Am. J. Trop. Med. Hyg., 76(2), 2007, pp. 392–395

COMPARISON OF IVERMECTIN AND BENZYL BENZOATE LOTION FOR SCABIES IN NIGERIAN PATIENTS

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Abstract. Few studies have compared ivermectin directly with topical agents in developing countries. We compared the effectiveness of oral ivermectin (200 μg/kg) with topical 25% benzyl benzoate and monosulfiram soap in 210 subjects of age 5 to 65 years with scabies. Subjects with persistent lesions after 2 weeks received a second course of treatment. All lesions had resolved after 2 weeks in 77 of 98 (79%) subjects treated with ivermectin and in 60 of 102 (59%) subjects treated topically ($P = 0.003$). The improvement in severity score was greater in the ivermectin group than in the topical treatment group ($P < 0.001$). The overall cure rate after 4 weeks was 95% in the ivermectin group and 86% in the topical treatment group ($P = 0.04$). Compared with topical benzyl benzoate and monosulfiram in the treatment of scabies, ivermectin was at least as effective and led to more rapid improvement.

INTRODUCTION

Scabies occurs worldwide with a widespread distribution in the tropics. The highly contagious skin infection, caused by the mite *Sarcoptes scabiei* var. *hominis*, is one of the most common pruritic dermatoses.[1] Scabies is endemic in many developing countries,[2–7] usually associated with conditions of overcrowding, low socioeconomic standards, and poor hygiene.[4,6,8] Prevalence of scabies in African children can be as high as 40–80%,[9,10] although a figure of 4.7% has been reported in Nigerian school children.[7] Introduction of a single case of scabies into crowded living conditions can result in an epidemic.[11,12] Scabies causes considerable discomfort and can result in severe secondary complications such as impetigo, cellulitis, pyoderma, bacteremia, and post-streptococcal glomerulonephritis.[2,13,14] Scabies occurs in 2–4% of patients with HIV infection.[1]

Various options for the treatment of scabies exist.[1,15] Topical treatment has the disadvantages of being cumbersome, time-consuming, and associated with treatment failure caused by poor compliance, insufficient application of scabicide, inappropriate frequency or technique of application, and inadequate treatment of close contacts.[14] Because effective topical scabies treatment relies on judicious and simultaneous application of cream or lotion to prevent re-infection, accomplishing this on a community or institutional scale is difficult. Oral ivermectin is safe in humans and easy to use in individuals and families and on a large scale.[2,15–17] It has also proven useful in HIV-related scabies and after treatment failures with topical agents.[12,18–21]

Ivermectin has been used in Nigeria for onchocerciasis control,[22,23] but limited work on the use of ivermectin in scabies has been reported.[24] Although ivermectin has been demonstrated to be effective in treating scabies, few studies have compared ivermectin directly with topical agents in developing countries. We compared the effectiveness of oral ivermectin with the standard topical treatment used in Nigeria (25% benzyl benzoate lotion and monosulfiram soap).

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METHODS

Subjects of age 5 years and above, weighing more than 15 kg, presenting at the General Outpatient Department of Jos University Teaching Hospital with clinically suspected scabies were eligible for the study. Subjects were excluded for any of the following reasons: serious illness, pregnant or lactating women, or treatment of scabies within the preceding 1 month. The study was approved by the Jos University Teaching Hospital Ethical Committee. Written informed consent was obtained from adult subjects and from the parents or guardians of children.

One experienced family physician (HMS) recorded demographic and clinical data and plotted the distribution of lesions (burrows, papules, vesicles, crusts) on a body diagram. The severity of disease was recorded as mild (10 or fewer lesions), moderate (11–49 lesions), severe (50 or more lesions), or crusted. Severity scores of 1, 2, 3, and 4 were assigned to scabies cases recorded as mild, moderate, severe, and crusted, respectively. Burrows were identified with a magnifying lens, and microscopy of skin scrapings was performed to search for mites, eggs, or fecal pellets.

Criteria for the diagnosis of scabies were: history of contact with a person infected with scabies, pruritus, presence of burrows or secondary lesions (papules, nodules, excoriations, crusts, or folliculitis) in characteristic sites, or gross scaling with hyperkeratotic plaques and fissuring. Three or more positive findings were accepted as diagnostic of scabies even without positive microscopy. However, a positive microscopy result was considered diagnostic.

