

# Post-therapy Parasite Clearance in subjects with mixed infection of Onchocerciasis and Plasmodiasis in Garaha-Dutse, Nigeria

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## Abstract

This study was conducted to determine the treatment regimen that produces the highest parasite clearance in subjects with co-infection of onchocerciasis and plasmodiasis. One hundred and eight (108) inhabitants of Garaha-Dutse village, Adamawa State of Nigeria who were earlier tested positive for onchocerciasis and plasmodiasis were treated with ivermectin and chloroquine using three different approaches. The infected subjects were divided into test group, control group A and control group B each consisting of thirty-six subjects. The test group was administered with both drugs concurrently and also by one after the other. Control group A and control group B were treated with ivermectin and chloroquine respectively. The baseline parasite density, post therapy parasite density and parasite clearance were estimated. Post-therapy drug reactions were also recorded. The findings showed that the highest parasite clearance (74.7%) was recorded in subjects with mixed infection when chloroquine administration preceded ivermectin therapy. Also the drug reaction mostly experienced by the subjects was pyrexia 9(25.0%) and it was more frequent 5(15.2%) when administration of ivermectin preceded chloroquine therapy. Statistical analysis however showed no significant association between the treatment method and the post-therapy drug reaction ( $P > 0.05$ ). Also, there was no significant difference in post-therapy parasite clearance with respect to age and gender ( $P > 0.05$ ).

## INTRODUCTION

Onchocerciasis, otherwise referred to as river blindness is a parasitic infection of human skin. The causative agent is microfilaria of *Onchocerca volvulus*. About 15 million people of the total world estimate infected with onchocerciasis lives in Africa (1,2) while not less than 3.3 million reside in Nigeria alone (3). Similarly, malaria is a human parasitic infection, caused by four species of Plasmodium (P) namely: *P.falciparim*, *P. vivax*, *P. malariae* and *P. ovale*. All the species infect human red blood cells and the liver. In Nigeria, and indeed the entire Africa, *P. falciparim* is responsible for most cases of malarial infection (4). Over 300,000 deaths are recorded yearly in Nigeria as a result of malarial infection while not less than 20 million new cases are reported annually (5,6).

Although many treatment failures due to chloroquine had been reported in the past (7,8), it is still considered the first line of drug for malarial treatment in many rural communities of Nigeria due to its lower cost, affordability and availability. Also, because of some serious adverse reactions of many anti-filariasis drugs, ivermectin is still

considered safer and more effective against onchocerciasis in Africa (9). Non-compliance with treatment regimen by the infected people is one of the major causes of drug resistance which in turn constitutes a major problem against the control of infections in different parts of the world.

In this study, we have focused on the assessment of post-treatment parasite clearance in subjects with concurrent infection of onchocerciasis and plasmodiasis with the aim of comparing the drug performance by simultaneous treatment regimen with that of separate therapy.

## SUBJECTS AND MATERIALS

### STUDY AREA AND POPULATION

This study was conducted in Garaha – Dutse community in the Hong Local Government Area of Adamawa State, Nigeria. The community is situated within Dugwada district which lies on latitude 10° 20' to N 10° 30' N and longitude 12° 40' E to 12° 50'E. The study was carried out between May 2003 and March 2004 on four hundred and twenty-eight volunteers aged 11-70 years randomly selected within the village. Only permanent residence of the village who

were tested positive for *O. volvulus* or/and malarial parasite were included in the treatment stage of the study. All uninfected subjects were excluded. Prior to the beginning of the study, an approval from the State Ministry of Health was obtained while the informed consent of each subject sought.

### **MICROSCOPIC EXAMINATION OF SUBJECT SPECIMENS**

Two capillary tubes filled with peripheral blood collected from each subject were employed in this study. The fingertips of each subject were sterilized with methylated spirit before sample collection. The blood samples were firstly used for making thick films in duplicates on geese-free slides, the films were allowed to dry and stained by Giemsa method as described by Monica (10). Thin blood films were then made from the blood samples, dried and stained by Leishman technique as described by Ramnik (11). Stained thick films were examined under x 100 objective lens of a microscope with the aid of immersion oil for any stage of malarial parasite and were scored as negative, + or ++. The thin films were also examined to determine the average number of parasitized red blood cells per hundred red blood cells differentiated with Erlich's eye piece.

Similarly, to detect the presence of dermal *Onchocerca volvulus* and determine its intensity in each subject, skin snips were taken in duplicates using the standard technique in which biopsy punch was used to take 2mm skin snips from the right iliac crest and right calf of each subject. The specimens were separately weighed and dropped in microlitre plates containing three drops of saline to enable the microfilariae emerge within 24-hours of incubation at room temperature. The preparations were then examined for the presence of microfilariae under x 40 objective lens of the microscope and the microfilaria (mf) intensity of each subject was expressed as number of microfilaria per skin snip. The average mf number per positive subject was calculated.

