

RESEARCH ARTICLE

Effectiveness of Combined Oral and Topical Ivermectin Compared to Topical Treatments in Patients with Scabies

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ABSTRACT

Background: Scabies is a common parasitic skin infestation transmitted mainly through direct skin contact. Permethrin was considered the standard treatment; however, due to increasing resistance against permethrin, recent research investigates the effect of other topical preparations like ivermectin as an alternative treatment.

Aim of the study: This study aim to evaluate the efficacy and safety of ivermectin whether its topical alone or combined with oral form of ivermectin in the same time on scabietic lesions compared to permethrin.

Patient and method: 236 patients with uncomplicated scabies participated in the study. The study population was selected and divided randomly into three groups. The first group received permethrin, the second group received topical ivermectin, and the third group received a combination of topical and oral ivermectin. Each patient received two doses one week apart. The patients were followed up for the first, second, and fourth week of treatment.

Results: At the first week, the group who received the combination of treatments has a significant decrease in both severity of itching and number of lesions, the reduction percentage is (77.6, 53.9%), respectively compared to (61.8, 55.2%) with topical ivermectin and (8.3, 19%) with permethrin. At the 4th week, 15.8% of patients in the combination treatment group reported severe itching, significantly lower than the corresponding values in the other groups.

Conclusion: The combination of topical and oral ivermectin is safe and more effective than topical ivermectin or permethrin alone. It achieves a remarkable effect in the first week.

Keywords: Combination of topical and oral ivermectin, Oral ivermectin, Permethrin, Permethrin resistance, Scabies, Topical ivermectin.

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INTRODUCTION

Scabies is a distressing dermatological problem that is common worldwide.¹ WHO reported that more than 200 million people of different ages, race, gender, and levels of social and economic status are infested with the parasite.^{2,3} In Iraq; the prevalence of scabies infestation varies from one place to another, it was 10.7 and 6.54% at Karbala and Najaf, respectively.^{4,5} While 5.5, 2.76, 1.2% at Duhok, Kirkuk and Tikrit, respectively.^{6,7} At Basrah was 3.3%.⁸

Considering the impact of the scabies infestation, many treatments were used, such as permethrin. It is widely used and effective. However, due to the frequency and intensity of this infestation, scabies mites apparently were able to develop resistance against permethrin. In addition, to the unpleasant side effects associated with its used, therefore, it was suggested

to use topical preparation of ivermectin as an alternative.^{9,10} Ivermectin is (from bacteria) that has been discovered at 1981. And it was called the wonder drug.

MATERIALS AND METHODS

There were a total of 236 patients with scabies infestation, of whom 55% were female and 45% were male; the mean age was 30 years. The study was carried out in dermatological clinics at Alsader teaching hospital in addition to private clinics. The study was explained to the patients, and they signed a research agreement with the possibility of withdrawing at any time. All patients provided written permission for the research, which was authorized by the Faculty of Medicine's ethics committee at the University of Basrah. The standards on which the inclusion of patients is based on is to be generally healthy. However, once the patient has one or more of the following,

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they will be excluded: younger children under the age of five and under 15 Kg; females who are expecting or breastfeeding, Norwegian scabies. Patients who had immunosuppression or immunity problems, history of ivermectin hypersensitivity, received a recent scabies remedy (within one month). Patients were excluded from the study if they had serious chronic conditions such as kidney or liver illness, severe asthma, or migraine. A dermatologist made the diagnosis after obtaining a thorough patient history. In addition, a thorough physical examination was performed to identify the location and nature of the lesions and to look for telltale scabies symptoms such as the evident borrow in the web, urticaria, secondary infection, and scratch marks, as well as any eczema-like lesions. A microscopic investigation was undertaken in rare situations when the diagnosis could not be confirmed via clinical examination.

Study Design

The patients were chosen randomly and allocated to three groups; the first group included 84 patients who got permethrin cream in doses of 5% for adults and 2.5% for children. Permethrin was administered topically twice, 7 days apart. The second group had 76 patients who got topical ivermectin emulsion at a dosage of 50 gm for adults and 25 gm for children. Ivermectin was administered topically twice, one week apart. The third group of 76 participants got a combination of oral and topical ivermectin (200 mg/Kg orally), which was repeated one week later. For both children and adults, the topical application dosage is the same as previously mentioned. (The combined therapy was administered twice, one week apart).

