



## Original Research Article

## A prospective and comparative study of efficacy of topical ivermectin to other scabidicidal agents in Tertiary care center in South India

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## ABSTRACT

**Introduction:** Scabies has been a major health problem in many countries worldwide because of its very high prevalence. The estimated prevalence varies from 0.2 to 71%. Nearly hundred million people are affected worldwide. Scabies remains a major problem in terms of its contagious nature and the secondary infections which occur as a result of the disease.

**Aims:** To compare the efficacy of Topical Ivermectin and other scabidicidal agents. To assess the improvement in severity of pruritus and severity of lesions.

**Materials and Methods:** This was an prospective and comparative study conducted in dermatology OPD of Madras Medical College, a tertiary care centre in south India between Oct ' 2015 and Aug' 2016. About 90 clinically diagnosed Scabies cases were randomly segregated into three factions [Group G (GBHC) = 30 cases of scabies treated with 1% GBHC lotion, Group P (Permethrin) = 30 cases of scabies treated with 5% Permethrin cream and Group I (Ivermectin) = 30 cases of scabies treated with 0.5% Ivermectin cream. Patients response to treatment was followed up with severity of pruritus score and severity of lesions score at baseline, third and sixth week of treatment. Based on the assessment of these scores, the response to treatment was categorized into good, moderate and poor. Data was compiled and analyzed with the help of Statistical Package for Social Science (SPSS).

**Results:** Mean age of the study population was 27.66 years. Forty seven subjects were males (52.2%) and forty three subjects were females (47.8%). In Group I (Ivermectin) , 86.6%(26 out of 30 cases) had good response to treatment when compared to Group P (Permethrin) 36.7% (11 out of 30 cases) and Group G (GBHC) 10%(3 out of 30 cases). Group I (Ivermectin) compared favorably to the other two drugs with nearly more than three fourth of the cases having significant improvement at an earlier stage while Group P (Permethrin) showed better response after twice application when compared to Group G (GBHC).

**Conclusions:** From this study, it can be concluded that topical 0.5% Ivermectin can be considered as the first line of treatment modality for scabies among other available agents as it causes earlier and maximum therapeutic response. This study further emphasizes the need for newer effective drugs for treatment of scabies.

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### 1. Introduction

Scabies has been a major health problem in many countries worldwide because of its very high prevalence. The estimated prevalence varies from 0.2 to 71 %.<sup>1</sup> Nearly hundred million people are affected worldwide. It affects people of all races and social classes.<sup>2</sup> It spreads rapidly

in crowded conditions.<sup>2</sup> Institutions like nursing homes, prisons and extended care facilities are often sites for outbreaks of scabies. It is a common, intensely pruritic dermatosis, caused by the mite *Sarcoptes scabie* Materials and methods

This prospective and comparative study included 90 cases that attended the dermatology OPD of Madras Medical College, a tertiary care centre in south India between Oct' 2015 and Aug' 2016. The protocol of the

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study was approved by the Institutional ethical committee before commencing the study. Informed written consent was obtained from all the patients before inclusion into the study. The Inclusion criteria for the study were 1. Patients of above 5 years and below 60 years of age 2. Patients of both sexes 3. Patients willing for topical therapy 4. Primary case of scabies 5. Patients willing for follow-up in the third and sixth week. The exclusion criteria were 1. Children below 5 years and elderly patients more than 60 years 2. Pregnant and lactating women 3. Patients who were not willing to come for follow-up 4. Any serious systemic illness 5. Prior use of topical or systemic scabicide in last 4 weeks 6. Patients on radiotherapy, steroids or other immunosuppressive drugs for any systemic or cutaneous indication 7. Hypersensitivity to permethrin or ivermectin. All patients were explained about the disease, benefits and possible side effects of treatment. Informed written consent was obtained from all patients before initiation of treatment. Detailed case history of each patient with reference to the duration of itching, worsening during night, similar illness in family members or inmates was noted. Clinical features like classical site of involvement, morphology of lesions, and other associated systemic and cutaneous disorders were noted. Thorough clinical examination of classical sites with magnifying lens, burrow ink test or examination after applying mineral oil application was done. The diagnosis was made after detailed history and clinical examination. In doubtful cases, demonstration of scabies mite, eggs or faeces was done by scraping from burrows or finger nails. The 90 clinically diagnosed Scabies cases were randomly segregated into three factions [Group G (GBHC) = 30 cases of scabies treated with 1% GBHC lotion, Group P (Permethrin) = 30 cases of scabies treated with 5% Permethrin cream and Group I (Ivermectin) = 30 cases of scabies treated with 0.5% Ivermectin cream.

