

Selective mass treatment with ivermectin to control intestinal helminthiases and parasitic skin diseases in a severely affected population

Jörg Heukelbach,¹ Benedikt Winter,² Thomas Wilcke,² Marion Muehlen,² Stephan Albrecht,² Fabíola Araújo Sales de Oliveira,¹ Lígia Regina Sansigolo Kerr-Pontes,¹ Oliver Liesenfeld,² & Hermann Feldmeier²

Objective To assess the short-term and long-term impact of selective mass treatment with ivermectin on the prevalence of intestinal helminthiases and parasitic skin diseases in an economically depressed community in north-east Brazil.

Methods An intervention was carried out in a traditional fishing village in north-east Brazil where the population of 605 is heavily affected by ectoparasites and enteroparasites. The prevalence of intestinal helminths was determined by serial stool examination and the prevalence of parasitic skin diseases by clinical inspection. A total of 525 people out of a target population of 576 were treated at baseline. The majority of these were treated with ivermectin (200 µg/kg with a second dose given after 10 days). If ivermectin was contraindicated, participants were treated with albendazole or mebendazole for intestinal helminths or with topical deltamethrin for ectoparasites. Follow-up examinations were performed at 1 month and 9 months after treatment.

Findings Prevalence rates of intestinal helminthiases before treatment and at 1 month and 9 months after mass treatment were: hookworm disease 28.5%, 16.4% and 7.7%; ascariasis 17.1%, 0.4% and 7.2%; trichuriasis 16.5%, 3.4% and 9.4%; strongyloidiasis 11.0%, 0.6% and 0.7%; and hymenolepiasis 0.6%, 0.4% and 0.5%, respectively. Prevalence rates of parasitic skin diseases before treatment and 1 month and 9 months after mass treatment were: active pediculosis 16.1%, 1.0% and 10.3%; scabies 3.8%, 1.0% and 1.5%; cutaneous larva migrans 0.7%, 0% and 0%; tungiasis 51.3%, 52.1% and 31.2%, respectively. Adverse events occurred in 9.4% of treatments. They were all of mild to moderate severity and were transient.

Conclusion Mass treatment with ivermectin was an effective and safe means of reducing the prevalence of most of the parasitic diseases prevalent in a poor community in north-east Brazil. The effects of treatment lasted for a prolonged period of time.

Keywords Nematode infections/drug therapy; Skin diseases, Parasitic/drug therapy; Ivermectin/therapeutic use/adverse effects; Albendazole/therapeutic use; Pyrethrins/therapeutic use; Mebendazole/therapeutic use; Treatment outcome; Brazil (source: MeSH, NLM).

Mots clés Nématodes, Infections/chimiothérapie; Dermatose parasitaire/chimiothérapie; Ivermectine/usage thérapeutique/effets indésirables; Albendazole/usage thérapeutique; Mébendazole/usage thérapeutique; Pyrèthrine/usage thérapeutique; Evaluation résultats traitement; Brésil (source: MeSH, INSERM).

Palabras clave Infecciones por nematodos/quimioterapia; Dermatopatías parasitarias/quimioterapia; Ivermectina/uso terapéutico/efectos adversos; Albendazol/uso terapéutico; Mebendazol/uso terapéutico; Piretrinas/uso terapéutico; Resultado del tratamiento; Brasil (fuente: DeCS, BIREME).

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Introduction

More than 1 billion people are infected with intestinal helminths worldwide (1–3). The morbidity associated with these parasites is strongly related to parasite burden; it includes nutritional

disorders, such as stunting and anaemia; deficient cognitive functions; and impaired performance at school (1, 4, 5). The disease burden is particularly high in developing countries and among school-age children (1, 6).

¹ Department of Community Medicine, Faculty of Medicine, Federal University of Ceará, Rua Prof. Costa Mendes 1608, Fortaleza, CE 60931-140, Brazil. Correspondence should be addressed to Dr Heukelbach at this address (email:samsa@mcanet.com.br).

² Department of Medical Microbiology and Immunology of Infection, Institute for Infection Medicine, Charité, Campus Benjamin Franklin, Germany.

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Because it is difficult to eliminate the factors that make individuals vulnerable to infection with intestinal helminths, such as a lack of sanitation, poor hygiene and overcrowding, mass treatment with a broad spectrum anthelmintic drug is considered to be the key strategy for controlling morbidity among impoverished populations (1, 3, 4, 6).

Parasitic skin diseases also affect several hundred million individuals worldwide (7, 8). Like intestinal helminths, parasitic skin diseases primarily affect resource-poor populations and are associated with considerable morbidity (9–12). In particular, tungiasis, pediculosis, scabies and cutaneous larva migrans have an important impact on society as a whole and on the mental health of the individual. However, these skin diseases are rarely acknowledged as public health problems (8, 13).

