

East African Medical Journal Vol. 78 No. 10 October 2001

VALIDATION OF REPORTS OF NODULES DISSOLUTION AFTER REPEATED IVERMECTIN TREATMENT OF ONCHOCERCIASIS IN SOUTHEASTERN NIGERIA

C. C. Ukaga, BSc, MSc, PhD, Senior Lecturer, I. N.S. Dozie, BSc, MSc, Senior Lecturer and B.E.B Nwoke, BSc, MSc, PhD, Professor, Medical Parasitology and Entomology Research Laboratory, College of Sciences, Imo State University Owerri, PMB 2000, Owerri, Nigeria.

Request for reprints to: Dr I. N.S. Dozie, Medical Parasitology and Entomology Research Laboratory, College of Sciences, Imo State University Owerri, PMB 2000, Owerri, Nigeria.

**VALIDATION OF REPORTS OF NODULES DISSOLUTION AFTER REPEATED IVERMECTIN TREATMENT OF ONCHOCERCIASIS IN SOUTHEASTERN NIGERIA**

C. C. UKAGA, I. N.S. DOZIE and B.E.B. NWOKE

**ABSTRACT**

**Objective:** To ascertain the validity of the claims by villagers in endemic communities in southeastern Nigeria that repeated ivermectin treatment cause disappearance or dissolution of onchocercal nodules.

**Design:** From baseline epidemiological data, four communities (Amuro, Aku, Nzerem Ikpem and Awuchinimo) were randomly chosen as the study sites. A total of 324 adults (hitherto had onchocercal nodules), aged  $\geq 20$  years from these communities were enlisted in the study. After clinical examination, each of the villager was interviewed with structured, pre-tested questionnaire. Also personal and focus group discussion was held.

**Results:** Sixty nine (21.30%) respondents; 16.67% from Amuro, 32.26% from Aku, 19.05% from Nzerem Ikpem and 15% from Awuchinimo claimed that their nodules gradually dissolved or disappeared. A significant ( $p < 0.05$ ) proportion (82.61%) attributed this phenomenon to repeated doses of ivermectin; 4.35% claimed it was not due to ivermectin therapy while 13.04% were not sure of the cause.

**Conclusion:** The results have opened challenges in our understanding of the role of ivermectin therapy in endemic communities and calls for further studies of nodule dissolution in other onchocerciasis endemic communities.

**INTRODUCTION**

In Nigeria and other west African countries, human onchocerciasis is a serious public health problem(1,2), especially among the farming populations who produce the bulk of the food and industrial raw materials(3). This disease is a clinical syndrome partly or entirely characterised by severe skin lesions, nodules, ocular and lymphatic pathologies and sometimes systemic manifestations. The pattern of socio-economic/cultural liability that has emerged due to this parasitic disease has been particularly damaging to infected individuals and endemic communities. Hence National (Nigerian) Onchocerciasis Control Programme(NOCP) in collaboration with United Nation Agencies (WHO, UNICEF) and NGDO coalition started community distribution of ivermectin (Mectizan<sup>®</sup>) as a control strategy in endemic areas in 1991.

Ivermectin, technically is not a macrofilaricide but in course of routine evaluation and monitoring of the ongoing Community Directed Distribution of Ivermectin (CDTI) in endemic communities in the rain forest of south-eastern Nigeria, some villagers reported the disappearance or dissolution of onchocercal nodules after repeated treatment with ivermectin. Challenged by this field observation, this present study was carried out to

ascertain the validity of this claim with a view to generate an important baseline data for further studies.

**MATERIALS AND METHODS**

The study was carried out in four onchocerciasis hyperendemic communities of Amuro, Aku, Nzerem Ikpem and Awuchinimo(4) in the tropical rain forest zone of the Imo River Basin of South-eastern Nigeria. Located between Lat.  $5^{\circ} 35'$  and  $5^{\circ} 56'N$  and Long.  $7^{\circ} 15'$  and  $7^{\circ} 25'E$ , this area has a lot of permanent river systems which are breeding foci of the vectors of the disease, *Simulium damnosum* s.l(5).