Patients response to treatment was followed up with severity of pruritus score and severity of lesions score at second, third and sixth week of treatment. Severity of pruritus was evaluated by Visual Analogues Scale (VAS). VAS was considered as a 10 cm line, in which point 0 (zero) refers to existence of no pruritus and point 10 refers to the most severe pruritus. According to this scale, we scored pruritus of the patients as a) Point 1 to 3 - Mild pruritus b) Point 4 to 6 - Moderate pruritus c) Point 7 to 10 - Severe pruritus. Severity of the disease is measured according to the number of lesions present. It can be graded as a) Mild - less than or equal to 10 lesions b) Moderate - 11-49 lesions c) Severe - more than or equal to 50 lesions or crusted. Based on the assessment of these scores, the response to treatment was categorized into a) Good Responders - Complete resolution of lesions b) Moderate Responders - Patients post treatment, >50% improvement in pruritus and severity of lesions score and c) Poor Responders - Patients post treatment improvement less than or equal to 50%.

Cases were followed up for a period of two more months to look for relapse in the patients. In patients who had relapsed, demonstration of mites was done to confirm the diagnosis. Data was compiled and analyzed with the help of Statistical Package for Social Science (SPSS).

## 2. Results

Ninety cases from the outpatient department of age group above 5 years and below 60 years of age, diagnosed clinically as scabies and not undergone any treatment prior were enlisted in the study. The mean age group of the study population was 27.66 years. Of these 90 cases, 38(42.2%) were male sex, 34(37.8%) were female sex and 18(20.0%) were children. Overall significance of treatment groups was assessed by using Friedman test to find out the p value and chi square value. Post hoc analysis was done with Wilcoxon Signed Rank tests to determine which group had significant improvement. Using Friedman test, the severity score for pruritus of the three groups at baseline were compared and the analysis revealed Chi square value of 8.083 at degree of freedom of 2 and p value of .018 which was insignificant. Table 1 At baseline the comparison of severity scores for pruritus using Wilcoxon signed rank test and the p values obtained for pruritus were insignificant. The severity score for lesions of 3 groups at the baseline was compared using Friedman test and it revealed Chi square value of 2.526 at degree of freedom 2 and there was no significant difference in the severity scores (0.283). Table 2 At baseline the comparison of severity scores for lesions using Wilcoxon signed rank test and the p values obtained for lesions were insignificant.

At the time of first follow up at the end of 3 weeks after completion of two applications of scabidical agents, improvement in terms of severity of pruritus and severity of lesions in each group were again reassessed to find out the effects of the drug. The pruritus severity score of the three groups were compared using Friedman test and the analysis revealed Chi square value of 51.185 at degree of freedom of 2. p value being less than 0.001 revealed significant difference in pruritus severity scores in the three groups. To find out which group had caused significant improvement in severity of pruritus - Post hoc analysis with Wilcoxon signed-rank tests was conducted with a Bonferroni correction applied, resulting in a significance level set at  $p < 0.017$ . Median (IQR) perceived effect levels for Group G, Group P and Group I were 5, 4 and 1 respectively. There were no significant differences between Group P and Group G lesions score trials ( $Z = -1.808$ ,  $p = 0.071$ ). However, there was a statistically significant reduction in pruritus severity in the Group I vs Group G ( $Z = -4.829$ ,  $p = <0.001$ ) and Group I vs Group P ( $Z = -4.821$ ,  $p = <0.001$ ). Table 3

The lesions severity score of the three groups were compared using Friedman test. Statistical analysis revealed

Chi square value of 43.948 at degree of freedom of 2.  $p$  value being less than 0.001 revealed significant difference in lesions severity scores in the three groups. To assess which group had caused statistically significant improvement in severity of lesions - Post hoc analysis with Wilcoxon signed-rank tests was conducted after applying Bonferroni correction, which resulted in a significance level set at  $p < 0.017$ . Median (IQR) perceived effect levels for the Group G, Group P and Group I were 12.5, 12.0 and 1.5 respectively. Group P and Group G lesions score revealed no significant differences between these groups ( $Z = -1.893$ ,  $p = 0.058$ ). However, there was a statistically significant reduction in lesions severity in the Group I vs Group G ( $Z = -4.790$ ,  $p = <0.001$ ) and Group I vs Group P ( $Z = -4.551$ ,  $p = <0.001$ ). Table 4

