PRELIMINARY ASSESSMENT OF THE IMPACT OF IVERMECTIN IN THE TREATMENT OF ONCHOCERCIASIS IN EZZA NKWUBOR AND UMUHU COMMUNITIES IN ENUGU STATE, NIGERIA

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ABSTRACT

Blackflies have been implicated over the years as the vector of onchocerciasis (River blindness). Ivermectin on the other hand has been the drug of choice for the treatment of onchocerciasis and to a great extent indirectly serving as systemic insecticide thereby breaking the transmission cycle of the disease. This study tried to evaluate the impact of ivermectin in Ezza Nkwubor and Umuhu communities of Enugu East and Isi Uzor LGAs of Enugu State, respectively. Epidemiological survey was carried out to check for the presence of microfilariae in skin snip samples collected from both left and right iliac crests of subjects living in the community. A total of 147 subjects were evaluated in the two communities. There was a significant difference p = 0.266 in the age distribution and also in the gender distribution p = 0.316. It was observed that the knowledge of ivermectin in the study areas was significantly different p = 0.012 and for those that have been skin snipped before there was also a statistically significant difference p = 0.000. More so, all samples subjected to microscopic analysis tested negative. It will be hasty to conclude that onchocerciasis has been eliminated from these communities. Further studies on the presence of the vector and their vectorial capacity could also assist in determining the actual status of onchocerciasis in the study areas.

Keywords: Epidemiological survey, Onchocerciasis, Ivermectin, Microfilariae, Ezza Nkwubor and Umuhu communities, Enugu State, Nigeria

INTRODUCTION

Onchocerciasis is a vector-borne parasitic disease caused by a filarial nematode worm *Onchocerca volvulus*. The adult worms (macrofilariae) lodge in palpable nodules under the skin of infected humans, although they can also be found free in subcutaneous tissue (Nnochiri, 1964; Samba, 1994). The microfilariae are found in the intercellular fluid, including that of the eye, and their death and subsequent disintegration result in inflammatory reactions. If microfilarial load is high following a prolonged period of exposure to massive infection, this may lead to serious visual impairment including blindness. In addition, the microfilariae give rise to intensely itching rashes, to wrinkling, thickening and depigmentation of the skin, to lymphadenitis resulting in hanging groins and elephantiasis of the genitals and to general debilitation, including loss of weight (Samba, 1994). The disease affects rural communities and is a major cause of blindness and skin disease in endemic areas usually accompanied with serious morbidity, psychosocial problems and reduced work, especially reduced agricultural productivity in populations affected by the disease. Estimates

shows that approximately 500,000 people are blind due to onchocerciasis (Boussinesq *et al.,* 2001; TDR, 2005; WHO, 2011). Globally it is estimated that 37 million people are infected with onchocerciasis and more than 99 percent of cases occur in 27 countries in sub-Saharan Africa with 120 – 122.9 million at risk of the disease (WHO, 1995; Gemade *et al.,* 1998). In Nigeria, onchocerciasis is widespread and the cause of blindness in most rural communities. Of all the countries of the world, Nigeria is worst hit and has the greatest number of persons with onchocerciasis (WHO, 1995). Visual impairment due to onchocercal eye disease can be demonstrated in about 30% of children aged 5 years who live in hyper-endemic communities in Nigeria; 35% of males and 27% of females in such communities are visually impaired at the age of 30 years (Edungbola *et al.,* 1993; Gemade *et al*., 1998). The disease is endemic in much of tropical Africa and parts of Central and South America and Yemen (Gemade *et al*., 1998). In the warm tropical environment, the disease thrives under conditions favorable for their development all year round (Gemade and Utsalo, 1990). Duke (1972) described the disease in Africa, as a disease of the future because as the development of the hinterlands proceed, particularly as dams and water projects increase, it will cease to be a disease affecting only small, isolated, poverty stricken and primitive communities in the bush and will become more and more a threat to sophisticated development personnel and other workers. It is thus expected that the battle for control of onchocerciasis will require more effort. There have been reports on different epidemiological patterns of infection between savanna and forest regions. Blindness and impaired vision are the most dangerous disabilities associated with the disease and are seen more among endemic communities living around the foci of transmission (Murdoch *et al.,* 2002). In West African savanna areas, ocular onchocerciasis is common; it particularly affects the anterior segment of the eye, though the posterior eye segment can also be affected. The risks of visual impairment increase, in part, as the prevalence and intensity of infection in a community rises (Crosskey, 1990; Nwoke and Ikonne, 1993). Onchocercal blindness is more common in the savanna bio-climatic zone than in the rain forest zone with sclerosing keratitis standing out as the ocular lesion with the highest prevalence (Murdoch *et al.,* 2002). In African forest areas with a comparable intensity of onchocerciasis as savanna areas, onchocercal skin disease predominates, with much less blindness. Furthermore, ocular lesions, when present, usually involve the posterior eye segment (Murdoch *et al.,* 2002).

