Ivermectin for *Sarcoptes scabiei* Hyperinfestation

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**ABSTRACT**

Objectives: Crusted (Norwegian) scabies is an unusual variant of scabies caused by hyperinfestation with *Sarcoptes scabiei*. It has high morbidity, and secondary bacterial skin sepsis may result in life-threatening bacteremia. An open label study of oral ivermectin was carried out in patients with crusted scabies refractory to topical therapy.

Methods: Patients with refractory crusted scabies were prescribed oral ivermectin, one to three doses of 200 μg/kg at 14-day intervals, combined with topical scabicide and keratolytic therapy.

Results: Of the 20 patients who received ivermectin, 8 had a complete initial clinical response, a partial response was achieved in 9, and minimal improvement occurred in 3. Three doses of ivermectin were curative for 8 of 10 cases, but recurrence of scabies from presumed reinfection occurred in at least half of these.

Conclusion: The authors conclude that ivermectin is effective for crusted scabies; however, multiple doses may be required to achieve a cure, and recurrence 6 or more weeks after completing treatment is common.

Key Words: ivermectin, *Sarcoptes scabiei*, scabies


Crusted or Norwegian scabies is an unusual variant of scabies first described in a group of leprosy patients in Norway. It is caused by hyperinfestation with *Sarcoptes scabiei* and is characterized by hyperkeratosis, scaling, and crusted lesions over a wide distribution of the body. It is usually seen in association with underlying predisposing conditions, including human immunodeficiency virus (HIV), hematologic malignancy, immunosuppressive therapy, connective tissue diseases, and neurologic illness. Scabies is endemic in many remote aboriginal communities of Australia with prevalence in children up to 50%. Crusted scabies has been associated with human T-cell lymphotropic virus type I (HTLV-I) in central Australia. In remote aboriginal communities in the tropical north of the Northern Territory, HTLV-I is not endemic, and HIV has not been documented in that region. The majority of aboriginal patients with crusted scabies in these communities have no identified specific immunosuppression. Crusted scabies has a high morbidity and secondary bacterial skin sepsis may result in life-threatening bacteremia. It is highly infectious and may cause widespread outbreaks of scabies.

Therapy is usually with topical scabicides; however, success with crusted scabies is often limited. Ivermectin is a chemically modified avermectin, a class of antiparasitic agents produced by the actinomycete *Streptomyces avermitilis*. It has a broad spectrum of activity against nematodes (excluding human hookworm) and arthropod parasites. It is used widely as an antiparasitic drug in veterinary practice, including for sarcoptic mange. Ivermectin has been used in humans most extensively for onchocerciasis and more recently for strongyloidiasis.

The authors performed an open label study of 22 patients from the tropical north of the Northern Territory, with crusted scabies refractory to topical therapy, who were prescribed ivermectin for compassionate use in a protocol adapted from the regimen of Meinking et al.

**MATERIAL AND METHODS**

The diagnosis of crusted scabies was made on clinical findings plus positive skin scrapings for *S. scabiei* mites. All patients had crusted lesions that had inadequately responded to multiple topical scabicide treatments. Management in most cases involved hospitalization for at least 1 week and an intensive regimen of topical therapy with three supervised applications of permethrin 5% topical scabicide, spaced over the week, the cream being applied from the scalp down, left overnight, and washed off the following morning. On the days when permethrin was not used, keratolytic therapy with urea 10%, and lactic acid 5% cream was applied. Oral ivermectin was given on
an empty stomach at a single dose of 200 µg/kg, and in most cases subsequent doses of ivermectin were planned for day 14 and day 28. Administration of this medication, supervision of further topical therapy, and environmental control measures, such as treatment of household contacts, advice regarding washing of linen and clothes, and fumigation of the house with synthetic pyrethroid-containing insecticide, were done through the health clinic in the patient's community. Responses to treatment were judged on clinical assessment of the skin and were graded as minimal, partial, or complete. As the full effect of scabies therapy may not be evident for several weeks, a complete response was defined as normal skin 4 weeks or longer after the last dose of ivermectin. Whereas recurrence after partial response was assumed to be recrudescence of the original scabies infestation, recurrence after complete response was assumed to be reinfection. Fisher's exact test was used to compare outcomes of therapy.

