

Comparative Study of Cost effectiveness, Efficacy and Safety of Topical Gamma Benzene Hexachloride, Topical Permethrin and Oral Ivermectin in the Treatment of Scabies

*DrVidyullatha Balivada¹, DrRamya Gajam², DrAbilash Jain Bhansali³,
DrChaithanya Kamalla⁴, DrSunil Kumar Yadav⁵

^{1,2,4,5}(Department of Pharmacology, Osmania Medical College, Hyderabad, Telangana, India), ³(Department of Family Medicine, Baptist Hospital, Bangalore, Karnataka, India)

Corresponding Author: *Dr Vidyullatha Balivada

Abstract: Scabies is a common parasitic infection with a worldwide prevalence of about 300 million cases annually. An open label, prospective, parallel group study was conducted in out-patient department of Dermatology in Osmania General Hospital to compare the cost effectiveness, efficacy and safety of topical 1% Gamma Benzene hexachloride, topical 5% Permethrin and oral Ivermectin 200µg/kg in the treatment of 90 scabies patients of age group 5-60 years of either sex, divided in to three groups of 30 patients each. Clinical grading score and Itch grading score were recorded at baseline, 1 week, 2 weeks and 3 weeks of treatment. Any adverse effects of the treatment were also recorded. ANOVA test was used to compare the efficacy and chi-square test was used to analyze the cure rate between the three treatment groups. The cost effectiveness was calculated on the basis of total expenditure on medicine (in INR) at the end of the third week. Oral ivermectin is more cost-effective treatment with equal efficacy and safety profile when compared to benzene hexachloride and Permethrin. But the rate of decreasing pruritus is better with Permethrin may be due to its rapid onset of action.

Keywords: Scabies, Gamma Benzene hexachloride, Permethrin, Ivermectin.

Date of Submission: 18-09-2019

Date of Acceptance: 03-10-2019

I. Introduction

Scabies is a parasitic skin disease caused by the mite *Sarcoptes scabiei* var. *hominis*, which is an obligate human parasite. The infection is contagious as it can spread from person to person via direct skin contact, including sexual contact. It occurs throughout the world, but it is more prevalent in the areas of poor sanitation, overcrowding, and social disruption, and is endemic in many resource-poor countries.

It is estimated that the global prevalence of scabies is 300 million, but the level of infection varies between countries and communities[1]. There is some seasonal variation with incidence being greater in the winter than the summer, perhaps related to the tendency for more indoor overcrowding in colder weather[2].

Various drugs have been developed to treat scabies, and herbal and traditional medicines are also used. Treatments such as sulfur compounds, which have been used for centuries; benzyl benzoate (BB); crotamiton; gamma benzene hexachloride (GBHC or Lindane); malathion; permethrin; and oral ivermectin[3].

There are many factors which determine the choice of therapy such as age, cost of treatment, efficacy, safety etc. Several studies were conducted to compare various antiscabietic drugs for scabies. It is important to choose the best intervention for scabies with more efficacy, safety, and cost-effectiveness and with better compliance[4].

Oral Ivermectin has been gaining popularity in the treatment of scabies due to its convenience of dosing and better compliance than other topical medications.

In this study, oral ivermectin will be compared to the topical Gamma benzene hexachloride (GBHC) and topical permethrin in terms of efficacy, safety and cost-effectiveness.

The present study will be conducted to compare three commonly used anti-scabietic drugs - Permethrin, Gamma benzene hexachloride and Ivermectin to find out the best intervention at minimal cost, better efficacy, and safety.

1.1 Aims and objectives

- To compare the efficacy of the topical Gamma benzene hexachloride, topical permethrin and oral ivermectin.
- To find out the cost-effective drug for the treatment of the scabies out of topical GBHC, topical permethrin and oral ivermectin.
- To monitor any adverse drug reactions with the study drugs.

II. Patients And Methods

2.1 Site of study:

Patients attending dermatology OPD at Osmania General Hospital, with clinically diagnosed Scabies were included in the study after obtaining approval from Institutional ethics committee and informed consent.

2.2 Period of Study: 1 year – 10/2015 to 10/ 2016.

2.3 Inclusion Criteria

- Patients of either sex aged 5 to 60 years with clinically-diagnosed scabies.
- History of involvement of family member or similar symptoms in contacts.
- Patients who gave informed consent.

2.4 Exclusion criteria:

- Patient treated with any topical scabidical therapy in the month before entry.
- Patients taking any topical or systemic antibiotic therapy in the week before entry into the study.
- Immunologically-compromised patients.
- Having scabies with atypical presentation like crusted scabies or scabies incognito.
- Patients with secondary bacterial infection.
- Pregnant and lactating females.

2.5 Methodology:

96 Patients fulfilling the above inclusion criteria and exclusion criteria were randomly allocated to three treatment groups. They were explained about the drugs to be given for their condition and how to use the medications and an informed consent taken from the patients. Consent obtained from the parent or guardian if the patient belongs to paediatric group or if the patient is illiterate.

2.6 Method of collection of data:

A case report form containing the detailed information about patient's medical history and general examination was prepared. Demographic profile of the patient, detailed general examination of the patient, medical history of the patient, family history of the patient were documented. Total 6 patients were lost to follow up, 2 patients from group 1 lost to follow up at the end of 1st week and 1 patient from group 2 didn't come for follow up at the end of 2nd week and another patient from group 2 lost to follow up at the end of 2nd week and 2 patients from group 3 were lost to follow up at the end of 1st week, hence excluded from the study.

Excluding the dropouts the study was continued and completed with 90 patients. The patients from each group received treatment as follows: Group 1 received Topical 1% Benzene Hexachloride (GBHC), Group 2 received topical 5% Permethrin, Group 3 received Oral Ivermectin 200 mcg/kg.

2.7 Interventions:

The patients were randomly allocated to three groups.

Group 1:

Single application of gamma benzene hexachloride (GBHC) 1% lotion, half bottle i.e. 25 ml was applied over whole body below neck and bath was taken 8 hours later. This procedure was repeated after one week. The price of the 50 ml bottle is INR 32/-.

Group 2:

A Single application of permethrin 5% lotion, half bottle i.e. 15 ml was applied over whole body below neck and bath was taken 8 hours later. This process was repeated after one week. The price of the 30 ml bottle is INR 70/.

Group 3:

A single dose of Tab. Ivermectin 200mcg/kg was advised to take any time of the day and repeated after 1 week. The price of the single tablet is INR 12/-.

2.8 Grading scores:

The patients were graded according to the number of lesions and the severity of itch present at the time of enrollment. The baseline itch and clinical grade scoring was done. All the details were recorded. The efficacy was assessed on basis of the two parameters.

Clinical grading score:(CGS)

The primary efficacy parameter was lesion subsidence. Severity of lesions was clinically graded on a scale of 0 to 3 arranged as follows:

- 0 = Free of lesions (no lesions),
- 1 = 10 or fewer lesions (mild),
- 2 = 11- 49 lesions (moderate),
- 3 = 50 or more lesions (severe).

Itching grading score: (IGS)

The secondary efficacy parameter was the assessment of reduction in severity of itch, considering the pruritus at first visit as 100%. The patient was asked for reduction in pruritus on subsequent visit and on basis of that grading was done. Pruritus was graded on a scale of 0 to 4 on basis of severity.

Grading was done as:

- 0 = 0% (no pruritus),
- 1 = 1-25% (mild pruritus),
- 2 = 26-50% (moderate pruritus),
- 3 = 51-75% (severe pruritus),
- 4 = 76-100% (very severe pruritus).

2.9 Method of assessment:

Efficacy and Safety assessment:

The patients of all of the three groups were followed up at the end of 1st week, 2nd week and 3rd week to assess the efficacy and safety. At each of the three follow ups, a detailed clinical examination was performed. The patients with all the remaining scabietic lesions are compared to the baseline clinical grading score and were also asked about the itching and compared it to the baseline itch grading score.

