A comparison of the efficacy of single doses of albendazole, ivermectin, and diethylcarbamazine alone or in combinations against *Ascaris* and *Trichuris* spp.

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Objective To determine the efficacy of single doses of albendazole, ivermectin and diethylcarbamazine, and of the combinations albendazole + ivermectin and albendazole + diethylcarbamazine against common intestinal helminthiases caused by *Ascaris* and *Trichuris* spp.

Methods In a randomized, placebo-controlled trial, infected children were randomly assigned to treatment with albendazole + placebo, ivermectin + placebo, diethylcarbamazine + placebo, albendazole + ivermectin, or albendazole + diethylcarbamazine. The Kato–Katz method was used for qualitative and quantitative parasitological diagnosis. The χ^2 test was used to determine the significance of cure rates, repeated measures analysis of variance for the comparison of mean log egg counts, the Newman–Keuls procedure for multiple comparison tests, and logistic regression for the comparison of infection rates at days 180 and 360 after treatment.

Findings Albendazole, ivermectin and the drug combinations gave significantly higher cure and egg reduction rates for ascariasis than diethylcarbamazine. For trichuriasis, albendazole + ivermectin gave significantly higher cure and egg reduction rates than the other treatments: the infection rates were lower 180 and 360 days after treatment.

Conclusion Because of the superiority of albendazole + ivermectin against both lymphatic filariasis and trichuriasis, this combination appears to be a suitable tool for the integrated or combined control of both public health problems.

Keywords Albendazole/administration and dosage; Ivermectin/administration and dosage; Diethylcarbamazine/administration and dosage; Ascaris/drug effects; Trichuris/drug effects; Drug combinations; Placebos; Treatment outcome; Child; Randomized controlled trials; Comparative study; Philippines (*source: MeSH, NLM*).

Mots clés Albendazole/administration et posologie; Ivermectine/administration et posologie; Diéthylcarbamazine/administration et posologie; Ascaris/action des produits chimiques; Trichuris/action des produits chimiques; Association médicamenteuse; Placebo; Evaluation résultats traitement; Enfant; Essai clinique randomisé; Etude comparative; Philippines (*source: MeSH, INSERM*).

Palabras clave Albendazol/administración y dosificación; Ivermectina/administración y dosificación ; Dietilcarbamacina/administración y dosificación; Ascaris/efectos de drogas; Trichuris/efectos de drogas; Combinación de medicamentos; Placebos; Resultado del tratamiento; Niño; Ensayos controlados aleatorios; Estudio comparativo; Filipinas (*fuente: DeCS, BIREME*).

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Voir page 41 le résumé en français. En la página 41 figura un resumen en español.

Introduction

The drug regimens currently recommended for programmes aiming to eliminate lymphatic filariasis are based on the annual administration of single doses of two-drug combinations (*1*) involving the use of albendazole (400 mg) + ivermectin (200 μg/kg) or albendazole (400 mg) + diethylcarbamazine (6 mg/kg). Albendazole is also effective against intestinal helminth infections if administered more than once yearly (*2*, *3*); however, ivermectin is not registered for the control of helminth infections, and its use is not indicated.

The efficacy and long-term effects of these medications against intestinal helminth infections have not been fully defined. Because combinations of the drugs are used at yearly intervals in filariasis elimination programmes, it is important to define the concomitant effects on intestinal helminth infections and to compare the use of two co-administered drugs with that of standard single-drug regimens in the treatment of intestinal parasites.

This study had the following aims:

– to compare the efficacies of single oral doses of 400 mg albendazole, 200 μg/kg ivermectin, 150 mg diethylcarbamazine; and of 400 mg albendazole + 200 μg/kg ivermectin and 400 mg albendazole + 150 mg diethylcarbamazine against common intestinal helminth infections; and
– to assess the frequency and intensity of infection with common intestinal helminths 180 and 360 days after treatment.

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Methods

Study site and population

The study was conducted in the second half of 1998 in the Dela Paz Elementary School Main, a public school in the municipality of Biñan, province of Laguna, Philippines, which is attended by 1199 boys and 1085 girls. In early 1998 the cumulative prevalence of common intestinal helminth infections in the area was 94%.

