

Treatment of *Dracunculus medinensis* infection with cotrimoxazole in endemic populations of Ebonyi, South Eastern Nigeria

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ABSTRACT

Background: The aim of this study was to determine the effectiveness of cotrimoxazole (Septrin[®], Wellcome, England) on *Dracunculus medinensis* and the response of infected persons on mass cotrimoxazole therapy in an endemic rural farming population. **Method:** During the peak transmission season of 1998/1999 epidemiological years, 12,158 persons were examined for guinea worm infections in endemic populations of Ebonyi state, southeastern Nigeria. Eight hundred and sixty-four (864) active cases as well as persons with painful non-emergent worms were systematically treated with cotrimoxazole. Dosage was adjusted according to body weight given in tablets at 20 mg/kg in 2 divided doses for 5 days. **Results:** Of the 864 treated cases, 539 and 125 were females and males respectively. Eight hundred and twelve (812) patients had 1-3 worms, while 52 patients showed poly-parasitism of up to 28 worms per person. Inflammation signs subsided within the first 2-4 days of treatment with cotrimoxazole. Specifically, symptoms were more in the untreated than in the treated group. The drug enhanced healing of septic wounds, reduced both swollen legs and pains in over 67% of the cases. **Conclusion:** Cotrimoxazole appears to be effective without serious adverse effects in the treatment of dracunculiasis. It's efficacy in the amelioration of symptoms and cure of the disease is encouraging and should prove a useful weapon against dracunculiasis in Nigeria. [Report and Opinion. 2009; 1(3):41-46]. (ISSN: 1553-9873).

Keywords: Dracunculiasis, guinea worm, cotrimoxazole, prodromal signs, Nigeria

INTRODUCTION

Treatment of dracunculiasis in endemic foci may involve either surgery or chemotherapy. Surgical removal of dracunculus is widely practiced in several endemic areas, when the outline of a worm can be seen or palpated. This approach is however not effective if the worm has burst in the tissue or has broken the skin more than a few days previously (1, 2). It is also difficult to remove the worm when it is embedded in deep fascia (1). Over the years, a number of therapeutic substances have been employed in the treatment of dracunculiasis. Among the earliest trial substances used in West Africa and India were palm oil, kerosene and concoction of leaves placed over the ulcer (4). In most endemic areas, various oral portions such as raw sugar and tartar emetics have also been recommended (5, 6). Most of these concoctions, though with deep bearing in local beliefs are not of much value in the treatment of dracunculiasis. Although other medicaments like diethylcarbamazine (DEC) appear to be without action on the adult worms, Rousset (7) presented circumstantial evidence that DEC kills the developing stages of *D. medinensis* including

larval stages inside cyclops (8).

Chemotherapy of dracunculiasis received a boost with the discovery of niridazole, thiabendazole, metronidazole and mebendazole in the mid 20th century. Trial/ field treatments with these drugs have continued to yield varying results (1, 10, 11, 12). Metronidazole for example, was useful but also requires 7 days of application to achieve appreciable result (10).

Mass chemotherapy against dracunculiasis has not received much attention in Nigeria, probably because of general lack of effective cure with the drugs currently in use (13, 12, 4). More so, these drugs have been shown to be toxic and relatively expensive for peasants, who constitute majority of clinical cases (14). In southeastern Nigeria, information on the treatment of the disease is non-existent (15, 16, 17). We present our findings on Ebonyi state, which was the most endemic state in Nigeria by 1998/99 epidemiological year. In an area of renewed outbreak reported in previous studies (17, 2) trial doses of cotrimoxazole (Septrin[®]) were therefore administered to infected subjects following parasitological and clinical examinations. Earlier point trial with cotrimoxazole had yielded some encouraging results amongst patients on its effectiveness in ameliorating pains and improving worm expulsion/extraction (18). The objective of the present study is to determine the effectiveness of the cotrimoxazole on *D. medinensis* and the responses of infected patients to mass therapy with the drug during an outbreak of infection in four most endemic local Government Areas of Ebonyi State, Nigeria.