The improvement was graded as Mild= CGS (grade 2 or 3) + IGS (grade 3 or4), Moderate= CGS (grade 1)+ IGS (grade 1or2), Good = CGS (grade 0)+ IGS (grade 0). Patients with moderate and good improvement were considered cured. The patients with no improvement in the pruritus, non-healing of old skin lesions, appearance of new lesions and with mild improvement were considered not cured.

The treatment was considered effective only if at the end of the three weeks, the pruritus was reduced and lesions were improved without appearance of any new lesions from initial visit. The patients were asked for any adverse events occurred during the course of treatment.

Cost effectiveness assessment:

The cost effectiveness was calculated on basis of total expenditure on medicine (in INR) at the end of the third week and cure rate and the three drugs were compared on the basis of amount needed to treat one case successfully.

2.10 Data analysis:

In this study, at each visit, the improvement in both clinical grading score and itch grading score were analyzed. Data were presented as mean ± standard deviation. Efficacy was measured by using ONEWAY ANOVA as statistical test and cure rate was analyzed by using Chi-square test. Percentages were calculated to assess the improvement in clinical grading score (severity of lesions) and itch grading score (severity of itch) during the follow ups.

P value:

- A p-value of < 0.05 was considered significant.
- A p-value of > 0.05 was considered not significant.

III. Observations And Results

Table 1: Baseline characteristics of the three treatment groups

Parameters	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)
Mean age(±SD) in years	35.63 ± 13.88	24.56 ± 16.37	29.93 ± 13.69
Gender (male %/female %)	60 / 40	53.3 / 46.7	50 / 50
Nocturnal pruritus(%)	100	100	100
Family history of pruritus(%)	70	76.6	80
Clinical Grading Score (%)			
Severe	33.33	30	36.67
Moderate	56.67	56.67	53.33
Mild	10	13.33	10
Itch grading Score (%)			
Very severe	33.33	30	36.67
Severe	66.67	70	63.33
Moderate	0	0	0
Mild	0	0	0

Table 2: Distribution of the patients according to age in Group 1, 2 and 3

Age group	Group 1 (GBHC)	Group 2 (Permethrin)	Group 3 (Ivermectin)
5 to 20 yrs	4	18	8
21 to 40 yrs	18	5	16
41 to 60 yrs	8	7	6

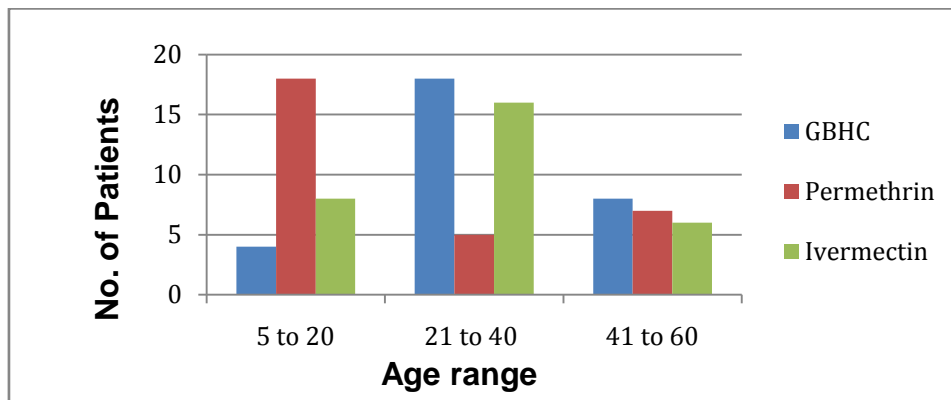


Figure 1: Distribution of the patients according to age in Group 1, 2 and 3

In the present study patients were taken between the age group of 5 to 60 years. The mean age of all patients in this study is 30 ± 15.2.

Table 3: Distribution of the patients according to gender in Group 1, 2 and 3

Sex	Group 1(GBHC)	Group 2 (Permethrin)	Group 3 (Ivermectin)
Male	18	16	15
Female	12	14	15

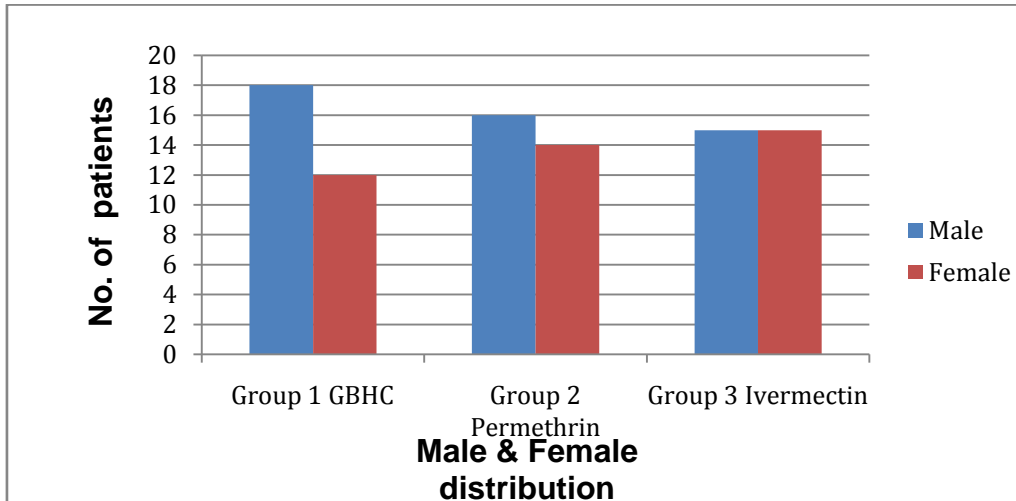


Figure 2: Distribution of the patients according to gender in Group 1, 2 and 3

Table 4: Distribution of the patients in group 1, 2 and 3 according to gender and family history of Pruritus

Gender	Group 1 (GBHC)	Group 2 (Permethrin)	Group 3 (Ivermectin)
Males with family h/o pruritus	12	11	11
Females with family h/o pruritus	9	12	12

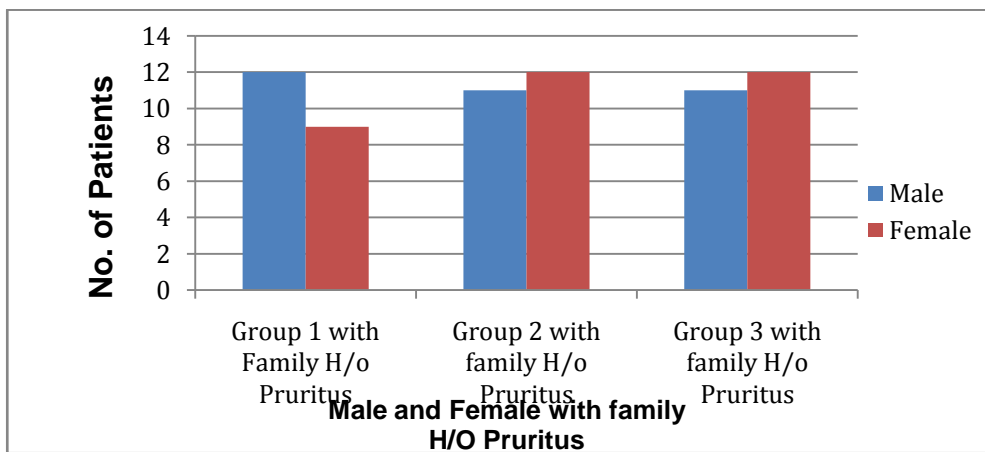


Figure 3: Distribution of the patients in group 1, 2 and 3 according to gender and family history of Pruritus

Table 5: Baseline clinical grading score of group 1, 2 and 3 at the time of enrollment

Group	Severe (%)	Moderate (%)	Mild (%)	No lesions (%)
Group 1 (GBHC)	33.33	56.67	10	0
Group 2 (Permethrin)	30	56.67	13.33	0
Group 3 (Ivermectin)	36.67	53.33	10	0

