Targeted chemotherapy for parasite infestations in rural black preschool children

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Objective. To investigate whether targeted chemotherapy can reduce parasite prevalence rates in rural black preschool children.

Design. The study consisted of a before/after trial. Stool and urine samples were analysed on four occasions over a 21-week period.

Setting. Crèches in two rural areas of southern KwaZulu/Natal (coastal and inland).

Patients. Two hundred children of 4 - 6 years of age attending 19 crèches in the area.

Intervention. Targeted chemotherapy using albendazole for nematode infestations, praziquantel for trematode and cestode infestations and metronidazole for protozoal infections was administered twice at an interval of 14 weeks.

Main outcome measure. Prevalence rates.

Results. The prevalences of *Ascaris lumbricoides, Trichuris trichiura* and *Necator americanus* infestation decreased significantly after treatment. Reinfestation rates 12 weeks after treatment were 16% for *A. lumbricoides,* 33% for *T. trichiura,* 24% for *Giardia lamblia* and 3% for *N. americanus.* No reinfestation was noted for *Schistosoma haematobium, Hymenolepsis* or *Taenia* species.

Conclusion. The study suggests that parasite prevalence rates in children can be reduced by the administration of appropriate chemotherapy at regular intervals. However, the provision of clean water and adequate sewerage facilities remains a high priority for black communities living in rural areas of South Africa.

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Although the mortality rate associated with parasite infestations is negligible, morbidity such as impaired physical and mental development is significant. This is confirmed by studies on nematode and cestode infestation in children.[1-3] In Jamaica prevalence and intensity of infection with *Trichuris trichiura* were found by Nokes *et al.*[4] to be greater among academically less able pupils. Boivin *et al.*[5] reported that after successful treatment for infestation with serious types of chronic intestinal parasites children in Zaïre

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demonstrated significant improvement in spatial memory. A combination of vermifuge and iron supplement resulted in higher cognitive performance.[6] Kvalsvig[7] working in KwaZulu/Natal noted that spontaneous energetic activity increased in children treated for schistosomiasis relative to controls, and that poor performance on an attention task showed an association with parasite infection.[3]

Intensity of infestation affects morbidity, while lack of clean water and adequate sanitation are major contributors to infestation and reinfestation. Many individuals also host more than one parasite infestation simultaneously.[3] The question of whether children's nutritional status is affected by their worm load has been the subject of repeated discussion.[8-10] Simeon and Grantham-McGregor[11] suggest a relationship between mental development and mild-to-moderate undernutrition. Recent work on children suffering from mild-to-moderate undernutrition has tended to use height for age and weight for height.[11] Treatment of helminth infestation resulted in an improvement in these indices. Improvement in physical fitness has been noted as a result of the successful treatment of ascariasis and trichuriasis.[12]

This study examined the prevalence of parasite infestations (helminths and protozoa), and the efficacy of targeted chemotherapy and reinfestation rates after chemotherapy in rural black preschool children using the following single-dose drug protocols: (*i*) praziquantel (Biltricide; Bayer) for schistosomiasis and cestodiasis; (*ii*) albendazole (Zentel; SmithKline Beecham) for nematode infestation (*Ascaris lumbricoides, T. trichiura* and *Necator americanus*); and (*iii*) metronidazole for *Giardia lamblia*.

Material and methods

This study formed part of an investigation into the effects of parasite infestations on behaviour and cognitive processes in children living in areas with a high prevalence of common helminth parasites.[3]

Two hundred preschool children attending 19 crèches from a coastal (Mtwalume) and an inland (Nqabeni) region of southern KwaZulu/Natal were included after informed parental consent had been obtained. All children present were investigated for all parasites at each survey and received treatment targeted at the infections/infestations. The inaccessibility of some of the crèches precluded repeated visits by the researchers for follow-up purposes. The number of subjects in each of the four surveys therefore differs.

Phase 1 (N = 153) consisted of all children who were available at both survey 1 and survey 2. Any child who presented at just one of the two surveys was excluded from the analysis. Phase 2 (N = 145) consisted of all children presenting at both survey 3 and survey 4.