At the time of second follow up in the sixth week, amelioration in terms of severity of pruritus and severity of lesions in each group were reassessed again to find out the effects of the drug. The pruritus severity score of the three groups were compared using Friedman test and the analysis revealed Chi square value of 52.541 at degree of freedom of 2.  $p$  value being less than 0.001 revealed significant difference in pruritus severity scores in the three groups. To determine which drug had caused significant improvement in severity of pruritus - Post hoc analysis with Wilcoxon signed-rank tests was conducted after applying Bonferroni correction, resulting in a significance level set at  $p < 0.017$ . Median (IQR) perceived effect levels for the Group G, Group P and Group I were 3, 1 and 0 respectively. There were statistical significant differences between Group P and Group G lesions score ( $Z = -4.463$ ,  $p < 0.001$ ). There was a statistically significant reduction in pruritus severity in the Group I vs Group G ( $Z = -4.463$ ,  $p = <0.001$ ) and Group I vs Group P ( $Z = -4.758$ ,  $p < 0.001$ ). Table 5 The lesions severity score of the three groups were compared using Friedman test. Statistical analysis revealed Chi square value of 46.137 at degree of freedom of 2.  $p$  value being less than 0.001 revealed significant difference in lesions severity scores in the three groups. To assess which group had caused statistically significant improvement in severity of lesions - Post hoc analysis with Wilcoxon signed-rank tests was conducted with Bonferroni correction applied, which resulted in a significance level set at  $p < 0.017$ . Median (IQR) perceived effect levels for the Group G, Group P and Group I were 6, 2 and 0 respectively. Group P and Group G lesions score trials revealed significant differences between these groups ( $Z = -4.098$ ,  $p = 0.058$ ). However, there was a statistically significant reduction in lesions severity in the Group I vs Group G trial ( $Z = -4.634$ ,  $p = <0.001$ ) and Group I vs Group P trial ( $Z = -4.026$ ,  $p = <0.001$ ) Table 6

On comparing the severity of pruritus for all the 3 groups on regular follow up in group G (GBHC), there was 20% reduction in the severity score for pruritus at the time of second application. In Group P also there was 20%

reduction in the severity score for pruritus during second application. Whereas in Group I there was 66.1% reduction in the score at time of second application of medication. Table 7 The mean Severity of pruritus score across all the treatment groups when compared showed that, patients treated with Ivermectin had the fastest and the maximal response. Both the initial response and the end point was better in Group I patients. Second best response was seen in Group P. Table 8 The average of Severity of lesions score across all the treatment groups when compared showed that, patients treated with Ivermectin had the fastest response. But later on all the drugs had similar response at the sixth week follow up. Table 9

The response to study groups on treatment revealed that more than 86% of patients treated with Ivermectin had good response to treatment while only 36.7% of those treated with permethrin and 3% of those treated with GBHC had good response to treatment. Poor response was seen in 33.3% of GBHC patients compared to the 0% in patients receiving Permethrin and Ivermectin. Table 10 No side effects was observed in all the study groups.

Out of the 90 patients studied, there was a relapse in 7(7.8%) of patients. Of the 7 relapsed patients, 5 belonged to Group G (GBHC) and 2 patients belonged to Group P (Permethrin). There was no relapse in Group I (Ivermectin). Treatment group is significantly associated with relapse. In Group P and Group G, significant association with relapse and treatment group noted with degree of freedom being 2 and at  $p$  value of 0.053. On using chi square test for assessing the treatment response, It was found that 86.6% good response was seen in Ivermectin group compared to 36.7% response in Permethrin group and 10% in GBHC group at the time of second application. This is statistically significant with chi square value of 64 and at  $p$  value of  $<0.001$  and degree of freedom being 2.

### 3. Discussion

This prospective, observational and comparative study was conducted among 90 clinically diagnosed patients with Scabies with a view to compare the efficacy of GBHC, Permethrin and Ivermectin as modalities of treatment. The age group of 90 cases ranged from 8 to 52 years. Mean age of the study population was 27.66 years and standard deviation 13.213 years. Forty seven cases were males (52.2%) and forty three cases were females (47.8%). The 90 cases in the study were divided into three groups of 30 cases each and started on respective treatment regimen. In GBHC group, there were 16 male cases and 14 female cases. In Permethrin group, there were 15 male cases and 15 female cases. In Ivermectin group, there were 16 male cases and 14 female cases. The treatment response was analysed in all the treatment groups based on reduction in the severity of pruritus score and severity of Lesions score. The response was then graded as good, moderate and poor.

