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Short Communication

Status of forest onchocerciasis in the Lower Cross River Basin, Nigeria: Change in clinical and parasitological indices after 6 years of ivermectin intervention

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Onchocerciasis is commonly known as river blindness because the most devastating effect caused by the microfilariae of *Onchocerca volvulus* is damage to the eyes that leads to blindness. Less appreciated but definitely more widespread are onchocercal skin lesions.[1] Nigeria remains one of the most affected countries in the world with over 6 million people infected, 13 million at risk of having the disease, over 100 000 blind, and an estimated 1 million presenting with various skin abnormalities.[2]

The strategy used to control onchocerciasis in Nigeria is mass drug administration through community-directed treatment with ivermectin. This strategy, adopted by the African Programme for Onchocerciasis Control (APOC), is being employed

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in countries outside the WHO's Onchocerciasis Control Programme in West Africa. Although mass ivermectin distribution and treatment is still in place in communities endemic for onchocerciasis, reports on the effectiveness of treatment are still scanty in view of the fact that the disease pattern varies in distribution, endemicity and treatment coverage among endemic countries. As APOC aims to close in 2010, studies on the effect of ivermectin from various onchocerciasis endemic areas in Africa would indicate whether or not it is necessary for APOC to extend the control programme in these communities. In the 6-year period from 1995 to 2001, repeated annual ivermectin distribution took place in all endemic communities of the Lower Cross River Basin, Nigeria. The aim of this study was to evaluate the impact of six successive mass treatments of a population on the parasitological and clinical indices of onchocerciasis in eight hyperendemic communities of Lower Cross River Basin, Nigeria.

Cross River State is situated within the Cross River Basin, between latitudes 5°32′ and 4°27′ north and longitudes 7°50′ and 2°20′ east (Fig. 1). The study area has been described elsewhere.[3] The communities reported in this study were among a host of villages from Cross River State, Nigeria from which pretreatment (baseline) epidemiological data were collected by the National Onchocerciasis Control Programme (NOCP) in 1994, just before the

