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The post-treatment effects of enterobiasis on the occurrence of enuresis among children in Calabar, Nigeria

Iquo B Otu-Bassey, Monday F Useh*, Anyanwu A Alaribe

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Medical Microbiology/Parasitology Unit, Department of Medical Laboratory Science, Faculty of Allied Medical Sciences, University of Calabar, Calabar, Nigeria

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ABSTRACT

Objective: To investigate the relationship between enterobiasis and enuresis before and after albendazole therapy among 632 children, aged, 5-14 years, in Calabar, Nigeria. Methods: The scotch tape (cellotape) technique was used for the detection of eggs of Enterobius vernicularis (E. vermicularis) while questionnaire-based interviews were used for screening for anal itching and/or enuresis among study participants. All subjects found positive for Enterobius infection as confirmed by the presence of eggs and those with persistent anal itching (both enuretic and nonenuretic) were treated with 400 mg of albendazole given as a single dose. The treated subjects were re-assessed post-treatment to ascertain whether they were cured and also to determine their enuretic status (for the enuretics). Results: The overall prevalences of Enterobius infection, anal itching, and enuresis prior to albendazole therapy were 6.8%, 42.9%, and 35.6% respectively. There was no statistically significant difference in the prevalence of these parameters by the socio-economic class of subjects (P = 0.462, P = 0.647, and P = 0.610, respectively). The pretreatment prevalences of enuresis among Enterobius and anal itching-positive subjects were 53.5% and 49.8%, respectively versus 34.3% and 24.9%, respectively among their negative counterpart (P = 0.012 and P < 0.001, respectively). Four (20%) out of the 20 enuretic children found Enterobius egg-negative after albendazole therapy were equally cured while 8(40%) had reduction of their enuresis, thus giving a total resolution rate of 60%. Similarly, 64.2% resolution (25% cure and 32.8% reduction) of enuresis was observed amongst 120 anal itching-cured/ enuretic children. Enuretic status of the Enterobius-/anal itching-uncured subjects, on the other hand, remained unchanged post-treatment. Conclusions: This study is suggestive of the involvement of *E. vermicularis* in the aetiology of enuresis in Calabar. Children presenting with, especially, uncomplicated enuresis should be screened for enterobiasis.

1. Introduction

Enterobiasis is a common intestinal helminthic infection caused by the nematode, *Enterobius vermicularis (E. vermicularis)*. It is commonly referred to as pinworm, or thread worm^[1]. The disease is distributed worldwide and is estimated to infect over 1 000 million people globally^[2]. It is a group infection which predominates in children (aged 5–14 years) and the poor but is no respecter of socio–economic status, age, race, and sex or season^[2,3]. The transmission of infection is usually by oro–anal contact and is facilitated by factors such as overcrowding (as in orphanages, schools and

family groupings) and poor personal/group hygiene[1].

Most pinworm infections are asymptomatic. In symptomatic cases, the commonest symptom is anal itching (pruritus ani) which may be intense and induce the victim to scratch the affected area resulting in excoriations, haemorrhages and secondary infections^[2]. Other common symptoms of the disease include abdominal discomfort^[4,5], insomnia (persistent difficulties to sleep) and restlessness, anorexia (loss of appetite), weight loss, irritability, and emotional instability^[1].

Available evidence has shown that enterobiasis which is often underrated and thought to be restricted to the temperate regions could cause more significant morbidity, particularly in the tropics, than previously thought. For example, the pinworm may occasionally cause severe ectopic diseases (extra–intestinal enterobiasis) and other complications in various parts of the body, including enuresis^[2,6] and urinary tract infections^[7,8]. Pathological

^{*}Corresponding author: Prof. Monday F Useh, Medical Microbiology/Parasitology Unit, Department of Medical Laboratory Science, Faculty of Allied Medical Sciences, University of Calabar, Calabar, Nigeria.