Study design

Stool samples were obtained and examined 7–14, 180, and 360 days after the treatment of 784 children with proven intestinal helminthiasis who had been randomly assigned to the above regimens. In this single-blind study, a placebo resembling albendazole was used together with the one-drug treatments in order to make it appear that all pupils were receiving a combination of two drugs. The study was conducted in accordance with good clinical practice, the Declaration of Helsinki, and national guidelines.

Screening and baseline assessment

During the screening visit on day 0, written informed consent was obtained from each participant's parent or guardian. The research staff then obtained a full medical history and conducted a complete physical examination of each patient.

The inclusion criteria were as follows: male or female; age 6–12 years; informed consent; *Ascaris lumbricoides* and/or *Trichuris trichiura* eggs in stool samples; and compliance with protocol, requiring stool samples at the specified times after treatment.

The exclusion criteria were as follows: previous hypersensitivity reaction to benzimidazole, ivermectin, diethylcarbamazine, or any related compound; other helminths without the target helminths listed; diarrhoeal disease; receipt of any anthelminthic in the two weeks before enrolment; receipt of an anthelminthic during the study period; and concomitant infection or underlying disease compromising evaluation of the response to the medications being studied.

Stool samples were obtained for qualitative screening by the Kato thick smear method (*4*). Those found to be positive for helminth infection underwent baseline quantitative assessment by the Kato–Katz method. Quantitative findings were reported as the number of eggs per stool. Intensities of infection were classified as light, moderate, or heavy in accordance with WHO guidelines (*5*).

Treatment

Following randomization, each participant received a single dose of 400 mg albendazole (SmithKline Beecham Pharmaceuticals, France) + placebo, 200 μg/kg ivermectin (Merck, Sharpe & Dohme, Netherlands) + placebo, 150 mg diethylcarbamazine (Pharmamed, Malta) + placebo, 400 mg albendazole + 200 μg/kg ivermectin, or 400 mg albendazole + 150 mg diethylcarbamazine. The treatments were given under the supervision of the project physician, who confirmed that the drugs were swallowed. This was recorded on a case report form, one for each participant. Each patient received sealed plastic containers for the collection of stool samples 7–14, 180, and 360 days after treatment.

Follow-up visits 7–14, 180, and 360 days after treatment

At all follow-up visits a stool sample was supplied by the patient and sent for qualitative and quantitative analysis. At the first follow-up visit, information was collected on adverse experiences and on concomitant therapy subsequent to treatment. At the second and third follow-up visits, information on anthelminthic therapy was obtained.

Quality control

Quality control was undertaken in order to verify the consistency of the microscopic readings during the baseline and follow-up surveys. A reference microscopist who had no knowledge of the initial results (gold standard) examined a random selection of 10% of the positive smears and all the negative slides. Discrepancies of up to 10% were allowed. Attempts were made to identify and correct the reasons for larger discrepancies.

The accuracy and completeness of case report forms were checked by senior research staff. Data from these forms were encoded and re-encoded using Epi-Info and data entry errors were corrected.

Data-handling and analysis

Cure rates were compared for the intention-to-treat and per-protocol populations. The χ^2 test was performed to compare the efficacies of the treatments (*6*). Only patients satisfying the criteria for the per-protocol efficacy analysis were included. Analysis of variance was used to compare the logarithmically transformed egg counts before and after treatment. A value of 1 was added to each egg count to permit calculation of the logarithm in case the number of eggs per gram was 0. When a significant overall test was obtained, multiple tests were performed in order to identify significant differences between treatments.

Logistic regression analysis (*6*) was used to compare infection rates on day 180 after treatment, taking into account the effect of intensity of infection and infection status at baseline, and 7–14 days following treatment. Only individuals for whom there were complete data on infection status from baseline to day 180 were included in this analysis. Because there were few subjects in some categories, data on intensity were grouped into "negative-to-light" and "moderate-to-heavy" categories. A similar analysis was performed on infection rates 360 days after treatment, using a 5% level of significance. Where overall significance was identified, further tests were performed in order to determine which treatments were significantly different from each other.

The egg counts at days 180 and 360 were compared using arithmetic and geometric means as well as the logarithmically transformed data as described above. The mean log-transformed egg counts were compared by repeated measures analysis of variance. The effects of time and its interaction with treatments on egg counts were assessed. If the time and treatment interaction was significant, tests on simple effects were performed by means of the Newman–Keuls procedure (*7*).