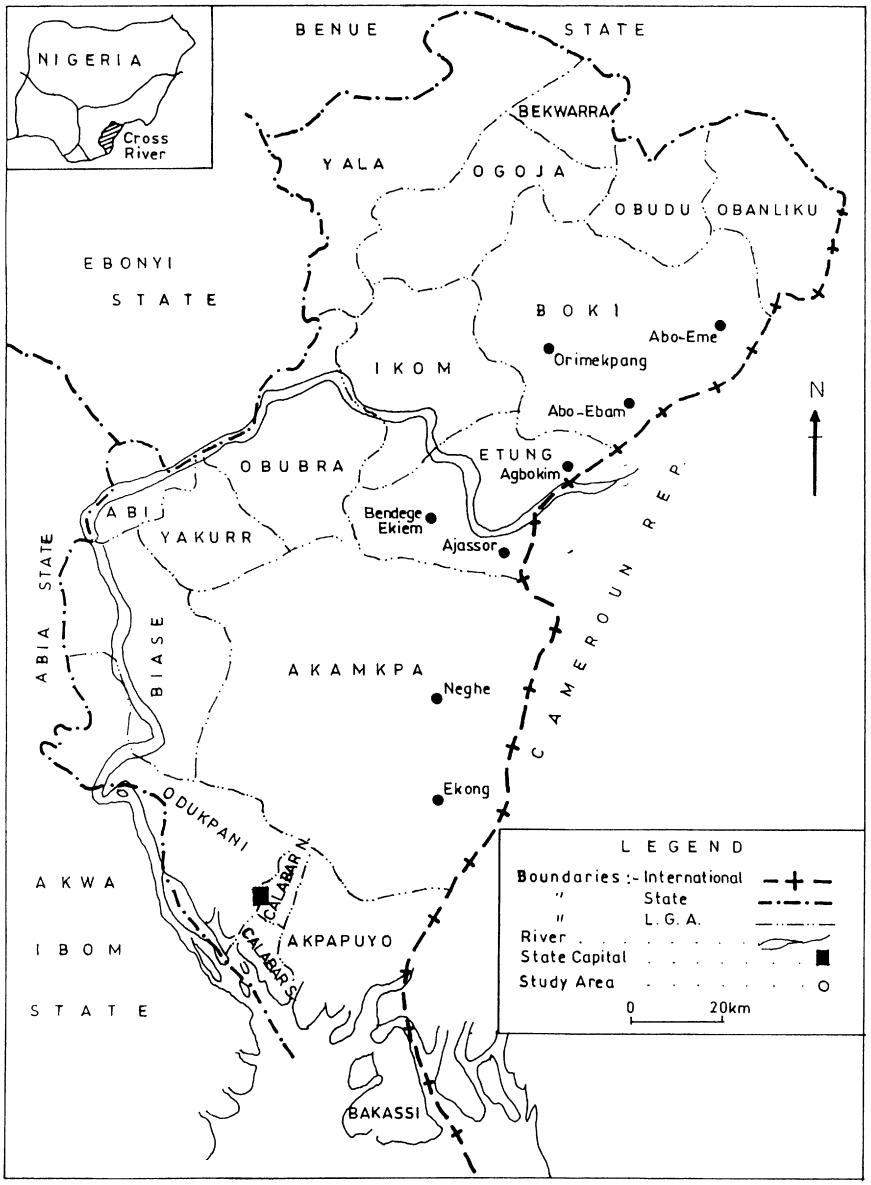

Figure 1 Map of Cross River State showing study sites.

commencement of mass drug administration. The communities were selected on the basis of their hyperendemic status, and they are currently receiving treatment with ivermectin. A cohort selected at random from the hyperendemic communities was examined because of the significant public health importance of controlling disease in these communities. In total, 916 subjects were examined in the pretreatment epidemiological survey in 1994, and 2065 subjects were examined in the treatment evaluation study in 2001. The Cross River State Ministry of Health, Calabar, Nigeria approved the study, and informed consent was sought and obtained from communities and individuals.

All subjects who voluntarily presented themselves at the screening centre for the survey were asked for identification data (name, age, sex, occupation, number of years resident). Bloodless skin snips were obtained from the right and left iliac crests of those examined using a 2 mm Holth Corneoscleral Punch (Storz Instrument to GMBH, Heidelberg, Germany), and examined for microfilariae of *O. volvulus* as described previously.[2,4] Each subject underwent a physical examination, and was asked to undress in an enclosed area with adequate illumination. They were examined for leopard skin and asked if they had nodules (local name 'Ekikoi or Ekpuk', meaning swelling). Thereafter, nodules were palpated for around the lower ribs and back, waist, iliac crests, hips and legs as described previously.[5] Other skin manifestations (papular lesions) were also investigated. No attempt was made to distinguish between acute papular onchodermatitis and chronic papular onchodermatitis. Blindness was defined as the inability to count three fingers at 3 m distance or less. Complete ophthalmological examinations were not performed on the subjects.

Ivermectin treatment of onchocerciasis began in Cross River State in July 1995 as a combined effort of the State Ministry of Health and the United Nations Children Fund (UNICEF). Successive treatments were given between the months of February and March each year. In 1998, Cross River State began receiving APOC's support with the initiation of community-directed treatment with ivermectin. In each of the communities examined, community-directed distributors (CDDs) were responsible for ivermectin distribution. The height of all subjects was determined and the manufacturer's exclusion criteria were adopted in drug administration. For all those who accepted the drug, individual compliance was ensured as the subject was made to ingest the drug in the presence of the CDD. The full name, sex, age and height of all treated subjects were recorded at every treatment period and the dose was noted. The total number of people treated from each community between 1998 and 2001 was retrieved from the community treatment register and the annual summary treatment statistics kept by NOCP, Calabar Office, Nigeria.

All statistical analyses were performed using a commercial statistical package (Analyseit+General 1.71 version statistical software, Analyse it, USA). Differences in prevalence between 1994 and 2001 were tested using Chi-squared (χ^2) test. The comparison of intensity was tested by Student's *t*-test. Pre- and post-treatment endemicity data were analysed by means of parasitological indices. The community microfilarial load (CMFL) is the geometric mean number of microfilariae per skin snip among adults aged 20 years or over in the community, including those with negative counts. This mean was calculated using a log (x+1) transformation.

