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Long-term effect of mass chemotherapy, transmission and risk factors for *Schistosoma mansoni* infection in very low endemic communities of Venezuela

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ABSTRACT

The prevalence of *Schistosoma mansoni* infection in Venezuela has changed from high to low due mostly to successful control activities, including mass chemotherapy and molluscicide applications. This study examined the impact of mass chemotherapy on *S. mansoni* transmission and risk factors for infection 12 years after administration of praziquantel in Venezuela. Two relatively isolated rural communities were studied, one with snail control (Manuare) and the second without (Los Naranjos). A cross-sectional survey of randomly selected households included 226 (Manuare) and 192 (Los Naranjos) consenting participants. *S. mansoni* prevalence was determined using a combination of coprological (Kato-Katz) and serological (circumoval precipitin test, alkaline phosphatase immunoassay and Western blot) tests. Data on epidemiological and socioeconomic risk factors were obtained through individual structured interviews. Univariate analysis and multivariate logistic regression models identified independent risk factors for infection. Water sites were examined for the presence of *Biomphalaria glabrata* snails. Only one participant was positive by coprology. The overall prevalences according to the combined tests were 32.7% in Manuare and 26.6% in Los Naranjos. Lower prevalences (12.7% in Manuare and 13.2% in Los Naranjos) were found in children <12 years of age representing those born after mass chemotherapy. Social demographic variables associated with infection in both communities were older age (>25 years), contact with specific water sites, and being a farmer/non-specialised worker. Mass treatment with praziquantel applied once to endemic communities led to an important and long-lasting sustained reduction of *S. mansoni* infections independent of the application of snail control. A degree of low active transmission of *S. mansoni* persisted in the treated areas which was associated with similar factors in both communities.

1. Introduction

Schistosomiasis remains one of the world's most prevalent parasitic infections and a global public health problem (WHO, 2002). It is estimated that 779 million people are at risk of schistosomiasis while 207 million are infected worldwide (Steinmann et al., 2006). The global burden due to schistosomiasis infection is estimated at 3.3 million disability-adjusted life years (DALYs) (Murray et al., 2012). Schistosomiasis is endemic in 76 countries and territories (Engels et al., 2002). It is usually a rural disease that occurs in areas with poor sanitary conditions. The distribution of schistosomiasis has changed over the past 50 years due to a number of successful control measures. These include mass treatment and control of

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intermediate host snails through the use of molluscicides and the introduction of competitive snails (Chitsulo et al., 2000; Pointier et al., 2011; Qing-Wu et al., 2002; WHO, 2002).

Venezuela is an example of a country in which control projects have played a significant role. The prevalence and transmission of *Schistosoma mansoni* have changed from high to low in Venezuela, mostly due to snail control, improved water provision and better means of faecal disposal carried out by the Schistosomiasis Control Program (SCP) established in 1943. Mass treatment with praziquantel was used in a small village of Carabobo state (Caserío El Veinticinco) for the first time in 1987 and thereafter in other endemic regions of Venezuela. However, human cases and infected snails continued to emerge, although at a very low rate in the states of Aragua, Carabobo, Guárico, Miranda and Vargas (Alarcón de Noya et al., 1999, 2007). An example of this low persistent transmission may be occurring in the valleys of Los Naranjos and Manuare in Carabobo state, south of Valencia Lake in north-central Venezuela. Both valleys showed high transmission up to the beginning of the 1990s (Alarcón de Noya et al., 1992; Delgado et al., 1993; Jove and Marszewski, 1955) even after selective chemotherapy.

In 1996, mass treatment with praziquantel was applied to approximately 75% (SCP Inspector Gonzalez, personal communication) of the inhabitants of Los Naranjos and of the whole Manuare valley by the SCP. At the time of the 1996 mass treatment, limited amount of snails had been detected in Manuare probably due to the repeated long lasting molluscicide treatment programme. No snail control was done in Los Naranjos. For the Manuare valley the efficiency of these control measures (mass chemotherapy and snail control) was evaluated in a control village (Fectifero, next to Manuare town), resulting in the absence of new cases (García et al., 1997). After 1998 no further research took place in any of the valleys.