In phase 1, survey 1 determined the prevalence of infestation and survey 2 the efficacy of treatment and new cases. In phase 2, survey 3 assessed reinfestation in subjects who had been successfully treated in phase 1, while survey 4 assessed the efficacy of the second treatment, and new cases.

The treatment schedule took place over 21 weeks.
Phase 1. Week 0 (survey 1) — stool/urine sampling and analysis; week 4 — treatment of identified parasites; week 10 (survey 2) — evaluation of treatment.
Phase 2. Week 16 (survey 3) — evaluation of reinfestation; week 18 — treatment of identified parasites; week 21 (survey 4) — evaluation of treatment.

Faecal samples were examined microscopically for the presence of eggs of *A. lumbricoides* (roundworms), *T. trichiura* (whipworm), *N. americanus* (hookworm), *Schistosoma mansoni* (bilharzia), *Taenia* spp., *Hymenolepis nana* (tapeworm) and *G. lamblia* (protozoa), while urine samples were examined for *S. haematobium* eggs.

Where children tested positive (faecal and urine sampling) the following treatment schedule was used: (*i*) schistosomiasis and cestodiasis — single oral dose of praziquantel (40 mg/kg); (*ii*) nematode helminthiases, i.e. *Ascaris* and/or *Trichuris* and/or *Necator* — single oral dose of albendazole (400 mg); (*iii*) mixed helminthiases — both albendazole and praziquantel; and (*iv*) protozoan infection, i.e. *G. lamblia* — single oral dose of metronidazole (800 mg), given together with albendazole or praziquantel where required.

Efficacy of treatment was determined by repeat stool and urine analysis 6 weeks after drug treatment (phase 1) and 3 weeks after drug treatment (phase 2). Reinfestation rates were determined by repeating stool and urine examination (survey 3) 12 weeks after the first course of chemotherapy. McNemar's test was used to compare the change in the prevalence before and after treatment. Statistical significance was assumed at $P < 0,05$.

Results

Of the 200 children included in the study, 183 participated in survey 1, 165 in survey 2, 174 in survey 3 and 151 in survey 4. The study population comprised children aged 4 - 6 years (mean age (± SD) 4,81 ± 0,34 years); 83 children were aged 4 - 4½ years, 116 5 - 5½ years and 1 6 years. Weights ranged from 12 to 24 kg (mean 16,66 ± 1,94 kg) and heights from 89 to 114,8 cm (mean 105,17 ± 1,94 cm).

The prevalences of parasite infestation measured in survey 1 for the coastal area around Mtwalume and the inland area around Nqabeni are shown in Table I. There were multiple infestations in 77% of cases, with 4,9% of children simultaneously harbouring as many as 4 parasite species and only 5,5% being free of infestation. Species identified as commensals were *Escherichia coli* (47%), *Entamoeba histolytica* (6%), *E. hartmanni* (9,8%), *Iodamoeba butschlii* (7,7%) and *Chilomastix mesnili* (9,8%).

Table I. Prevalence of parasite infestations in coastal and inland areas

	Coastal (Mtwalume) (N = 114)		Inland (Nqabeni) (N = 69)		Total (N = 183)	
	No.	%	No.	%	No.	%
A. lumbricoides	93	82	56	81	149	81
T. trichiura	109	96	39	57	148	81
N. americanus	50	44	3	4	53	29
S. haematobium	7	6	1	2	8	4
H. nana	2	2	1	2	3	2
Taenia spp.	0		3	4	3	2
G. lamblia	21	18	2	3	23	13