The interval therapeutic coverage for the study area over the 6-year period was 74% (range 52–90%), and the annual therapeutic coverage for the communities ranged from 38% to 98%. To evaluate the impact of this treatment coverage on the disease, changes in prevalence and infection were monitored in 2065 subjects from the eight endemic communities in 2001. In 1994, 70% of the 916 subjects examined were positive for *O. volvulus* microfilariae in their skin snips. In 2001, microfilariae could only be detected in 44.9% of the 2065 subjects examined, representing a 35.9% reduction [range 2.1–78.9%; $\chi^2 = 70.83$; odds ratio (OR) 7.5; 95% confidence interval (CI) 6.31–9.14; $P<0.001$] (Table 1). There was a remarkable reduction in the prevalence of skin microfilariae (PMF) in Neghe from 76.5% in 1994 to 16.1% in 2001, and this was followed by Ajassor with a 59.1% reduction in PMF. There was a significant ($P<0.05$) reduction in PMF in all the communities except for Ekong. The CMFL in all the treated communities was also reduced during the period of investigation. The overall CMFL for the study area was 8.01 microfilariae/skin snip in 1994, and this reduced to 3.20 microfilariae/skin snip in 2001, representing a 60.1% reduction (range 35.52–74.05%; $t = 13.52$; OR 4.5; 95% CI 3.72–5.30; $P<0.001$) (Table 1). Overall, ivermectin intervention reduced papular dermatitis significantly ($P<0.05$) from 43.1% to 12.0%, representing a reduction of 72.2% (range 50.0–81.0%; $\chi^2 = 18.34$; OR 4.2; 95% CI 3.51–5.22; $P<0.05$); reduced nodule prevalence from 43% to 25.2%, representing a reduction of 40% (range 32.4–65.5%; $\chi^2 = 39.81$; OR 2.54; 95% CI 2.16–3.00; $P<0.05$); and reduced the rate of

Table 1 Prevalence of skin microfilariae (PMF) and community microfilarial load (CMFL) in eight communities receiving ivermectin

Community	PMF			CMFL (microfilariae/skin snip)			Total number examined	
	1994	2001	Reduction (%)	1994	2001	Reduction (%)	1994	2001
Orimekpang	67.2	50.0	25.6	7.42	3.27	55.92	90	364
Abo-Emeh	66.5	56.3	15.3	7.24	3.10	57.18	83	160
Abo-Ebam	67.1	53.6	20.1	6.85	3.01	56.06	124	220
Ajassor	66.5	27.2	59.1	5.63	1.56	72.29	142	368
Agbokim	75.5	56.3	25.4	8.44	3.22	61.85	144	238
Bendeghe-Ekiem	66.0	40.2	39.1	7.25	2.15	70.35	154	408
Ekong	60.0	73.4	2.1	9.32	6.01	35.52	95	158
Neghe	76.5	16.1	78.9	8.44	2.19	74.05	84	149
Total	70.0	44.9	35.9	8.01	3.20	60.10	916	2065
P-value	<0.05			<0.05				

Table 2 Prevalence of selected morbidity indicators in eight hyperendemic communities of Lower Cross River Basin before treatment (1994) and after treatment (2001)