Tel: 2348033363670

E-mail: francisuse@yahoo.co.uk

conditions such as vaginitis, vulvovaginitis (pruritus vulvae)[7], granulomatous endometritis, and lesions such as pelvic inflammatory disease (PID)[9], salpingitis, pelvic peritonitis, tubo-ovarian abscess^[10] and prostatitis (in males)^[11] leading to sterility have been reported[9]. Other studies have associated enterobiasis with ear and eye infections and the facilitation of the transmission of *Dientamoeba fragilis*^[12]. *Enterobius* is capable of invading the gastric mucosa with resultant ulcers/haemorrhages, secondary infections and sub mucosal abscesses, necrosis and nerve injury, which may lead to nervous symptoms, and enuresis^[13]. Invasion of human tissues by the parasite may lead to the formation of granulomas14 which may be difficult to diagnose^[15,16]. Enterobiasis has also been associated with acquired immune deficiency syndrome (AIDS), probably because it can be sexually transmitted, especially through homosexual and oro-anal sexual contacts[17]. It has been associated with appendicitis^[18,19], low intelligence quotient in children aged 6-12 years^[20], and malnutrition and growth retardation in children^[21]. Several drugs, including albendazole are used for the treatment of pinworm infection. Albendazole is one of the broad-spectrum antihelminthics recommended for mass treatment of, preferably ectopic enterobiasis^[22].

Enuresis is an unintended release of urine at least once a week in an individual old enough (usually 4–5 years) to achieve bladder control, which leads to bedwetting, especially at night (nocturnal enuresis). Enuresis may date from birth (primary enuresis, *i.e.*, never dry) and may even persist to adulthood or may occur after a dry period of up to 6 months or more *i.e.*, after bladder mastery has been achieved (secondary enuresis)^[23].

Enuresis is a common childhood problem worldwide, affecting about 5–7 million children in the United States and more boys than girls wet in the ratio of 3:1[24]. There are isolated studies on enterobiasis and its relationship with enuresis. A few studies have linked enterobiasis with enuresis, particularly secondary enuresis[6.25]. In Nigeria, information on the endemicity of enterobiasis is very scanty. There is no study on its possible relationship with enuresis, except the preliminary report by Otu–Basssey, *et al*[13] where it was suggested that *E. vermicularis* could bring about enuresis directly by causing nerve injury, nervous breakdown and subsequent enuresis or indirectly by inducing urinary tract infection (which had earlier been associated with secondary enuresis) or that the two problems may simply share a risk factor.

Enuresis is a health problem with multifactoral and somewhat controversial aetiology, social and psychological consequences and management difficulties. Efficient management of enuresis depends on proper identification and treatment of the cause. Unfortunately, only about one third of the families with this problem seek medical help^[24]. In the present study, *Enterobius*-infected/enuretic children were treated with albendazole. The post-treatment statuses of both disorders were followed up to determine the role of enterobiasis in the aetiology of enuresis among school-age children in Calabar, Nigeria.

2. Materials and methods

2.1. Study area

The investigation was carried out in Calabar, the capital of Cross River State in South South Nigeria between January and December, 2007. Calabar is a coastal urban city comprising two local government areas, namely Calabar Municipal and Calabar South with a metropolitan and urban slum setting. It has annual rainfall of 1 500-2 000 mm which is usually confined to a single rainy season each year (April-October). The metropolitan areas are planned, less crowded with near adequate infrastructure and social amenities but with good sanitation. A greater number of the residents in the metropolitan area are high-income earners and include senior civil/public servants and chief executive officers from the organized private sector. The urban slums, located at the suburbs, are overcrowded with limited infrastructure, social amenities and poor drainage system. Most of its dwellers operate on low incomes, with poor standard of hygiene and sanitation and are comprised mainly of peasant farmers, artisan workers, casual laborers, petty traders, and junior civil servants.