A multi-country study in highly endemic forest communities found that itching affected 42 percent of the population aged ≥20 years, and onchocercal skin lesions affected 28 percent of the population aged ≥5 years. Strong associations were found between the prevalence of skin lesions and troublesome itching and onchocercal endemicity (Remme *et al.,* 1989).

The drug of choice for onchocerciasis is ivermectin, which has been shown to reduce the occurrence of blindness and severity of skin symptoms. Ivermectin kills the microfilariae (larvae), but not the adult worms. Treatment has to be continued annually for at least 15 years in order to cover the life span of the adult worms (WHO, 2011). Contraindications for administration of ivermectin include being younger than 5 years or 90 cm in height, being pregnant or and lactation of infant less than one week of age, having serious health problem, e.g. asthma, renal or hepatic disease (WHO, 2011).

MATERIALS AND METHODS

Study Area: The study was undertaken in Umuhu and Ezza Nkwubor communities of Isi Uzor and Enugu East Local Government Area of Enugu State, respectively. Isi Uzor is a Local Government Area of Enugu State, Nigeria bordering Benue State and Ebonyi State. Its headquarter is in Ikem town. It has an area of 877 km² and a population of 148,415 at the 2006 census. It is located around 6°47′N 7°43′E. Umuhu is a rural community located in Eha-Amufu, Isi-Uzor, Enugu State, located at 5.8° N 7.2° E. The soil is of lateritic type and the vegetation is mostly composed of lowland forest trees, mainly *Piptadeniastrum africanum,*

Uapaca spp*., Pycanthu* spp., *Lophiraalata* and *Khaya ivorensis*.

The area rises up to 300 m above sea level and is dominated by a tropical interland climate with an average temperature of over 27° C. The total annual precipitation is 2000 – 3000 mm (Wikipedia, 2014). Umuhu is a village where residents are predominantly farmers. There is a common river called 'Ebonyi' where all the community gets their source of water for drinking, bathing and washing. The highest educational institution in the village is secondary school both private and public. Enugu East is a Local Government Area in Enugu State, Nigeria. Its headquarter is in the town of Nkwo Nike. It has an area of 383km^2 and a population of 279,089 at the 2006 census. Ezza Nkwubor is a village in Emene located on latitude 6.30115°, longitude 7.37001° (Maplandia, 2014). It is basically a farming community with secondary school being the highest educational institution. University. The rivers commonly used by some of the community dwellers are River Oboja and River Owo which are between 0.6 – 1 km from the village settlement.

Study Design: A descriptive epidemiological study was used to carry out the research. A cross sectional type of descriptive study was employed.

Limitation of Study: Wider population coverage would have been better, but unfortunately, only a small proportion of people in the community presented themselves for skin snipping. More so, entomological observations were to be done simultaneously but it was not possible.

