin and topical 5% permethrin was concluded to be more efficacious and safer in scabies than other drugs. Finally, it is concluded that combination therapy is now a real possibility to treat patients with ease and accuracy. This should decrease the potential for escalating mite resistance and provide another means of controlling scabies in highly affected areas in developing countries like India.

J Popul Ther Clin Pharmacol Vol 29(1):e87–e96; 15 March 2022.

AUTHOR'S CONTRIBUTION:

SD - Concept and design of study, manuscript preparation, data collection, statistically analyzed and interpreted the data, critical revision of the manuscript.

VS - Collected data, statistically analyzed and interpreted the data, critical revision of the manuscript.

PK - Collected data, statistically analyzed and interpreted the data, critical revision of the manuscript.

WORK ATTRIBUTED TO

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SOURCE OF FUNDING

Self-funding

CONFLICT OF INTEREST

None

REFERENCES

1. Karthikeyan K. Treatment of scabies: Newer perspectives. Postgrad Med J. 2005;81:7–11. https://doi.org/10.1136/pgmj.2003.018390
2. Lee B, Groth P. Scabies: transcutaneous poisoning during treatment. Pediatrics dermatol. 1977;59:643. https://doi.org/10.1542/peds.59.4.643
3. Davies JE, Dadhia HW, Morgade C, Barquet A, Maibach HI. Gamma benzene hexachloride Poisoning. Arch Dermatol. 1983;119:142-44. https://doi.org/10.1001/archderm.1983.01650260050017
4. Zargari O, Golchai J, Sobhani A, Dehpour AR, Sadr-Ashkevari S, Alizadeh N et al., Comparison of the efficacy of topical 1% gamma benzene hexachloride vs 5% permethrin in scabies: A randomized, double-blind study. Indian J Dermatol Venerol Leprol. 2006;72: 33–6. https://doi.org/10.4103/0378-6323.19715
5. Roth WI. Scabies resistant to lindane 1% lotion and crotamiton 10% cream. J. of the American Acad. of Dermatol. 1991;24(3):502–503. https://doi.org/10.1016/S0190-9622(08)80078-3
6. Delmar SM, McKinster CD, Orozco CL. Treatment of 18 children with scabies or cutaneous larva migrans using ivermectin. Clin Exp Dermatol. 2002;27:264–7. https://doi.org/10.1046/j.1365-2230.2002.01050.x
7. Sharma R, Singhal A. Topical permethrin and oral ivermectin in the management of scabies: a prospective, randomized, double blind, controlled study. Indian Journal of Dermatology, Venereology and Leprology. 2011;77:581–6. https://doi.org/10.4103/0378-6323.84063
8. Macotela-Ruíz E, Peña-González G. The treatment of scabies with oral ivermectin. Gac Med Mex. 1993;129:201–5.
9. Usha V, Gopalakrishnan TV. A comparative study of oral ivermectin and topical permethrin cream in the treatment of scabies. J Am Acad Dermatol. 2000;42:236–40. https://doi.org/10.1016/S0190-9622(00)90131-2
10. Bachewar NP, Thawani VR, Mali SN, Gharpure KJ, Shingade VP, Dakhale GN et al. Comparison of safety, efficacy, and cost effectiveness of benzyl benzoate, permethrin, and ivermectin in patients of scabies. Indian J Pharmacol. 2009;41:9–16. https://doi.org/10.4103/0253-7613.48882
11. Chouela EN, Abeldaño AM, Pellerano G, La-Forgia M, Papale RM, Garsd A et al. Equivalent therapeutic efficacy and safety of ivermectin and gamma benzene hexachloride in the Treatment of Human Scabies. Arch Dermatol. 1999;135:651–5. https://doi.org/10.1001/archderm.135.6.651
12. Scheinfeld N. Controlling scabies in institutional settings: A review of medications, treatment models, and implementation. Am J Clin Dermatol. 2004;5:31–7. https://doi.org/10.2165/00128071-200405010-00005
13. Sule HM, Thacher TD. Comparison of ivermectin and benzyl benzoate lotion for scabies in Nigerian

patients. Am J Trop Med Hyg. 2007;76:392–5. https://doi.org/10.4269/ajtmh.2007.76.392

14. Victoria J, Trujillo R. Topical ivermectin: A new successful treatment for scabies. Pediatr Dermatol. 2001;18:63–5. https://doi.org/10.1046/j.1525-1470.2001.018001063.x
15. Madan V, Jaskiran K, Gupta U. Oral ivermectin in scabies patients: a comparison with 1% topical gamma benzene hexachloride lotion. J Dermatol. 2001;28:481–4. https://doi.org/10.1111/j.1346-8138.2001.tb00015.x
16. Taplin D, Meinking TL, Chen JA, Sanchez R. Comparison of crotamiton 10% cream (Eurax) and permethrin 5% cream (Elimite) for the treatment of scabies in children. Pediatr Dermatol 1990;7:67–73. https://doi.org/10.1111/j.1525-1470.1990.tb01078.x
17. Schultz MW, Gomez M, Hansen RC, Mills J, Menter A, Rodgers H et al. Comparative study of 5% permethrin cream and 1% gamma benzene hexachloride lotion for the treatment of scabies. Arch Dermatol. 1990;126:167–70. https://doi.org/10.1001/archderm.1990.01670260037006
18. Bachewar NP, Thawani VR, Mali SN, Gharpure KJ, Shingade VP, Dakhale GN et al. Comparison of safety, efficacy, and cost effectiveness of benzyl benzoate, permethrin, and ivermectin in patients of scabies. Indian J Pharmacol. 2009;41:9–16. https://doi.org/10.4103/0253-7613.48882
19. Elgart ML. A risk benefits assessment of agents used in the treatment of scabies. Drug Safet. 1996;14:386–93. https://doi.org/10.2165/00002018-199614060-00004
20. Burkhart CG, Burkhart CN. Optimal treatment for scabies remains undetermined. J Am Acad Dermatol. 2001;45:637. https://doi.org/10.1067/mjd.2001.113454
21. Barkwell R, Shields S. Deaths associated with ivermectin treatment of scabies. Lancet. 1997;349:1144–5. https://doi.org/10.1016/S0140-6736(05)63020-6
22. Conti-Diaz IA. Treatment of human scabies with oral Ivermectin. Revista Instituto Medicina Tropical. 1999;41:259–61. https://doi.org/10.1590/S0036-46651999000400011
23. Dourmishev AL. Efficacy and tolerance of oral Ivermectin in scabies. J European Dermatology. 1998;11:247–51. https://doi.org/10.1111/j.1468-3083.1998.tb00977.x