

# An Interventional Study to Evaluate the Efficacy of Topical Ivermectin in the Management of Uncomplicated Scabies

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## ABSTRACT

**Introduction:** Scabies is a common itching dermatoses caused by *Sarcoptes scabiei*. It presents with scabies rash and nocturnal itching. Though oral ivermectin has been found to be a safe and effective alternative to other scabicides, there is very little data on topical ivermectin preparations in management of uncomplicated scabies. So present study was conducted to evaluate the efficacy of topical ivermectin formulation in the management of human scabies.

**Material and Methods:** Fifty patients of uncomplicated scabies were enrolled in an open-labelled prospective interventional study and were prescribed 0.5% topical ivermectin cream, two applications, one week apart. Scabies was categorized as mild (<10 lesions), moderate (11-49 lesions) or severe scabies (>50 lesions). Pruritus severity was assessed on the Visual Analogue Scale as mild (1-3cm), moderate (4-6cm) or severe (7-10cm). The patients were examined at baseline and followed up at the end of 1<sup>st</sup>, 2<sup>nd</sup> and 4<sup>th</sup> week and scabies severity and pruritus severity was noted at each visit. Wilcoxon-Signed Rank Test was applied as test of significance. P value < 0.05 was cut off.

**Results:** Majority of the patients (76%) had moderate to severe scabies and pruritus was severe in 36% patients at baseline. After one application, there was decrease in scabies severity (P<0.001) and pruritus severity (P<0.001), but only one patient was cured. After the second application, 98% patients had no scabietic lesions (P<0.001) while 80% were pruritus free (P<0.001).

**Conclusions:** Topical ivermectin cream (0.5%), two applications, one week apart is effective in treatment of uncomplicated scabies.

**Keywords:** Scabies, Topical Ivermectin, Scabies Severity, Visual Analogue Scale

## INTRODUCTION

Scabies is a contagious skin infection caused by the mite *Sarcoptes scabiei* and is one of the most common causes of itching dermatoses.<sup>1</sup> Almost 300 million people worldwide are affected annually and World Health Organization (WHO) in 2013 listed scabies as a neglected tropical disease.<sup>2</sup> Though all ages, genders and ethnicities are susceptible to scabies, it is frequently seen in crowded living conditions, which is common in resource-poor countries.<sup>3</sup> Outbreaks of scabies are frequently reported from institutional environments such as hospitals, nursing homes, old-age homes, prisons and refugee camps.<sup>4</sup>

The classical features are presence of a “scabies rash” and “intense itching” which is worse at night. The rash begins as an erythematous papule and can progress to vesicles or

pustules. The web spaces between fingers, flexor surface of wrist and elbow, axilla, female breasts, waist band and groin are commonly affected sites.<sup>5</sup> Currently there are few safe and effective scabicides with variation in treatment modalities between clinical settings. Oral ivermectin has been found to be as effective as 5% permethrin and better than other topical agents such as lindane, 10% crotamiton and benzyl benzoate.<sup>6-11</sup>

Recently topical route for ivermectin delivery has been introduced but topical ivermectin has been little explored in the management of scabies. Though topical ivermectin formulations are being used for management of head lice infestation since 2012 and were given approval by FDA in 2014 for use in other cutaneous ectoparasitic conditions, there is scarcity of data of their efficacy in scabies.<sup>12</sup> So present interventional study was conducted in a tertiary care hospital to evaluate the efficacy of topical ivermectin formulation in the management of human scabies.

## MATERIAL AND METHODS

An open-labelled prospective interventional study was carried over a period of one year to evaluate the efficacy of topical ivermectin in the management of human scabies in the Skin Out Patient Department of a tertiary care hospital in North India. Institutional Ethical Committee clearance was taken before commencement of the study. Informed consent was obtained from all the participants. Registration was sought with Clinical Trial Registry of India with reference no: REF/2017/01/013142. Patients of 18-65 years of age, of both genders, and diagnosed with scabies based on history and clinical examination were candidates for the study. Only patients willing to report for follow up at 1<sup>st</sup>, 2<sup>nd</sup> and 4<sup>th</sup> week were included in the study. Patients with Norwegian crusted scabies, history of use of any topical or systemic acaricide in the previous four weeks, history of seizures, immunosuppressive disorders, diabetes, congestive heart failure, renal and hepatic insufficiency and pregnant and

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lactating women were excluded from the study.

A total of 50 treatment-naive patients of scabies were included in the study and prescribed two applications of topical ivermectin (0.5% cream) at an interval of one week. All the patients were educated and also given an instruction leaflet in the vernacular language regarding correct application of the drug and other general measures. None of the patients were prescribed anti-histaminics at the initial visit. Only patients whose pruritus did not resolve by the end of 2<sup>nd</sup> week were prescribed oral antihistaminics. The family members were simultaneously treated with 5% topical permethrin cream.