Ethical Review: Ethical clearance was obtained from the University of Nigeria Teaching Hospital Ethics Committee. Clearance from the State Ministry of Health and the State Onchocerciasis unit was also obtained before visiting the communities. Informed consent of all eligible subjects was obtained verbally before they were sniped.

Data Collection: Skin-snip surveys were done in Umuhu and Ezza Nkwubor communities and were carried out between September 2013 and February 2014.

In each village, all subjects above the age of 10 year who agreed to participate. The questions on the validated and pre-tested questionnaire sought information on the age, sex, occupation, knowledge of the fly, disease caused by the black fly, duration of stay in study area and knowledge of ivermectin.

Epidemiological Evaluation: The age of the cohort range from 10 – 75 years. Subjects were selected at convenience for the skin snip. Although majority of the subjects that presented themselves declined to be registered for the skin snip. All members of a family present at the venue of registration were all registered in one form bearing the "Family name" for easy access should there is any positive case. The surveys used established skin-snip examination methods in which the National Onchocerciasis Control Program (NOCP) had previously been trained by the WHO African Programme for Onchocerciasis Control (APOC). Two skin biopsies were obtained from the right and left iliac crests of all individuals who presented themselves for the survey. A 2 mm Holth Corneoscleral Punch (MDP^{CE} IW811) was used to obtain the skin biopsies. After each series of two bloodless skin-snip obtained from a subject, the scleral punch was sterilized sequentially in sodium hypochlorite solution, distilled water and then autoclaved by pressure for 15 minute. The entire process was to ensure that blood-borne infections are not transferred to individuals in the community. The samples were microscopically examined after 24 hours incubation in normal saline to allow the microfilariae (larvae) to emerge.

Data Analysis: The analytical tool employed in the study includes descriptive statistics and chi-square test of independence. It was used to obtain the frequencies and percentages of the research variables. Chi-square symbolically represented as χ^2 was used to compare actual observed distribution with the hypothesis or expected distribution. The test was done at 95% confidence level.

RESULTS

Only 75 subjects agreed to be registered in Umuhu community and these were the number that was snipped. The turnout was similar in Ezza Nkwubor with only 68 persons agreeing to be registered but only 65 of them yielded to be snipped. In total, 143 subjects registered but only 140 were snipped in both communities yielding to 97.9% compliance, and 2.1% refusal (Table 1).

Age and Sex Distribution: Out of the 65 subjects that were snipped in Ezza Nkwubor, 23(35.4%) were below the age range <35 years and 45(69.2%) were >35 years with the P = 0.266 showing that there is significant difference in the age of subjects that were snipped in both communities. In Umuhu community, 19(25.3%) were in the age range <35 years while a greater proportion 56(74.7%) were in the age group >35. There was a significant difference in the gender of the subjects in both rural and urban P = 0.316, although in Ezza Nkwubor community 27(41.5%) were males 38(58.5%) were females likewise Umuhu community, 25(33.3%) were males and 50(66.7%) were females (Table 1).

Knowledge of Ivermectin and Skin Snip: Among those that were registered in the Ezza Nkwubor, 45(66.2 %) were aware of ivermectin and have been given ivermectin by the CDDs and 23(33.8%) had no knowledge on ivermectin distribution nor have taken it before. While in Umuhu community 34(45.3 %) were also aware of ivermectin distribution and have been taking the annual rounds. There was a significant difference P = 0.012 between the two community on the knowledge of ivermectin distribution. Moreso, none of the subjects had any knowledge of being snipped before. Whereas in the rural area, 39(55.7%) remembered they have been snipped before in the community while 31(44.3 %) have never been skin snipped before. Knowledge on previous skin snip information was statistically significant at p = 0.000 (Table 2).

Microfilariae: All samples subjected to microscopic analysis after 24 hours incubation were confirmed negative for microfilariae.