### **TREATMENT AND EVALUATION OF INFECTED SUBJECTS**

Of the subjects examined in the study, 108 infected were given treatment based on the type of infection. The infected subjects were grouped into three: The test group, control group A and control group B. The test group consisted of thirty-six subjects infected with both onchocerciasis and plasmodiasis. Twelve were treated with chloroquine preceding ivermectin therapy, the next twelve were treated with ivermectin administration before chloroquine therapy

while the last twelve subjects were given both drugs concurrently. The control group A were another thirty-six subjects infected with onchocerciasis only and they were administered ivermectin while the last thirty-six subjects were the control group B infected with malaria parasite alone and they were treated with chloroquine. Before the treatment, the heights of the subject to be treated with ivermectin were determined with metre rule. Ivermectin was administered with respect to height in line with World Health Organization Standard (12). Height from 1.2 metres to 1.39 metres was given a dose of 6mg of the drug, 1.4 metres to 1.59 metres was administered with 9mg and any height above 1.59 metres was given a dose of 12mg of the drug to be taken at once. Chloroquine tablets were administered at an adult dosage of 600mg starting dose for the age between 16 and 70 years followed by 300mg after six hours and another 300mg daily for two days. Subjects from age of 11 to 15 years were given half of the adult dosage. All the drugs were administered orally with the assistance of community health officers. Structured interview on subject age and drug reactions experienced after the treatment was conducted on them.

Before and after each treatment, the parasite density and parasite clearance were calculated weekly for two weeks using the formulae:

#### **Figure 1**

$$\text{Parasite density} = \frac{\text{Sum of average number of parasite in each subjects divided by total number of subjects infected.}}{\text{Total number of subjects infected.}}$$
$$\text{Parasite clearance} = \frac{\text{Pre-therapy density minus Post-therapy density}}{\text{Pre-therapy density}} \times 100$$

The data obtained in the study were analysed by percentage and simple means before statistical analysis using Chi-square test.

### **RESULTS**

The parasite intensity of subjects with concurrent infection of onchocerciasis and plasmodiasis fourteen days post-therapy is as shown in table 1. The table also shows the density of the parasites in single infection of *onchocerca volvulus* and plasmodiasis as control groups. Before the drug administration, the Baseline mean parasite density of the thirty-six subjects with concurrent infection was 4.3 parasites per field; while 8.5mf /skin snip and 9.6 mp/100rbc were the mean baseline densities for control A (*onchocerciasis*) and control B (*plasmodiasis*) respectively. Two weeks after administration of ivermectin and

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chloroquine to the subjects, the mean parasite density of the test group fell to 1.3 parasites/field while that of control A dropped to 1.1mf/skin snip and control B to zero malaria parasite.

### Figure 2

Table 1: Post-therapy variation in parasite density of subjects infected with and malarial parasites.

Infection	Mean Parasite Density/field		
	Pre-therapy	Post-therapy	
	D <sub>0</sub>	D <sub>7</sub>	D <sub>14</sub>
Co-infection n = 36	4.3	1.6	1.3
Control A Onchocerciasis n = 36	8.5	2.0	1.1
Control B Plasmodiasis n = 36	9.6	0	0

- n = Number of subjects treated  
 D<sub>0</sub> = Before drug administration  
 D<sub>7</sub> = Seven days post-therapy  
 D<sub>14</sub> = Fourteen days post-therapy

Table 2 shows the parasite clearance rate in subjects with co-infection of *O. volvulus*. and malaria parasites. When chloroquine was first administered before ivermectin was given to the subjects, a highest parasite clearance was obtained (76.7%) and closely followed by this was when both drugs were given simultaneously (69.7%) while the least clearance of parasite was recorded when administration of ivermectin preceded chloroquine (58.1%).

### Figure 3

Table 2: Post-treatment parasite clearance in subjects with concurrent infection of onchocerciasis and plasmodiasis.

Treatment	Mean Density of <i>O. volvulus</i> and malaria parasites/field		Parasite Clearance (%)
	Pre-therapy	Post-therapy	
Ivermectin before Chloroquine	4.3	1.8	58.1
Chloroquine before Ivermectin	4.3	1.0	76.7
Chloroquine and Ivermectin combined	4.3	1.3	69.7

The data in table 3 shows the frequency of some drug reactions experienced by the subjects after administration of ivermectin and chloroquine. Pyrexia was the most commonly experienced reaction 9(25.0%) and it was more frequent 5(15.2%) when administration of ivermectin preceded chloroquine and least when both drugs were given concurrently 1(2.8%). The next drug reaction often experienced by the subjects after taking the drugs was itching 8(22.2%) almost equally observed among the subjects irrespective of the treatment regimens. The least experienced reaction by the subjects was dizziness 3(8.3%) which was observed only when chloroquine was administered before ivermectin therapy 2(5.6%) and also when both drugs were administered at the same time 1(2.8%).

### Figure 4

Table 3: Post-treatment drug reactions experienced by the subjects.