WHO recommends four drugs for the control of intestinal nematodes, namely albendazole, mebendazole, levamisole, and pyrantel (14). Although ivermectin is known to be a safe and potent broad spectrum anthelmintic (15, 16) that also has a proven effect against different ectoparasites, it is recommended for the treatment of only some filarial diseases. A few randomized or open trials have shown that ivermectin has a high efficacy when used to treat skin diseases such as scabies (17, 18), head lice (19), and cutaneous larva migrans (20). Ivermectin is a comparatively cheap drug, and some have suggested that it could be used to treat individuals infected by a number of parasites in situations where specific diagnoses are difficult to establish due to a lack of appropriate health infrastructure (21).

Because the simultaneous occurrence of intestinal and skin parasites is common among resource-poor populations, ivermectin may be the ideal treatment to control ectoparasites and enteroparasites at the community level. To assess the effectiveness of ivermectin in such a setting, we performed an intervention study based on mass treatment with ivermectin in a poor fishing community heavily affected by intestinal helminthiasis and parasitic skin diseases.

Methods

Study area and population

The study was performed in the village of Balbino (Cascavel Municipality), approximately 60 kilometres south of Fortaleza, the capital of Ceará State (north-east Brazil). The village is situated on sand dunes near the coast, and the people mainly depend on fishing for their livelihood. The community comprises 141 families, and there are a total of 605 inhabitants. The population is poor; streets are not paved; and many houses are built on sandy soil. About 75% of the households have electricity, and 86.4% have a latrine. Slightly more than 84% of houses have a private well. About 95% of families have some type of domestic pet: 84.1% have a dog and 68.9% have a cat (22).

Study design

Each household in the community was visited, and plastic vials for stool specimens were distributed. A staff member visited the households to collect the specimens. To compensate for day-to-day variation of egg excretion, three faecal samples were collected at intervals of 3–4 days. The samples were collected in plastic vials without preservatives, and they were analysed in a field laboratory on the same day.

Stool samples were examined before treatment and 4 weeks after treatment. To assess the long-term effect of mass treatment with ivermectin, another follow-up examination was performed 9 months after treatment.

Stool samples were processed by the sedimentation method as described by Hoffman et al. (23). Briefly, with this method helminth eggs are concentrated by passing a faeces–water suspension through gauze and allowing spontaneous sedimentation to occur. After 24 hours, the sediment is collected from the bottom of the receptacle with a pipette. In this study, the method was adapted to use a centrifuge instead of spontaneous sedimentation. (Samples were centrifuged for 3 minutes at 3000 rpm.) One slide per faecal sample was prepared. *Strongyloides stercoralis* larvae and hookworm larvae were differentiated using established morphological criteria (24). If the stool sample was negative for *S. stercoralis* by the Hoffman method, another sample was prepared using the Baermann method, as adapted by Willcox & Coura (25). This modification of the Baermann method uses polypropylene tubes with small plastic filters (Parasito Kit, Biologica, São Paulo, Brazil), making gauze and laboratory equipment unnecessary. All specimens were examined by the same three investigators (BW, TW, SA).

Quality control was performed during baseline and the follow-up examinations. After the slides had been read by one of the microscopists, 10% were randomly selected for cross-reading by another microscopist, who was blind to the results of the first reading. If the results diverged, a new slide was prepared from the original sample and read by an expert microscopist who was blind to the previous results. Diverging results between the three routine microscopists occurred in < 5% of the specimens.

To recruit participants with parasitic skin diseases, all households were visited twice by the same investigator (TW). Each member of the family was thoroughly examined for the presence of scabies, tungiasis, head lice and cutaneous larva migrans. Diagnoses were made clinically. Pubic lice were not looked for. Body lice, ticks and myiasis do not occur in the study area.

Parasitic skin diseases were defined as shown in Box 1.

Box 1. Diagnostic criteria used for parasitic skin diseases among participants

| Parasitic skin disease | Diagnostic criteria |
|-------------------------|--|
| Cutaneous larva migrans | Presence of characteristic linear or serpiginous lesions associated with itching |
| Pediculosis | The entire head was clinically examined after parting the hair; special attention was paid to the nape of the neck and behind the ears. Active pediculosis was defined as the presence of nymphs or adult lice on the scalp of the hair; pediculosis as the presence of nits or parasites or both |
| Scabies | Presence of erythematous papular, vesicular, pustular or bullous lesions associated with itching |
| Tungiasis | Diagnosed according to Eisele et al. (26); flea in statu penetrandi; a red-brownish itchy spot with a diameter of 1–2 mm (early lesion); lesions presenting as a white patch with a diameter of 3–10 mm with a central black dot (mature lesion); or a brownish-black circular crust with or without surrounding necrosis of the epidermis (dead parasite) |

