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Interruption of the transmission of *Onchocerca volvulus* in the Kashoya-Kitomi focus, western Uganda by long-term ivermectin treatment and elimination of the vector *Simulium neavei* by larviciding

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ABSTRACT

Uganda is the only country in sub-Saharan Africa whose onchocerciasis elimination programme extensively uses vector control and biannual treatment with ivermectin. The purpose of this study was to assess the impact of combined strategies on interrupting onchocerciasis transmission in the Kashoya-Kitomi focus. Mass Drug Administration annually (13 years) followed by biannual treatments (6 years) and ground larviciding (36 cycles in 3 years) with temephos (Abate®, EC500) against *Simulium neavei* were conducted. Routine fly catches were conducted for over seven years in six catching sites and freshwater crabs *Potamonautes aloysiisabaudiae* were examined for immature stages of *Simulium neavei*. Epidemiological assessments by skin snip were performed in 2004 and 2013. Collection of dry blood spots (DBS) from children <10 years for IgG4 antibodies analysis were done in 2010 and 2013.

Treatment coverage with ivermectin improved with introduction of biannual treatment strategy. Microfilaria prevalence reduced from 85% in 1991 to 62% in 2004; and to only 0.5% in 2013. Crab infestation reduced from 59% in 2007 to 0% in 2013 following ground larviciding. Comparison of total fly catches before and after ground larviciding revealed a drop from 5334 flies in 2007 to 0 flies in 2009. Serological assays conducted among 1,362 children in 2010 revealed 11 positive cases (0.8%; 95% CI: 0.4%–1.2%). However, assessment conducted on 3246 children in 2013 revealed five positives, giving point prevalence of 0.15%; 95% CI: 0.02%-0.28%. Four of the five children subjected to O-150 PCR proved negative. The data show that transmission of onchocerciasis has been interrupted based on national and WHO Guidelines of 2012 and 2016, respectively.

1. Introduction

Human onchocerciasis, a parasitic disease found in 28 African countries, six Latin American countries and Yemen, causes blindness and severe dermatological disease (WHO, 1995). Vector control was used by the Onchocerciasis Control Programme (OCP) of West Africa from 1974 to 2002 and considerably contributed to reduction of the burden on onchocerciasis in 11 western African countries (WHO, 2010). The objective was to eliminate onchocerciasis as a public health importance, and as an obstacle to socioeconomic development in the programme area, thus allowing the repopulation and development of those valleys previously almost deserted because of onchocerciasis (WHO, 1991). However,

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with the registration of ivermectin in 1987, efforts to control this disease shifted from vector control approaches to the mass distribution of ivermectin, a drug donated by Merck & Co. (Thylefors et al., 2008). In the Americas, the Onchocerciasis Elimination Programme of the Americas (OEPA) has been highly successful and has brought the disease close to elimination since 1993. Colombia and Ecuador announced the elimination of onchocerciasis in 2013 and 2014, respectively (WHO, 2013, 2014). In Guatemala and Mexico, treatment has also been stopped in seven foci where it has been replaced by surveillance to detect possible recrudescence (The Carter Center, 2014). Similarly, in sub-Saharan Africa evidence has emerged of the successful elimination in isolated foci in Senegal and Mali, Uganda and Sudan (Diawara et al., 2009; Katabarwa et al., 2014; Higazi et al., 2013). These are commendable successes that need to be adopted by other African countries if onchocerciasis elimination is to be achieved in the continent.

In Uganda, onchocerciasis was endemic in 36 out of 112 districts. In 1998 it was estimated that over 2.0 million people were at risk of infection, with some 1.4 million infected (Ndyomugyenyi, 1998). Most of the endemic districts have been under Mass Drug Administration (MDA) with ivermectin for over 15 years and in some isolated foci MDA has been supplemented by ground larviciding (Ndyomugyenyi et al., 2007; Garms et al., 2009). Kashoya-Kitomi is one of the foci in western Uganda with a history of over 20 years of ivermectin treatment. However, annual treatment with ivermectin alone was reported not to achieve interruption of onchocerciasis transmission (Ndyomugyenyi et al., 2004). Infection rates of parous *S. neavei* at Kitomi Bridge declined from over 50% in 1991–20% in 2003 but disease transmission remained intense. A vector control intervention was therefore initiated on the Kitomi river system in July 2003 to enhance the effect of Community Directed Treatment with Ivermectin (CDTI) towards the interruption of transmission. A first series of seven riverine treatments of R. Kitomi and its tributaries (Fig. 1) with the organophosphorous larvicide temephos (Abate® EC500) at monthly intervals reduced biting densities and transmission; the routine catching site along R. Kitomi recorded zero and suppressed crab infestation rate to about 1%. However, in 2004, there was re-infestation from outside sources due to incomplete mapping of the focus. In 2007, following the launching of the Ugandan onchocerciasis elimination policy, vector elimination was initiated in this focus addressing the earlier challenges recorded in 2004. Herein, we report the impact of the two interventions on interrupting onchocerciasis transmission in Kashoya-Kitomi focus.