Drug Reaction	Number Examined	Reaction by Treatment Regimen		
		Iver Before Chloroquine	Chloro. before Ivermectin	Ivermectin and Chlor. combined
Nausea	5	1	1	3
Head ache	4	1	1	0
Pyrexia	9	5	3	1
Itching	8	3	2	3
Dizziness	3	0	2	1
No Reaction	7	2	1	4
Total	36	12	12	12

Post-therapy parasite clearance rate in relation to age and

gender is as shown in table 4. The highest clearance (100.0%) was recorded among age-group 11-20 years while the least (70.2%) was recorded within 61-70 years age bracket. Generally, as the age increases the clearance rate reduces. Statistical analysis however shows no significant difference in parasite clearance rate in relation to age, ( $P > 0.05$ ). Similarly the parasite clearance among the male subjects was higher (84.0%) than in their female counterparts (78.0%).

Statistical analysis by Chi-square also showed no significant difference in the parasite clearance by gender ( $P > 0.05$ ).

**Figure 5**

Table 4: Post-therapy parasite clearance in relation to age and gender.

Age group (Year)	Number Infected	Parasite density/ field in:		parasite Clearance (%)
		Baseline	Post-therapy	
11 - 20	4	1.4	0	100.0
21 - 30	6	2.6	0.2	92.3
31 - 40	4	2.3	0.1	86.9
41 - 50	5	2.9	0.6	79.3
51 - 60	8	3.1	0.8	74.2
61 - 70	9	3.9	1.1	70.2
<b>Sex</b>				
Male	1.6	2.5	0.4	84.0
Female	2.0	4.1	0.9	78.0

**DISCUSSION**

Our findings in this study revealed a better drug performance in subjects with concurrent infection of onchocerciasis and plasmodiasis when administration of chloroquine precedes ivermectin. This assessment was deduced from the highest post-therapy parasite clearance (76.7%) recorded with this treatment regimen as against the lower rates by the other regimens. The study also showed that infected subjects experienced a highest pyretic drug reaction 5(15.2%) when treated with ivermectin before the administration of chloroqui.

Although several studies had previously reported (<sub>13,14</sub>) chloroquine resistance and treatment failure of malaria, the present finding obtained from thirty-six subjects with single infection of malaria (control group B) did not record any treatment failure. The reason for the difference between the

present study and the previous ones could probably be due to lack of abuse of chloroquine among the inhabitants of Garaha village where the research was conducted. Another reason could be due to the quality of chloroquine (Mayer and Baker) and the type of treatment regimen employed in this study. Conversely, 1.1% treatment failure was observed in single onchocerciasis infection (control group A) when treated with ivermectin. The probable reason for this finding could be due to the short period of evaluation of the performance of the drug against the parasite.

Although the highest parasite clearance (76.7%) was recorded when administration of chloroquine preceded ivermectin, there was no case of complete clearance when the subjects were treated concurrently with both drugs. However, simultaneous administration of the drugs gave a higher parasite clearance (69.7%) than when ivermectin was given to the subjects before chloroquine was administered (58.1%).

By critically assessing the post-treatment drug reactions experienced by the subjects, pyrexia was observed to be more frequently experienced 9(25.0%), closely followed was itching 8(22.2%) while dizziness was the least observed drug reaction. The frequency of Pyrexia was highest 5(15.2%) when ivermectin therapy preceded chloroquine, indicating that the post-therapy febrile condition was probably initiated by ivermectin administration and later potentiated with chloroquine administration. This scenario was reduced 3(9.1%) when the treatment regimen was reversed with chloroquine preceding ivermectin and was at the minimum 1(2.8%) when both drugs were simultaneously given.

Statistical analysis by Chi-square however showed no significant association between the treatment regimen of the concurrent infection and the post-therapy drug reaction ( $P > 0.05$ ).

Post-therapy parasite clearance with respect to age showed a diminishing rate as the age of the subjects increases. Among the youngest age group of 11-20 years, the highest parasite clearance (100%) was recorded while the lowest rate (70.2%) was recorded within the oldest age bracket of 61-70 years. The reason for this trend could probably be associated with diminishing immunity of the subjects as they get older, making them to respond poorly to treatment hence poor parasite clearance after treatment. Although the present findings is in consonance with the previous results (<sub>15,16</sub>), statistical analysis shows no significant difference in post-

therapy parasite clearance in relation to the age of the infected subjects ( $P > 0.05$ ).

Similarly, the parasite clearance rate in males (84.0%) is higher than in the females (78.0%) indicating that infected males responded better to the treatment than their female counterparts. Statistically however, there is no significant difference in the parasite clearance rate with respect to the sex of the infected subjects ( $P > 0.05$ ).

## CONCLUSION AND RECOMMENDATIONS

With these present findings, we wish to suggest further research work on the long-term effect of ivermectin on subjects with mixed infection of onchocerciasis and plasmodiasis while this result could serve as baseline information for future studies. Also since some skin infections have been reported (17) to be in association with HIV pandemic, a study on the relationship between onchocerciasis and the dreaded virus is recommended.

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