**Table 1:** Comparison of pruritus score at baseline (n=90)

| GROUP   | G (n=30)          | P (n=30)          | I (n=30)          |
|---|-------------------|-------------------|-------------------|
| G(n=30)                                       | -NA-              | -1.225 ( P 0.209) | -1.852 ( P 0.064) |
| P(n=30)                                       | -1.225 ( P 0.209) | -NA-              | -0.729 ( P 0.429) |
| I (n=30)                                      | -1.852 ( P 0.064) | -0.729 ( P 0.429) | -NA-              |
| Chi square value : 8.083 degree of freedom: 2 |                   |                   |                   |

**Table 2:** Comparison of lesion score at baseline (n=90)

| Group   | G (n=30)          | P (n=30)          | I (n=30)          |
|---|-------------------|-------------------|-------------------|
| G (n=30)                                      | -NA-              | -0.729 ( P 0.466) | -2.189 ( P 0.029) |
| P (n=30)                                      | -0.729 ( P 0.466) | -NA-              | -0.809 ( P 0.418) |
| I (n=30)                                      | -2.189 ( P 0.029) | -0.809 ( P 0.418) | -NA-              |
| Chi square value : 2.526 degree of freedom: 2 |                   |                   |                   |

**Table 3:** Comparison of pruritus score at third week (n =90)

| GROUP  | G (n=30)           | P (n=30)           | I (n=30)           |
|--|--------------------|--------------------|--------------------|
| G (n=30)                                       | -NA-               | -1.808 ( P 0.071)  | -4.829 ( P <0.001) |
| P (n=30)                                       | -1.808 ( P 0.071)  | -NA-               | -4.821 ( P <0.001) |
| I (n=30)                                       | -4.829 ( P <0.001) | -4.821 ( P <0.001) | -NA-               |
| Chi square value : 51.185 degree of freedom: 2 |                    |                    |                    |

**Table 4:** Comparison of lesion score at third week (n =90)

| GROUP  | G (n=30)           | P (n=30)           | I (n=30)           |
|--|--------------------|--------------------|--------------------|
| G (n=30)                                       | -NA-               | -1.893 ( P 0.058)  | -4.790 ( P <0.001) |
| P (n=30)                                       | -1.893 ( P 0.058)  | -NA-               | -4.551 ( P <0.001) |
| I (n=30)                                       | -4.790 ( P <0.001) | -4.551 ( P <0.001) | -NA-               |
| Chi square value : 43.948 degree of freedom: 2 |                    |                    |                    |

**Table 5:** Comparison of pruritus score at sixth week (n =90)

| Group  | G (n=30)           | P (n=30)           | I (n=30)           |
|--|--------------------|--------------------|--------------------|
| G(n=30)  | -NA-               | -4.463 ( P <0.001) | -4.758 ( P <0.001) |
| P(n=30)  | -4.463 ( P <0.001) | -NA-               | -4.667 ( P <0.001) |
| I(n=30)  | -4.758 ( P <0.001) | -4.667 ( P <0.001) | -NA-               |
| Chi square value : 52.541 degree of freedom: 2 |                    |                    |                    |

**Table 6:** Comparison of lesion score at sixth week (n =90)

| Group  | G (n=30)          | P (n=30)          | I (n=30)          |
|--|-------------------|-------------------|-------------------|
| G(n=30)  | -NA-              | -4.098( P <0.001) | -4.634( P <0.001) |
| P(n=30)  | -4.098( P <0.001) | -NA-              | -4.026( P <0.001) |
| I(n=30)  | -4.634( P <0.001) | -4.026( P <0.001) | -NA-              |
| Chi square value : 46.137 degree of freedom: 2 |                   |                   |                   |

**Table 7:** Comparison of severity of pruritus (n =90)

| Group    | At Presentation | Second Week | Third Week | Sixth Week |
|----------|-----------------|-------------|------------|------------|
| G (n=30) | 86.7%           | 66.7%       | 10%        | 0%         |
| P (n=30) | 90.0%           | 70%         | 0%         | 0%         |
| I (n=30) | 86.7%           | 20.6%       | 0%         | 0%         |

**Table 8:** Comparison of average of pruritus in each group at subsequent visits (n =90)

| Group   | At Presentation | Second Week | Third Week | Sixth Week |
|---------|-----------------|-------------|------------|------------|
| G(n=30) | 10              | 9           | 7          | 5          |
| P(n=30) | 10              | 9           | 6          | 2          |
| I(n=30) | 10              | 4           | 1          | 0          |