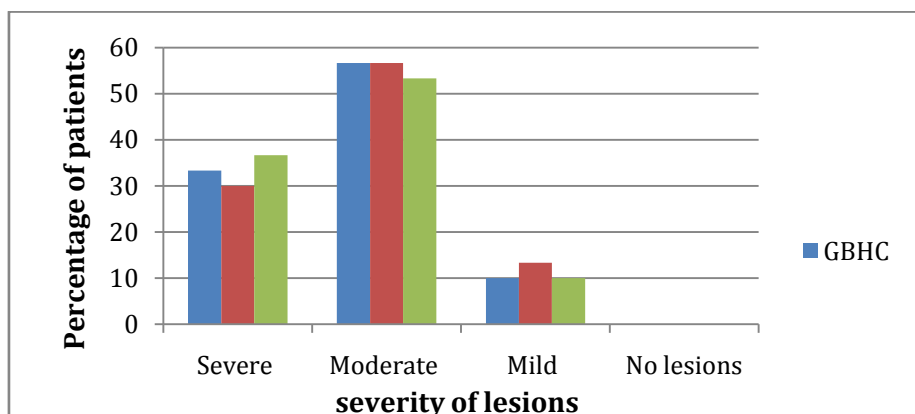


Figure 4: Baseline clinical grading score of the patients from group 1, 2 and 3 at the time of enrollment

In the present study, there is statistically no difference between the baseline clinical grading score among the three treatment groups with p value > 0.05, as calculated by ANOVA.

Table 6: Improvement of Clinical grading score in group 1, 2 and 3 at the end of 1st week

Group	Severe (%)	Moderate (%)	Mild (%)	No lesions (%)
Group 1 (GBHC)	20	46.66	43.33	0
Group 2 (Permethrin)	13.33	43.33	43.33	0
Group 3 (Ivermectin)	10	46.66	43.33	0

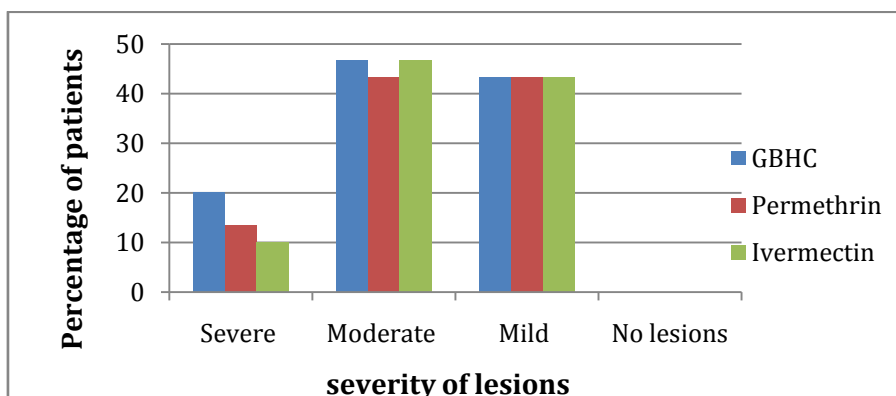


Figure 5: Improvement of Clinical Grading score in group 1, 2 and 3 at the end of 1st week

In the present study, there is statistically no significant difference between the clinical grading score at the end of 1st week among the three treatment groups with p value > 0.05, as calculated by ANOVA.

Table 7: Improvement of Clinical grading score in group 1, 2 and 3 at the end of 2nd week

Group	Severe (%)	Moderate (%)	Mild (%)	No lesions (%)
Group 1 (GBHC)	6.66	13.33	80	0
Group 2 (Permethrin)	3.33	10	63.33	23.33
Group 3 (Ivermectin)	6.66	26.66	66.66	0

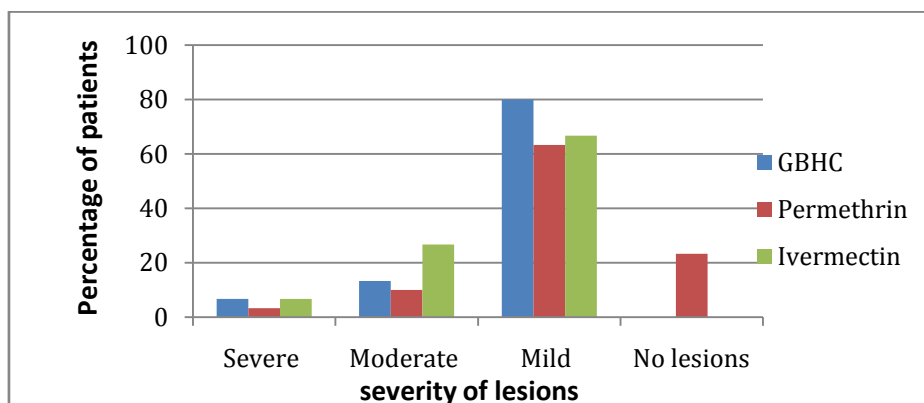


Figure 6: Improvement of Clinical grading score in group 1, 2 and 3 at the end of 2nd week

In the present study, there is statistically no significant difference between the clinical grading score at the end of 2nd week among the three treatment groups with p value > 0.05, as calculated by ANOVA.

Table 8: Improvement of Clinical grading score in group 1, 2 and 3 at the end of 3rd week

Group	Severe (%)	Moderate (%)	Mild (%)	No lesions (%)
Group 1 (GBHC)	6.67	0	56.67	36.66
Group 2 (Permethrin)	3.33	3.33	43.33	50
Group 3 (Ivermectin)	0	0	36.66	63.33

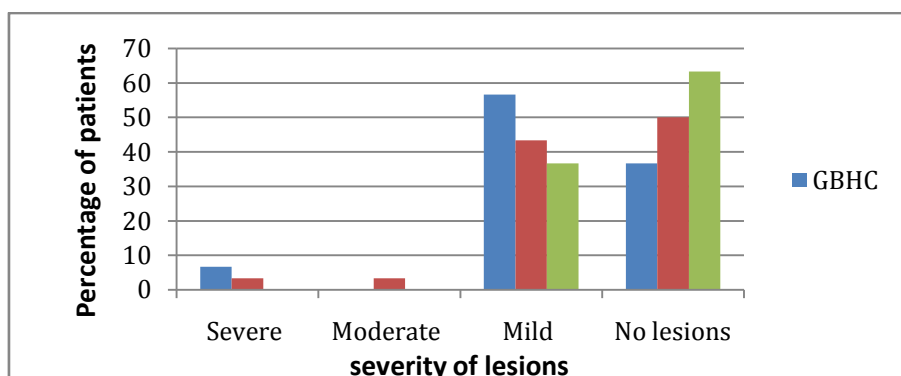


Figure 7: Improvement of Clinical grading score in group 1, 2 and 3 at the end of 3rd week

In this study there is statistically no significant difference between the clinical grading score at the end of 3rd week among the three treatment groups with p value > 0.05, as calculated by ANOVA.

Table 9: Baseline Itch grading score of group 1, 2 and 3 at the time of enrollment

Group	Very severe (%)	Severe (%)	Moderate (%)	Mild (%)	No Pruritus (%)
Group 1 (GBHC)	33.33	66.67	0	0	0
Group 2 (Permethrin)	30	70	0	0	0
Group 3 (Ivermectin)	36.67	63.33	0	0	0

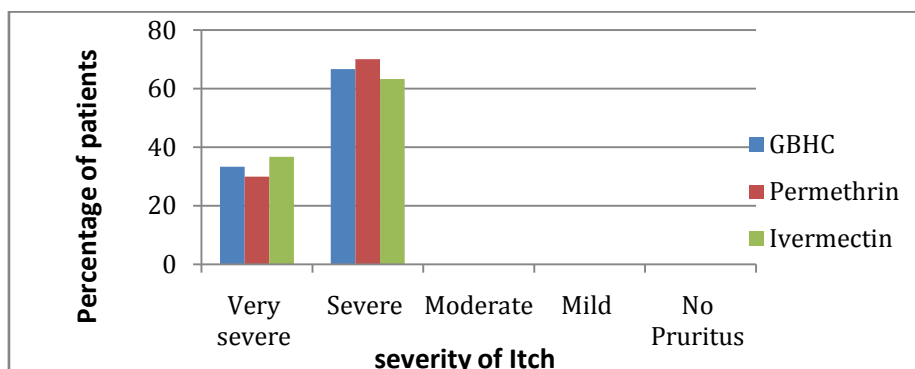


Figure 8: Baseline Itch grading score of group 1, 2 and 3 at the time of enrollment

In this study, the baseline itch grading score of the patients enrolled in to the three treatment groups shows statistically no significant difference with a p-value > 0.05, as calculated by ANOVA.