Table II. Prevalence of parasite infestations and efficacy of chemotherapy

	Phase 1 (N = 153)							Phase 2 (N = 145)						
	Survey 1, prevalence		Survey 2					Survey 3, prevalence		Survey 4				
			Prevalence		Cured		Mean egg reduction in			Prevalence		Cured		Mean egg reduction in
	No.	%	No.	%	No.	%	non-cured cases	No.	%	No.	%	No.	%	non-cured cases
A. lumbricoides	123	80	10	7	113	92	98%	28	19	4	3	27	96	87%
										(3 new cases)				
T. trichiura	125	82	97	63	28	22	37%	85	59	83	57	12	14	33%
										(10 new cases)				
N. americanus	45	29	5	3	40	89	80%	3	2	3	2	3	100	–
										(3 new cases)				
S. haematobium	5	3	11	7	1	20	2 453%	2	1	5	3	1	50	1 167%
			(7 new cases)				increase			(4 new cases)				increase
H. nana	2	1	4	3	1	50	50%	1	0,7	2	1	1	100	–
			(3 new cases)							(2 new cases)				
Taenia spp.	3	2	1	0,7	3	100	–	0		0		–		–
			(1 new case)											
G. lamblia	20	13	17	11	17	85	0%	13	9	20	14	10	77	0%
			(14 new cases)							(17 new cases)				

The efficacy of targeted chemotherapy is shown in Table II. As a result of the initial treatment (phase 1) there were cure rates of 92% for *Ascaris,* 22% for *Trichuris* and 89% for *Necator* (P < 0,01). In phase 2 of the study cure rates were 96% for *Ascaris,* 14% for *Trichuris* and 100% for *Necator* (P < 0,01).

Table III. Parasite reinfestation rates* after chemotherapy

	No. at survey 2 who were successfully treated	No. who subsequently became infested at survey 3
A. lumbricoides	105	17 (16%)
T. trichiura	24	8 (33%)
N. americanus	40	1 (3%)
S. haematobium	1	0
H. nana	1	0
Taenia spp.	3	0
G. lamblia	17	4 (24%)

* Only children who participated in surveys 2 and 3 were considered for the study on reinfestation rates.

In this study there were few *Ascaris* and *Trichuris* egg counts over 10 000 eggs per gram (epg) faeces. In other studies, counts of less than 2 000 epg have been considered mild and counts between 2 000 and 10 000 epg moderate.[13] In order to analyse the extent to which light infestations were effectively treated by albendazole, egg loads were divided into groups of < 2 000, 2 000 - 10 000 and > 10 000 epg.

The *Ascaris* load in survey 1 showed 6 children with egg counts greater than 10 000 epg, the highest count being 37 587 epg. At survey 3, 1 child had an *Ascaris* egg count of 12 177 epg; however, at the end of the study all children not cured of infestation had counts considerably less than 500 epg. For *Trichuris* infestations, 26 of the 28 patients cured in phase 1 and 11 of the 12 patients cured in phase 2 had egg counts less than 2 000 epg. Four children had egg counts above 10 000 epg, and these were reduced to considerably below 10 000 epg after treatment. The largest *Necator* load was 446 epg.

Only 16 children with *S. haematobium* infestations were identified, with samples containing 2 to 1 107 eggs per millilitre. The number of cases in each survey was small. Of the 5 children who received treatment after survey 1, 1 was cured; the egg count decreased in another and increased in 3. Seven new cases were noted in phase 1 and 4 new cases in phase 2. No case of *S. mansoni* infestation was detected. The prevalence of tapeworm infestation (*Taenia* spp. and *Hymenolepis*) was low, and praziquantel appeared to be highly effective in eradicating infestation in both phases of the study (1 child in phase 1, however, was not cured but showed a reduction in egg load). Of 20 children with *G. lamblia* infection, 17 were cured after treatment in phase 1; in phase 2 10 of 13 were cured. A large number of new cases of *Giardia* infection were noted at surveys 2, 3 and 4.

Discussion

Although in the 1920s white children in the Eastern Transvaal were treated for parasitic diseases by the Medical Officer of Health attached to the Transvaal Education Department on the grounds that these diseases affected their school work, some 5 decades later prevalence rates among black children remain high and for the most part the diseases remain untreated.[14] High prevalence rates for *A. lumbricoides* (81%) and *T. trichiura* (81%) were observed. Evans *et al.*[15] reported prevalences in KwaZulu of 64,5% for *Ascaris* and 61,1% for *Trichuris.* While the coastal and inland regions showed similar prevalences for *Ascaris,* there was a higher prevalence of *Trichuris, Necator* and *Giardia* in the coastal areas. Whether these differences were due to population density, climatic conditions or soil type is not known. However, further investigation of these regional variations may help direct remedial measures.