Evaluation of Patients

Patients were thoroughly examined at the diagnosis stage and their symptoms were evaluated in detail. Visual analogue scale (VAS), a scale printed on a sheet of paper ranging from 1 to 10, was used to quantify the degree of itching. Patients were instructed on how to use scale and asked to point their fingers to the area that best described their level of itching. Eventually, 3 categories resulted: mild, moderate and severe itching.¹¹ Lesion severity was determined by the number of lesions and categorized into less than 10 lesions as mild, 11 to 49 as moderate, or 50 or more as severe.¹² During the 1st, 2nd, and 4th weeks, the patient's condition, satisfaction, infestation severity, and appearance of new lesions or whether a new individual became infected were monitored. Also, document any serious adverse effects of the medications.

Changes in the VAS score (reduction of nocturnal itching or decrease in lesions number) and no more new lesions defined as a response.

At the end of the trial, patients' opinions regarding their treatments were solicited in order to evaluate their treatment satisfaction.

RESULTS

SPSS version 21 and Microsoft Excel (2013) were used to estimate descriptive and analytical statistics. There were three basic parameters were used to assess

therapeutic efficacy. one of them is itching severity, where the study started with no significant difference between the treatment groups (p -value = 0.134) at the time of diagnosis (zero time). Where 96.4, 92.1, 98.7% of the patients had severe itching with VAS score ≥ 7 in permethrin, ivermectin (topical), combined oral and topical ivermectin groups, respectively. During the first week of follow-up, the percentage of cases in each group decreases significantly, indicating that topical preparation of ivermectin alone and a combination of oral and topical ivermectin treatment were efficacious when used once in a 1-week period. In the course of the second week of treatment, 54.8% of patients on permethrin still had severe itching, compared to 30.3 and 13.2% on ivermectin and combination therapy, respectively. By the end of the study (4th week), 34.5% of the patients in the permethrin group reported severe itching, whereas only 17 and 16% of the patients in the other groups had itching. These data are presented in Table 1.

The other parameter is lesions' number. At zero time (the time of diagnosis), there was no significant difference among the three treatment groups. Oral and topical ivermectin rapidly reduced the proportion of individuals with severe scabies infestation. After one week of therapy, lesions dropped from 93.4 to 14.5%. (Figure 1). After the 4th week of therapy, the proportion of patients with severe infestations increased after a consistent decrease. Topical ivermectin reduced the number of patients with severe scabies. The initial 77.6% of patients with severe lesion infestation dropped to 50, 22.4, and 17.1% after the first, second, and fourth weeks of therapy. These two treatments reduced severe scabies infestations more than permethrin. Figure 1 shows these data.

Throughout the course of the study, participants report a range of side effects, including headaches, dizziness, and a burning or itching sensation. None of these were serious enough to call for stopping the medication.

At the first, second, and fourth weeks of follow-up, 80, 68, and 60% of patients reported irritation from permethrin. In contrast to the incidence found with permethrin, only 7.9% of patients receiving topical ivermectin alone experienced irritation during the course of treatment (p -value > 0.05). In

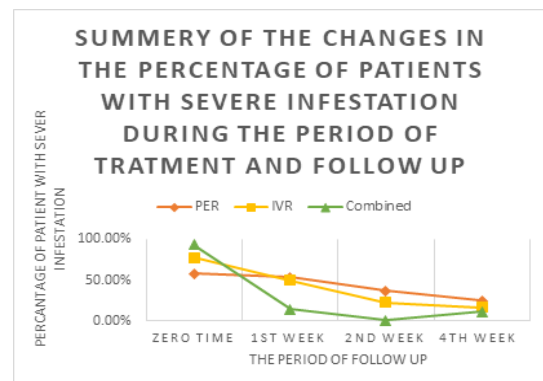


Figure 1: Summary of changes in the frequency/percentage of severe infestation. PER= permethrin, IVR= topical ivermectin, combined=topical and oral ivermectin

Table 1: The effect of different treatments on the itching severity in patients with scabies infestation

Treatment	Severe itching a visual analog score equal or more than 7			
	On diagnosis (%)	First week (%)	Second week (%)	Fourth week (%)
Permethrin	96.4	88.1	78.6	34.5
Ivermectin	92.1	30.3	30.3	17.1
Oral and topical ivermectin	98.7	21.1	13.2	15.8

the combination group, none of the patients had discomfort, and once more, this incidence differed dramatically from that previously reported (p -value >0.05) with topical ivermectin or permethrin.