**Table 9:** Comparison of average of lesions in each group at subsequent visits (n =90)

| Group   | At Presentation | Second Week | Third Week | Sixth Week |
|---------|-----------------|-------------|------------|------------|
| G(n=30) | 56              | 45          | 3          | 0          |
| P(n=30) | 54              | 35          | 2          | 0          |
| I(n=30) | 56              | 25          | 0          | 0          |

**Table 10:** Response to treatment in study groups (n =90)

| Group   | MildNo. of patients (%) | ModerateNo. of patients (%) | GoodNo. of patients (%) |
|---------|-------------------------|-----------------------------|-------------------------|
| G(n=30) | 10(33.3%)               | 17(56.7%)                   | 3(10.0%)                |
| P(n=30) | 0                       | 19(63.3%)                   | 11(36.7%)               |
| I(n=30) | 0                       | 4(13.3%)                    | 26(86.6%)               |

Among the thirty cases treated with GBHC, three cases (10%) had good response to treatment, with seventeen cases (56.7%) showing moderate response and ten cases (33.3%) showed poor response to treatment. Of the thirty cases managed with permethrin, eleven cases (36.7%) patients showed good response to treatment. Nineteen cases (63.3%) showed moderate response to treatment with permethrin. In cases treated with Ivermectin group, twenty six cases (86.6%) showed good response to treatment whereas only four cases (13.3%) showed moderate response to treatment. Ivermectin compared favourably to the other two drugs with nearly more than three fourths of the cases having significant symptomatic improvement and improvement in lesions at an earlier stage. While Permethrin group had better response after twice application of medicine when compared to GBHC group. Age and sex seemed to have no effect on the response to treatment, with cases across all age groups showing same pattern of response in all the three treatment groups.

On analysing the severity of pruritus and severity of lesions scores, the Ivermectin group cases showed the maximal reduction in severity of pruritus and severity of lesions score between baseline and second application and at third week follow up. The value at second week after first application of medicine was significant with a drop of more than 86% seen in cases. Permethrin group cases also had a higher reduction in Severity of pruritus score and severity of lesions score soon after completion of second application of medicine. At the time of third week follow up after second application of medicine, cases showed more than 90% improvement in symptoms and disease. In the GBHC group, the initial response is lower than that of Ivermectin and Permethrin with decrease in only 20% of lesions at the time of second application of medicine. While at the time of third week follow up, there was nearly 76.7% improvement in skin lesions. The end points are comparable in each response group separately. Ivermectin group had earlier improvement in symptoms and cutaneous signs with nearly 86.7% reduction in severity of pruritus score and 87.8% reduction in severity of lesions score soon after a week of

first application. In permethrin group and GBHC group, the initial response was 20% reduction in the severity of pruritus and lesions score at the time of second week follow up after first application, whereas at the time of third week follow up after second application of medicine, Permethrin group had 70% reduction in severity of pruritus and lesions score while GBHC group had only 56.7% improvement of severity of pruritus and lesions scores.

None of these cases surprisingly showed any signs of adverse effects. Out of the 90 cases studied, there was a relapse in 7(7.8%). Out of the 7 relapsed cases, 5 belonged to Group A (GBHC) and 2 cases belonged to Group B (Permethrin). There was no relapse in group C (Ivermectin). In Goldust et al<sup>11</sup> study, it was shown that topical ivermectin was more effective than Crotamiton 10% cream when used twice over a period of four weeks which correlates with our study showing much better response when compared to other scabicial agents in our treatment groups. In 1986, Taplin et al<sup>12</sup> showed a cure rate of 91% for permethrin in comparison with 65% for lindane in treating scabies at 4-week post-treatment. In another trial, Schultz et al<sup>13</sup> reported cure rates of 91% and 86.3% with permethrin and lindane respectively. These two studies correlates with our studies as in our study permethrin has shown cure rate of more than 90%.

Scabies is a common cutaneous infestation affecting the population of any age but more common in young individuals.<sup>14</sup> It is a distressing disease encountered frequently in clinical practice. The current mainstay of therapy is the use of topical permethrin and oral ivermectin along with anti-histamines.<sup>15</sup> However, topical ivermectin is a newer drug which can be used in scabies patients.<sup>16</sup> In our study we have compared the efficacy of GBHC, Permethrin and Ivermectin in the treatment of Scabies. The following conclusions were reached. Young individuals were the most commonly involved group. Children and young individuals in the age group of 16-25 was the susceptible age group. There was no significant difference gender wise. This is in accordance with other Indian studies regarding the epidemiology of the disease. In the Ivermectin group, all

