



Short Communication

Effect of Therapeutic Doses of Ivermectin on Subjects Infected with Onchocerciasis

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Abstract

Impact of Onchocerciasis and the efficacy of doses of Ivermectin chemotherapy was carried out in Udi and Igbo-Etiti Local Government Area of Enugu State using rapid assessment method (RAM) and skin biopsies for onchocercal microfilaria (MF). Out of the 1362 subjects examined and dosed with Ivermectin at a standard dosage of 150 mg/15kg body weight, 1158 (85%) were infected with onchocerciasis. Individual onchocercal signs recorded were microfilaria 498 (36.6%), leopard skin 486 (35%), nodules 756 (55.5%), visual impairment 534 (39.2%) and blindness rate of 57 (4.2%). Post-drug survey was carried out in three of the communities after 6 months interval and in one community after 3 months interval to monitor the effect of Ivermectin chemotherapy in the treated communities using RAM and re-skin snipping of the subjects. Results obtained showed that there are significant reductions in the disease prevalencies when compared to the pre-drug onchocercal prevalencies ($P < 0.05$). Results obtained are; microfilaria 158 (15.9%), leopard skin 278 (28.0%), nodules 508 (51.1%), Visual impairment 262 (26.4%) and blindness receded to 0 (0.0). Ivermectin was also found to be most efficient when taken at 6 month intervals when compared to 3 month dosing. Treatment with Ivermectin was also best when height instead of weight is used in dosing the subjects. A single case of adverse side reaction following treatment in the form of mazzoti and hanging groin was recorded.

Keywords: Ivermectin, Onchocerciasis, leopard skin, blindness and microfilaria.

Introduction

Onchocerciasis is a disease of public health importance; about 18 million people worldwide are infected with filarial nematode *O. volulus* – transmitted from person to person by the blackfly of genus *Simulium*. About 1 million of these are blind or have severe visual impairment from onchocerciasis and more than 80 million living in endemic areas of sub-Sahara African, central and South America are at risk of the disease¹. Ivermectin, a sem-synthetic macrocyclic lactone marketed under the name mectizans is a widely used drug in veterinary medicine. It was introduced in 1987 for the treatment of human onchocerciasis. It is a derivative of avermectin, a fermentable product of streptomyces avermitilis. As an anti parastic agent, it is claimed to have consideration promise in the treatment of onchocerciasis²⁻⁴. Onchocerciasis is a disease found in all states of Nigeria including Abuja^{5,6}. In Cross River State of Nigeria, the prevalence of the disease has been established in 42 of the 46 villages⁷⁻⁹. Ivermectin is receiving wide usage in the treatment of endemic onchocerciasis distributed free of charge. Formally, control measures of onchocerciasis involved nodulecetomy and chemotherapy, which lacked merit when compared to mass control programme. The search for alternative control measure lead to the use of Abate (temephos), a phosphorus biodegradable insecticide which is effective

against *S. damnosum* which also posses greater safety in terms of toxicity and cost-effectiveness.

The adoption and launching of large-scale distribution of Ivermectin as a national strategy for control offered a laudable interventions¹⁰. The introduction of Ivermectin by Mack sharp and Dome (the manufacturer) for use, in conjunction with the technical material and moral support provided to the NOCP by non-governmental organization, United Nations Agencies and other donors facilitated and encouraging take off of control measures. The development of rapid assessment method (RAM) for community diagnosis of onchocerciasis will enhance the efficiency of large scale distribution of mectizan¹¹. The use of RAM is also innovative, valuable and timely. Clearly important to note, onchocerciasis is an economically important disease, it is not a killing disease¹². Down here at the present study, in spite of intervention measures, no investigation has been carried out at Nze, Uzueme, Useh and Orda communities in Udi and Igbo Etiti Local Government Areas of Enugu State, Nigeria. Although there was early information¹³ about onchocerciasis in the two local government (Ukehe and Nachi). This study is aimed at i. determining the prevalence of onchocerciasis in the communities, ii. determining whether there is any significant difference in the efficacy of Ivermectin on onchocerciasis in relation to treatment peridodicity and iii. determining whether

there is any significant difference in the efficacy of Ivermectin on Onchocerciasis in relation to dosing schedules.