Selective mass treatment was performed as follows. The target population was defined as all individuals from households where at least one individual was found to be infected with at least one intestinal helminth or one ectoparasite species. All members of these households were treated with ivermectin (200 µg/kg; Revectina, Solvay Farma, São Paulo, Brazil), provided there were no contraindications. The dose was repeated after 10 days. Contraindications for administration of ivermectin were: being younger than 5 years, weighing < 15 kg, being pregnant or breastfeeding, or having renal or hepatic disease. Mebendazole or albendazole were administered to children who were < 5 years: mebendazole in a dose of 100 mg twice daily for three days (children < 6 months were treated only if at least one stool examination was positive; children aged 6 months to 2 years were treated if at least one family member had a positive stool). Children aged 2–4 years were treated with 400 mg albendazole in a single oral dose. Women who were pregnant or breastfeeding at baseline were treated at the end of the study; breastfeeding women were treated at this time only if their children had been weaned. All oral drugs were administered under supervision.

In cases of pediculosis or scabies, topical deltamethrin lotion (Deltacid, Solvay Farma, São Paulo, Brazil) was given to individuals for whom ivermectin was contraindicated if the individual or at least one family member had pediculosis or scabies. Participants were instructed to use the lotion for three consecutive nights on their head (in cases of pediculosis) or their body (in cases of scabies).

Households were visited by one of the investigators (MM) 2–5 days after treatment, and individuals were interviewed about adverse events. An adverse event was defined as the occurrence of symptoms or signs after treatment regardless of whether a pharmacological relation to the drug was assumed. Details of the adverse events were recorded as signs, symptoms, the date and time the event started and ended, how long it occurred after taking the drug, the duration of the event, the severity of the event, the action taken by the participant, and the outcome.

Statistical analysis

Data were entered into a database twice using EpiInfo software (version 6.04d) and checked for errors that could have

occurred during data entry. EpiInfo was used to calculate 95% confidence intervals of point prevalence rates. The χ^2 test was used to determine the significance of differences between relative frequencies.

Ethical considerations

In preparation for the study, several community meetings were held, and the objectives of the study were explained. In addition, meetings were held with representatives of the community associations (*associações dos moradores*). The representatives decided unanimously that the community should support the study. Ethical clearance was obtained from the institution legally responsible for monitoring public health interventions using registered drugs, in this case the ethical committee of Cascavel Municipality. Before an individual was included in the study, informed oral consent was obtained. In the case of minors, carers were asked for consent.

The study was conducted in accordance with good clinical practice and the Declaration of Helsinki as amended in 2001 (27).

Findings

The target population consisted of 576 individuals with a mean age 26.4 years. There were 279 males (48.4%) and 297 females (51.6%). At baseline, 1419 stool samples from 516 inhabitants (85.3% of the total population) were analysed. At the first follow-up visit, 1124 stool samples from 475 individuals (78.5% of the total population) were analysed; and at the second follow-up visit 998 samples from 403 individuals (66.6% of the total population) were analysed.

At baseline, 548 individuals (90.6% of the total population) were examined for parasitic skin diseases. At the time of first follow-up 505 people were examined (83.5% of total population); and at the time of the second follow-up examination 535 people were seen (88.4% of the total population).

The number of individuals examined and the number of those who received ivermectin, albendazole, mebendazole, or topical deltamethrin are shown in Table 1. A total of 88 individuals (41 females, 47 males; mean age 32.6 years) were not treated. This is 14.5% of the total population.

Table 1. Number of participants examined at each visit by diagnosis and treatment

| Diagnosis | No. examined at baseline | No. treated at baseline ^a | No. examined 1 month after selective mass treatment | No. examined 9 months after selective mass treatment |
|----------------------------------|--------------------------|--------------------------------------|---|--|
| Intestinal helminthiases | | | | |
| Ivermectin | 419 | 478 (83.0) | 396 | 324 |
| Albendazole | 23 | 24 (4.2) | 20 | 19 |
| Mebendazole | 13 | 15 (2.6) | 9 | 8 |
| No treatment ^b | 61 | 88 (15.3) | 50 | 52 |
| Parasitic skin diseases | | | | |
| Ivermectin | 443 | 478 (83.0) | 411 | 431 |
| Deltamethrin | 41 | 41 (7.1) | 34 | 36 |
| No treatment ^b | 64 | 86 | 60 | 68 |
| Any treatment^c | 495 | 525 (91.1) | 454 | 473 |

^a Numbers in parentheses are percentage of the target population ($n = 576$) as defined in Methods.

^b Some participants were not treated because there were contraindications or they refused treatment.

^c Number of participants treated with at least one dose of ivermectin, albendazole, mebendazole, or topical deltamethrin.