Results

Ascaris sp. was seen in 67.4% of the 784 infected children and *Trichuris* sp. in 96.8%. Both parasites were seen in 64.2% (503 out of 784) of the infected children (Table 1).

Table 1. **Parasites found at baseline**

Parasites	No. of pupils
Ascaris sp. only	25 (3.2)[a]
Trichuris sp. only	254 (32.4)
Ascaris and *Trichuris* spp.	499 (63.6)
Trichuris and *Enterobius* spp.	1 (0.1)
Trichuris and hookworm	1 (0.1)
Ascaris sp., *Trichuris* sp. and hookworm	2 (0.3)
Ascaris sp., *Trichuris* sp. and *Enterobius* sp.	2 (0.3)
Total	**784 (100.0)**

[a] Figures in parentheses are percentages.

In all treatment groups a majority of the participants exhibited moderate-to-heavy infection. The proportions of heavy intensity of infection at baseline for *Ascaris* sp. and *Trichuris* sp. were not significantly different ($\chi^2 = 8.35$, $P = 0.40$ and $\chi^2 = 7.91$, $P = 0.40$, respectively) (Table 2).

Cure rates

Among the children with ascariasis at baseline, 12 were lost to follow-up or withdrew from the study and were considered not to have been cured in the intention-to-treat analysis.

The overall χ^2 test on the intention-to-treat population showed that at least one of the cure rates for ascariasis was significantly different from the rest ($\chi^2 = 103.40$, $P<0.001$). Among 516 participants in the per-protocol efficacy analysis, the overall χ^2 test showed that at least one of the cure rates was significantly different from the rest ($\chi^2 = 108.87$, $P<0.001$). Similar results were obtained using the intention-to-treat and per-protocol populations because of very few withdrawals/losses to follow-up.

For the per-protocol population, the residuals were examined to determine which of the treatments made significant contributions to the total χ^2 test result. It emerged that the diethylcarbamazine treatment made the largest contribution, i.e. it differed significantly from the other regimens. The albendazole, ivermectin, albendazole + ivermectin, and albendazole + diethylcarbamazine treatments produced significantly higher cure rates than diethylcarbamazine on its own.

Among the children with trichuriasis at baseline, 17 were lost to follow-up or withdrew from the study and were considered not to have been cured in the intention-to-treat analysis. The overall χ^2 test on the intention-to-treat population showed that at least one of the cure rates for trichuriasis was significantly different from the rest ($\chi^2 = 150.16$, $P<0.001$). This was also shown for 742 participants in the per-protocol population ($\chi^2 = 150.96$, $P<0.001$). The similarity between the two populations arose because there were few withdrawals or losses to follow-up.

With respect to ascariasis, the analysis of residuals showed that both the diethylcarbamazine and the albendazole + ivermectin treatments made significant contributions to the χ^2: the latter produced a significantly higher cure rate and the former having a significantly lower cure rate than the other drug regimens. The albendazole and the ivermectin treatments made almost the same contribution, with infection rates slightly lower than in the albendazole + diethylcarbamazine group, i.e. the latter combination tended to produce a lower cure rate than the albendazole and ivermectin on their own (Table 3).

For *Ascaris* sp. the overall test of significance showed that at least one treatment regimen had a mean egg count reduction that was significantly different from the rest ($P<0.001$). The decreases in egg counts for the albendazole, albendazole + ivermectin, albendazole + diethylcarbamazine and ivermectin treatments did not differ significantly from one another but all were significantly different from that of the diethylcarbamazine treatment.

For *Trichuris* sp. at least one treatment had a mean egg count reduction that was significantly different from the rest ($P<0.001$). Multiple comparison tests showed that only the differences between the decreases in egg counts in the albendazole and ivermectin treatments and between those in

Table 2. **Intensity of *Ascaris* and *Trichuris* spp. infection at baseline by treatment**