For each patient, the number of scabietic lesions were counted and recorded at baseline and each follow-up and clinical grading score was given as:<sup>8</sup>

No scabies: 0 lesions

Mild scabies: <10 lesions

Moderate scabies: 11-49 lesions

Severe scabies: >50 lesions

Severity of pruritus was evaluated by Visual Analogue Scale (VAS), which is a 10 cm line, where point 0 (zero) denotes “no pruritus” and point 10 refers to “most severe pruritus.” Patients were asked to mark the severity of pruritus experienced at baseline and subsequent follow-ups. Severity of pruritus according to the VAS scale was graded as:

Point 0 = No pruritus

Point 1-3 = Mild pruritus

Point 4-6 = Moderate pruritus

Point 7-10 = Severe pruritus

Efficacy was evaluated by disappearance of lesions and relief of symptoms. Treatment failure was defined as either lack of initial cure or appearance of new lesions.

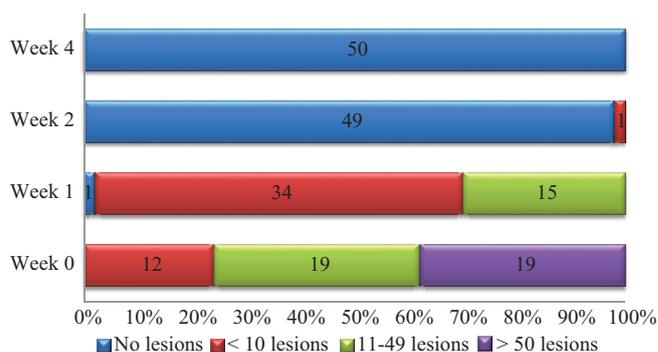
## STATISTICAL ANALYSIS

Data processing was done using Statistical Package for Social Sciences, Version 23. Wilcoxon-Signed Rank test was applied to evaluate statistically significant difference in response to treatment at each visit. P value less than 0.05 was considered as significant.

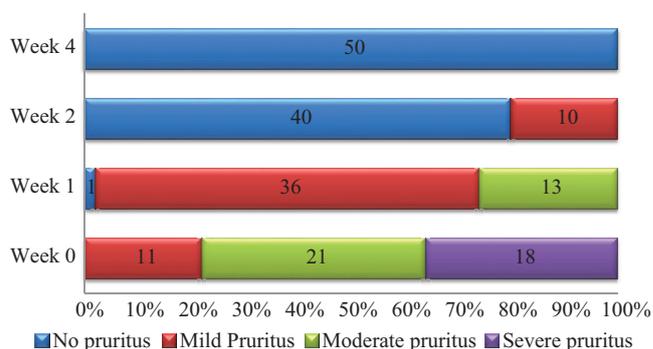
## RESULTS

The mean age of patients in our study was  $28.92 \pm 11.14$  years with a male: female ratio of 1.31 and rural: urban ratio of 1.12. As illustrated in Figure 1, of the 50 patients of scabies, 12 patients (24%) had mild scabies, 19 patients (38%) had moderate scabies and 19 patients (38%) had severe scabies. At the end of 1<sup>st</sup> week, only one patient reported with no scabietic lesions, 34 patients (68%) had mild scabies and 15 patients (30%) had moderate scabies ( $P < 0.001$ ). At the end of 2<sup>nd</sup> week, only one patient still reported with mild scabies, while 49 patients (58%) had no evidence of any lesion ( $P < 0.001$ ). This further improved by the 4<sup>th</sup> week, with no patient presenting with any scabietic lesions. (Fig 1)

Figure 2 shows that at baseline, 11 patients (22%) had mild pruritus, 21 (42%) had moderate pruritus while 18 (36%) had severe pruritus. At the end of 1<sup>st</sup> week, one patient reported that the pruritus had resolved completely while 36 patients (72%) had mild pruritus and 13 (26%) patients had



**Figure-1:** Bar diagram depicting the distribution of scabies severity in patients treated with topical ivermectin at baseline and at the end of week 1, week 2 and week 4. Wilcoxon-Signed Rank test comparing the difference in scabies severity distribution at each successive visit was highly significant. P value < 0.001.



