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Impact of 3 years ivermectin treatment on onchocerciasis in Yanomami communities in the Brazilian Amazon

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ABSTRACT

In the current study, it was assessed, for the first time, the effect of ivermectin treatment administered twice a year on the prevalence and morbidity of onchocerciasis in the hyperendemic Yanomami communities of the Roraima State (Brazil). Physical and parasitological examinations were carried out every 6 months until six drug rounds of treatment were completed. The coverage during the six rounds of ivermectin treatment ranged from 89% to 92% of the eligible Yanomami population. Overall, comparison of results at pre-treatment with results after six rounds of treatment, the prevalence of infection had declined from 87% to 42% ($P < 0.0001$, CI 95% = 0.05–0.22); the community microfilarial load (CMFL) fell from 1.17 to 0.53 Mf/mg of skin; and the crude intensity of infection (MFL-Total) decreased from 18.95 to 1.96 Mf/mg of skin during the same period ($P < 0.0001$, for both microfilarial loads). Although no significant difference was observed between microfilarial densities in skin snips from iliac crest and scapula after the 6th round of ivermectin treatment it was observed that the prevalence of positive skin snips was significantly higher when skin snips were taken from iliac crest (42%) than from scapula (8%) ($P = 0.001$, CI 95% = 3.41–22.67). After six rounds of ivermectin treatments, no significant differences were observed in the prevalences of palpable nodules and of onchodermatitis in relation to pre-treatment prevalences, from 45% to 41% and from 17% to 20% ($P > 0.05$, for both).

These findings suggest that mass population treatment should continue without interruption and achieve higher levels of drug coverage in order to alleviate disease manifestations and interrupt infection transmission to hasten the elimination of onchocerciasis in Yanomami communities. In addition, the sensitivity of iliac crest snips for parasitological assessment in epidemiological surveillance of Yanomami communities may increase the acceptance of the population in biopsy sampling and seems to be a good choice for assessing the success of control programs.

1. Introduction

Human onchocerciasis caused by the filarial parasitic nematode *Onchocerca volvulus*, has remained an important public health problem in Tropical Africa, Latin America, and the Yemen with over 37 million people infected and a risk population of over 120 million, mostly in Africa (Basáñez et al., 2006; WHO, 2000).

Onchocerciasis is transmitted by the blackfly *Simulium* spp. which inject infective larvae during blood meal. These larvae mature to female and male worms within a year and are located in subcutaneous nodules. The females release approximately 1000 microfilariae per day over a 9–14-year period (Schulz-Key, 1990). These microfilariae induce the pathology characteristic of the disease as dermatitis, skin atrophy, eye lesions leading to blindness (Hoerauf et al., 2003). Up to 500,000 cases of severe visual impairment and 270,000 of blindness have been attributed to onchocerciasis (WHO, 2000).

Onchocerciasis endemic areas in Brazil are located in the Amazon rain forest along the Brazilian–Venezuelan border where about 9500 Amerindians, mainly Yanomami, live in at least 28 small isolated communities of which 18 are endemic (Marcano et al., 2004; Shelley, 2002). The Yanomami are seminomadic, with different patterns of migration, with both micromovements of community and surroundings as well as macromovements (Chagnon, 1992). They support themselves by hunting, fishing and subsistence farming which are predisposing factors to biting simuliids. The introduction of onchocerciasis in the Brazilian Yanomami communities is

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not well established but the first case was reported over 35 years ago (Bearzoti et al., 1967).

The control of onchocerciasis, in the endemic areas, is based mainly upon the large-scale distributions of Mectizan® (ivermectin), a potent oral microfilaricide drug, in order to reduce transmission by lowering the microfilarial load in infected individuals besides to mitigate the health consequences of infection. In the six Latin America countries where this disease is endemic (Ecuador, Venezuela, Columbia, Guatemala, Mexico and Brazil,) twice a year treatment regimen was preconized by Onchocerciasis Elimination Program for the Americas (OEPA). Ivermectin-based elimination efforts have been under way in Brazil for the past decade, beginning in 1995 with some Yanomami communities but only achieved more communities in 2002 due to the difficult access to these remote communities and their seminomadic habits.

This work reports for the first time the evaluation of the impact of 3 years of ivermectin treatment administered twice a year on onchocerciasis in Yanomami communities (Roraima, Brazil) living in a highly endemic area.

2. Materials and methods

2.1. Study population

Aratha-ú and Xiriana are two communities (malocas) in Yanomami Area, situated in north Roraima State 347 km from the Boa Vista city, Capital of the State of Roraima (northern Amazon: 03°09′39.6″N 63°46′53.2″W) close to the border of Venezuela. Its population was estimated at 201 individuals. This area was selected for this study because of its high prevalence of onchocerciasis (Shelley, 2002) and these communities were recently contacted by the Brazilian government and were never treated with ivermectin. These facts were used to establishing the pre-ivermectin treatment base-line data.