Intensity of infection[a]	Parasite	Albendazole No.	Ivermectin No.	Diethyl-carbamazine No.	Albendazole + ivermectin No.	Albendazole + diethylcarbamazine No.
Light	*Ascaris* sp.	35 (35.4)[b]	31 (30.4)	29 (28.4)	33 (31.4)	41 (34.2)
	Trichuris sp.	58 (38.9)	51 (33.1)	50 (33.1)	61 (41.0)	50 (31.4)
Moderate	*Ascaris* sp.	50 (50.5)	43 (42.2)	47 (46.1)	42 (40.0)	53 (44.2)
	Trichuris sp.	74 (49.7)	80 (52.0)	74 (49.0)	68 (45.6)	75 (47.1)
Heavy	*Ascaris* sp.	14 (14.1)	28 (27.4)	26 (25.5)	30 (28.6)	26 (21.6)
	Trichuris sp.	17 (11.4)	23 (14.9)	27 (17.9)	20 (13.4)	31 (19.5)
Total	***Ascaris* sp.**	**99 (100.0)**	**102 (100.0)**	**102 (100.0)**	**105 (100.0)**	**120 (100.0)**
	***Trichuris* sp.**	**149 (100.0)**	**154 (100.0)**	**151 (100.0)**	**149 (100.0)**	**156 (100.0)**

[a] Classification of intensities of infection (ref. 5):

	Ascaris sp.	*Trichuris* sp.
Light	1–4999 eggs per g (epg)	1–999 epg
Moderate	5000–49 999 epg	1000–9999 epg
Heavy	⩾ 50 000 epg	⩾10 000 epg

[b] Figures in parentheses are percentages.

Table 3. **Distribution of children with *Ascaris* and *Trichuris* spp. according to outcome at first follow-up (day 7–14)**

Treatment	Parasite infection	No. of pupils at baseline	No.of pupils cured at day 7–14	No. of pupils withdrawn or lost to follow-up
Albendazole	*Ascaris* sp.	99	69 (69.7)[a]	3 (3.0)
	Trichuris sp.	149	47 (31.5)	4 (2.7)
Ivermectin	*Ascaris* sp.	102	80 (78.4)	3 (3.0)
	Trichuris sp.	154	54 (35.1)	3 (1.9)
Diethylcarbamazine	*Ascaris* sp.	102	24 (23.5)	2 (2.0)
	Trichuris sp.	151	4 (2.6)	4 (2.7)
Albendazole + ivermectin	*Ascaris* sp.	105	82 (78.1)	3 (2.9)
	Trichuris sp.	149	97 (65.1)	3 (2.0)
Albendazole + diethylcarbamazine	*Ascaris* sp.	120	93 (77.5)	1 (0.8)
	Trichuris sp.	156	30 (19.2)	3 (2.0)
Total	***Ascaris* sp.**	**528**	**348 (65.9)**	**12 (2.3)**
	***Trichuris* sp.**	**759**	**232 (30.6)**	**17 (2.2)**

[a] Figures in parentheses are percentages.

the albendazole and albendazole + diethylcarbamazine treatments were not significantly different from each other (P = 0.34 and 0.38, respectively).

The decrease in egg counts obtained with albendazole + ivermectin was significantly higher than the decreases obtained with either the albendazole or the ivermectin treatment (P<0.001). Moreover, it was significantly higher than that obtained with albendazole + diethylcarbamazine. The decrease in egg counts obtained with the diethylcarbamazine treatment was significantly lower than the decreases obtained with the other treatments (P<0.001) (Table 4).

Infection rates on days 180 and 360 after treatment

The *Ascaris* sp. infection rate on day 180 among the 736 children given the diethylcarbamazine treatment was significantly different from the infection rate among those who received the other four treatments (P<0.001). The lowest infection rate was seen among those on the albendazole + ivermectin treatment. However, the infection rates on day 180 with all four treatments did not differ significantly from each other when the baseline levels and the responses on day 7–14 were taken into account. There were no significant differences between treatments on day 360 (Table 5).

Analysis of the *Trichuris* sp. infection rate on day 180 showed it to be significantly higher among those on the diethylcarbamazine treatment than in the ivermectin and albendazole + ivermectin treatments (P<0.001), but it did not differ significantly from the rates in those on the albendazole or the albendazole + diethylcarbamazine treatment. The infection rates among those on these three treatments were significantly different from those on the ivermectin and albendazole + ivermectin treatments. The albendazole + ivermectin treatment produced the lowest infection rate on day 180, significantly lower than the one obtained with ivermectin

Table 4. **Mean *Ascaris* and *Trichuris* spp. egg counts before and after treatment**