**RESULTS**

The patients were aboriginal (12 male and 10 female) and between 21 and 76 years of age (mean, 42.8 y). Crusted lesions involved all four limbs and the trunk, in the majority, and skin scrapings invariably showed numerous *S. scabiei* mites. Most had documented clinical scabies for over 1 year, the longest being for 12 years. Eight patients had been admitted to hospital at least once, and one patient had been admitted 12 times for secondary sepsis. Two patients who were intended to be treated died prior to receiving ivermectin. One was a 35-year-old woman who died of polymicrobial sepsis and the other, a 51-year-old woman with a history of treated leprosy, who died following amputation of a severely infected arm. Preceding conditions included treated leprosy in two, noninsulin-dependent diabetes in three, and steroid therapy for chronic lung disease in one. There was no evidence of HIV in 14 patients tested or HTLV-I in 13 patients, with both viruses not known to be present in any of the communities involved. No underlying malignancies were detected.

A complete initial response was achieved in 8 of 20 (40%) patients, 9 of 20 (45%) had at least a partial response (3 of these possibly had a complete response, but this was not confirmed) and 3 of 20 (15%) had minimal improvement after ivermectin therapy. Four of the eight patients with a complete initial response had recurrence of scabies, occurring 6 to 40 weeks after the last ivermectin dose and usually progressing to crusted scabies. Two of these were retreated, with again a complete response, but both had further recurrence 8 and 16 weeks after ivermectin. One of these had a third treatment course, but again developed recurrent severe crusted scabies. This last patient has had a total of 10 ivermectin doses over 12 months.

Of the 25 treatment courses given to 20 patients, there was significantly better clinical response in those who received three doses of ivermectin (Table 1), but in two cases even three doses of ivermectin was not curative. One man who had a partial response after only one dose of ivermectin received a full course of three doses of ivermectin 1 year later, with complete response. No adverse effects of the drug were observed.

**DISCUSSION**

In uncomplicated scabies, single-dose ivermectin was found to be at least as effective as topical therapy. As noted by Meinking et al, reported ‘treatment failures’ may be explained by the sometimes slow resolution of skin signs after therapy or by reinfection after ivermectin tissue activity has ceased. The authors' observations of empirical therapy of crusted scabies with ivermectin support the findings of Meinking et al that single dose ivermectin may be inadequate with severe scabies hyperinfection and that further, second weekly doses are beneficial in such cases. Whether more frequent dosing or doses higher than 200 µg/kg will have better outcomes requires further study. The concomitant use of topical scabicides and keratolytics seems justified by concerns that ivermectin may not penetrate thick crusts adequately.

With one or two doses of ivermectin, a partial response was often followed by deterioration, suggesting recrudescence after failure to eradicate parasites. While three doses usually resulted in a complete clinical response, recurrent scabies commonly occurred 6 or more weeks after therapy. With the high prevalence of scabies in these communities, reinfection is not surprising. Currently, molecular typing methods for *S. scabiei* are being developed, to better define recrudescence versus reinfection following scabies therapies. Although regularly repeated or intermittent ivermectin therapy may be of benefit for individuals with recurrent crusted scabies, emphasis should be placed on coordinated entire-community interventions to break the cycles of transmission of *S. scabiei* that lead to infestation.

**Table 1. Number of Doses of Ivermectin Received and Clinical Response**

<table>
<thead>
<tr>
<th>Response</th>
<th>One Dose</th>
<th>Two Doses</th>
<th>Three Doses*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Partial</td>
<td>5</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Minimal</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

*Complete response versus minimal or partial response was significantly greater for three doses than for one or two doses of ivermectin; P = 0.005, Fisher's exact test.*
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REFERENCES