

# A COMPARISON OF MEBENDAZOLE AND ALBENDAZOLE IN TREATING CHILDREN WITH *TRICHURIS* *TRICHIURA* INFECTION IN DURBAN, SOUTH AFRICA

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**Objective.** To compare the efficacy of mebendazole 500 mg and albendazole 400 mg single-dose treatments of *Trichuris trichiura* infection in children in the Durban area of KwaZulu-Natal, South Africa.

**Design.** A single-blind randomised trial in children with a documented moderate infection of *T. trichiura*. Ova were counted in stool specimens before and 10 days after treatment by the formal-ether concentration method.

**Setting.** Two shelters for abandoned and orphaned children in Durban.

**Participants.** Ninety-six children aged between 2 and 12 years.

**Outcome measures.** The number of children who showed reduced *T. trichiura* ova counts after the treatments, and reductions in ova counts, both expressed as percentages. Statistical analysis using the Wilcoxon 2-sample test and the chi-square test.

**Results.** Eighty-two children completed the trial; 42 received mebendazole and 40 albendazole. Of the mebendazole group 85% showed a reduction in *T. trichiura* ova count, compared with 75% of children who received albendazole.

Mebendazole treatment was associated with a median percentage reduction in ova count of 72.2%, which significantly exceeded the 44.1% reduction after albendazole ( $P = 0.024$ ).

**Conclusion.** The mebendazole 500 mg single-dose therapy was more efficacious than the albendazole 400 mg single-dose therapy in treating *T. trichiura* infection in these children.

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Trichuriasis is an extensive worldwide health problem with estimates indicating that some 500 million people are infected with *Trichuris*.<sup>1</sup> Although found in all communities, parasitic diseases tend to be associated with poverty, and one estimate of the prevalence of *T. trichiura* infections in school-going children in a peri-urban area of KwaZulu-Natal is 47%.<sup>2</sup> Intestinal parasitic infections impact on morbidity widely. Trichuriasis has been associated with protein energy malnutrition,<sup>3</sup> which in turn has behavioural and cognitive effects. In a Jamaican study by Simeon *et al.*<sup>4</sup> it was shown that *T. trichiura* infection combined with poor nutritional status had an adverse effect on school performance. Trichuriasis has also possibly been linked with poor attention in school-going children.<sup>2</sup> *T. trichiura* infection is one of the most difficult parasitic infections to treat effectively. For example, Hall and Nahar<sup>5</sup> found that although albendazole initially appeared to inhibit ova production, it was later resumed. Results of other investigations also support the fact that trichuriasis is more difficult to treat than other parasitic infections such as ascariasis and hookworm.<sup>6,7</sup>

Mebendazole and albendazole are both benzimidazole carbamate drugs. Mebendazole has a broad spectrum of anthelmintic activity, including trichuriasis, hookworm, ascariasis, enterobiasis, strongyloidiasis and tapeworm. The drug is not absorbed from the host's intestine to any significant degree and appears to work by irreversibly blocking glucose uptake in the parasite, leading to depletion of the parasite glycogen, decreased formation of adenosine triphosphate and cell death.<sup>8</sup> Albendazole has a similar spectrum of activity to mebendazole, but its mode of action differs in that it is absorbed from the host's intestine.<sup>8</sup>

Mebendazole has been available as a multiple daily dose formulation on the South African market for many years. The advent of the single-dose regimen for mebendazole and the availability of albendazole for human treatment prompted the decision to conduct this comparative trial in South Africa.

## METHODS

### Subjects and stool specimens

One hundred and seventy-five children between the ages of 2 and 12 years (mean 8 years) were screened for this study. The children lived in one of two shelters for abandoned and orphaned children in the Durban area of KwaZulu-Natal, South Africa. Initial screening was performed to determine which children were infected with *T. trichiura*. Stool specimens were collected in 30 ml plastic screw-cap stool jars and preserved in 10% formal-saline. Formed stool specimens were covered with preservative; in the case of a semi-formed stool an equal volume of 10% formal-saline was added to the jar. One-gram samples were then processed in duplicate by means of the formal-ether concentration method. Total egg counts were performed on the concentrate using a compound

microscope, and dilute Lugol's iodine was used as a stain. The counts were expressed as eggs per gram of stool. Ninety-six children with a moderate infection (5 - 70 ova per cover slip on low power) were selected for the trial.

### Treatment and follow-up

These children then received either a single 500 mg dose of mebendazole (Vermox; Janssen-Cilag) or a single 400 mg dose of albendazole (Zental; SmithKline Beecham). The drugs were packaged identically and administered under the supervision of a clinician in a single-blind manner according to a randomisation schedule prepared by the Janssen Research Foundation, Belgium. The staff supervising the children were asked to note any adverse experiences reported by them, particularly during the 24-hour period following drug administration. Ten days after treatment stool collections were repeated and 1 g duplicate samples of each specimen were processed for quantitative *T. trichiura* ova counts, as above.

### Statistics

In order to show a 25% difference in parasite reduction between the two treatment groups, with 80% power and significance at the 5% level, 80 children were required to complete the study. The distribution of the ova counts, as well as the percentage reduction in ova counts, deviated significantly from normality and so the results were summarised in terms of medians and interquartile ranges. The significance of the difference between groups was assessed using the Wilcoxon 2-sample test. The chi-square test was used to compare the groups with respect to the percentage of children showing a reduction in ova burden.