2.2. Subjects and consents

Six hundred and thirty two (632) children (470 from high and 125 from low density area), aged 5-14 years, whose parents were either of high or low economic status was enrolled in the study. Prior to the investigation, written ethical clearance was obtained from the "Cross River State Government Committee on Health Research Ethics". Written parental consent was sought and obtained through house-to-house visits and issuing of information/consent letters by the investigators. The participants were briefed about the intended study, its objectives, procedures, potential risks and benefits. The study households in both local government areas were randomly selected and once parental consent had been obtained, all the children in each household within the study age group were screened for Enterobius infection, anal itching and enuresis. Parents were asked not to bathe the children or wash their anus (nor allow them to do so by themselves) after defecation (but to use toilet paper only) on waking on the day of screening. All the subjects found positive for *Enterobius* eggs and anal itching were treated without charge.

2.3. Pre-treatment screening for Enterobius infection, anal itching and enuresis

2.3.1. Collection of anal swabs

For parasitological screening, anal swab was collected from each child, using an 8 cm \times 2 cm piece of transparent adhesive tape (Cellotape, Henkel Consumer Adhesives, Winsford, UK) held sticky side out, over the end of a glass microscope slide^[26]. The tape was briefly patted on the perianal area of a subject and then reversed, so that it stuck to the glass slide, with the sample trapped between the tape and the glass. All samples were collected between 06:00 and 08:00, just after the children had woken up but before they had bathed. Each subject was sampled only once due to poor co-operation of the subjects and/or their parents.

2.3.2. Screening for anal itching and enuresis

After the anal swabs had been obtained, each of the subjects was interviewed in the presence of at least one of his or her parents or guardians based on a standard questionnaire. The ages and gender of the subjects were recorded before they were asked if they suffered from any anal itching and/or bedwetting (and if so, for how long). They were asked also if they had felt the movement of, or seen worms emerging from their anus. For the purpose of this work, only subjects who wetted themselves frequently and night wetters were considered enuretic since about 85% of enuretics are night wetters^[27].

2.4. Detection of ova of E. vermicularis

To each anal swab, 2 drops of xylene were added, between the slide and the tape, and spread over the entire length of the slide to dissolve the mucilage in the sample^[26]. Each slide was then carefully examined under a light microscope, at 10× and 40×, for the characteristic ova of *E. vermicularis*.

2.5. Treatment of Enterobius egg- and anal itching-positive subjects

All subjects (enuretic and non-enuretic) found positive for Enterobius eggs and those reported as having anal itching in the initial screening, except those who opted out were administered with a single oral dose of 400 mg of albendazole^[22] (supplied as Zentel and manufactured by Glaxo Wellcome Nigeria Ltd., Lagos, Nigeria) following their clinical assessment by the study physician, who also monitored them for any adverse effects. Anal itchingpositive but *Enterobius* egg-negative individuals were treated to ascertain to what level syndromic management of helminths infections undermine the determination of the true prevalence of enterobiasis.

2.6. Post-treatment screening for Enterobius eggs, anal itching and enuresis

The cure rates of *Enterobius* infection and anal itching were assessed among treated subjects following treatment by repeat screening for *Enterobius* eggs and anal itching using the same procedure as used during pre-treatment. All the enuretic subjects found *Enterobius* egg and/or anal itching negative (cured) and their positive (uncured) counterparts were further interviewed to determine their enuretic status post-treatment.

2.7. Data analysis

A child was only considered cured of enterobiasis if no eggs were detected in his/her anal swab or if no anal itching was reported post-treatment for those who had anal itching but were egg-negative. Proportions were compared using χ^2 tests. A two-tailed *P*-value of < 0.05 was considered indicative of a statistically significant difference.