The villagers who are mainly rural farmers are continuously exposed to the bites of these vector flies and transmission of the disease is by way of residential proximity or by way of occupational exposure. In view of the widespread and severity of the disease in this area, NOCP in collaboration with Global 2000 River Blindness Programme (GRBP) commenced the distribution of ivermectin in this area in 1992. At the time of this study, these communities were on the fourth treatment cycle (1992-95).

The villagers used for this study were randomly selected resident male and female adults aged  $\geq 20$  years, from the study communities who hitherto (before treatment) had onchocercal nodules from the epidemiological records. Based on the descriptive information from the preliminary observation (during the monitoring and evaluation of the program), revised structured pre-tested questionnaire was administered to the villagers after clinical examination of the nodule locations and size/texture. Also personal and focus group discussions (5-10 persons per

group) were held to strengthen the response of the questionnaire. The answers to the questions were recorded directly into individual questionnaires and analysed using the Epi-Info Chi-square test statistics.

## RESULTS

A total of 324 randomly, chosen infected villagers were interviewed in this study. From the four communities which constituted the study, the results showed that 16.67% from Amuro, 32.26% from Aku, 19.05% from Nzerem Ikpem and 15% from Awuchinimo claimed that their onchocercal nodule(s) gradually dissolved or disappeared (Table 1). On the whole, 69(21.30%) out of the 324 villagers claimed that their onchocercal nodule(s) disappeared/dissolved.

**Table 1**

*Number of persons per study population in endemic communities with experience of dissolved/disappeared nodules*

Study area	Total number of persons interviewed	No. of persons who experienced dissolution of nodules (%)
Amuro	108	18(16.67)
Aku	93	30(32.26)
N. Ikpem	63	12(19.05)
Awuchinimo	60	9(15.00)
Total	324	69(21.30)

Furthermore the results in Table 2 showed that a significant ( $p < 0.05$ ) proportion (82.61 %) of those who reported that their onchocercal nodules dissolved or disappeared claimed that the phenomenon was due to repeated ivermectin treatment. The other 4.35% reported that it was not due to the ivermectin therapy while 13.04% were not sure of the cause for the disappearance of the nodules.

**Table 2**

*Perceived causation for disappearance of nodules*

Study area	Total number of persons who experienced dissolution of nodules	Causation for nodule dissolution (%)		
		Ivermectin (%)	Not ivermectin (%)	Not sure (%)
Amuro	18	18 (100)	0 (0)	0 (0)
Aku	30	21 (70)	3 (10)	6 (20)
N. Ikpem	12	9 (75)	0 (0)	3 (25)
Awuchinimo	9	9 (100)	0 (0)	0 (0)
Total	69	57 (82.61)	3 (4.35)	9 (13.04)

During the personal and group discussions, the majority (73.68%) of the respondents gave descriptive accounts of how their nodules which were initially big, hard and firm got smaller and softer after the first dose of ivermectin treatment and later dissolved following the

subsequent doses. This was more or less confirmed, when the individuals were palpated. In about 21 cases, the dissolving nodules were felt, whereas in others they could not be located anymore. The respondents attributed the dissolution/disappearance of their nodule(s) to repeated annual dose of ivermectin. Other respondents who still had their nodules and had heard of the dissolution/disappearance phenomenon wondered why theirs were yet to dissolve.

On the assessment of health problems in the area, the majority (62%) of the participants noted that malaria was a more serious health problem than onchocerciasis while 27% of them reported that the disease especially the oncho-skin disease was a more serious problem in the community. Despite the seemingly low ranking of onchocerciasis as a serious public health problem in the area, a great majority of participants indicated their continued willingness to participate in the on-going distribution of ivermectin because of the many benefits.