2. Materials and methods

2.1. Study area

Kashoya-Kitomi onchocerciasis focus is located around the Kashoya–Kitomi forest reserve in Western Uganda, which covers an area of approximately 399 km^2 and traverses the districts of Kamwenge, Ibanda, Buhweju and Rubirizi. The main rivers are Kitomi, Ngoro and Buhindagi, draining into Lake George (Fig. 1). The vector species breeding in these river systems was *S. neavei*. Prior to the introduction of CDTI a Rapid Epidemiological Mapping of Onchocerciasis (REMO) was conducted in the focus between 1996 and 1997. This was to provide accurate estimates of the population living in high risk areas for the disease and to identify communities to be given priority treatment with ivermectin. The REMO teams comprised of epidemiologists, geographers and entomologists who used topographical maps (1:250,000) to select sampled villages. In each community, 50 adult males who had lived in the area for at least 10 years were randomly selected and examined for the presence of palpable onchocercal nodules (Ngouma and Walsh, 1993). The results from REMO allowed the programme to categorize hyper- and meso-endemic areas for mass treatment with ivermectin (Ndyomugyenyi, 1998). The focus has 385 communities of which 352 were categorized as hyper-endemic and 33 as meso-endemic. With a total population at risk of 209,275 Kashoya-Kitomi is considered to be geographically isolated from other foci of onchocerciasis (Walsh et al., 1996) because of the distance to other foci in comparison to the limited flight range of *S. neavei*.

2.2. Mass drug administration with ivermectin

The communities in the Kashoya-Kitomi focus have had over 20 consecutive treatment rounds of Mass Drug Administration (MDA) with ivermectin. Control of onchocerciasis by MDA with ivermectin started in 1991 with support of the German Technical Cooperation (GTZ). In order to ensure effective coordination of onchocerciasis control activities, in 1992 the Ministry of Health, Uganda, established the Onchocerciasis Control Programme. During this early period mass treatment with ivermectin was through community based distributors chosen by their communities. Mobile teams had the responsibility of training Community health workers (CHWs) in ivermectin distribution methods in their villages. This strategy was reported in other parts of Africa to have improved ivermectin treatment coverage (Hopkins, 1998). In this focus, GTZ Basic Health services were supporting the distribution of ivermectin which they initiated as early as 1991. However, in 1999, a new approach of Community Directed Treatment with ivermectin (CDTI) was introduced with support from the African Programme for Onchocerciaisis Control (APOC). In CDTI, communities were empowered to take responsibility of ivermectin distribution, and they were responsible for planning, selecting treatment venue, medicine distributors, selecting period for treatment and collection of medicines from the nearest health facilities (WHO, 1996a,b). In 2007, the objective of the Ugandan programme was changed from control to elimination, which allowed the inclusion of communities in hypo-endemic areas based on the national guidelines (MOH, 2012). Vector control was piloted in 2003 to supplement MDA and due to its positive results it allowed the introduction and expansion of vector elimination in 2007.

2.3. Ground larviciding using temephos (Abate® EC500)

In the Kashoya-Kitomi focus a high level of onchocerciasis transmission was reported despite ivermectin MDA (Lakwo, 2004). Larviciding was therefore aimed at breaking the transmission of onchocerciasis. The focus has intricate river systems that required comprehensive vector mapping to determine larvicide dosing points. Most of the mapping activities were conducted between 2003 and 2004 and included extensive insecticide carry trials on R. Kitomi and R. Ishangwe. In 2007, with the initiation of vector elimination, completion of mapping *S. neavei* breeding sites was done on R. Nkurungu, R. Nyamuswiga and R. Buhindagi including its tributaries.

Insecticide carry-trials were conducted on R. Buhindagi and its tributaries where it was not earlier done. Temephos (Abate® EC500) was applied against *S. neavei* immature stages at a rate of 0.2–0.4 mg/L. Application of temephos was done at an interval of 4 weeks for the first 6 months of operation and once all the sites have freshwater crabs free from the immature stages of *S. neavei* vector, decision was then made to shift to 8-weekly interval (Garms et al., 2009). The insecticide was pre-mixed in a 15 l knapsack sprayer and applied for a period of 30 min at the established dosing points. Effect of larviciding on *S. neavei* immature stages was assessed every 4 weeks prior to the next application cycle and this was done in all the established sites in the focus (Lakwo et al., 2013).