Eligible subjects were alternately assigned to receive oral ivermectin (Mectizan; Merck & Co., Rahway, NJ) at 200 μg/kg body weight or topical treatment with benzyl benzoate lotion (Scabcare BB 25% w/w, Vitabiotics, Nigeria Ltd., Ikeja, Nigeria) and tetraethythiuram monosulfide 5% soap (Tetmosol, Jagal Pharma Ltd., Ikeja, Nigeria). Topical treatment consisted of a thorough bath with the monosulfiram soap followed by application of benzyl benzoate lotion to the entire body below the neck, repeated daily for 3 consecutive days. Subjects in both groups were instructed to wash their clothing and bed linens in hot water, dry them in the sun, and press them with a hot iron. Where possible, close contacts of subjects with scabies were examined, and those clinically confirmed to have scabies were invited to enroll in the study.

Asymptomatic contacts were also treated but not enrolled. All subjects and close contacts were treated simultaneously.

Subjects were followed up at 2 weeks to assess compliance and examine the patient. A single investigator (HMS), who was not blinded to the treatment received, recorded the number of lesions present. Only those with new or persistent lesions and pruritus were treated with a second course of their assigned treatment, and they were evaluated again 2 weeks later. Criteria for cure were absence of pruritus and absence of new lesions.

Statistical analysis was done using Epi Info 2000 (CDC, Atlanta, GA). Differences in proportions were compared with the χ^2 statistic. Severity scores were compared using the Mann-Whitney test, because they were ordinal and without a normal distribution. Multiple linear regression (analysis of covariance) was used to adjust for baseline severity in comparing subsequent severity scores between treatment groups. Logistic regression was used to determine the adjusted odds of treatment success while controlling for confounding factors. P values < 0.05 were considered significant. In calculating the sample size, we assumed cure rates of 95% and 75% with ivermectin and benzyl benzoate, respectively. A sample size of 83 in each treatment group would provide 95% power to detect this difference with 95% confidence. We sought to enroll 100 in each treatment group to allow for incomplete follow-up.

RESULTS

A total of 210 subjects were recruited (Table 1). Their mean (± SD) age was 16.2 (12.9) years (range, 5–65 years); 99 (47.1%) were male, and 111 (52.9%) were female. Of these, 10 were lost to follow-up after the initial treatment (7 received ivermectin, and 3 received topical treatment). Two-thirds (66%) of the subjects were children 5–14 years of age.

TABLE 1
Characteristics of 210 Nigerian subjects with scabies treated with ivermectin or topical benzyl benzoate

Characteristic	Ivermectin (N = 105)	Topical treatment (N = 105)	P value
Age (years)			0.17
5–14	68	71	
15–24	14	14	
25–34	10	12	
35–44	7	8	
≥ 45	6	0	
Sex (M/F)	55/50	44/61	0.12
Weight (kg)	34.1 ± 16.5	33.3 ± 15.3	0.52
Pruritis	105	105	1.0
History of contact	105	105	1.0
Types of lesions			
Burrows/vesicles	41	45	0.57
Papules/nodules/excoriations	104	101	0.37
Crusts	3	0	0.25
Distribution of lesions			
Head	4 (4%)	3 (3%)	0.50
Hands/arms	96 (91%)	99 (94%)	0.42
Trunk	35 (33%)	32 (31%)	0.66
Buttocks	86 (49%)	89 (51%)	0.58
Genital	47 (45%)	49 (47%)	0.78
Thighs/legs	66 (52%)	60 (48%)	0.40
Positive microscopy	58 (55%)	53 (50%)	0.49

Of the 200 subjects who completed the study, 98 received ivermectin and 102 received topical treatment.

Of the 98 subjects who received ivermectin, 53 (54.1%) had moderate lesions, 42 (42.8%) had severe lesions, and 3 (3.1%) had crusted lesions. Of the 102 subjects who received topical treatment, 75 subjects (73.5%) had moderate lesions, 27 (26.5%) had severe lesions, and none had crusted lesions. None of the subjects in either group had mild lesions at presentation. Prior to treatment, the severity score of the ivermectin group (2.5 ± 0.6; median, 2.0) was significantly greater than that of the topical treatment group (2.3 ± 0.4; median, 2.0; $P = 0.004$).