Table 10: Improvement in Itch grading score in group 1, 2 and 3 at the end of 1st week

Group	Very severe (%)	Severe (%)	Moderate (%)	Mild (%)	No Pruritus (%)
Group 1 (GBHC)	0	36.66	63.33	0	0
Group 2 (Permethrin)	0	33.33	66.66	0	0
Group 3 (Ivermectin)	0	53.33	46.66	0	0

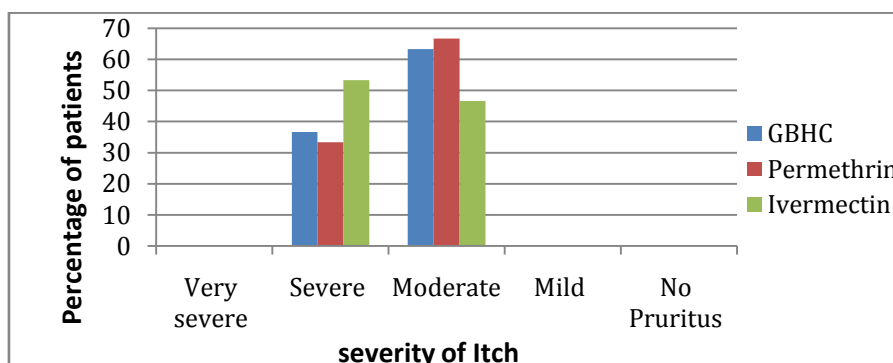


Figure 9: Improvement in Itch grading score in group 1, 2 and 3 at the end of 1st week

In this study, improvement in the percentage of itch at the end of 1st week between the three treatment groups shows a statistically significant difference with a p-value < 0.05 (p = 0.006) as calculated by ANOVA. Permethrin group showed more improvement in itch than other two groups of drugs.

Table 11: Improvement in Itch grading score in group 1, 2 and 3 at the end of 2nd week

Group	Very severe (%)	Severe (%)	Moderate (%)	Mild (%)	No Pruritus (%)
Group 1 (GBHC)	0	3.33	63.33	33.33	0
Group 2 (Permethrin)	0	3.33	73.33	23.33	0
Group 3 (Ivermectin)	3.33	13.33	53.33	30	0

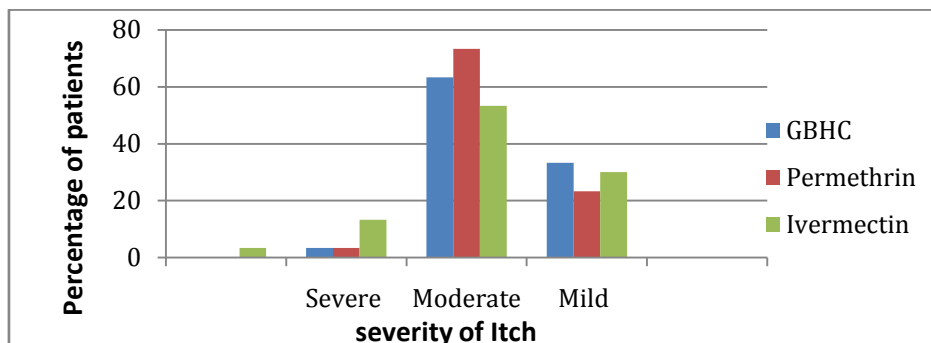


Figure 10: Improvement in Itch grading score in group 1, 2 and 3 at the end of 2nd week

In this study, the improvement of itch grading score (percentage of itch) between the three treatment groups, group 1, 2 and 3 at the end of 2nd week shows statistically no significant difference with p-value > 0.05, as calculated by ANOVA.

Table 12: Improvement in Itch grading score in group 1, 2 and 3 at the end of 3rd week

Group	Very severe (%)	Severe (%)	Moderate(%)	Mild(%)	No Pruritus(%)
Group 1 (GBHC)	0	3.33	0	63.33	36.67
Group 2 (Permethrin)	0	0	3.33	63.33	36.67
Group 3 (Ivermectin)	0	0	0	40	60

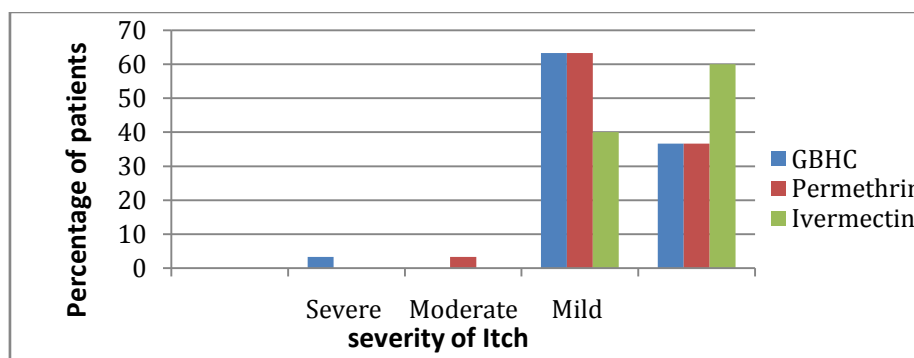


Figure 11: Improvement in Itch grading score in group 1, 2 and 3 at the end of 3rd week.

In this study, the improvement in the % of itch among the three treatment groups at the end of 3rd week shows no statistically significant difference with a p-value > 0.05, as calculated by ANOVA.

Table 13: Comparison of improvement in Clinical grading score between group 1, 2, and 3

	Group 1 GBHC	Group 2 Permethrin	Group 3 Ivermectin	P value
Baseline	38.5 ± 19.47	36.73 ± 18.12	42.3 ± 17.27	0.48
At the end of 1st week	23.53 ± 17.8	23.46 ± 15.38	27.16 ± 17.62	0.62
At the end of 2nd week	11.66 ± 13.02	7.43 ± 9.32	13.3 ± 11.96	0.13
At the end of 3rd week	6.53 ± 13.65	4.5 ± 9.56	2.36 ± 3.48	0.26

Table showing the improvement in clinical grading score in terms of Mean ± SD at each week follow up for each drug group.

In this study, there is no significant difference in the improvement of clinical grading score (no. of lesions) between the three treatment groups, group 1, 2 and 3 at the end of 1st week, at the end of 2nd week and at the end of 3rd week after 3 weeks of follow up with a p-value > 0.05, as calculated by ANOVA.

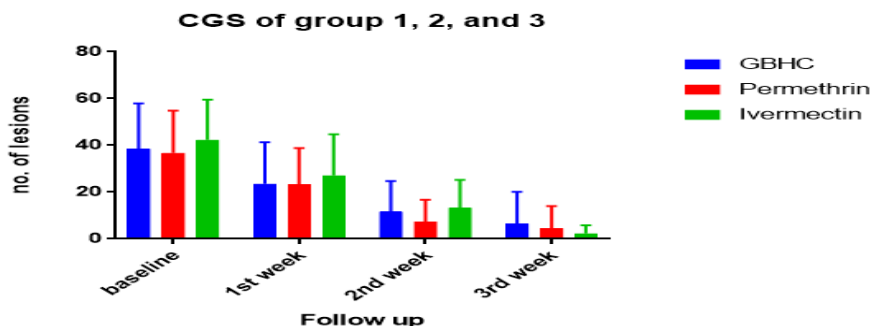


Figure 12: Comparison of improvement in Clinical grading score between group 1, 2, and 3

Figure showing the improvement in clinical grading score (no. of lesions.)