MATERIAL AND METHODS

Volunteers with obvious acute manifestations of dracunculiasis such as abscess, itching, erythema, blister, bleb formation, pain and cellulitis were randomly selected for the study from the four most endemic local Government Areas (LGA) of Ebonyi State, Nigeria. These included Ikwo, Ozibo, Ebonyi and Ezza North LGAs. A total of 12,158 persons were examined, and of these, 864 persons including active cases of dracunculiasis as well as persons with non-emergent worms and village based health workers (VBHWs) were treated with cotrimoxazole (Septrin[®], Wellcome, England). Cotrimoxazole is a combination of trimethoprim and sulphonamides. Trimethoprim is a diaminopyrimidine derivative, which inhibits the conversion of dihydrofolate to trihydrofolate by inhibiting the enzyme dihydrofolate reductase in bacteria and protozoa (19, 20). Used alone, it is not particularly effective against bacteria and resistance develop easily (21, 22). However, in combination with sulphonamides, a synergistic action, which results in a segmental blockage of microbial enzyme systems through the blocking of different reactions in the same pathway occur with broad spectrum bactericidal consequence (20). Although an old drug, it still finds useful application in the management of numerous bacterial infections (23, 24, 25, 26).

The drug was administered orally in tablet form according to manufacturer's instruction, which was translated to 20 mg/kg body weight in two divided doses daily for five days. The efficacy in the amelioration of symptoms as well as cure of the infection was monitored. The clinical course of the disease in other patients not administered the Septrin[®] was equally monitored.

The clinical signs such as exudation, pain, redness and swelling were ranked using the method of Sastry et al (27) as follows: 0 = nil; 1 = mild; 2 = moderate; 3 = severe and 4 = incapacitating (very severe). The effect of the cotrimoxazole on *D. medinensis* was also scored using the method of Sastry et al (27) in classifying response to treatment as poor=no response, fair = slow, or delayed response, good = easy extractability of worms, with relief of inflammation and very good = spontaneous extrusion of worms and dramatic subsistence of inflammation. In subjects with multiple lesions, maximum grading of clinical manifestation was noted, while reports of prodromal symptoms and signs were recorded.

The patients progress was noted on the 3rd, 6th, 9th, 12th and 15th days. These intervals were necessary to the team for appropriate case management, while the lesion usually would have shown reasonable response and healing. Adverse reactions to the drug in treated subjects and their intensity were equally scored on a 0-3 basis as follows: 0= absent; 1 = mild or occasionally present; 2 = severe and continuous; 3 = stop treatment. Data generated from the study were analyzed using simple descriptive statistics such as simple averages and percentages.

RESULTS

Table 1 showed that of the 12,158 persons examined, 864 (7.1%) were infected with guinea worm. This included active cases as well as persons with painful non-emergent worms. Treated subjects varied across

the study area with Ikwo LGA (30%) as the highest and Ozibo as the least (17.1%). Of the 864 patients treated with Septrin[®], 529 were females and the rest males, with the number of persons infected reaching a peak in the 11-20 years-age bracket before a gradual decrease with increase in age of patients (Table 2).

Majority of the clinical manifestations were moderate (Table 3), while over 70% of the predilection sites of worm emergence were the lower limbs (Table 4). Three cases of lesions each were observed on the scrotum, chin and breast respectively. The treated subjects showed good tolerance to the drugs, with many reporting relief of pain, while the clinical course of the disease in the untreated group extended up to 13 weeks before subsidence of acute manifestations. Inflammatory manifestations disappeared in the treated group within 2-3 days of treatment.

In 864 cases, there was spontaneous extrusion of the worm or the worm could be extracted manually without any resistance (Table 5). Abscess formation or encystment was not observed after drug therapy. Worms which were previously palpable could not be felt as a cord presumably due perhaps, to migrations of the worms to deeper fascia or lyses. There were reports of prodromal symptoms and signs in most patients prior to the emergence of adult fertilized female worms. These were observed in both treated and control groups.

