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TRANSMISSION OF *ONCHOCERCIASIS* IN NORTHWESTERN UGANDA

Transmission of *Onchocerca volvulus* Continues in Nyagak-Bondo Focus of Northwestern Uganda after 18 Years of a Single Dose of Annual Treatment with Ivermectin

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Abstract

The objective of the study was to determine whether annual ivermectin treatment in the Nyagak-Bondo onchocerciasis focus could safely be withdrawn. Baseline skin snip microfilariae (mf) and nodule prevalence data from six communities were compared with data collected in the 2011 follow-up in seven communities. Follow-up mf data in 607 adults and 145 children were compared with baseline (300 adults and 58 children). Flies collected in 2011were dissected, and poolscreen analysis was applied to ascertain transmission. Nodule prevalence in adults dropped from 81.7% to 11.0% ($P < 0.0001$), and mf prevalence dropped from 97.0% to 23.2% ($P < 0.0001$). In children, mf prevalence decreased from 79.3% to 14.1% ($P < 0.0001$). Parous and infection rates of 401 flies that were dissected were 52.9% and 1.5%, respectively, whereas the infective rate on flies examination by polymerase chain reaction (PCR) was 1.92% and annual transmission potential was 26.9. Stopping ivermectin treatment may result in onchocerciasis recrudescence.

INTRODUCTION

Onchocerciasis, a leading cause of blindness, is caused by infection with *Onchocerca volvulus*, a filarial nematode parasite. The female worms that live in the nodules produce microfilariae (mf), which inflame the skin. The mf may also enter the eyes, giving rise to

subsequently provided 5 years of financial assistance for implementation and establishment of mechanisms to sustain the CDTI program. APOC continued providing financial support to the program for 3 additional years to replace capital items and provide some training and advocacy. Subsequently, the CDTI project was expected to sustain annual mass treatment using only national resources. However, the national government did not take over the funding of CDTI activities.[13] Therefore, APOC continued to provide some assistance for specific activities alongside regular CDTI support from The Carter Center in Nebbi and Zombo districts and recently, Arua district by USAID funds for Neglected Tropical Diseases through RTI International. Overall, with the support of these agencies, annual ivermectin treatment has been provided to the at-risk population of Nyagak-Bondo for a period of 18 years. The objective of the present study was to determine whether annual mass treatment with ivermectin for 18 years could be withdrawn in Nyagak-Bondo onchocerciasis focus like in Mali and Senegal without the risk of disease recrudescence

MATERIALS AND METHODS

Mf assessments.
At baseline, 300 adults ages 20 years and over who had lived in their respective communities for at least 10 years and 58 children at 5 years of age from six baseline communities were assessed for mf prevalence. In the 2011 follow-up study, 607 resident adults and 145 resident children less than 10 years of age (born after mass treatment in all seven communities had started) were skin snipped. The procedure for skin snipping involved cleaning the site with an antiseptic; then, a piece of skin raised with the help of a disposable sterile dermal hook was carefully removed with a sterilized surgical blade. Two skin snip samples were taken from the posterior iliac crests of every selected person. Every person that was skin snipped had his or her own dermal hook and surgical blade, which were carefully disposed of after use.
The skin samples were placed immediately in wells of microtiter plates containing a sterile normal saline solution; they were kept at room temperature for 12–24 hours and examined microscopically for mf.[17–19] The results were expressed for each individual as positive or negative and recorded in the study registration form. Mf prevalence was expressed as a percentage.[4] The follow-up results were compared with baseline mf prevalence data of 1993 from adults and children.

ENTOMOLOGICAL ASSESSMENT

Crab infestation.
Crab trapping was conducted in the months of July and December of 2010 and continued through the months of January, March to June, and September to December of 2011 at a number of sites on the Nyagak, Agoi, and Wariki river systems. The crabs carrying larval and pupal stages of *S. neavei* were counted, and infestation rate (number of crabs positive for young stages of the fly) was expressed as a percent of the total number of crabs captured.[20]

Fly collection and analysis.
Two *Simulium* fly collection sites were set up at selected breeding points on the Agoi and Wariki rivers. Organized full-day catches were conducted for 7 consecutive days, 1 month in June, and September to December of 2010. Human landing collections were carried out from 07:00 to 18:00 daily.[19] A total of 401 flies collected during the period were dissected to determine parity, infection, and infective rates.[21,22] Examination of the larval stages of *O. volvulus* involved dissection of the abdomens, thoraces, and heads of the collected *Simulium* flies. The numbers of flies with larval stages (L1, L2, and L3) were counted, and monthly infection and infective rates were calculated. The result was expressed as a percentage of the total number of flies dissected × 100.[4]
Additional *Simulium* flies were caught from routine fly collections in 2011 from two previous

children, mf prevalence had reduced from 79.3% (with a range of 36.4–100% in 1993) to 14.1% (with a range of 0% to 36.8%, $P < 0.0001$) (Table 4).

Entomology.

In the Nyagak-Bondo onchocerciasis focus, crab infestation rate was 21.4% ($N = 3,245$), with a monthly range of 8.3–43.9% in an intermittent 11-month survey from July of 2010 to December of 2011 (Figure 2). The *S. neavei* parous rate investigated from June and September to December (a period of 5 months) was 52.9% ($N = 401$), with a monthly range of 0–67.8%. The infection rate (L1, L2, and L3 larval stages) was 1.50%, with a monthly range of 0–3.85%, whereas the infective rate was zero (Table 5). Pool screening of 22 head pools (1,100 flies) resulted in a single confirmed positive pool, which revealed a prevalence of infective flies of 1.92% (95% upper limit = 7.4/2,000 flies). In addition, the ATP was estimated at 26.9 (95% confidence interval = 0–66) third-stage (L3) larvae per person per year.

DISCUSSION

The results showed that, after 18 years of annual mass treatment with ivermectin, there was a significant reduction in infection. However, the children born well after ivermectin distribution commenced were still getting infected with *O. volvulus,* and a substantial proportion of adults were still positive for mf. This finding was not surprising, because breeding of *S. neavei* was ongoing, with mean crab infestation at 21.4%, a fly parous rate of 52.9%, infection rate of 1.50%, and poolscreen infective rate of 1.92% with the ATP of 26.9.

Nodule and mf rates.

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Interruption of transmission is considered to have been attained if the calculated upper 95% confidence interval of the ATP is less than 5–20 L3/person or the prevalence of flies carrying infective larvae is less than ½,000 in the overall fly population (< 0.05%).[33] The point estimate of the ATP in Nyagak-Bondo was still 26.9, with a point estimate of the prevalence of infective flies of 1.92/2,000 flies. The upper bound of the 95% confidence interval for both metrics was considerably higher than the accepted cutoffs indicative of transmission suppression. These

Although an annual dose of ivermectin given over a period of 18 years has reduced onchocerciasis infection significantly, it has not interrupted the transmission of *O. volvulus*. Although the reports from Senegal and Mali show that, in some areas, onchocerciasis can be eliminated with 15–17 years of annual treatment, the Nyagak- Bondo focus of northwestern Uganda showed that it was not possible. This finding alludes to the fact that local variations in the ecology of transmission of onchocerciasis could determine the ultimate success of an elimination program. Hence, it is imperative to focus on new innovative and flexible approaches to meet the needs of varying ecological conditions that determine the level of onchocerciasis transmission if onchocerciasis elimination becomes the goal throughout Africa.

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TABLE 1 - Population and treatment coverage of the eligible population from 1993 to 2010

TABLE 2 - Comparing data on baseline nodule prevalence of 1993 with data from the follow-e(9a)4(33(i)-2 U)-