In this study, there is no significant difference in the improvement of clinical grading score between the three treatment groups, group 1, 2 and 3 at the end of 1st week, at the end of 2nd week and at the end of 3rd week after 3 weeks of follow up with a p-value > 0.05, as calculated by ANOVA.

Table 14: Comparison of improvement in Itch grading score between Group 1, 2, and 3

	Group 1 GBHC	Group 2 Permethrin	Group 3 Ivermectin	P value
Baseline	75.56 ± 14.83	73.26 ± 14.65	76.86 ± 15.26	0.64
At the end of 1st week	45.93 ± 14.79	41.46 ± 13.02	53.56 ± 15.5	0.006
At the end of 2nd week	29.23 ± 10.38	28.06 ± 8.34	33.2 ± 17.63	0.26
At the end of 3rd week	6.23 ± 10.05	5.7 ± 9.46	3.03 ± 4.27	0.28

Table showing the improvement in itch grading score in terms of Mean ± SD at each week follow up for each drug group.

In this study, the improvement of itch grading score (% of itch) between the three treatment groups, group 1, 2 and 3 at the end of 1st week shows a significant difference in the improvement in the percentage of itch with a p-value < 0.05 (p = 0.006) and there is no significant difference in the improvement in the percentage of itch at the end of 2nd week and 3rd week with a p-value > 0.05, as calculated by ANOVA.

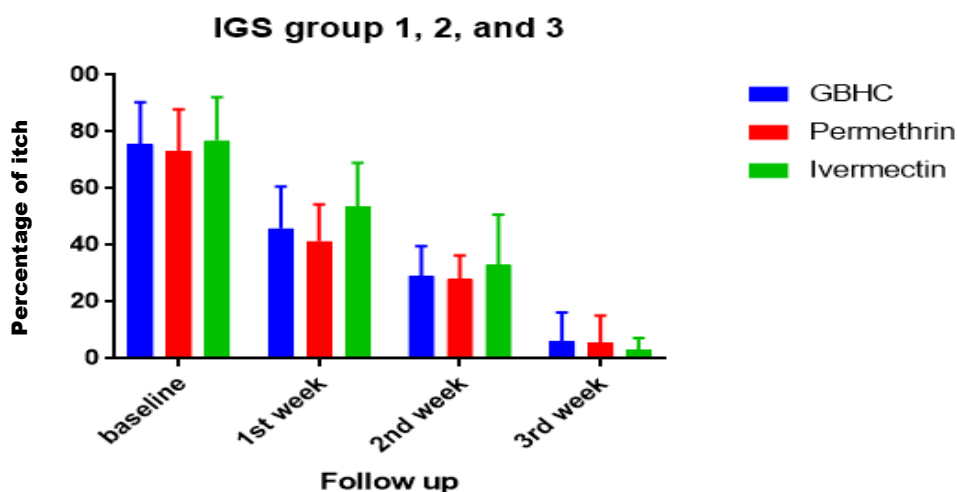


Figure 13: Comparison of improvement in Itch grading score between Group 1, 2, and 3

In this study, there is a significant difference in the improvement in the percentage of itch at the end of 1st week in group 2 with a p-value < 0.05 (p = 0.006). Permethrin group showed more improvement in itch than other two groups of drugs. There is no significant difference in the improvement in the percentage of itch between the three treatment groups at the end of 2nd week and 3rd week with a p-value > 0.05, as calculated by ANOVA.

Table 15: Clinical cure rate in terms of improvement in both Clinical grading score and Itch grading score in group 1, 2 and 3

Drug group	No. of patients in each group	Cure rate at the end of 1 st week	Cure rate at the end of 2 nd week	Cure rate at the end of 3 rd week
Group 1 (GBHC)	30	40%	76.66%	93.33%
Group 2 (Permethrin)	30	40%	83.33%	96.66%
Group 3 (Ivermectin)	30	36.66%	60%	100%

Table showing the overall cure rate at each week follow up.

In this study, there is no statistically significant difference in the overall cure rate at each week follow up of the patients of the three treatment groups with p-value > 0.05, as calculated by chi-square test.

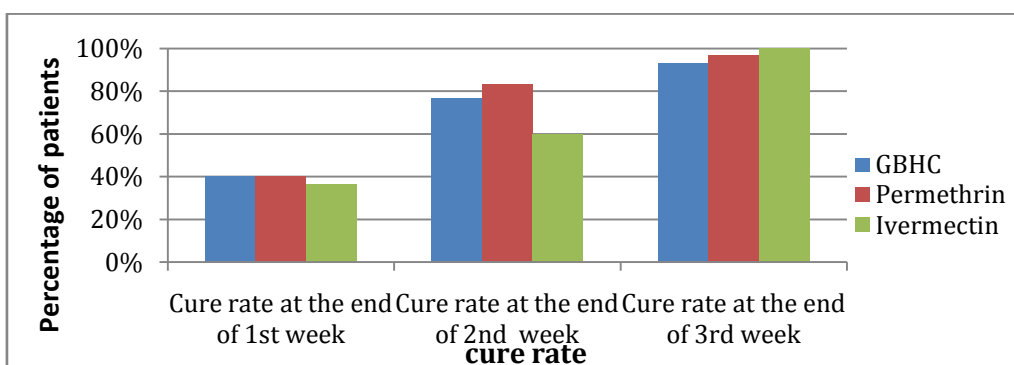


Figure 14: Clinical cure rate in terms of improvement in both Clinical grading score and Itch grading score in group 1, 2 and 3.

Figure showing the overall cure rate among the three treatment groups at each follow up

In this study, the overall cure rate at each week follow up of the patients of the three treatment groups shows no significant difference with a p-value > 0.05, as calculated by chi-square test.

Table 16: Cost-effectiveness of each study drug at the end of 3rd week based on the overall cure rate

Parameters	GBHC	Permethrin	Ivermectin
Cost in INR for 100 participants	32 × 100 = 3200	70 × 100 = 7000	24 × 100 = 2400
Overall Cure rate (%)	93.33	96.66	100
Cost effectiveness	3200 for 93.33 participants	7000 for 96.66 participants	2400 for 100 participants
Cost to treat one case	34	72	24

Table showing the cost-effectiveness of the drugs used in this study

The cost incurred to treat one case successfully is less with Ivermectin as compared to GBHC and permethrin. So ivermectin is more cost-effective than the other two drug groups.

IV. Discussion

Scabies is the common parasitic infestation in poor people due to overcrowding and unhygienic conditions which helps in transmission. The patients of all age group and both sex are susceptible. The treatment options are topically applied medicines like benzyl benzoate, gamma benzene hexachloride, permethrin etc. Now an oral medicine Ivermectin has been found to be effective. The objective of this study was to determine the safe and cost effective treatment for Scabies.

A large number of studies were done to prove the cost effectiveness of Ivermectin in the treatment of Scabies; however the standard treatment remains Permethrin due to its rapid onset of action. This study was done to determine the best treatment modality in Scabies in terms of efficacy, safety, cost-effectiveness and also the compliance of the patients to the treatment given.

Gamma benzene hexachloride is a neurotoxin that interacts with the GABA-A receptor chloride channel complex at the picrotoxin binding site and disrupts GABA neurotransmission, this results in death of mite[5].

Permethrin is a neurotoxin and it blocks the movement of sodium ions from outside to inside of the nerve cells. This causes delayed repolarisation and paralysis and death. Permethrin acts on ubiquitous sodium channels so it acts at all stages of the life cycle of the mite[6].