DISCUSSIONS

Several studies have indicated that elimination of onchocerciaisis with long term mass drug administration with ivermectin is achievable. Such studies have been carried out in Mali and Senegal (Diawara, 2009) where treatment had started as early as 1988/1989 and also in Kaduna State, Nigeria where more evidence have shown elimination of onchocerciaisis with long term mass ivermectin administration (Tekle *et al.,* 2012).

This study tried to evaluate the impact of ivermectin within the study area through the skin snip method to check for the presence of microfilariae in the skin of the subjects. The statistically significance that was observed in the age distribution of subjects could be that most of the subjects that fall on this range <35 are students and very youthful and feel they are not sick. Many of them most have gone to school or may have travel to neighboring town in search of greener pastures. Oyekanmi (2010) in a study in Kwara State, Nigeria found out that males were more prone to migration. This could be a reason why we had more female subjects compared to the males. The age range >35 was considered aged because majority of them were far above 40 years of age. They might have presented themselves to be snipped because of the feeling of ill health usually attributed to age and will seek and respond to any health intervention program. There was a significant difference on previous skin snip information on both communities. It was clear from the study that there was a more active CDTI and CDDs in Umuhu community compared to Ezza Nkwubor community. Umuhu community dwellers perceived onchocerciasis to be a burden in their community compared with the community dwellers in Ezza Nkwubor. This perceived risk might have changed the attitude of subjects towards the demand for Ivermectin.

Table 1: Socio-demographic parameters of Ezza Nkwubor and Umuhu communities in Enugu State, Nigeria preliminary assessed on the impact of ivermectin in the treatment of onchocerciasis

Variables	Umuhu community n=75 Frequency (%)	Ezza Nkwubor community n=68 Frequency (%)	Total n=143 Frequency (%)	X^2 value	P-value
Age in years				1.239	0.266
< 35	19 (21.0)	23(33.8)	42 (29.4)		
> 35	56 (74.7)	45 (66.2)	101 (70.6)		
Sex				1.004	0.316
Male	25 (39.7)	27 (33.3)	52 (38.5)		
Female	50 (66.7)	38 (66.3)	88 (61.5)		

Statistically significant at p<0.05

Table 2: Knowledge of the use of ivermectin and skin snip among members of Ezza Nkwubor and Umuhu communities in Enugu State, Nigeria preliminary assessed on the impact of ivermectin in the treatment of onchocerciasis

Variables	Umuhu community n=75 Frequency (%)	Ezza Nkwubor community n=68 Frequency (%)	Total n=143 Frequency (%)	X^2 value	P-value
Knowledge of ivermectin				6.267	0.012
Yes	34 (45.3)	45(66.2)	79(55.2)		
No	41 (54.7)	23(33.8)	64(44.8)		
Skin snip information				52.810	0.000*
Snipped before	39(55.7)	0(0.0)	39(28.3)		
Not been snipped	31(44.3)	68 (100.0)	99 (71.7)		

**Statistically significant at p<0.05*

Microscopic analysis revealed that all 140 samples of skin snips examined were negative. The fact that no skin microfilariae were found indicated that there might not be adult worms in the subjects that were evaluated or even if there are still adult worms in the subjects, they may not longer be productive or may be producing too few microfilariae to be detected by microscopic analysis of the skin snip. It was also observed that drug distribution was not carried out routinely. There were irregularities with drug administration. It might be that subjects took in ivermectin just a few days or week prior to evaluation of the skin biopsy. It has been proven that ivermectin can clear 85% of the microfilariae within the first 24 hours of intake and 98 – 99% after 1 – 2 months (Basanez *et al.,* 2008).

Recommendation: The study focused only on the epidemiological aspects of the community dwellers using skin snip diagnosis, it is therefore important to undertake an entomological survey to ensure the actual and present situation of the vectorial capacity of the flies through dissection to detect microfilaria. It is evident that mass drug distribution is effective. It is therefore important to encourage the CDDs in their task of ivermectin distribution. Moreso, there is the need for more awareness, sanitization and epidemiological survey prior to drug administration.

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