Treatment	Parasite	No. of pupils	Mean epg[a] before treatment	Mean epg after treatment	Egg reduction rate
Albendazole	*Ascaris* sp.	96	21 656.0	1520.2	93.0
	Trichuris sp.	145	6376.2	2930.8	54.0
Ivermectin	*Ascaris* sp.	99	36 485.5	2072.7	94.3
	Trichuris sp.	151	6340.3	833.9	86.8
Diethylcarbamazine	*Ascaris* sp.	100	43 556.0	28 953.7	33.5
	Trichuris sp.	147	7364.3	5895.2	19.9
Albendazole + ivermectin	*Ascaris* sp.	102	41 011.4	198.8	99.5
	Trichuris sp.	146	4948.1	122.5	97.5
Albendazole + diethylcarbamazine	*Ascaris* sp.	119	32 821.4	1113.3	96.6
	Trichuris sp.	153	7544.2	1557.6	79.4

[a] epg = eggs per g.

Table 5. ***Ascaris*** **infection rates by treatment for baseline and days 180 and 360**

Treatment	Follow-up day	No. of subjects	No. of infected subjects at baseline	No. of infected subjects at follow-up
Albendazole	180	149	94 (63.1)[a]	39 (26.2)
	360	130	84 (64.6)	68 (52.3)
Ivermectin	180	146	93 (63.7)	39 (26.2)
	360	116	71 (61.2)	60 (51.7)
Diethylcarbamazine	180	147	96 (65.3)	83 (56.5)
	360	121	79 (65.3)	72 (59.5)
Albendazole + ivermectin	180	147	98 (66.7)	35 (23.8)
	360	121	81 (66.9)	65 (53.7)
Albendazole + diethylcarbamazine	180	147	110 (74.8)	42 (28.6)
	360	128	93 (72.7)	74 (57.8)
Total	**180**	**736**	**491 (66.7)**	**238 (32.3)**
	360	**616**	**712 (97.0)**	**339 (55.0)**

[a] Figures in parentheses are percentages.

alone ($P<0.001$). On day 360 the diethylcarbamazine treatment produced the highest infection rate and albendazole + ivermectin produced the lowest rate. The infection rate among those on the diethylcarbamazine treatment was significantly higher than the rates for those on either the ivermectin or the albendazole + ivermectin treatment ($P<0.001$). The results of the comparisons of the five treatments made at day 360 were similar to those seen at day 180. The findings on *Ascaris* and *Trichuris* spp. infection rates took into account the baseline levels and the responses 7–14 days after treatment (Table 6).

Egg counts

Of the 528 children with *Ascaris* sp. at baseline, 409 for whom there were complete data on egg counts from day 0 to day 360 were included in the analysis. The effect on mean log *Ascaris sp.* egg counts of at least one treatment was significantly different from that of the others ($P<0.001$). The mean log egg counts in all regimens differed significantly over time ($P<0.001$). At least one treatment was superior to the others in all follow-up periods, but because of significant interaction ($P<0.001$) the difference varied at each follow-up.

A significant interaction indicates that the effect of a given treatment varies from one time to another. The nature of the interaction is best understood by comparing the means of log egg counts for a particular follow-up time by means of tests on simple effects. The absence of interaction yields a parallel line when the means of the response variable are plotted in a graph for various follow-up periods. Interactions are indicated by deviations from parallelism with the horizontal axis.

The Newman-Keuls procedure indicated significant differences between treatments in the *Ascaris* sp. egg counts on days 180 and 360. On day 180 the egg counts in the albendazole and albendazole + ivermectin treatments were not significantly different from each other. Each of these treatments produced significantly lower egg counts than the ivermectin, albendazole + diethylcarbamazine, and diethylcarbamazine treatments. The egg counts in the ivermectin and albendazole + diethylcarbamazine treatments did not differ significantly from each other. However, the diethylcarbamazine treatment produced significantly higher egg counts. At 360 days the egg counts were significantly different from each other except for those in the ivermectin and albendazole + diethylcarbamazine treatments. Compared with the other treatments, the albendazole regimen produced a significantly reduced egg count, while the diethylcarbamazine treatment produced a significantly higher egg count.

Of the 759 children with *Trichuris* sp. at baseline, 595 for whom there were complete data on egg counts from day 0 to day 360 were included in the analysis. Repeated measures analysis of variance showed that the effect of treatment on *Trichuris* sp. egg counts of at least one treatment was significantly different from that of the others ($P<0.001$). The egg counts differed significantly over time ($P<0.001$). At least one treatment was shown to be superior to another in all follow-up periods, but because of significant interaction ($P<0.001$) the difference varied at each follow-up period.