Although there was a higher prevalence of schistosome infestations in children living at the coast, both the incidence and the prevalence of these infestations in children of 4 - 6 years of age are low. This would appear to be the result of differences in behaviour, older children being more likely to play in contaminated water and thus get infected. Bundy and Cooper[2] noted that mean intensity of infestation related convexly to age. Infestation intensity rises rapidly among infants, reaching a maximum in the 4 - 10-year group, and declines in young adults to a stable low value. Although a similar proportion of adults and children are infested, adults tend to harbour significantly fewer worms.

The high prevalences of *Ascaris* and *Trichuris* infestation in the southern KwaZulu/Natal area suggest that these children are at risk of impaired physical and mental development.[3,16]

The results of treatment of *Ascaris* infestation in phase 1 indicated a substantial decrease in prevalence subsequent to treatment, and in children not cleared of infestation its intensity had decreased to less than 500 epg. Between treatments some children were reinfested, but intensity of infestation was greatly reduced from the initial levels. In the present study cure rates for *Trichuris* infestation of 22% and 14% were achieved in phases 1 and 2 respectively, but treatment failures occurred with egg counts greater than 2 000 epg. When infestation was mild (< 2 000 epg) cure rates were appreciably higher and consistent with the 61 - 73% reported by Maisonneuve *et al.*[13]

It has been postulated that minor increases in infestation in high-prevalence areas may result in a significant increase in morbidity.[17] The success in reducing both prevalence and intensity of infestation suggests that regular treatment with a suitable anti-parasitic agent may have a major impact on morbidity reduction, since the effects of repeated intervention may change both parasite transmission characteristics and the pattern of infestation.

Many intestinal parasites may cause diarrhoea. It is common in trichuriasis and giardiasis, especially when infestation is heavy. Diarrhoea is frequently reported among children in crèches, and the high prevalence of trichuriasis may be an additional burden.

Albendazole was effective as a single-dose treatment for *Ascaris* and *Necator* infestation, but less so for *Trichuris.* Single-dose treatment has obvious advantages for mass chemotherapy, but further investigation including repeated doses of drugs and the use of alternative compounds are needed in respect of heavy infestations of *Trichuris.*

Although the literature suggests a 3 - 7-day course of treatment with metronidazole for *G. lamblia* infection,[18] in this study a single dose of 800 mg was empirically chosen with a view to improving patient compliance. The success of this regimen suggests that single-dose treatment with metronidazole should be investigated further.

The unacceptably high reinfestation rates (Table III) are a reminder that improvement in the socio-economic status of these communities and the provision of clean water and adequate sewerage facilities are high priorities in South Africa.

Conclusions

The prevalences of *Ascaris* and *Trichuris* infestation among the preschool children were notably higher than those of *Necator* and *Schistosoma* infestation. Although the prevalence of *Ascaris* infestation was similar at Mtwalume and Nqabeni, there were higher prevalences of *Trichuris* and *Necator* infestation among children living in the coastal areas. Whether this relates to differences in population density is not known.

The problem of reinfestation was noted with *Ascaris, Trichuris* and *Giardia* after a 12-week interval. Reinfestation is a problem because in the southern KwaZulu/Natal area where this study was conducted most people do not have clean water or adequate sewerage facilities. While ongoing repeated courses of chemotherapy may help, provision of pure water and adequate sanitation facilities is vital in ensuring the long-term health of communities.

Recommendations

The World Health Organisation has stated that 'school children harbour some of the most intense helminth infections with adverse effects on health, growth and school performance' and that 'treatment without prior individual screening of the whole population is recommended where the surveys of school-age children indicate that the prevalence of intestinal helminths or schistosome infection exceeds 50%'.[19]

In the interest of limiting costs, treatment should be targeted and not universal. Primary and preprimary children should be targeted for intestinal helminths and primary school children for schistosomiasis, because prevalence and intensity of parasite infections is usually greatest in these groups. The national health authorities should investigate and negotiate the best possible prices for the drugs used, given that safe and effective treatment programmes are available.

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