The study population consisted of 113 subjects previously chosen for ivermectin treatment by national onchocerciasis control programs (National Foundation of Health/FUNASA). It was composed of 58 women and 55 men, most of them (64%) were adults ($\geq$18 years) ($P < 0.0001$) with ages ranging from 5 to 60 years old (mean ± SD age = 27 ± 15 years). The study was approved and registered by the Ethical Committee of the Ministry of Health of Brazil (no. 1186/2000) and National Indian Foundation/FUNAI (no. 012/CGEP/01).

The field examinations and data collecting procedures were performed by the official health professionals (FUNASA/Roraima and Brazilian non-governmental Yanomami Health Services/URIHI). The verbal and written consent was given by each participant by an official fellow tribe member familiar in both Yanomami and Portuguese languages.

2.2. Mass drug administration

Twice a year mass ivermectin (Mectizan®) treatments were initiated in April 2001 and six rounds were given until April 2004. Eligible individuals were treated with ivermectin at a dose of 150–200 μg/kg of body weight by the Ministry of Health (FUNASA). Physical evaluation and parasitological examination were conducted immediately before the 1st (pre-treatment), 3rd, 4th, 5th, 6th and 7th drug administration. Unfortunately the parasitological examinations could not be conducted before 2nd treatment. Some persons ($n = 88$) were excluded from treatment based on the usual exclusion criteria for ivermectin treatment (children aged <5 years or weighed less than 15 kg, pregnant women, nursing mothers, history or symptoms of neurological disorder).

2.3. Physical and parasitological examinations

Each eligible individual was examined for onchocercal skin disease and for the presence of characteristic subcutaneous onchocercal nodules (by palpation) around the lower ribs and back, waist, iliac crest, sacrum, hips, legs and head. After physical examination, two skin snips (weighing 1–2 mg) were taken one from the left scapula and other from the right iliac crest of each person using a 2 mm Holth-type corneoscleral punch in order to ascertain the level of microfiladermia. Snips were incubated in normal saline for about 24 h at room temperature, emerging microfilariae (Mf) were counted and the intensity of infection estimated per mg of skin (Mf/mg). Community microfilarial load (CMFL) was calculated as the geometric mean of the microfilarial load, calculated after $\log(n+1)$ transformation, of all eligible individuals aged $\geq$20 years including negative counts, where n is the individual microfilarial load (Remme et al., 1986). The individual microfilarial load for each eligible individual was calculated as the arithmetic mean of the microfilarial counts of the two skin snips. The crude intensity of infection (MFL-Total) was calculated as the geometric mean of microfilarial load among eligible individuals with positive counts. The geometric means of the microfilarial load of iliac crest (MFL-IC) skin snips and scapula (MFL-Sc) skin snips were also recorded separately from each snip among individuals with positive counts. The crude prevalence of infection was calculated according to the percentage of positive Mf skin snips in eligible population.

In order to verify the coexistence of other microfilarial pathogens, blood sample was collected by finger prick technique and used to make thin and thick blood smears that were stained by Giemsa and examined microscopically.

2.4. Statistical analysis

Data were stored in the dBASE data bank software (*Ashton Tate*, *Borland*, *CA*). GraphPadPrism4 (*GraphPadSoftware*, *Dan Diego*, *CA*) and the EpiInfo version 6 (*Centers for Disease Control and Prevention*, *Atlanta*, *GA*) statistical software programs were used for data analysis. Mann–Whitney *U* test was used to analyze differences in mean values of community microfilarial load (CMFL), crude intensity of infection (MFL-Total), microfilarial load of iliac crest (MFL-IC) and microfilarial load of scapula (MFL-Sc) skin snips (Mf/mg of skin). Chi-square test was applied to compare the prevalence of infection, prevalence of palpable nodules and prevalence of onchocercal skin disease. Spearman's rank coefficient test was used to analyze the correlation between variables.

3. Results

The coverage during the six rounds of ivermectin treatment ranged from 89% to 92% of the eligible Yanomami population ($n = 113$). Since treatments were provided after completion of each epidemiologic survey, these surveys evaluated the effects of treatments that were given 6 months before. The discrepancy between the number of ivermectin-treated Yanomami and the number of the parasitological and physical examinations recorded in each round of treatment is explained by the absence of some individuals during the survey due to the high mobility of the population, which often travels for hunting or social purposes or by their refusal to participated in biopsy sampling or in physical examination. The Yanomami who were absent during the main ivermectin distribution period received the treatment afterward independently of their participation in the study.