We aimed to assess the long-term effect of mass treatment with praziquantel given 12 years before this work with (Manuare) and without (Los Naranjos) snail control, by determining whether transmission still occurred and if so, identifying risk factors for current *S. mansoni* infection.

2. Materials and methods

2.1. Study design and study area

A cross-sectional survey was performed in 2009 in two rural communities in northern Venezuela with previous high *S. mansoni* endemicity. Households were randomly selected and individuals invited to participate in the study through house-to-house visits. Structured interviews to determine risk factors for *S. mansoni* infection were applied to consenting individuals, and blood and stool samples were obtained to estimate current prevalence of infection.

Los Naranjos had an estimated population of 1205 inhabitants living in 241 houses as estimated for 2009. The main watercourse (mostly used for agriculture and eventually for domestic or recreational use) is Los Naranjos River. There is an artificial lagoon fed by a creek (Agua Fría lagoon and Agua Fría creek), heavily used for recreation until mass treatment of schistosomiasis in 1996. There is an indoor water supply system initially from a creek built 45 years ago and currently from an underground well. All houses in 1996 and in 2009 were connected to the water supply system. Faecal disposal is done in WCs leading to septic tanks; there is no main piped sewage system in the village and this has not changed since 1996.

Manuare had an estimated population of 1500 inhabitants living in approximately 300 houses as estimated in 2009. The main watercourse is Manuare River, which is used in a similar way as Los Naranjos River. There is an indoor water supply system from creeks coming from nearby mountains and underground wells since the 1940s. This system is used by all type of houses and the situation was similar in 1996. Faecal disposal is done in WCs, with sewage pipes going directly to Manuare River, with no treatment other than a sedimentation tank for retention of solids. Although this type of faecal disposal has been in place earlier than 1996, some recently built precarious dwellings or shacks have “home-made” septic tanks instead of sewage pipes.

2.2. Study population and ethical considerations

Sixty households in Los Naranjos and 75 households in Manuare were randomly selected. Individuals aged ≥3 years with a written informed consent were included in the study. A written informed consent signed by the parents or carers was obtained for children younger than 18 years. Community consent was obtained from the community head and its committee (Junta Comunal) of Los Naranjos and Manuare. All procedures were performed according to the Venezuelan laws. The University of Carabobo Ethical Committee approved the project. Members of the SCP of the Ministry of Health were present at all times of the field work. Results of laboratory tests were handed out to the participants. Treatment of infected participants with praziquantel was guaranteed.

2.3. Interview

A structured interview was conducted, consisting of: (a) household characteristics and living conditions and (b) an individual questionnaire: part (1) the household head was questioned on the type of house (determined by the nature of the floor, walls and roof), monthly income, water supply, number of inhabitants and number of children; part (2) individual questionnaires were applied to all consenting household members. Variables included age, gender, relationship within the family, knowledge and medical history of schistosomiasis, symptoms, place of defecation and water contacts within- and around Manuare and Los Naranjos. Schistosomiasis is more commonly known as bilharzia; therefore this term was used in the interviews. Knowledge was measured by asking people if they have ever heard about bilharzia and its mode of transmission.

2.4. Diagnostic methods

To determine the prevalence of *S. mansoni*, four diagnostic methods were used: coprology by Kato-Katz, antibody detection by circumoval precipitin test (COPT), alkaline phosphatase immune assay (APIA) and Western blot. The combination of these tests was used to define a case of *S. mansoni* infection as follows: (i) persons having *S. mansoni* eggs in the stools or (ii) having a positive COPT (≥10%) or (iii) having both antibody-based methods positive: APIA and Western blot.

2.4.1. Kato-Katz

One stool sample per participant was collected. Out of each collected stool sample, duplicate Kato-Katz thick smears were made (Katz et al., 1972) the following day after collection of samples. Samples were kept at 4 °C in a humid chamber in the dark, before clarification and examination. Additionally, faecal samples were fixed with merthiolate–iodine–formaldehyde (MIF) as soon as reaching the laboratory.

2.4.2. Circumoval precipitin test (COPT)

The COPT was carried out according to Oliver-González (1954). The COPT was considered positive when the proportion of positive eggs (with precipitates in their surfaces) was >15%, weakly positive