## DISCUSSION

The present results showed a very high frequency of claims by respondents that their nodules dissolved/disappeared after repeated ivermectin therapy. Scattered field reports within the bioecological zone also point to this phenomenon. Again, a consistent description of respondents was that their nodule(s) which were hard before the treatment gradually became soft and at times smaller in size with repeated therapy; and eventually dissolved/disappeared. The inability to locate visible/palpable onchocercal nodule(s) in hitherto nodule-carrying villagers tend to support these claims.

Ivermectin is not technically a macrofilaricide but the studies of Duke and his colleagues(6) noted that 12 monthly dose of ivermectin killed a proportion of adult worms (21% males and 22% females) leaving the rest of the worms relatively unaffected. In a similar study, Chavasse *et al*(7) observed an increasing number of discoloured and calcified worms with a possible trend towards mortality after four to five doses of ivermectin. Even though ivermectin does not show a clear cut universal macrofilaricidal effect as seen after adequate dose with suramin(8), the results(6,7) tend to support the claims of villagers in the present study. For instance, if ivermectin could by some unidentified mechanism result in the death of the adult worms, subsequent degeneration and re-absorption might call forth a process, possibly enzymatic that could result in the softening, dissolution/disappearance of nodules. It could also be possible that the putative macrofilaricidal action of repeated ivermectin therapy may vary from person to person perhaps in relation to individual physiologic composition and host-immune response and subsequent pharmacokinetics of the drug in the infected persons. This may explain why some affected respondents reported dissolution/disappearance of nodule(s) after repeated ivermectin therapy while others did not. The present results have opened up a lot of

questions in our understanding of the importance and other benefits of ivermectin therapy in onchocerciasis control.

#### ACKNOWLEDGEMENTS

We are very grateful to Global 2000 River Blindness Programme (GRBP) for logistic support and to the villagers for co-operation in the course of the study.

#### REFERENCES

1. Prost A. The burden of blindness in adult males in the savannah villages of West Africa exposed to onchocerciasis. *Trans. roy Soc. trop. Med. Hyg.* 1986; **80**: 522-527.
2. Nwoke B.E.B. The socio-economic aspects of human onchocerciasis in Africa: the present appraisal. *J. Hyg. Epidem. Microbiol. Immunol.* 1990; **34**:37-44.
3. Gemade E.I.I., Jiya Y., Nwoke B.E.B., Ogunba, E.O., Edegere H., Akoh J.I. and Omojola A. Human onchocerciasis: current assessment of the disease burden in Nigeria by rapid epidemiological mapping. *Ann. trop. Med. Parasit.* 1988; **92** (suppl. 1): 579-583.
4. Nwoke B.E.B., Edungbola L.D., Mencias B.S., Njoku A.J., Abanobi O.C., Nkwogu F.U., Nduka F.O. and Oguariri R.M. Human onchocerciasis in the rainforest zone of south eastern Nigeria. I. Rapid assessment for community diagnosis in the Imo River Basin. *Nig. J. Parasit.* 1994; **15**:7-18.
5. Nwoke B.E.B. and Uwazie O.U. Studies on the blackflies *Simulium* of Imo State Nigeria. The distribution of immature stages in Isiukwato Okigwe area. *Nig. J. Parasit.* 1991; **12**:29-37.
6. Duke B.O.L., Fea - Flores G., Castro J., Cupp E.W. and Munoz B. Effects of multiple monthly doses of ivermectin on adult *Onchocerca volvulus*. *Amer. J. trop. Med. Hyg.* 1990; **43**:657-664.
7. Chavasse D.C., Post R.J., Lemoh P.A. and Whitworth J.A.G. The effect of repeated doses of ivermectin on adult of female *Onchocerca volvulus* in Sierra Leone. *Trop. Med. Parasit.* 1992; **43**:256-257.
8. Duke B.O.L. Suramin and the time it takes to kill *Onchocerca volvulus*. *Trop. Med. Parasit.* 1991; **42**: 346-350.