Lesions were still present 2 weeks after treatment in 21 subjects (21%) in the ivermectin group and in 42 subjects (41%) in the topical treatment group ($P = 0.003$). In the ivermectin group, 15 (15%) had mild lesions, 6 (6%) had moderate lesions, and none had severe or crusted lesions. In the topical treatment group, 26 (25%) had mild lesions, 16 (16%) had moderate lesions, and none had severe or crusted lesions (Figure 1). The improvement (reduction) in severity score was significantly greater in the ivermectin group (–2.2 ± 0.6; median, –2.0) than in the topical treatment group (–1.7 ± 0.8; median, –2.0; $P < 0.001$, adjusting for baseline severity). Of those with persistent lesions, 5 subjects (24%) in the ivermectin group had positive microscopy compared with 19 (45%) in the topical treatment group ($P = 0.10$). All subjects with persistent lesions received a second course of their assigned treatment. Two weeks after the second treatment, 5 of

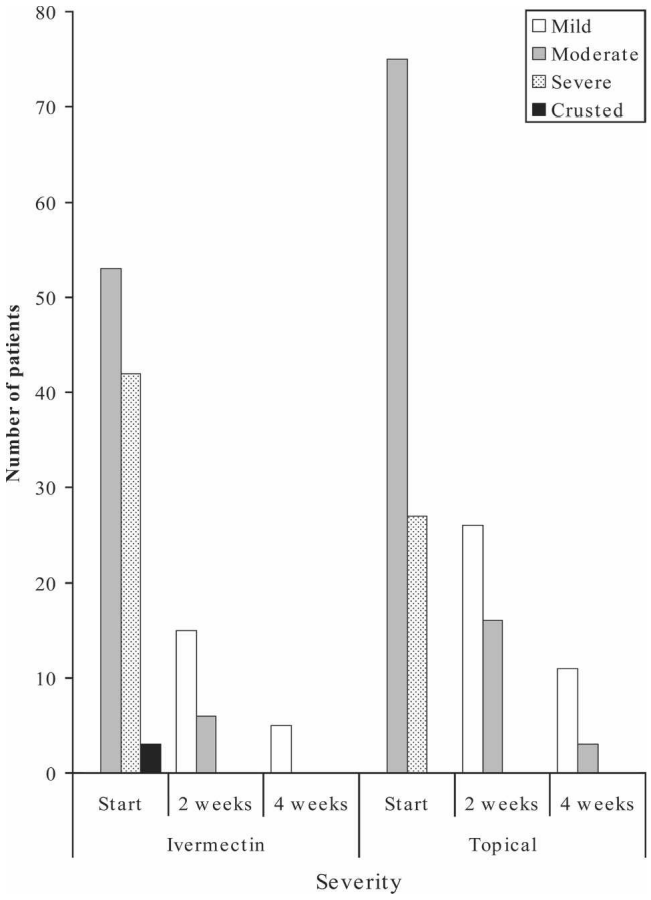

FIGURE 1. Change in severity of lesions with treatment.

21 (24%) in the ivermectin group had lesions (all mild) compared with 14 of 42 (33%) in the topical treatment group (11 had mild lesions, and 3 had moderate lesions), but this difference was not significant ($P = 0.44$), and the mean reduction in severity score was the same in both groups (–1.0). Of the 3 subjects with crusted lesions, 2 were completely cured after 2 doses of ivermectin.

The overall cure rate after 4 weeks was 95% in the ivermectin group and 86% in the topical treatment group ($P = 0.04$). A stratified analysis did not suggest any difference in response between children and adults ($P = 0.66$). The results were also analyzed on an intention to treat basis with the 10 dropouts included as treatment failures. By this analysis, 89% of the ivermectin group and 84% of the topical treatment group achieved cure, but this difference was not significant ($P = 0.32$).

In a logistic regression analysis with cure rate after 4 weeks as the dependent variable and treatment group, age, sex, positive microscopy, and initial severity as independent variables, only treatment group ($P = 0.007$) and initial severity ($P = 0.003$) were significant predictors of cure. Compared with topical treatment, ivermectin was significantly more likely to result in cure (adjusted odds ratio 5.2; 95% CI: 1.6 to 17).

DISCUSSION

We found that ivermectin has similar or better efficacy compared with the commonly used topical treatment of 25% benzyl benzoate lotion and monosulfiram soap. These results are similar to those of other workers. A single dose of ivermectin resulted in resolution of pruritus after 4 weeks in 93% of patients in southern Nigeria, compared with 48% who received benzyl benzoate.[24] A lower dose of ivermectin (100 μg/kg) achieved a 70% response rate in French Polynesia compared with a 48% response rate in those treated with 10% benzyl benzoate, but these differences were not significant.[25] In contrast, complete resolution of skin lesions was observed in only 56% of patients with scabies who received a single dose of ivermectin compared with 51% of those who were treated with 10% benzyl benzoate in Vanuatu.[26] The authors attributed the relatively low response rate to the possible persistence of papules and nodules without scabies mites at the final assessment, 3 weeks post-treatment. In a study of HIV-associated scabies, 63% of patients responded to a single dose of ivermectin, primarily those classified with mild or moderate severity, compared with 47% of patients who received benzyl benzoate.[21] The combination of ivermectin with benzyl benzoate was effective in all 17 cases in which it was used, including in severe and crusted forms.