Community	Papular dermatitis			Nodules			Blindness			Leopard skin		
	1994	2001	Reduction (%)	1994	2001	Reduction (%)	1994	2001	Reduction (%)	1994	2001	Reduction (%)
Orimekpang	30.4	10.6	65.1	44.8	30.3	32.4	10.0	6.2	38.0	10.6	9.4	11.3
Abo-Emeh	31.0	9.3	70.1	44.3	23.9	46.1	10.2	7.6	25.5	23.9	22.9	4.2
Abo-Ebam	30.5	6.1	80.0	44.7	27.1	39.4	9.7	7.4	23.7	29.1	28.3	2.8
Ajassor	20.3	6.9	66.0	44.3	22.4	49.4	14.6	5.9	59.6	15.1	14.4	4.6
Agbokim	21.0	6.6	68.4	50.0	24.4	51.2	14.4	8.9	38.2	12.6	11.7	7.1
Bendeghe-Ekiem	18.5	3.5	81.0	44.0	25.3	42.5	14.0	6.0	57.1	16.5	15.9	3.6
Ekong	75.8	37.9	50.0	40.0	20.5	48.8	15.3	14.1	7.8	22.4	21.8	2.7
Neghe	59.6	13.8	76.8	51.0	17.6	65.5	14.7	12.6	14.3	21.6	19.4	10.2
Total	43.1	12.0	72.2	42.3	25.2	40.0	12.9	8.6	33.3	18.9	18.0	4.8
P-value	<0.05			<0.05			<0.05			>0.05		

blindness from 12.9% to 8.6%, representing a reduction of 33.3% (range 7.8–59.6%; $\chi^2 = 4.93$; OR 1.81; 95% CI 1.41–2.33; $P > 0.05$) (Table 2). Out of the 220 subjects who were considered to be blind in 1994 due to their inability to count three fingers at a distance of 3 m or less, 12.9% tested positive for microfilariae of *O. volvulus*, while out of the 112 subjects who were considered blind in 2001, seven (8.6%) were positive for microfilariae of *O. volvulus*. There was no significant ($P > 0.05$) reduction in the blindness rate in Ekong. There was no significant change in the prevalence of leopard skin (18.0%) ($\chi^2 = 6.69$; OR 1.14; 95% CI 0.93–1.39; $P > 0.05$] (Table 2).

The findings from this study show that after 6 years of annual ivermectin treatment, the hyperendemic status of the study area has been reduced to mesoendemic. However, these effects varied from one community to another. These results show that onchocerciasis in still a public health problem in the Lower Cross River Basin. There was a remarkable reduction in PMF and CMFL in the study area, which is consistent with a previous report[2], which found that initial treatment with ivermectin brings about a dramatic decrease in skin microfilarial densities, whereas subsequent doses are followed by more gradual reduction. In this investigation, the degree of reduction was higher for CMFL than PMF. The impact is more on microfilarial densities than prevalence. The varied percentage reduction observed in PMF and CMFL in all the communities may be due to the different treatment coverage patterns in the river basin. Although Orimekpang, Abo-Emeh, Abo-Ebam and Agbokim had interval treatment coverage (>70%), the reduction in PMF values was not remarkable. However, the opposite was true for CMFL. The impact of ivermectin on PMF and CMFL in Ekong was

very poor, and the poor coverage (<55%) may have had an adverse effect on this phenomenon. There were serious adverse reactions following ivermectin treatment in this community. Hence, there was complete rejection of ivermectin in Ekong. Absenteeism and poor community leadership in the community may also have played major roles in the poor treatment outcome. However, due to the poor acceptance and compliance with annual ivermectin treatment, the people were properly mobilized by explaining the expected adverse reactions and the advantages of ivermectin, and reassured about efficacy and safety. This was done before the seventh round of treatment. This may lead to an increase in treatment coverage. It has been suggested that close monitoring of drug treatment and distribution by the CDDs and strict enforcement of compliance by every eligible member of the endemic community are needed if the campaign against river blindness is to be achieved. From the present study, it is possible that the reservoir of skin microfilariae available to the local fly population has continued to decrease and this progressive reduction may have led to a decrease in the transmission of onchocerciasis between 1994 and 2001 in the study area.[3] This observation is true because CMFL is an index of the public health importance of the disease, and onchocerciasis is considered to be a public health problem when the CMFL exceeds 5–10 microfilariae/skin snip.[6] The present study found that CMFL decreased from a pretreatment value of 8.01 microfilariae/skin snip to 3.20 microfilariae/skin snip following treatment. Since ivermectin has been reported to reduce the number of microfilariae in the skin,[2,6,7] the drug was expected to affect clinical signs and symptoms by arresting the progression of existing disease and preventing the development of new lesions. The finding of a significant reduction in the severity of the two morbidity indicators (dermatitis, nodules) shows that clinical improvement in certain types of skin lesions may become evident after repeated doses of ivermectin. Papular dermatitis can be due to causes other than onchocerciasis, including other infectious agents such as scabies, pediculosis, larva migrans, dermatophytes, insect bites and contact allergens. Ivermectin is effective against scabies, pediculosis and larva migrans,[8] thus the decrease in papular lesions noted in this study may be attributed to the beneficial side effects of mass ivermectin administration. Onchocerciasis is only one of the major causes of blindness in endemic areas, and differentiating onchocercal blindness from other causes such as trachoma, cataracts, glaucoma and diabetes requires complete ocular examination by an ophthalmologist. This aspect of the work was not investigated. However, subjects who were considered to be blind due to onchocerciasis were those subjects who tested positive for microfilariae of *O. volvulus* after their inability to count three fingers at a distance of 3 m or less. Improvement in onchocerciasis lesions following treatment appears to be variable, which may be due to the fact that some established lesions are irreversible or even continue to progress despite treatment, especially if small numbers of skin microfilariae persist.[9,10]