Intestinal helminthiases

Prevalence rates of intestinal helminthiases at baseline are shown in Table 2. The prevalence rates of the most common infections (hookworm disease, ascariasis, trichuriasis and strongyloidiasis) decreased significantly after one month (all $P < 0.001$), and they remained significantly lower when compared to the baseline survey 9 months after selective mass treatment (all $P < 0.001$). Prevalence rates of ascariasis and trichuriasis increased significantly between the first follow-up and the second ($P < 0.001$), whereas the prevalence of hookworm disease was lowest 9 months after treatment ($P < 0.001$).

Parasitic skin diseases

Prevalence rates of parasitic skin diseases at baseline and during follow-up are shown in Table 3. The prevalence of pediculosis (defined as the presence of nits, nymphs or adult parasites) decreased slightly, though significantly, after one month ($P = 0.01$). Nine months after selective mass treatment prevalence had decreased further and was about half the baseline value ($P < 0.001$). Active pediculosis (defined as individuals presenting with nymphs or adult parasites) virtually disappeared 1 month after ivermectin treatment ($P < 0.001$). After 9 months, the prevalence of active pediculosis was still significantly lower when compared to baseline ($P < 0.001$). The prevalence of scabies decreased at the time of first follow-up ($P < 0.01$) and remained stable for the next 9 months compared to baseline ($P = 0.02$). Cutaneous larva migrans was found in four patients at baseline, but none was found to be infected during follow-up. The prevalence of tungiasis remained unchanged 1 month after mass treatment. However, there was a significant decrease in the prevalence of tungiasis 9 months after administration of ivermectin when compared to baseline ($P < 0.001$).

The relative reduction in prevalence rates obtained 9 months after selective mass treatment is shown in Table 4.

Adverse events

Ivermectin was well tolerated. After a total of 904 doses of ivermectin, adverse events were reported in 85 (9.4%) individuals receiving the drug (Table 5). All events were of mild or moderate severity. Of the 71 events reported in 64 individuals after the

first dose (14% of those taking ivermectin), 28 were considered probably to be related to the drug and 29 were considered to be possibly related. Two events were considered completely unrelated, and 12 were unlikely to be related to the drug (data not shown). After the second ivermectin dose, significantly fewer adverse events were reported (21 individuals, 4.7%; $P < 0.001$). Eight events were considered to be probably related to treatment, and 11 were considered to be possibly related. One case was unrelated, and two other events were unlikely to have been related to the drug. The majority of events occurred in individuals with helminth eggs present in stool samples while having treatment.

Discussion

In developing countries, intestinal helminthiases and parasitic skin diseases are not only highly prevalent but also associated with important morbidity (1, 11, 21). What is less well known is that intestinal helminthiases and parasitic skin diseases commonly coexist in resource-poor communities, and many individuals are concomitantly infected with enteroparasites and ectoparasites.

Mass treatment with a broad spectrum anthelmintic drug is considered to be an effective means of controlling intestinal helminths at the population level (1, 3, 4). The benefit of periodic treatment with drugs such as albendazole and mebendazole has been shown clearly in terms of a reduction in worm burden and morbidity (1, 5, 28, 29). At least in children, regular treatment has been shown to reduce the parasite load to such a low level that helminth-associated morbidity may completely disappear (3, 28). Until now, similar data on parasitic skin diseases have been scanty, although it may be assumed that mass treatment would reduce the prevalence of ectoparasitoses and their associated morbidity (21, 30, 31). The key to successfully controlling morbidity associated with ectoparasites and enteroparasites is to use a drug with a high efficacy against all types of parasites expected to occur among impoverished populations.

Ivermectin is a promising candidate for such an approach. It is highly effective against a number of intestinal nematodes, and it is considered the drug of choice for treating strongyloidiasis (1). It is also effective against scabies, pediculosis and

Table 2. Prevalence of intestinal helminthiases at baseline, 1 month after treatment, and 9 months after treatment

| Disease and organism | Baseline ($n = 516$) ^a | | 1 month after treatment ($n = 475$) ^a | | 9 months after treatment ($n = 403$) ^a | |
|---|-------------------------------------|-------------------------|--|-------------------------|---|-------------------------|
| | No. testing positive | Prevalence ^b | No. testing positive | Prevalence ^b | No. testing positive | Prevalence ^b |
| Hookworm disease (<i>Ancylostoma duodenale</i> , <i>Necator americanus</i>) | 147 | 28.5 (24.7–32.6) | 78 | 16.4 (13.3–20.1) | 31 | 7.7 (5.4–10.9) |
| Ascariasis (<i>Ascaris lumbricoides</i>) | 88 | 17.1 (14.0–20.6) | 2 | 0.4 (0.1–1.7) | 29 | 7.2 (5.0–10.3) |
| Trichuriasis (<i>Trichuris trichiura</i>) | 85 | 16.5 (13.4–20.0) | 16 | 3.4 (2.0–5.5) | 38 | 9.4 (6.8–12.8) |
| Strongyloidiasis (<i>Strongyloides stercoralis</i>) | 57 | 11.0 (8.5–14.2) | 3 | 0.6 (0.2–2.0) | 3 | 0.7 (0.2–2.3) |
| Hymenolepiasis (<i>Hymenolepis nana</i>) | 3 | 0.6 (0.2–1.8) | 2 | 0.4 (0.1–1.7) | 2 | 0.5 (0.1–2.0) |

^a Number of participants who returned at least one stool sample.