Our study had a larger number of patients than other studies comparing ivermectin with benzyl benzoate and thus had greater power to detect a difference between these two treatments. However, when dropouts were included in the analysis as treatment failures, the difference between the two treatment groups was not statistically significant. Because the number of dropouts in the ivermectin group was greater than in the topical treatment group, comparison of the two groups by an intention to treat analysis demonstrated no significant difference in treatment response. However, it is unlikely that all of the dropouts represented treatment failures, because those who respond to treatment no longer have incentive to return for follow-up.[26] In addition, despite the greater severity of lesions at presentation in the ivermectin group than in the topical treatment group, the ivermectin group had a better response to treatment in those who completed the study.

At least two limitations of our study could introduce potential bias. The first is that patients were alternately assigned, rather than randomly assigned, to treatment groups. Consequently, we did not maintain allocation concealment. However, every eligible subject was enrolled, and the order of assigned treatment was not altered, thus minimizing potential selection bias. A second limitation is that the investigator who evaluated the response to treatment was not blinded to the treatment group assignment. However, we consider the criteria for evaluating the response to treatment (no. of lesions, patient's report of pruritus) sufficiently objective to prevent a major degree of bias.

Ivermectin has several clinical advantages that make it superior to topical treatment in developing countries. It is safe, inexpensive, simple to administer, easily supervised, and treats the entire skin surface without neglected areas.[27] Ivermectin is better tolerated than topical treatment in those with excoriations or open ulcerations.[26] The drug has successfully been used for mass treatment and in epidemics.[2,5,12] It also has the additional benefit of reducing the prevalence of other human parasitic infections common in the tropics, including onchocerciasis, *Ascaris* infection, lymphatic filariasis, pediculosis, cutaneous larva migrans, and strongyloidiasis.[17,23,27] Although ivermectin reduces *Loa loa* microfilaremia, life-threatening encephalopathy can occur in heavy infections, which warrants caution in endemic areas.[23] *L. loa* infection is infrequent in northern Nigeria, where this study was performed. Ivermectin is also superior to topical agents in treating immunocompromised persons with scabies,[21,27] which must be considered in African settings with a high prevalence of HIV infection (5% prevalence in Nigeria in 2003). Even when equivalent efficacy with benzyl benzoate is assumed, these additional advantages of ivermectin make it a superior choice in developing countries, like Nigeria, where conditions favor rapid spread that can quickly reach epidemic proportions. Long-term evaluation of the risk of re-infestation and rates of disease in close contacts warrants further study.

Received March 28, 2006. Accepted for publication November 2, 2006.

Acknowledgment: This work was submitted as a dissertation in part fulfillment of the Fellowship in General Medical Practice of the National Postgraduate Medical College of Nigeria.

Financial support: This study was funded in part by a dissertation grant of the Jos University Teaching Hospital. The funding agency had no role in the conduct of the study or the decision to publish the results. The American Society of Tropical Medicine and Hygiene (ASTMH) assisted with publication expenses.

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REFERENCES

1. Chosidow O, 2000. Scabies and pediculosis. *Lancet 355:* 819–826.
2. Lawrence G, Leafasia J, Sheridan J, Hills S, Wate J, Wate C, Montgomery J, Pandeya N, Purdie D, 2005. Control of scabies, skin sores and haematuria in children in the Solomon Islands: another role for ivermectin. *Bull World Health Organ 83:* 34–42.