The significant reduction in PMF, CMFL and clinical symptoms of onchocerciasis in the Lower Cross River Basin attests to the advantages of repeated mass treatment with ivermectin on the transmission of onchocerciasis. It is the authors' belief that if the treatment coverage is improved and sustained, the level of microfilariae will be reduced drastically to a level that the disease would no longer be a public health problem. Routine monitoring of ivermectin distribution and treatment is recommended. The awareness campaign of the multiple benefits of ivermectin should be intensified and sustained in endemic communities.

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References

1. Murdoch ME, Hay RJ, Mackenzie CD, Williams JF, Ghalib HW, Cousens S, Abiose, et al. A clinical classification and grading system of the cutaneous changes in onchocerciasis. *Br J Dermatol* 1993;**129**:260–9.
2. Oyibo WA, Fagbenro-Beyioky AF. Effect of repeated community based ivermectin treatment on the intensity of onchocerciasis in Nigeria. *Rur Rem Health J* 2004;**3**:211–6.
3. Opara KN, Fagbemi BO, Ekwe A, Okenu DMN. Status of forest onchocerciasis in the Lower Cross River Basin, Nigeria. Entomological profile after five years of ivermectin intervention. *Am J Trop Med Hyg* 2005;**73**:371–6.
4. Kirkwood B, Smith P, Marshall T, Prost A. Variations in the prevalence and intensity of microfilairae infection by age, sex, place and time in the area of the Onchocerciasis Control Programme. *Trans R Soc Trop Med Hyg* 1983;**77**:857–61.
5. Albeiz EJ, Buttner DW, Duke BO. Diagnosis and extirpation of nodules in human onchocerciasis. *Trop Med Parasitol* 1988;**39**(Suppl. 4):331–46.
6. World Health Organization. *Summary report of the OCP/TDR meeting on the impact of ivermectin on onchocerciasis transmission*. JPC 22-JAF/INF/DOC. 2002. p. 2.1–14.
7. Ndyomugyenyi R, Tukesiga E, Buttner DW, Garms R. The impact of ivermectin treatment alone and when in parallel treatment alone and when in parallel with Simulium neavei

elimination on onchocerciasis in Uganda. *Trop Med Int Health* 2004;**9**:882–6.
8. Del Mar Saez-De-Ocariz M, Mckinster CD, Orozco-Covarribias L, Tamayo-Sanchez L, Ruiz-Maldonado R. Treatment of 18 children with scabies or cutaneous larva migrans using ivermectin. *Clin Exp Dermatol* 2002;**27**:264–7.
9. Whitworth JAG, Morgan D, Maude GH, et al. A community trial of ivermectin for onchocerciasis in Sierra–Leone: clinical and parasitological responses to four doses given six-monthly intervals. *Trans R Soc Trop Med Hyg* 1992;**86**:277–80.
10. Boatin BA, Hougard JM, Alley ES, Akpoboua LKB, Yameogo L, Diembele N. The impact of mectizan treatment on the transmission of onchocerciasis. *Ann Trop Med Parasitol* 1998;**92**(Suppl. 1):547–60.