Ivermectin blocks chemical transmission across the nerve synapses that use glutamate-gated anion channels or γ -aminobutyric acid- gated chloride channels. Stimulation of γ -aminobutyric acid (GABA) release from presynaptic nerve endings and enhancement of the binding to the postsynaptic receptors accomplishes this[7,8]. Ivermectin does not affect synapses gated by other transmitter substances, such as acetylcholine, norepinephrine, and serotonin[9]. This leads to an increase in the permeability of the cell membrane to chloride ions with the hyper polarization of the cell, resulting in paralysis and death of the parasite[10,11].

A study entitled "Comparative study of cost effectiveness, efficacy and safety of topical gamma benzene hexachloride, topical permethrin and oral ivermectin in the treatment of scabies" undertaken at Dermatology and venereology department, Osmania General Hospital.

The patients attending dermatology OPD, with newly diagnosed mild to severe scabies within the age range of 5 to 60 years of either sex were taken in to the study.

The effects studied were:

- Decrease in the number of lesions (Clinical Grading Score)
- Decrease in the intensity of pruritus (Itch Grading Score)
- No appearance of new lesions
- Cost-effectiveness of the given medications
- Adverse drug reactions occurred if any.

Based on the above effects the efficacy, safety and cost-effectiveness of the three drugs, topical Gamma benzene hexachloride, topical permethrin and oral Ivermectin were compared.

All the three treatment modalities show effect by paralyzing the mite which results in its death. But the question is which one of them is more cost-effective and safe with better compliance. Previous studies showed that oral Ivermectin is cost-effective and more compliant for the patients due to its convenience of administration unlike the exhaustive application of topical agents which consumes time and messes with patient's compliance.

In this study, the Improvement in Clinical grading score is graded as number of mild cases and cases with no lesions in each group at each follow up at the end of 1st week, at the end of 2nd week, at the end of 3rd week. At the end of 1st week the patients in GBHC, Permethrin and ivermectin showed equal proportion of improvement in clinical grading score.

In this study, the improvement in Itch grading score is graded as number of moderate pruritus cases, mild pruritus cases and cases with no pruritus.

In Permethrin group there is a decrease in pruritus in some patients at the end of 1st week as compared to GBHC and Ivermectin which may be due to its rapid onset of action.

The mean age in this study among all the three treatment groups are 35.63 ± 13.88 in group 1 (GBHC), 24.56 ± 16.37 in group 2 (Permethrin), 29.93 ± 13.69 in group 3 (Ivermectin). The mean age of all patients in this study is 30 ± 15.2 .

At the time of enrollment, all the baseline characteristics, clinical grading score and itch grading score of the three treatment groups show no significant difference.

In Group 1 (GBHC) the percentage cure rate at the end of 1st week in Clinical Grading Score is 43.33%, that in Group 2 (Permethrin) is 43.33% and that in Group 3 (Ivermectin) is 43.33% with no significant difference in the improvement in Clinical Grading score between all the drug groups ($p > 0.05$.)

In group 1 the percentage cure rate at the end of 2nd week in Clinical Grading Score is 80%, that in group 2 is 86.66%, and that in group 3 is 66.66%. There is slight difference between Permethrin and Ivermectin group but there is no statistically significant difference ($p > 0.05$.)

In group 1 the percentage cure rate at the end of 3rd week in Clinical Grading Score is 93.33%, that in group 2 is 93.33%, and that in group 3 is 100%. There is no significant difference in the improvement in the clinical grading score between all the three treatment groups ($p > 0.05$.)

In group 1 the percentage improvement at the end of 1st week in Itch Grading Score is 63.33%, that in Group 2 is 66.67% and that in Group 3 is 46.66%, There is a significant difference between the three treatment groups in the improvement of itch grading score ($p = 0.006$). permethrin group showed more improvement in itch grading score than other two groups.

In group 1 the percentage improvement at the end of 2nd week in Itch Grading score is 96.66%, that in group 2 is 96.66%, and that in group 3 is 83.33%. There is no significant difference in improvement of Itch grading score between the three treatment groups ($p > 0.05$.)

In group 1, the percentage improvement at the end of 3rd week in Itch Grading score is 99%, that in group 2 is 100%, and that in group 3 is 100%. There is no significant difference between the three treatment groups in the improvement in Itch grading score ($p > 0.05$.)

When compared between the three groups using One-way ANOVA, the improvement in Clinical Grading Score and Itch Grading Score at the end of 3rd week shows no significant difference with p value > 0.05 .

The overall cure rate (both CGS and IGS) at the end of 1st week is 40% in GBHC group, 40% in Permethrin group and 36.66% in ivermectin group.

The overall cure rate (both CGS and IGS) at the end of 2nd week is 76.66% in GBHC group, 83.33% in Permethrin group and 60% in ivermectin group

The overall cure rate (both CGS and IGS) at the end of 3rd week is 93.33% in GBHC group, 96.66% in Permethrin group and 100% in ivermectin group.

There is no significant difference in the overall cure rate (both CGS and IGS) between the three treatment groups with p -value > 0.05 , as calculated by chi-square test.

In this study, two doses of Ivermectin was more cost-effective and efficacious than GBHC and Permethrin. A single application of permethrin is more efficacious in relieving itch at the end of 1st week than other two drugs.

In the present study, 90 patients who were attending Dermatology OPD and fulfilling the inclusion criteria were included. Out of the 90 patients Group 1(GBHC) has 18 Female patients and 12 male patients, Group 2 (Permethrin) has 16 male patients and 14 female patients, Group 3 (Ivermectin) has 15 male patients and 15 female patients. The mean age of each group in this study was 35.63 ± 13.88 in GBHC group, 24.56 ± 16.37 in Permethrin group, 29.93 ± 13.69 in Ivermectin group respectively.

Similar study was conducted by **Meenakshi et al** at Maharani Laxmi Bai Medical College, involving 210 newly diagnosed patients. Out of which Group A (Permethrin) has 49 male patients and 21 female patients, Group B (GBHC) has 51 male patients and 19 female patients, Group C (Ivermectin) has 41 male patients and 29 female patients[6].

Another study conducted by **Sunita B chaiyya et al** in 315 patients comparing the efficacy and safety of topical Permethrin, topical Ivermectin and oral Ivermectin at C. U. Shah Medical College, Gujarat, were randomly allocated to the 3 treatment groups. Out of the 315 patients, Permethrin group has 58 male patients and 47 female patients, Topical Ivermectin has 59 male patients and 46 female patients, and Oral Ivermectin has 58 male patients and 47 female patients[12].

In other study done by **Bachewar et al** in 103 patients comparison of safety, efficacy and cost-effectiveness of topical Benzyl benzoate, topical Permethrin and oral Ivermectin at Government Medical College and Hospital (GMCN), Nagpur, were randomly allocated to three groups. Out of 103 patients, Benzyl benzoate group has 23 male patients and 12 female patients, Permethrin group has 22 male patients and 12 female patients, Ivermectin group has 18 male patients and 16 female patients[13].

Meenakshi et al conducted an open labeled randomized study of antiscabietic drugs. The cure rate at the end of first week was 83.87% in Group A (Permethrin), 78.18% in Group B (GBHC) and 55.17% in Group C (Ivermectin), permethrin and gamma benzene hexachloride shows no significant difference while ivermectin was less efficacious to both permethrin and gamma benzene hexachloride. While cure rate in the three treatment groups at the end of third week was 93.55% in Group A, 80.00% in Group B and 98.28% in Group C, there was no significant difference between permethrin and ivermectin while both permethrin and ivermectin were more efficacious than gamma benzene hexachloride[6].

In the present study, the cure rate at the end of 1st week with Ivermectin is 36.66%, with GBHC (40%) and Permethrin (40%), and the cure rate at the end of 3rd week shows no significant difference between the three

treatment groups GBHC (93.33%), Permethrin (96.66%), Ivermectin (100%) which is supported by the study done by **Meenakshi et al.**

Narendra P Bachewar et al conducted another study by comparing the efficacy, safety and cost-effectiveness of topical Benzyl Benzoate, topical Permethrin and oral Ivermectin, in which the cure rate of Ivermectin group is less as compared to the Permethrin group and Benzyl Benzoate group. Ivermectin showed 100% cure rate after two weeks of treatment. Permethrin decreased pruritus by 76% at the end of one week and had significantly better cure rate than ivermectin[13].