3. Schmeller W, 1998. Community health workers reduce skin diseases in East African children. *Int J Dermatol 37:* 370–377.
4. Hegazy AA, Darwish NM, Abdel-Hamid IA, Hammad SM, 1999. Epidemiology and control of scabies in an Egyptian village. *Int J Dermatol 38:* 291–295.
5. Bockarie MJ, Alexander ND, Kazura JW, Bockarie F, Griffin L, Alpers MP, 2000. Treatment with ivermectin reduces the high prevalence of scabies in a village in Papua New Guinea. *Acta Trop 75:* 127–130.
6. Odueko OM, Onayemi O, Oyedeji GA, 2001. A prevalence survey of skin diseases in Nigerian children. *Niger J Med 10:* 64–67.
7. Ogunbiyi AO, Owoaje E, Ndahi A, 2005. Prevalence of skin disorders in school children in Ibadan, Nigeria. *Pediatr Dermatol 22:* 6–10.
8. Okoronkwo MO, 2003. Scabies among children in police and army barracks and at Mado Village of Jos, Plateau State of Nigeria. *Highland Med Res J 1:* 40–47.
9. Kristensen JK, 1991. Scabies and Pyoderma in Lilongwe, Malawi. Prevalence and seasonal fluctuation. *Int J Dermatol 30:* 699–702.
10. Terry BC, Kanjah F, Sahr F, Kortequee S, Dukulay I, Gbakima AA, 2001. Sarcoptes scabiei infestation among children in a displacement camp in Sierra Leone. *Public Health 115:* 208–211.
11. Andersen BM, Haugen H, Rasch M, Heldal Haugen A, Tageson A, 2000. Outbreak of scabies in Norwegian nursing homes and home care patients: control and prevention. *J Hosp Infect 45:* 160–164.
12. Obasanjo OO, Wu P, Conlon M, Karanfil LV, Pryor P, Moler G, Anhalt G, Chaisson RE, Perl TM, 2001. An outbreak of scabies in a teaching hospital: lessons learned. *Infect Control Hosp Epidemiol 22:* 13–18.
13. Dieng MT, Ndiaye B, Ndiaye AM, 1998. Scabies complicated by acute glomerulonephritis in children: 114 cases observed in two years in a pediatric service in Dakar [in French]. *Dakar Med 43:* 201–204.
14. Heukelbach J, Feldmeier H, 2006. Scabies. *Lancet 367:* 1767–1774.
15. Burkhart CG, Burkhart CN, Burkhart KM, 2000. An epidemiologic and therapeutic reassessment of scabies. *Cutis 65:* 233–240.
16. Leppard B, Naburi AE, 2000. The use of ivermectin in controlling an outbreak of scabies in a prison. *Br J Dermatol 143:* 520–523.
17. Heukelbach J, Winter B, Wilcke T, Muehlen M, Albrecht S, de Oliveira FA, Kerr-Pontes LR, Liesenfeld O, Feldmeier H, 2004. Selective mass treatment with ivermectin to control intestinal helminthiases and parasitic skin diseases in a severely affected population. *Bull World Health Organ 82:* 563–571.
18. Meinking TL, Taplin D, Hermida JL, Pardo R, Kerdel FA, 1995. The treatment of scabies with ivermectin. *N Engl J Med 333:* 26–30.
19. Gladstone HB, Darmstadt GL, 2000. Crusted scabies in an immunocompetent child: treatment with ivermectin. *Pediatr Dermatol 17:* 144–148.
20. Fawcett RS, 2003. Ivermectin use in scabies. *Am Fam Physician 68:* 1089–1092.
21. Alberici F, Pagani L, Ratti G, Viale P, 2000. Ivermectin alone or in combination with benzyl benzoate in the treatment of human immunodeficiency virus-associated scabies. *Br J Dermatol 142:* 969–972.
22. Emukah EC, Osuoha E, Miri ES, Onyenama J, Amazigo U, Obijuru C, Osuji N, Ekeanyanwu J, Amadiegwu S, Korve K, Richards FO, 2004. A longitudinal study of impact of repeated mass ivermectin treatment on clinical manifestations of onchocerciasis in Imo State, Nigeria. *Am J Trop Med Hyg 70:* 556–561.
23. Tielsch JM, Beeche A, 2004. Impact of ivermectin on illness and disability associated with onchocerciasis. *Trop Med Int Health 9:* A45–A56.
24. Nnoruka EN, Agu CE, 2001. Successful treatment of scabies with oral ivermectin in Nigeria. *Trop Doct 31:* 15–18.
25. Glaziou P, Cartel JL, Alzieu P, Briot C, Moulia-Pelat JP, Martin PM, 1993. Comparison of ivermectin and benzyl benzoate for treatment of scabies. *Trop Med Parasitol 44:* 331–332.
26. Brooks PA, Grace RF, 2002. Ivermectin is better than benzyl benzoate for childhood scabies in developing countries. *J Paediatr Child Health 38:* 401–404.
27. Dourmishev AL, Dourmishev LA, Schwartz RA, 2005. Ivermectin: pharmacology and application in dermatology. *Int J Dermatol 44:* 981–988.