Table 1: Distribution of guinea worm patients in relation to sampled areas

Local Government Area*	Number infected (%)
Ikwo	267(30.9)
Ozibo	148(17.1)
Ebonyi	202(23.4)
Ezza North	247 (28.6)
Number Infected	= 864

*These are the most endemic Local Government Areas in South eastern Nigeria during the 1998/1999 transmission season.

Table 2: The age and sex distribution of the patients

Ages in years	1-10	11-20	21-30	31-40	41-50	51-60	61-70	Total
Females	86	192	117	46	39	31	28	529
Males	49	78	60	51	45	23	19	325

Table 3: Ranking of clinical manifestations

Clinical Manifestation	Grading					Total
	0	1	2	3	4	
Swelling	25	42	373	364	60	864
Pain	13	49	398	339	65	864
Redness	34	220	305	211	94	864
Exudation	105	52	401	219	87	864

Table 4: Predilection sites of worm emergence

Predilection Site of lesion	Lower limb	Upper limb	Other sites	Total
No of lesion	715	134	88	937

Table 5: Observations on clinical response

Response to treatment	No of Cases	Percentage
Poor	61	7.1
Fair	53	6.1
Good	86	9.9
Very good	664	76.9
n	=	864

DISCUSSION

Numerous traditional remedies abound in the study area indicating absence of effective modern management of the condition in the area (28). These rural communities had neither functional hospitals nor medical centers. Thus ulcers arising from guinea worm infection were treated according to the subject's level of belief and understanding. Some sufferers superstitiously attributed the disease to the wrath of the gods or to witch craft and could not readily appreciate any link between it and drinking cyclops-infested water (28). Systematic health education in these communities on the treatment of dracunculiasis has been successful, but must be sustained.

About 67% of the infected subjects, with emerging adult female worms complained of prodromal symptoms a few days or hours before the emergence of the worms. Kale (14) similarly reported that 80% of patients had prodromal signs in dracunculiasis endemic area in western Nigeria. The prodromata usually lasts for less than 24 hours and consists of one or more of generalized urticarial rash accompanied by erythema, mild to moderate itching, fever and giddiness, dyspnoea, nausea, vomiting, diarrhoea and infrequently intra-orbital oedema and syncope. These symptoms were observed more in the control group than in those treated with Septrin®. Prodromata of dracunculiasis are allergenic in nature and results from the release of histamine-like substances triggered off by the presence of the worms (11).

Most antibiotics so far employed in the management of dracunculiasis have beneficial effects on the patients in that they relieve symptoms, speed up the expulsion of the worms from the body and promote the healing of illness. Because they have not been shown to affect the worm in any discernible way, Muller (1) has suggested that their beneficial action in the treatment of dracunculiasis derives from their anti-inflammatory properties. Again, significant amount of an intra-cellular bacterium and endosymbiont *wolbachia* has been observed in the body of some parasitic nematodes (29, 30, 31). Further studies are urgently needed to elucidate the possible involvement of *wolbachia* in *D. medinensis* infection vis-a-vis the effect of those antibiotics on the parasites and *wolbachia* when present.

The Septrin® equally enhanced healing of septic wounds, reduced both swollen legs and pains in over 67% of the cases. Some of the worms that could not be extracted clue to loss of cuticle, atrophied and died within 4-6 days in 664 cases, as revealed by spontaneous extrusion of the dead worms or ease of manual extraction. Simple treatment regime, availability, good tolerance and the dramatic effectiveness makes Septrin® a possible candidate drug for mass treatment of dracunculiasis in the study area. Since Septrin® brand of cotrimoxazole is relatively costly when compared with other brands in the Nigerian market, there is need to repeat the study with other cheaper brands in order to determine their effectiveness and use by poor rural farmers, who constitute the major sufferers of dracunculiasis in Nigeria (18). Cotrimoxazole could prove a useful weapon for agencies mandated with the eradication of dracunculiasis in Nigeria.

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