This observation supports our study with a slight difference in decreasing pruritus by Permethrin which is 66.67% at the end of 1st week. But the Ivermectin group in our study showed cure rate of 100% at the end of 3rd week, which is different from the above study.

Sunita B. chhaiya et al conducted a study comparing topical Permethrin, Topical Ivermectin and oral Ivermectin. The cure rate of lesions at the end of 1st week in Permethrin group is 99.8% and in oral Ivermectin group is 98% which is very different from our study where the cure rate of lesions at the end of 1st week in Permethrin group is 86.67% and in Ivermectin group is 70%. [12].

However in the above study the cure rate of patients with no lesions in Permethrin group is 74.8% and in Ivermectin group is 30% which is not consistent with our study where the percentage of patients with no lesions is 0% at the end of 1st week. The cure rate of lesions at the end of 3rd week in the above study in Permethrin group is 100% and in Ivermectin group is 100%, but in our study the cure rate of lesions at the end of 3rd week in Permethrin group is 96.67% and in Ivermectin group is 100%, which is supported by the above study. The cure rate of itch in the above study at the end of 1st week is 93.9% and in Ivermectin group is 65%, but in our study the cure rate of itch in Permethrin group is 56.67% and in Ivermectin group is 10% which is very less when compared to the above study. The cure rate of itch at the end of 3rd week in the above study in Permethrin group is 99.8% and in Ivermectin group is 100% , in our study the cure rate of itch at the end of 3rd week in Permethrin group is 96.67% and in Ivermectin group is 99.99%, which is supported by the above study.

Omid Zargari et al conducted a randomized double blind study comparing the efficacy of topical lindane (GBHC) and topical permethrin where the cure rate at 2 weeks post treatment in Permethrin group is 84.6% and in Lindane group is 48.9%. In our study the cure rate at the end of 2nd week in GBHC (Lindane) group is 76.66% and in Permethrin group is 83.33%, where the cure rate in GBHC group in our study is more when compared to the above study.[14].

In another study conducted by **Pramod kumar Manjhi et al** they compared the efficacy of oral Ivermectin to that of topical Permethrin, GBHC and Benzyl benzoate (BB lotion). In their study, the efficacy of ivermectin, permethrin, GBHC and BB lotion considering improvement in severity of pruritus as parameter were 85%, 90%, 75% and 68.33% respectively at 2nd follow-up. Similarly considering improvement in severity of lesion as parameter, results were 80%, 88.33%, 71.66% and 65% respectively at 2nd follow up.[15].

In our study, the efficacy of ivermectin, permethrin, GBHC considering the improvement in severity of pruritus were 83.33%, 96.66%, 96.66%, respectively at 2nd week follow up. Considering the severity of lesions, the results were 66.66%, 86.66%, 80% respectively at 2nd week follow up. The above study supports our study in the improvement in severity of lesions and pruritus except for the Ivermectin where the lesion severity is more in our study.

Alireza Mohebbipour et al conducted a double blind study comparing efficacy of single dose of Ivermectin and two applications of Lindane 1week a part, On follow-up, with a single dose by the first week, 41.9% patients in the ivermectin group and 29.3% patients in the lindane group were cured. At 2 weeks post-treatment, cure was observed in 58.6% patients of the ivermectin group and 44.3% patients in the Lindane group. This difference was not significant ($p=0.24$) and the non-responders received a repeat therapy. By the fourth week, 92.7% patients were cured with ivermectin, whereas 71.7% patients were cured with lindane which is less compared to our study by the 3rd week the cure rate with Lindane is 93.33% and with Ivermectin is 100%. [16].

In this study, two doses of Ivermectin was more cost-effective and efficacious than GBHC and Permethrin at the end of 3rd week i.e. the cost incurred to treat one case successfully with ivermectin is INR 24/- which is less than that with permethrin (INR 72/-) and GBHC (INR 32/-). However a single application of permethrin is more efficacious in relieving itch at the end of 1st week than other two drugs, and supported by the study done by **Meenakshi et al** where ivermectin is more cost-effective than GBHC and permethrin.[6].

Narendra P Bachewar et al conducted a study comparing cost-effectiveness, efficacy and safety, It was found that Benzyl benzoate and ivermectin each consecutively for two weeks were most cost effective regimens giving complete cure in four weeks, while ivermectin was the fastest regimen giving the 100% efficacy in two weeks, and permethrin gave the fastest symptomatic relief.[13]. This study supports our finding that ivermectin was more cost-effective and permethrin was effective in the improvement of itch.

Sunita B Chhaiya et al concluded that topical permethrin is more cost effective than oral ivermectin in treatment of uncomplicated scabies, where they used an antihistaminic along with the two antiscabietic drugs in

which the ivermectin group patients needed more antihistaminic when compared with permethrin group. Although permethrin 5% is priced higher compared to tab. ivermectin, the additional cost of antihistaminic and transport was less due to earlier response with permethrin. As tab. ivermectin had lower cure rate at the first visit compared to other two treatments, the number of visits increased and that increased the cost of therapy of tab. Ivermectin.[12].

However in our study, the ivermectin is more cost-effective in curing the scabies and the patients are advised not to take any other medications during the study period and also were not prescribed any antihistaminics.

Elgart ML et al conducted a risk benefit analysis and have shown that oral ivermectin 200 micrograms/kg is extremely effective. Oral administration eliminates the need to be certain that medication has been applied properly. Toxicity has been very limited.[17].

This study supported our finding that oral ivermectin is more cost-effective in the treatment of scabies, no adverse effects observed.

Dey S et al in their safety reporting study on 120 patients found that a total 4 ADRs were identified in 16 patients. In permethrin group, 10% patients, in ivermectin group, 20% patients had ADRs, in lindane group, 6.67% patients & in permethrin + ivermectin group, 16.67% patients developed adverse reactions during treatment. In our study no ADRs were reported with the study drugs.[18].

Guzzo CA et al found that the patients who were treated with ivermectin do not show any serious adverse effects. Ivermectin is generally well tolerated with no indication of associated CNS toxicity for doses up to 10 times the FDA approved dose of 200µg/kg. But in our study the dose of ivermectin given was only 200µg/kg as advised by FDA and no adverse effects were observed with the study drugs.[19].

Chouela EN et al compared the therapeutic efficacy and safety of ivermectin and lindane for the treatment of human scabies. Adverse effects were mild and transient for both treatments. The group treated with lindane, however, had a higher rate of headaches (6 patients vs 1 patient treated with ivermectin) whereas the group treated with ivermectin had hypotension (1 patient), abdominal pain (1 patient), and vomiting (1 patient). Laboratory test results revealed no significant difference between the 2 treatments.[22]. However in our study there were no adverse effects observed with the study drugs at all follow ups.

V. Conclusion

In the present study the patients newly diagnosed with scabies, who are attending dermatology OPD, Osmania General Hospital, were included. A total of 96 patients were randomly allocated to three groups – group 1, group 2 and group 3. Excluding the 6 dropouts who were lost to follow up, the study was continued with 90 patients.

Group 1 received topical 1% gamma benzene hexachloride

Group 2 received topical 5% permethrin

Group 3 received oral ivermectin 200µg/kg

Baseline characteristics like age, gender, and nocturnal pruritus, family history of pruritus, severity of lesions, and severity of itch of the patients were recorded and tabulated. They were followed up for 3 weeks from the time of enrollment in to the study.

The mean age among all the three treatment groups were 35.63 ± 13.88 in group 1 (GBHC), 24.56 ± 16.37 in group 2 (Permethrin), 29.93 ± 13.69 in group 3 (Ivermectin) in this study. The mean age of all patients in this study is 30 ± 15.2.