3. Results

3.1. Pre- and post-treatment prevalence of Enterobius infection, anal itching and enuresis

The pre-treatment prevalence of *Enterobius* infection was 43(6.8%) based on presence of ova in the anal swabs and 271(42.9%) based on the reporting of anal itching while enuresis occurred in 225(35.6%) of the subjects examined (Table1). There was no statistically significant difference in the prevalence of *Enterobius* infection, anal itching and enuresis, respectively by economic class of the subjects ($\chi^2 = 0.54$, df = 1; P = 0.462; $\chi^2 = 0.21$, df = 1; P = 0.647, and $\chi^2 = 0.26$, df = 1; P = 0.610, respectively).

Subjects who had *Enterobius* infection were more significantly associated with enuresis (53.5%) than those without infection (34.3%) ($\chi^2 = 6.39$, df = 1; P = 0.012). Similarly, subjects with anal itching alone were significantly more infected (49.8%) than those without anal itching (24.9%) ($\chi^2 = 26.40$, df = 1; P < 0.001).

Among the initial number of subjects (23) treated with albendazole, who were *Enterobius*-positive/enuretic, 20 (87%) tested egg-negative for *E. vermicularis* while 120 (89.3%) of the 135 subjects with anal itching alone/enuresis were relieved of their itching post-treatment.

3.2. Post-treatment effects of Enterobius infection and anal itching on the occurrence of enuresis

Table 2 shows the resolution rate of enuresis among enterobiasis-cured and -uncured subjects. In the context of this study, resolution of enuresis was defined as complete absence of or reduction (from frequent to occasional) in

Table 1

Prevalence of Enterobius infection, anal itchi	1 .	1	• 1 • • • •	
Prevalence of <i>Enterobius</i> infection, anal itchi	ng and enuresis amon	g subjects by socio-ecc	phomic class of their	parents in Calabar [n(%)].
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Socio-economic class	Examined(n) -	Preralence			
		Enterobius eggs	Anal itching	Enuresis	
High	162	9 (5.6)	67 (41.4)	55 (33.9)	
Low	470	34 (7.2)	204 (43.4)	170 (36.2)	
Total	632	43 (6.8)	271 (42.9)	225 (35.6)	

High socio-economic class: Children of senior civil/public servants/chief executive officers from the organized private sector, mostly residents of low density, affluent area. Low socio-economic class: Children of junior civil servants, agro allied workers, artisans and casual laborers, mostly residents of high density, low economic area.

318 Table 2

Enuretic subjects	E		Enuresis resolved $n(\%)$	
	Examined(n)	Cured	Reduced	Total cured or reduced
Enterobiasis-cured	20	4 (20.0)	8 (40.0)	12 (60.0)
Anal Itching–cured	120	30 (25.0)	47 (32.8)	77 (64.2)
Total	140	34 (24.3)	55 (39.3)	89 (63.6)

bedwetting for up to 1 week–3 months. A higher resolution rate of enuresis 12 (60%) [*i.e.*, 4 (20%) cure and 8 (40%) reduction] was observed amongst 20 enterobiasis–cured children than none (0.0%) among their 3 uncured (control) counterparts. This difference was statistically significant ($\chi^2 = 3.94$, df = 1; P = 0.047). Also, 30(25%) of the 120 anal itching–cured children tested were simultaneously cured while 47(32.8%) had reduction of their enuresis, thus giving a total resolution rate of 77(64.2%) compared to none (0.0%) among their 15 uncured (control) counterparts. The post– treatment effect of anal itching on the occurrence of enuresis was statistically significant ($\chi^2 = 22.67$, df = 1; P < 0.001).

Enterobius infection and anal itching were respectively and significantly related to enuresis before and after albendazole therapy ($\chi^2 = 6.39$, df = 1; P = 0.012, and $\chi^2 = 26.40$, df = 1; P < 0.001) versus ($\chi^2 = 3.94$, df = 1; P = 0.047, and ($\chi^2 = 22.67$, df = 1; P < 0.001), respectively.