^b Prevalences are shown as % (95% confidence interval).

Table 3. Prevalence of parasitic skin diseases at baseline, 1 month after treatment, and 9 months after treatment

| Disease | Baseline (n = 548) ^a | | 1 month after treatment (n = 505) ^a | | 9 months after treatment (n = 535) ^a | |
|---------------------------------|---------------------------------|-------------------------|--|-------------------------|---|-------------------------|
| | No. testing positive | Prevalence ^b | No. testing positive | Prevalence ^b | No. testing positive | Prevalence ^b |
| Pediculosis | 154 | 28.1 (24.4–32.1) | 107 | 21.2 (17.8–25.1) | 72 | 13.5 (10.7–16.7) |
| Active pediculosis ^c | 88 | 16.1 (13.1–19.5) | 5 | 1.0 (0.4–2.4) | 55 | 10.3 (7.9–13.2) |
| Scabies | 21 | 3.8 (2.4–5.9) | 5 | 1.0 (0.4–2.4) | 8 | 1.5 (0.7–3.0) |
| Cutaneous larva migrans | 4 | 0.7 (0.2–2.0) | 0 | 0 | 0 | 0 |
| Tungiasis | 281 | 51.3 (47.0–55.5) | 263 | 52.1 (47.6–56.5) | 167 | 31.2 (27.3–35.4) |

^a Number of participants examined for parasitic skin diseases.

^b Prevalences are shown as % (95% confidence interval).

^c Presence of nymphs or adults or both.

cutaneous larva migrans (17, 19, 20, 32, 33). However, ivermectin has been thought to be contraindicated in children younger than 5 years of age or weighing less than 15 kg because it is not certain whether the drug is neurotoxic in children, given their less developed blood–brain barrier (34). However, preliminary data indicate that ivermectin is well tolerated by children younger than 5 years of age (35).

As a first step in trying to control ectoparasites and enteroparasites with a single drug we decided to assess the short-term and long-term impact of selective mass treatment with ivermectin on the prevalence of intestinal helminthiases and parasitic skin diseases in a population severely affected by both types of parasites.

For intestinal helminths, the greatest reduction in prevalence was achieved for strongyloidiasis, hookworm disease and ascariasis (Table 4). After 9 months, when compared with baseline values, prevalence rates remained lower by a factor of 16 for strongyloidiasis, 3.7 for hookworm disease and 2.4 for ascariasis. Ivermectin has already been found to be highly effective in treating strongyloidiasis and ascariasis (36–41). In contrast, earlier studies found it was less effective against hookworm and *Trichuris trichiura* infection (37, 38, 41). The better performance observed in our study may be due to the fact that two doses of ivermectin were given 10 days apart. In fact, Naquira et al. (40) reported a cure rate of 100% in patients with trichuriasis when ivermectin was given twice. Because hookworm infection is associated with a high risk of iron-deficiency anaemia, the better efficacy found when two doses of ivermectin were given would be of considerable advantage. Further investigations should examine our findings of better effectiveness gained by giving two doses of ivermectin.

Controlling parasitic skin diseases with topical compounds is cumbersome: the compound has to be applied several times (in the case of scabies, it must be applied to the entire body); it may cause adverse dermatological, neurological or haematological events; and resistance of head lice and *Sarcoptes scabiei* to insecticides and scabicides has been reported and seems to be increasing (21, 42–46).

Oral ivermectin does not have the disadvantages of topical compounds, and it has been shown to be highly efficacious when used in clinical trials to treat scabies and cutaneous larva migrans (17, 32, 47, 48). It has also been found to be effective in intervention studies (30, 31). Our results show that two doses of ivermectin reduced the prevalence rates of scabies and

pediculosis 1 month after selective mass treatment. In the case of scabies, the reduction persisted for 9 months.

Although no cases of cutaneous larva migrans were observed during the two follow-up visits, the control of this disease obviously cannot be achieved solely through treating the human population: larvae do not develop in the human host, and therefore treatment of infected humans cannot reduce the incidence (8). However, because larvae may survive for months in the epidermis, and many individuals suffer simultaneously from several migrating larvae (12), treatment with ivermectin considerably reduces the morbidity associated with the disease.