Material and Method

Study Area: The study was carried out in three communities of Igbo-Etiti Local Government Area and one community (Nze) in Udi Local Government Area both in Enugu State, Nigeria. The four communities Nze, Uzueme, Useh and Orda are situated on the same latitude (7° latitude East and (6°, 8°) longitude North of the equator). They have an average rainfall of 1500-2000 ml, a temperature of 25-27°C on the average and relative humidity of 75-95%. The vegetation here is predominantly rainforest with strips and patches of highly wooded Savanna on the foothills. The four communities have the same geographical spread and are rimmed off by hills, which placed them in a valley. There is complete dearth of big water bodies in the communities except for springs prominent on the hills. Other water bodies are small streams that are sparsely distributed and some extinct streams. The only large water body “Adada” River is about 1.5km away from Useh community. In fact, all the studied communities are almost of the same land stretch to the Adada River. However, Orda and Nze are more inland than Useh and Uzueme. Over 95% of the populations are stable farmers at the shore and offshore range of their homes. Udi and Igbo-Etiti shared boundaries with Uzo-Uwani at the Western axis, which is a known endemic onchocerciasis area¹⁴. Onchocerciasis is as old as the study area since inhabitants steadily reported that they have always lived with the disease for ages.

Determining Whether the Efficacy of Ivermectin is Related to Treatment Periodicity: Post-treatment survey was carried out in one of the communities (Uzueme) within three monthly intervals and repeated at 6 months alongside with the remaining three communities. The result was compared with 6 month Post-

treatment survey to determine which of the periodicity offered the most innovative intervention for the treatment of onchocerciasis. Results were also tested statistically for significance difference.

Determining Whether the Efficacy of Ivermectin on Onchocerciasis is Related to Dosing Schedules: Two communities were used for this objective (Useh and Orda). Subjects at Useh community were dosed with Ivermectin in a standard dosage of 150mg/kg body weight while Orda community were dosed with Ivermectin in a standard dosage of 150mg/90cm total height of a subject after RAM and skin biopsies have been conducted. Pre-treatment RAM and skin MF was compared with post-treatment RAM and MF prevalence and tested statistically for any significant differences.

Statistical Analysis: All results were recorded and analyzed using chi-square test, correlation and regression analysis and analysis of variance (ANOVA).

Results and Discussion

From table 1 above Orda community recorded overall best performance to the dosing method of height. They recorded generally lower prevalent rate to all the onchocercal disease problems than Useh community that was doses with weight schedule.

From the table 2, Uzueme community was used for this study. The subjects were dosed with Ivermectin using weight schedule. Post-drug rapid/parasitological technique was used to ascertain the prevalencies of onchocerciasis at three and six months intervals.

Table-1

Post-drug comparative display on onchocerciasis in two communities (Useh and Orda) dosed differently with Weight and Height dosing schedule

Weight (USEH)				Height (ORDA)		
	No Examined	No Infected	% Prevalence	No Examined	No Infected	% Prevalence
Microfilaria	192	72	37.5	160	55	34.5
Nodules	192	88	45.8	160	75	46.8
Leopard Skin	192	56	29.2	160	30	18.8
Visual Impairment	192	48	25.0	160	30	18.8
Total	768	264	134.7	640	190	118.9

Table-2

Post-drug Comparative Distribution of 6 months / 3 months Monitoring Plan

3 MONTHS				6 MONTHS		
Onchocercal Disease	No Examined	No Infected	% Prevalence	No Examined	No Infected	% Prevalence
Microfilaria	321	60	18.7	210	15	7.1
Nodules	321	99	30.8	210	40	19.1
Leopard Skin	321	153	47.7	210	105	50.0
Visual Impairment	321	75	23.4	210	40	19.1
Total	1284	387	120.6	840	200	95.3

Discussion: Six-months monitoring and dosing recorded all lower prevalent rates to all the onchocercal diseases than the three monthly monitoring and dosing. Though nodular formation appeared to be undisturbed by all the parameters tested for a better results. On dosing method efficacy test, two different parameters weight and height were compared statistically to show which parameter was most efficacious. Height was found to record the best reduction value against the values obtained when the subjects were dosed by weight $P < 0.05$. The observed height efficacy should be attributed to the fact that microfilaria inhabits the skin and not the muscles, bones, or adipose tissues which made the weight of the body. Therefore dosing by weight may present an underdose to the microfilariae while dosing with height provides a direct proportional balance between skin size and microfilaria infestations. Comparative analysis of dosing interval showed that 6 months dosing monitoring interval produced better results than 3 months interval¹⁵ ($P < 0.05$) in a multicentre study on the effect of ivermectin, noted that treatment was most beneficial for treatment of onchocercal disease and that 6 months intervals provided maximum efficacy.

Conclusion

The effect of therapeutic doses of ivermectin on subjects infected with onchocerciasis was elucidated in Wistar rats fed mashed stock diet. Ivermectin being an anthelmintic drug and a microfilaricide must be administered repeatedly. In this study, post-drug rapid technique was used to ascertain the prevalences of onchocerciasis at three and six months intervals. Both three and six months ivermectin monitoring and dosing appeared to have effect on the prevalences of onchocerciasis, treatment have also shown to be dose dependent.

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