There is a 100% nocturnal pruritus in all the three treatment groups.

In group 1 the proportion of the patients with family history of pruritus is 70 %,

In group 2 the proportion of the patients with family history of pruritus is 76.6 %

In group 3 the proportion of the patients with family history of pruritus is 80 %.

Before the treatment, the patients were graded using

- Clinical grading score - mild, moderate and severe.
- Itch Grading Score - mild, moderate, severe and very severe.

After the treatment the improvement is graded as

- Mild = CGS (grade 2 or 3) + IGS (grade 3 or 4),
- Moderate = CGS (grade 1) + IGS (grade 1 or 2),
- Good = CGS (grade 0) + IGS (grade 0).

Statistical tests – ANOVA test was used to compare the efficacy among the three treatment groups and chi-square test was used to analyze the cure rate between the three treatment groups.

In this study, there is no statistical significant difference in the improvement of clinical grading score (no. of lesions) between the three treatment groups, group 1, 2 and 3 at the each week follow up with a p-value > 0.05, as calculated by ANOVA.

In this study, at the end of 1st week there is a statistical significant difference between the three treatment groups in the improvement of the percentage of itch with a p-value < 0.05 (p = 0.006), where Permethrin group showed more improvement in itch than other two group of drugs. At the end of 2nd week and 3rd week there is no statistical significant difference in the improvement in the percentage of itch with a p-value > 0.05, as calculated by ANOVA.

In this study, there is no statistical significant difference in the overall cure rate at each week follow up of the patients of the three treatment groups with p-value > 0.05, as calculated by chi-square test.

In this study, the cost incurred to treat one case successfully is less with Ivermectin (INR 24/-) as compared to GBHC (INR 34/-) and permethrin (INR 72/-). So ivermectin is more cost-effective than the other two drugs.

In this study, it has been found that Ivermectin is more cost-effective than GBHC and Permethrin in curing scabietic skin lesions. But the rate of decreasing pruritus is better with Permethrin may be due to its rapid onset of action. At the end of 3rd week all the three treatment modalities showed improvement in both clinical grading score and itch grading score with no significant difference. (p> 0.05) with more efficacy and cost-effectiveness with Ivermectin.

Two cases from GBHC group and one case from permethrin group had treatment failures with persistence of lesions and itch. GBHC failed cases were re-treated with permethrin and Permethrin failed patients are given oral ivermectin in combination with topical permethrin.

During the study period there were no adverse drug reactions were reported with the study drugs.

From the above observations, the study suggests that oral ivermectin is more cost-effective treatment with equal efficacy and safety profile when compared to other antiscabietic drugs topical GBHC and topical permethrin. As permethrin remains the standard treatment for scabies due to its rapid onset of action on itch, but due to its higher cost it may not be affordable by the poor patients. Further studies are needed to place oral ivermectin as a first line treatment for scabies.

Strengths of the study:

- Newly diagnosed scabies patients were included in the present study.
- The patients were randomly allocated to the three treatment groups (topical GBHC, topical permethrin and oral ivermectin) i.e. equal distribution of severity among all the three treatment groups.
- Sample size is adequate.

Limitations of the study:

- In the present study, blinding was not done because not all the three groups received only topical treatment, as one group were prescribed oral treatment
- Microscopy to detect the mite from skin scrappings was not done.
- In this study, only the patients with mild, moderate and severe scabies were taken and the patients with crusted scabies and Norwegian scabies were not included.

References

- [1]. Alexander, JO. Scabies. Arthropods and human skin. Berlin: Springer-Verlag, 1984:227–9.
- [2]. Downs AM, Harvey I, Kennedy CT. The epidemiology of head lice and scabies in the UK. *Epidemiology and Infection* 1999;122(3):471–7.
- [3]. Interventions for treating scabies (Review); The Cochrane Library 2010, Issue 10.
- [4]. Burns DA. Diseases Caused by Arthropods and Other Noxious Animals. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. *Textbook of Dermatology*. Wiley-Blackwell; 2010;38.36-38.45.
- [5]. Taplin D, Rivera A, Walker JG, Roth WI, Reno D, Meinking R. A comparative trial of three treatment schedule for eradication of scabies. *J Am Acad Dermatol* 1983;9:550-4.
- [6]. Meenakshi M, Sadhna K, Neeraj S, Deepak V, Renu p. An open label, randomized, comparative study of antiscabietic drugs permethrin, gamma benzene hexachloride and ivermectin in patients of un-complicated scabies. *Int J Pharmacol and ClinSci* 2014;3:15-21.
- [7]. Turner MJ, Schaeffer JM. Mode of action of ivermectin. In: Campbell WC, editor. *Ivermectin and Abamectin*, New York: Springer Verlag. 1989;73-88.
- [8]. Dent JA, Davis MW, Avery L. avr-15 encodes a chloride channel subunit that mediates inhibitory glutametric neuro transmission and ivermectin sensitivity in *Caenorhabditis elegans*. *EMBO J* 1997;16:5867-79.
- [9]. Burkhart CN, Burkhart CG. Ivermectin: a few caveats are warranted before initiating therapy for scabies. *Arch Dermatol* 1999;135:1549-50.
- [10]. Chhaiya SB, Mehta DS, Kataria BC. Ivermectin: pharmacology and therapeutic applications. *Int J Basic Clin Pharmacol*. (2012), [cited October 06, 2016]; 1(3): 132-139. doi:10.5455/2319-2003.ijbcp002712.
- [11]. Campbell WC. Ivermectin, an antiparasitic agent. *Med Res Rev* 1993;13:61-79.
- [12]. Chhaiya SB, Patel VJ, Dave JN, Mehta DS, Shah HA. Comparative efficacy and safety of topical permethrin, and oral ivermectin in patients of uncomplicated scabies. *Indian J DermatolVenereolLeprol* 2012;78:605-10.
- [13]. Bachewar NP, Thawani VR, Mali SN, Gharpure KJ, Shingade VP, Dakhale GN. Comparison of safety, efficacy, and cost effectiveness of benzyl benzoate, permethrin, and ivermectin in patients of scabies. *Indian J Pharmacol* 2009;41:9-14.

- [14]. Zargari O, Golchai J, Sobhani A, Dehpour AR, Sadr-Ashkevari S, Alizadeh N, et al. Comparison of the efficacy of topical 1% lindane v/s 5% permethrin in scabies: A randomized, double-blind study. *Indian J Dermatol Venerol Leprol* 2006;72:33-6.
- [15]. Manjhi PK, Sinha RI, Kumar M, Sinha KI. Comparative Study of Efficacy of Oral Ivermectin Versus Some Topical Antiscabies Drugs in the Treatment of Scabies. *Journal of Clinical and Diagnostic Research: JCDR*. 2014;8(9):HC01-HC04. doi:10.7860/JCDR/2014/9092.487.
- [16]. Mohebbipouret al Comparison of ivermectin vs. lindanelotion *Acta Dermatovenerologica Croatica* 2012;20(4):251-255.
- [17]. Elgart ML. A risk benefit assessment of agents used in the treatment of scabies. *Drug Safety* 1996;14:386-93.
- [18]. Dey S, Sayedda K and Ahmed QS safety reporting study of antiscabietic drugs in a tertiary care teaching hospital www.wjpr.net Vol 4, Issue 07, 2015.
- [19]. Guzzo CA, Furtek CI, Porras AG, Chen C, Tipping R, Clineschmidt CM, et al. Safety, tolerability and pharmacokinetics of escalating high doses of ivermectin in healthy adult subjects. *J Clin Pharmacol* 2002;42: 1122-33.
- [20]. Chouela EN, Abeldano AM, Pellerano G, Forgia ML, Papale RM, and Garsd A, et al. Equivalent Therapeutic Efficacy and Safety of Ivermectin and Lindane in the Treatment of Human Scabies. *Arch Dermatol* 1999;135:651-5.