The prevalence of tungiasis had significantly decreased 9 months after treatment. This finding is supported by a recent double-blind placebo-controlled trial showing that topical ivermectin has some effect on sand fleas that have penetrated into the epidermis (49). However, we cannot exclude the possibility that the observed effect is spurious: the transmission dynamics of this ectoparasitosis are not well understood, and attack rates may vary over time.

Adverse events associated with ivermectin were of only mild to moderate severity, and in all cases they resolved spontaneously. Abdominal discomfort, the most common adverse event, is probably caused by worms dying and disintegrating,

Table 4. Relative reduction in prevalence 9 months after selective mass treatment

| Disease | Relative reduction in prevalence (factor) |
|-------------------------|---|
| Hookworm disease | 3.7 |
| Ascariasis | 2.4 |
| Trichuriasis | 1.8 |
| Strongyloidiasis | 16 |
| Hymenolepiasis | 1.2 |
| Pediculosis | 2.1 |
| Active pediculosis | 1.6 |
| Scabies | 2.5 |
| Cutaneous larva migrans | NA |
| Tungiasis | 1.6 |

NA = Not applicable.

Table 5. Number of participants who had adverse events after treatment, by drug and type of event^a

| Adverse event ^b | Drug | | | |
|---|-------------------------------------|--------------------------------------|-------------------------|-------------------------|
| | Ivermectin, first dose (n = 458) | Ivermectin, second dose (n = 446) | Albendazole (n = 24) | Mebendazole (n = 15) |
| Abdominal pain or discomfort | 23 | 10 | 0 | 0 |
| Nausea | 15 | 3 | 0 | 1 |
| Loose stools | 12 | 3 | 1 | 0 |
| Skin rash or itching | 6 | 1 | 1 | 1 |
| Dizziness | 5 | 0 | 0 | 0 |
| Somnolence | 3 | 3 | 0 | 0 |
| Headache | 3 | 0 | 0 | 1 |
| Fever | 1 | 0 | 0 | 0 |
| Common cold | 1 | 2 | 0 | 0 |
| Paraesthesia | 1 | 0 | 0 | 0 |
| Lumbar pain | 1 | 0 | 0 | 0 |
| Total no. adverse events | 71 | 22 | 2 | 3 |
| Total no. of participants affected | 64 | 21 | 2 | 3 |

^a Information on adverse events associated with topical deltamethrin is not available.

^b More than one symptom or sign could be present simultaneously.

especially *Ascaris lumbricoides*. Adenusi et al. (36) reported adverse events from ivermectin treatment in 31% of patients infected with strongyloidiasis in Nigeria. Interestingly, abdominal discomfort was not observed. However, infection with nematodes other than *Strongyloides*, particularly *A. lumbricoides*, was not investigated.

In our study no medical interventions were necessary to treat adverse events. Our finding that ivermectin is well tolerated supports previous observations. For example, during campaigns to eliminate onchocerciasis and lymphatic filariasis, several million people have been treated with ivermectin. Severe adverse events have been rare and seemed to be related to the release of antigens from disintegrating microfilariae and not to any intrinsic toxicity of the drug (16, 50).

Critical appraisal of our data must take into account the fact that considerably fewer individuals participated in the first and second follow-up visits than participated at baseline. However, at baseline prevalence rates of the diseases under study were similar among individuals lost to follow-up and those that remained in the study (data not shown). Therefore it is unlikely that loss to follow-up was responsible for the observed differences in pre-treatment and post-treatment prevalence.

The decline in prevalence in this study, even though the study was conducted as an open trial and without a control group, is most likely due to the treatment; other factors, such as climatic conditions, are unlikely to have caused the effect, with the exception of tungiasis. The long-term nature of the effectiveness of treatment indicates that there was a pronounced reduction in reinfection after selective mass treatment. This is probably due to the high coverage within the community,

which should have reduced faecal contamination and, consequently, chances of reinfection.

We have shown for the first time that ivermectin — a drug that until now has been mainly used for mass treatment of filarial diseases — is highly effective for the simultaneous control of intestinal helminthiases and parasitic skin diseases. Two doses of ivermectin used in a selective mass campaign with high coverage may offer a highly effective strategy for controlling enteroparasites and ectoparasites in populations other than the one described here. This study used an ivermectin manufactured in Brazil and is the first published evidence on the effectiveness and safety of an ivermectin not produced by Merck Sharp and Dohme. ■

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Conflicts of interest: none declared.

Résumé

Traitement de masse sélectif par l'ivermectine contre les helminthiases intestinales et les dermatoses parasitaires dans une population sévèrement touchée

Objectif Évaluer l'impact à court et à long terme d'un traitement de masse sélectif par l'ivermectine sur la prévalence des helminthiases intestinales et des dermatoses parasitaires dans une communauté économiquement défavorisée du nord-est du Brésil.