Patients' Satisfaction

The patients' opinions about their preferred treatment option were recorded at the end of the study. Their evaluation was centered on the efficacy, length of the course of treatment, and side effects. Around 74 and 22% of patients who receive the dual therapy of topical and oral ivermectin expressed high satisfaction with their therapy. Just 3.9% of patients were really dissatisfied with the treatment, nevertheless. Only 22.4% were unhappy with the effect of topical ivermectin, compared to 44.7% who were extremely satisfied, 11.8% who were content, 19.7% who were unsure, and 44.7% who were not sure at all. In contrast, of the 34 patients who shared their opinions in the permethrin group, 34.1% were extremely unhappy, 21.9% were unsatisfied, and 19.5% were uncertain about the treatment. Permethrin only satisfied 4.8% of people. A substantial correlation between the type of treatment and patient's satisfaction was found through statistical research (p -value > 0.05).

DISCUSSION

Scabies infestation threatens all racial and socioeconomic backgrounds.¹³ It typically shows up in densely populated areas and places with significant humidity.⁴ Permethrin, crotamiton, and ivermectin are examples of therapy options. Each treatment has its own distinctive qualities, mode of function, expense, and method of administration. These therapies vary in adverse effects, relapse rate, the likelihood of reinfection, resistance, and effectiveness variation.

Treatment for scabies devolves due to the emergence of resistance to many of the existing anti-scabies medications. According to reports, scabies has developed a resistance to the majority of conventional medications, including lindane, and permethrin.^{14,15} Resistance may cause either a poor response to therapy or the inability to entirely destroy the parasite, resulting in new lesions. This issue can necessitate a dose, period, or frequency increase for the treatment, and this increase might be hazardous to the patients.

To the best of our knowledge, this is the second study in Iraq to examine the effectiveness of topical ivermectin; the previous trial was conducted in Baghdad.¹⁶ However, it is the first study that evaluates the combination of topical and oral ivermectin. Permethrin in the current study lowered the number of individuals experiencing severe itching to 54.8% at the

end of the second week. However the effect was less pronounced. As contrary to this, topical ivermectin reduced the severity of itching to 30% starting in the first week and even more with combination treatments. Ivermectin's quick action can be attributed to its lipophilic property, which is rapidly dispersed after ingestion.¹⁷ A further advantage of the combination therapy's early response is the significant decline in consequences related to skin infections primarily caused by *Streptococcus* or *Staphylococcus*. Counting the number of scabietic lesions, which is directly connected to the severity of the parasitic infestation, is another method used to evaluate the response to treatment. Permethrin was used in the current investigation to reduce the number of scabietic skin lesions; however, this reduction took two weeks to manifest. Permethrin and topical ivermectin both had effects that were equivalent in terms of their strength and speed of occurrence. The combination of topical and oral ivermectin, on the other hand, significantly reduced the number of skin lesions, with the added finding that this impact manifested earlier than with other single therapy regimens.

The current study's findings concur with those of earlier research conducted in Iraq. They also demonstrated that topical ivermectin worked faster than permethrin.¹⁶ 89.5% of those treated with topical ivermectin were cured at the end of the fourth week, compared to 84.2% of those treated with permethrin 2.5% cream, according to an Iranian study that demonstrated the efficiency of the drug.¹³ In a different trial conducted in Egypt, the effects of topical and oral ivermectin were examined. They were both risk-free, with 73.5 and 87.5% cure rates, respectively. The effect was astounding and became apparent within one week. To guarantee a full recovery, they advise using second dose of both therapies.¹⁸

According to the results of the current study, oral and topical ivermectin work together to treat scabies more effectively. It is customary to combine two medications with distinct modes of action; even though oral and topical ivermectin have the same mode of action, their combination showed a very wide range of efficacy. The anti-inflammatory and antioxidant properties of ivermectin¹⁹⁻²¹ may also have a palliative effect on itching.

The medications used was examined for their tolerability and safety. permethrin's main side effect was mild to moderate skin irritation, which did not result in treatment termination. It should be noted that eight patients in the permethrin groups dropped out of the research. In the topical ivermectin group, there was minimal skin discomfort and just one patient discontinued. None of the patients in the combination group dropped out of the study, and dizziness and headache were recorded in a few individuals. Total 96% of patients expressed

support for the combination as a therapy option. Whereas 76.2% of respondents were satisfied with topical ivermectin alone, just 24.3% were moderately satisfied with permethrin alone.

CONCLUSION

Oral and topical ivermectin was preferable and superior to topical permethrin in terms of high cure rates, enhanced patient compliance, promoted patient satisfaction, and fewer side effects.

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