**Figure-2:** Bar diagram depicting the pattern of pruritus severity in patients of scabies treated with topical ivermectin at baseline and at the end of week 1, week 2 and week 4. Wilcoxon-Signed Rank test comparing the difference in pruritus severity distribution at each successive visit was highly significant. P value < 0.001.

moderate pruritus. None of the patients had severe pruritus at the end of week 1. By the end of 2<sup>nd</sup> week, 40 patients (80%) had no complains of pruritus while 10 patients (20%) still reported mild pruritus which resolved by end of 4<sup>th</sup> week. The improvement in pruritus was statistically significant at each follow-up ( $P < 0.001$ ). (Fig 2)

## DISCUSSION

The whole of humanity continues to be susceptible to the acquisition of scabies, but it is the vulnerable populations like young, old, immunocompromised, war-torn and those living in resource poor countries who are at major risk. Moreover, *Sarcoptes scabiei* is notorious for its disregard for person, age, sex or race.<sup>13</sup> Ivermectin has revolutionized the treatment of scabies.<sup>12</sup> Ivermectin directly kills *Sarcoptes scabiei* by binding selectively to glutamate-chloride channels, found in nerve terminals. It also increases levels of GABA at nerve terminals, thus paralyzing the parasite and killing it. Ivermectin is well tolerated in human beings because the glutamate-gated ion channels and GABA-gated chloride channels are located in the central nervous system and ivermectin cannot cross the blood-brain barrier.<sup>14</sup> Though ivermectin is conventionally used orally in the management of human scabies, topical route for ivermectin

delivery has been introduced recently and successfully used in human lice infestation.<sup>15</sup> This study was conducted to evaluate the efficacy of topical ivermectin preparation in the management of human scabies.

Among the 50 cases of scabies, 24% patients (n=12) had less than 10 scabietic lesions and were categorized as mild scabies while 38% patients (n=19) had between 11-49 lesions and 38% patients (n=19) had more than 50 lesions. They were categorized as moderate and severe scabies respectively. At the 1<sup>st</sup> week of follow up, all the patients reported improvement in severity of scabies, but only one patient was completely cured and presented with no lesions. None of the patients in our study had severe scabies after one application of topical ivermectin 0.5% cream. Even though the cure rate at the 1<sup>st</sup> week was only 2%, there was a highly significant difference in the severity of scabies at 1<sup>st</sup> week and baseline (p value < 0.001). (Fig1) Chaiyya et al had reported a cure rate of 69.3% in the topical ivermectin group after single application at the end of 1<sup>st</sup> week.<sup>16</sup> The higher cure rate in the topical ivermectin group reported in comparison to our study could be because of varying strength of topical ivermectin. Chaiyya et al used 1% topical ivermectin lotion while we prescribed 0.5% topical ivermectin cream to our patients.

During the second follow-up after 2 weeks, the clinical cure rates escalated to 98%. Only one patient still had evidence of scabietic papules in examination, though the number of lesions was less than 10. The cure rates were significantly higher in comparison to baseline and cure rate at 1<sup>st</sup> follow-up (p value < 0.001). (Fig 1) This could be because the patients had received two applications of 0.5% cream of topical ivermectin by the 2<sup>nd</sup> week. Also repeated directions on how to use the topical medication could have resulted in correct application of the cream. By the end of 4<sup>th</sup> week, none of the patients presented with any clinical evidence of scabies. Youssef et al used 0.8% lotion of ivermectin for scabies and found that the patients were cured clinically and parasitologically within 48 hours after single application. However, itching persisted in majority of patients which required a repeat application after 1 week.<sup>17</sup> Victoria et al had used ivermectin 1% solution and reported that all the patients were cured with two applications at weekly interval.<sup>18</sup>

Though all the patients complained of pruritus as the chief presenting complain, almost 78% had moderate to severe pruritus and 22% had mild pruritus. We did not prescribe oral antihistaminic to any patient at baseline as it could compound the improvement in pruritus due to topical ivermectin. Though there was a statistically significant decline in the severity of pruritus at the end of 1<sup>st</sup> week and none of the patients complained of severe pruritus, only one patient was pruritus free. The poor improvement in our study can be explained as the treatment with topical ivermectin was still incomplete at the 1<sup>st</sup> follow up. After 2<sup>nd</sup> application of topical ivermectin, greater improvement was seen in the severity of pruritus at the 2<sup>nd</sup> follow up with 80% patients reporting "no pruritus" (P value < 0.001). Ten patients reporting mild pruritus at the end of 2<sup>nd</sup> week were prescribed oral antihistaminics. The

improvement in pruritus in our study at the 2<sup>nd</sup> week after two applications of 0.5% topical ivermectin cream was similar to results achieved by other studies with the use of 1% topical ivermectin lotion at the 1<sup>st</sup> week.<sup>16</sup>

The limitation of our study was that we did not have a second arm to compare topical ivermectin with other established treatments of scabies. Further studies are required to compare topical ivermectin with oral ivermectin and other established anti-scabicides,

## CONCLUSION

The presentation of scabies is mostly severe and itching is a cardinal and often incapacitating symptom associated with scabies. Topical preparation of ivermectin has shown great promise in the treatment of scabies.

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