Méthodes Une intervention a été réalisée dans un village de pêcheurs traditionnel du nord-est du Brésil dont la population (605 habitants) est sévèrement touchée par des ectoparasites et des parasites intestinaux. La prévalence des helminthes intestinaux a été déterminée par examen en série de selles et celle des dermatoses parasitaires par inspection clinique. Au total, 525 personnes sur les 576 de la population cible ont été traitées en début d'intervention. La plupart ont reçu de l'ivermectine (200 µg/kg, avec une deuxième dose au bout de 10 jours). Lorsque l'ivermectine était contre-indiquée, les participants étaient traités par l'albendazole ou le mébendazole contre les helminthes intestinaux ou par la deltaméthrine en application locale contre les ectoparasites. Des examens de contrôle ont été réalisés 1 mois et 9 mois après le traitement.

Résultats La prévalence des diverses helminthiases intestinales avant le traitement et au bout d'un mois et de 9 mois après le traitement était, respectivement, de : ankylostomiase 28,5 %, 16,4 % et 7,7 % ; ascariase 17,1 %, 0,4 % et 7,2 % ; trichocéphalose 16,5 %, 3,4 % et 9,4 % ; strongyloïdose 11,0 %, 0,6 % et 0,7 % ; et hyménolépiase 0,6 %, 0,4 % et 0,5 %. La prévalence des diverses dermatoses parasitaires avant le traitement et au bout d'un mois et de 9 mois était, respectivement, de : pédiculose active 16,1 %, 1,0 % et 10,3 % ; gale 3,8 %, 1,0 % et 1,5 % ; larva migrans cutanée 0,7 %, 0 % et 0 % ; et tungose 51,3 %, 52,1 % et 31,2 %. Des effets indésirables ont été observés avec 9,4 % des traitements. Il s'agissait dans tous les cas d'effets passagers, de gravité faible à modérée.

Conclusion Le traitement de masse par l'ivermectine était un moyen efficace et sans danger pour réduire la prévalence de la plupart des affections parasitaires présentes dans une communauté pauvre du nord-est du Brésil, et ses effets étaient durables.

Resumen

Tratamiento masivo selectivo con ivermectina contra las helmintiasis intestinales y las parasitosis cutáneas en una población gravemente afectada

Objetivo Evaluar el impacto del tratamiento masivo selectivo con ivermectina, a corto y a largo plazo, en la prevalencia de las helmintiasis intestinales y las parasitosis cutáneas en una comunidad económicamente deprimida del noreste del Brasil.

Métodos Se llevó a cabo una intervención en un pueblo tradicional de pescadores del noreste del Brasil cuya población, de 605 habitantes, está gravemente afectada por diversos ectoparásitos y enteroparásitos. La prevalencia de los helmintos intestinales se determinó mediante examen coproparasitológico seriado, y la prevalencia de las parasitosis cutáneas, mediante inspección clínica. En total se trató al principio del estudio a 525 personas, de una población destinataria de 576. La mayoría de ellas fueron tratadas con ivermectina (200 µg/kg de peso, con una segunda dosis al cabo de 10 días). Cuando la ivermectina estaba contraindicada, el participante era tratado con albendazol o mebendazol si tenía helmintos intestinales, o con deltametrina tópica si tenía ectoparásitos. Los exámenes de seguimiento se realizaron al cabo de un mes y 9 meses del tratamiento.

Resultados Las tasas de prevalencia de las helmintiasis intestinales antes del tratamiento y al cabo de un mes y 9 meses del tratamiento masivo fueron las siguientes: anquilostomiasis, 28,5 %, 16,4% y 7,7%; ascariasis, 17,1%, 0,4% y 7,2%; tricuriasis, 16,5%, 3,4% y 9,4%; estromboloidiasis, 11,0%, 0,6% y 0,7%; y himenolepiasis, 0,6%, 0,4% y 0,5%, respectivamente. Las tasas de prevalencia de las parasitosis cutáneas antes del tratamiento y al cabo de un mes y 9 meses del tratamiento masivo fueron las siguientes: pediculosis activa, 16,1% 1,0% y 10,3%; sarna, 3,8%, 1,0% y 1,5%; larva migrans cutánea, 0,7%, 0% y 0%; y tungiasis, 51,3%, 52,1% y 31,2%, respectivamente. Se registraron acontecimientos adversos en el 9,4% de los tratamientos, todos ellos entre leves y moderados y de carácter transitorio.

Conclusión El tratamiento masivo con ivermectina fue un método eficaz y seguro de reducción de la prevalencia de la mayoría de las enfermedades parasitarias prevalentes en una comunidad pobre del noreste del Brasil. El tratamiento tuvo efectos prolongados.