### Ethical approval

This study was approved by the Postgraduate (Ethics) Committee of the Faculty of Medicine, University of Natal, Durban.

## RESULTS

### Patient characteristics

One hundred and fifty-three (88%) of the 175 children screened were positive for *T. trichiura* infection; only 9 children were free of parasites. Eleven other parasite species were identified, with *Giardia duodenalis* (63% of children), *Entamoeba coli* (31%) and *Ascaris* and *Entamoeba histolytica/dispar* (both 17%) being the next most common parasites identified. Most (71%) of the faecal samples were formed, 24% were semi-formed, and the remaining 5% were fluid. Of the 96 children who had an appropriate level of *T. trichiura* infection and who entered the trial, 14 either were unable to provide a post-treatment stool specimen or were lost to follow-up. Eighty-two children were therefore included in the analysis, of whom 42 received



mebendazole and 40 albendazole. No adverse events were reported in either group.

### Ova counts

The randomisation schedule achieved comparable baseline counts for each treatment, and these are summarised together with percentage reductions in counts in Table I. Frequency of ova count reduction was 36/42 (86%) after treatment with mebendazole and 30/40 (75%) after albendazole ( $P = 0.054$ ). The percentage reduction after mebendazole (72%) was significantly greater ( $P = 0.024$ ) than after albendazole (44%).

Table I. Pre- and post-treatment ova counts (eggs per gram of stool)

	Albendazole (median (interquartile range))	Mebendazole (median (interquartile range))	P-value
Pre-treatment	1 045 (626 - 1 548)	899 (583 - 2 051)	NS
Post-treatment	567 (184 - 948)	278 (71 - 605)	0.054
Reduction	44% (7 - 72%)	72% (33 - 89%)	0.024

### DISCUSSION

The results presented here indicating different efficacies between mebendazole and albendazole in treating *T. trichiura* infection are reflected elsewhere in the literature.<sup>7,9,10</sup> In a comparative trial using the same dose regimens as this study, Albonico *et al.*<sup>9</sup> showed mebendazole to be significantly superior to albendazole for both cure rate ( $P < 0.01$ ) and percentage ova reduction ( $P < 0.001$ ) in children infected with *T. trichiura* in Zanzibar. In a comparative study using 400 mg of either mebendazole or albendazole, Bartoloni *et al.*<sup>7</sup> showed mebendazole to have a higher cure rate than albendazole (60% v. 33%), while albendazole was reported to have a higher ova reduction rate than mebendazole (45.7% v. 15%). However, only 25 children with *T. trichiura* infection participated in the study, which may have contributed to the inconsistent results. In a study using higher doses of both mebendazole and albendazole (600 mg and 1 g, respectively), Holzer and Frey<sup>10</sup> reported that both drugs had enhanced cure rates in *T. trichiura* infection. Albendazole cured 90% of subjects and mebendazole 93%.

Several authors have studied either mebendazole or albendazole in an open fashion in the treatment of trichuriasis. Ramalingam *et al.*<sup>11</sup> treated patients with 400 mg, 600 mg or 800 mg albendazole as a single dose. The ova reduction rates on day 21 were 39%, 85% and 73%, respectively, and the cure rate varied between 20% and 61%, again with the best result in the 600 mg group. In comparison to these results, Hall and Nahar<sup>5</sup> reported that single doses of 600 mg or 800 mg albendazole were ineffective and that 400 mg for 5 days was required to

produce a statistically significant reduced ova count of 80% in *T. trichiura*-infected individuals.

Good efficacy in treating *T. trichiura* infection was reported by Abadi<sup>6</sup> when he treated subjects from Unjung Pandang, Indonesia, with a single 500 mg dose of mebendazole. He reported a cure rate of 78% and an ova reduction rate of 93%. A study conducted previously in South Africa with the mebendazole 500 mg single-dose regimen showed a 100% cure rate for trichuriasis in a small number of children with low ova counts.<sup>12</sup>

The effects and implications of untreated parasitic infections in children, such as trichuriasis, are wider than may initially be apparent. Three studies among Kenyan schoolchildren have shown improved growth, appetite and spontaneous physical activity after treatment of their mixed parasitic infections, which included *T. trichiura*.<sup>13-15</sup> An important finding among Jamaican schoolchildren was that the children most likely to benefit from treatment were those with poor nutritional status and heavy *T. trichiura* infections.<sup>16</sup> Both in South Africa and elsewhere it has been shown that treatment of parasitic infections can have a positive effect on children's cognitive processes.<sup>2,4</sup> Simeon *et al.*<sup>4</sup> showed particular benefit in children who were undernourished.

Owing to the wide implications of parasitic disease, the control or elimination of gastro-intestinal infections such as trichuriasis is of paramount importance in the upliftment of socially and economically disadvantaged communities. In view of the type of communities where *T. trichiura* is most prevalent, the treatment of this parasitic infection must take into account not only efficacy of the medication but also its availability and cost. Both at the time of undertaking this research and when reporting these results mebendazole 500 mg was available without a doctor's prescription, making it simpler to administer and more accessible, while albendazole 400 mg was available only on prescription in South Africa. The price of the two products was comparable. Our results showed both drugs to be safe; however, mebendazole was shown to have superior efficacy in treating *T. trichiura* infections in this group of children.

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