4. Discussion

This study has confirmed a low endemicity rate (6.8%) of E. vermicularis infection among school-age children in Calabar based on egg positivity. This is lower than the 7.5% earlier reported in this locality by Otu-Bassey et al^[13] and in Sudan (7.4%)^[28], but considerably lower than that reported in Puerto Rico (30%)[29], after the examination of one sample per subject, or (71.3%) in Hatay/Turky[6], after the examination of three consecutive samples per subject. One of the limiting factors in the present study was the unwillingness of some parents and subjects to participate in the study because of the invasion of their privacy. They were also dissuaded as they believed that the results of the survey might be easily traced since house to house sampling was done. These factors also impacted negatively on the sample size with a likelihood of underestimating the true prevalence of the infection in Calabar.

The overall prevalences of anal itching and enuresis in the study were 42.9% and 35.6%, respectively. In an earlier study in Calabar, Otu–Bassey *et al*^[13]reported a strong correlation between Enterobius infection and anal itching and suggested that the presence of the later can be used as the basis of treating enterobiasis where laboratory facilities are lacking. Pre–treatment evaluation showed that the existence of *E. vermicularis* infection, reporting of anal itching and occurrence of enuresis were significantly related (P = 0.012 and P < 0.001, respectively). Anal itching has consistently been associated with enterobiasis. The results obtained from this study are clear evidence that the endemicity of this disorder is underestimated in this locality because of the difficulties associated with the diagnosis. This calls for a reconsideration of the earlier held view that the condition is mainly that of the Western world. We have equally shown that subjects with Enterobius infection were more significantly associated with enuresis than those without the infection (53.5% vs 34.3%), respectively. The same observation held for analysis of the relationship between the occurrence of anal itching and enuresis. Subjects with anal itching were more associated with enuresis (49.8%) than those without anal itching (24.9%). The difference in prevalence in both situations were statistically significant (P = 0.012 and P <0.001, respectively). This colliery further affirms the fact that enterobiasis has a role in the causation of enuresis. The theory behind the relationship of enterobiasis and anal itching with enuresis, particularly secondary enuresis which appears to be supported by the above findings has been explained in the past[13,25].

Albendazole was very efficacious in elimination of Enterobius infection and anal itching in the study (87% and 89.3%, respectively). This drug is given in this locality as a broad spectrum medication for the treatment of helminths infection. Its administration may be partly responsible for the non-reporting of this disease in this locality coupled with the difficulties associated with its diagnosis. This study has shown that of the 20 subjects cured of enterobiasis following albendazole therapy, 20% were completely cured of enuresis while 40% had remarkable reduction of their enuresis episodes. In effect, 60% of the subjects were completely cured or very substantially relieved of enuresis following therapy. Similarly, 25% of the subjects who were cured of their persistent anal itching following albendazole therapy were equally cured of their enuresis while 32.8% had theirs substantially reduced giving a total resolution of 64.2%. On the other hand, the subjects that were not cured of enterobiasis and those with continued reportage of anal itching following albendazole therapy all continued with persistent enuresis. This is a further confirmation of our earlier report in this locality^[13] which associated Enterobius infection with anal itching and suggested the infection as one of the probable aetiologies of enuresis.

The findings of this study may have been limited by the sample size used occasioned by the fact that anal swabs are used for diagnosis as the eggs are laid in the perianal region. Effective diagnosis demands that subjects are preferably examined at home early in the morning before bathing. This is only possible using house to house visits which were strongly resisted by some participants for fear of intrusion of their privacy.

In conclusion, we have shown that some children who

were treated of *Enterobius* infection or anal itching which is mostly an outcome of *Enterobius* infection in this locality had their enuresis cleared or substantially reduced. We conclude that *E. vermicularis* infection is one of the aetiologic factors of secondary enuresis in this locality. We recommend that physicians should request for the evaluation of children with persistent enuresis for *E. vermicularis* infection.

Conflict of interest statement

We declare that we have no conflict of interest.

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