ملخص

المعالجة الجموعية الانتقائية بالإيفرمكتين لمكافحة الديدان المعوية والأمراض الجلدية الطفيلية في المجتمعات الشديدة التأثر بهذه الأمراض

وبعد شهر من المعالجة ٠,٤٪ وبعد تسعة أشهر من المعالجة الجموعية ٧,٢٪؛ ولداء المسلكات قبل المعالجة ١٦,٥٪ وبعد شهر من المعالجة ٠,٦٪ وبعد تسعة أشهر من المعالجة الجموعية ٩,٤٪؛ ولداء الاسطوانيات قبل المعالجة ١١,٠٪ وبعد شهر من المعالجة ٠,٦٪ وبعد تسعة أشهر من المعالجة الجموعية ٠,٧٪؛ ولداء المحرشفات قبل المعالجة ٠,٦٪ وبعد شهر من المعالجة ٤٪ وبعد تسعة أشهر من المعالجة الجموعية ٠,٥٪. أما معدلات انتشار الأمراض الجلدية الطفيلية لداء القمل قبل المعالجة فكانت ١٦,١٪ وبعد شهر من المعالجة ١,٠٪ وبعد تسعة أشهر من المعالجة ١٠,٣٪؛ وللجرب قبل المعالجة ٣,٨٪ وبعد شهر من المعالجة ١,٠٪ وبعد تسعة أشهر من المعالجة ١,٥٪؛ ولداء هجرة اليرقات الجلدي قبل المعالجة ٥,٧٪ وبعد شهر من المعالجة وبعد تسعة أشهر من المعالجة ٠٪؛ ولداء الطوامر قبل المعالجة ٥١,٣٪ وبعد شهر من المعالجة ٥٢,١٪ وبعد تسعة أشهر من المعالجة ٣١,٢٪. وقد وقعت حوادث ضائرة في ٩,٤٪ من الحالات المعالجة، إلا أنها كانت جميعاً عابرة وتتراوح بين الخفيفة والمتوسطة، من حيث الوخامة.

الخلاصة: ثبت أن المعالجة الجموعية بالإيفرمكتين وسيلة فعالة ومأمونة للحد من انتشار معظم الأمراض الطفيلية المنتشرة في مجتمع فقير في شمال شرقي البرازيل. كما أن تأثير المعالجة قد استدام لفترة زمنية طويلة.

الغرض: تقييم الآثار الطويلة الأمد والقصيرة الأمد للمعالجة الجموعية الانتقائية بالإيفرمكتين على معدل انتشار الديدان المعوية والأمراض الجلدية الطفيلية في مجتمع يعاني من كساد اقتصادي في شمال شرقي البرازيل.

الطريقة: تم إجراء مداخل في قرية تقليدية تعيش على صيد الأسماك في شمال شرقي البرازيل حيث يتأثر سكانها البالغ عددهم ٦٠٥ أفراد بشدة بالطفيليات البرانية والطفيليات المعوية. وقد تم تحديد معدل انتشار الديدان المعوية عن طريق اختبار عينات البراز بصورة متسلسلة، أما معدل انتشار الأمراض الجلدية الطفيلية فتم تحديده بالفحص السريري. وتمت معالجة ٥٢٥ من بين إجمالي السكان المستهدفين البالغ عددهم ٥٧٦ فرداً معالجة أساسية، إذ عولج معظمهم بالإيفرمكتين (٢٠٠ ميكروغرام/كغم من الوزن، مع إعطاء جرعة ثانية بعد ١٠ أيام). وعند وجود ما يحول دون استعمال الإيفرمكتين، تمت معالجة المشاركين بالألبندازول أو الميندازول للقضاء على الديدان المعوية، أو بالدلتامثرين الموضعي للقضاء على الطفيليات البرانية. وتم إجراء اختبارات للمتابعة بعد مضي شهر وتسعة أشهر من المعالجة.

الموجودات: بلغت معدلات انتشار الديدان المعوية قبل المعالجة لداء الديدان الشخصية قبل المعالجة ٢٨,٥٪ وبعد شهر من المعالجة ١٦,٤٪ وبعد تسعة أشهر من المعالجة الجموعية ٧,٧٪؛ ولداء الصفر (الإسكارس) قبل المعالجة ١٧,١٪

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Erratum

In the article "The natural history of HIV-1 and HIV-2 infections in adults in Africa: a literature review" on pages 462–469 of Vol. 82, issue number 6, 2004 by Shabbar Jaffar et al:

Page 465: Under the heading "Survival after AIDS among individuals infected with HIV-1", the third sentence should begin "The median time to death was 9.2 months ..." (and not "The median time to AIDS ...").