The Newman-Keuls procedure indicated significant differences between treatments in *Trichuris* sp. egg counts on days 180 and 360. At day 180 the egg counts were significantly different from each other. The albendazole + ivermectin treatment resulted in the lowest egg count, followed by the ivermectin, albendazole, and albendazole + diethylcarbamazine treatments in increasing order. On day 360 the egg counts differed significantly between all treatments. The albendazole treatment produced a significantly lower egg count and the diethylcarbamazine treatment produced a significantly higher one (Table 7).

Discussion

Common intestinal helminth infections present important health problems in the school-age population. In this study, trichuriasis was more commonly encountered than ascariasis on baseline examination. Both occurred in a majority of infected children on both screening and baseline examinations. Of the infected children, a majority had *Ascaris* and

Table 6. ***Trichuris* sp. infection rates by treatment at baseline and days 180 and 360**

Treatment	Follow-up day	No. of subjects	No. of infected subjects at baseline	No. of infected subjects at follow-up
Albendazole	180	148	141 (95.3)[a]	123 (83.1)
	360	129	123 (95.4)	111 (86.0)
Ivermectin	180	145	141 (97.2)	107 (73.8)
	360	115	111 (96.5)	83 (72.2)
Diethylcarbamazine	180	147	143 (97.3)	139 (94.6)
	360	121	117 (96.7)	115 (95.0)
Albendazole + ivermectin	180	147	141 (95.9)	64 (43.5)
	360	121	116 (95.9)	65 (53.7)
Albendazole + diethylcarbamazine	180	147	146 (99.3)	135 (91.8)
	360	128	127 (99.2)	113 (88.3)
Total	**180**	**734**	**712 (97.0)**	**568 (77.4)**
	360	**614**	**594 (96.7)**	**487 (79.3)**

[a] Figures in parentheses are percentages.

Table 7. **Geometric mean *Ascaris* and *Trichuris* spp. egg counts by treatment on days 0, 7–14, 180 and 360**

Treatment	Parasite	*n*	Day 0	Day 7–14	Day 180	Day 360
Albendazole	*Ascaris* sp	84	2864.1	2.0	3.5	62.2
	Trichuris sp	123	665.1	18.5	125.2	156.0
Ivermectin	*Ascaris* sp	71	3983.8	1.4	7.0	94.6
	Trichuris sp	111	665.1	11.8	46.5	49.4
Diethylcarbamazine	*Ascaris* sp	79	4402.8	330.3	327.0	221.4
	Trichuris sp	117	845.6	347.2	492.7	468.7
Albendazole + ivermectin	*Ascaris* sp	81	4582.5	1.2	4.5	129.0
	Trichuris sp	116	550.0	1.9	5.5	10.0
Albendazole + diethylcarbamazine	*Ascaris* sp	94	3197.1	1.6	7.0	94.6
	Trichuris sp	128	678.6	34.1	208.5	198.3

Trichuris spp. infections of moderate-to-heavy intensity in all treatment groups. This finding has important implications for morbidity and transmission rates.

The cure rate for ascariasis given with albendazole alone was 69.7%, whereas cure rates ranging from 85% to 100% have been reported previously (*8*). This may be partly explained by the fact that a majority of the children with ascariasis who received the albendazole treatment had moderate-to-heavy intensity infections. However, at 93.0% the level of egg reduction was satisfactory.

The cure rate for trichuriasis obtained with albendazole used alone was poor at 31.5% but within the range of previously reported cure rates, viz 10% to 67% (*8*). The egg reduction rate of 54.0% was lower than previously reported, viz 73% to 87% (*8*).

The ivermectin treatment gave cure rates of 78.4% and 35.1% for ascariasis and trichuriasis, respectively, not markedly different from the values for albendazole. In terms of egg reduction rate and monotherapy, ivermectin compared favorably with albendazole, especially against trichuriasis. This trial is one of few that have investigated the use of ivermectin for the treatment of intestinal helminths (*9*, *10*). Clearly, diethylcarbamazine alone did not result in acceptable cure and egg reduction rates for ascariasis and trichuriasis.

For ascariasis the efficacy of monotherapy with either albendazole or ivermectin compared favourably with that of combination drug therapy, in terms of both cure and egg reduction rates. For trichuriasis, however, albendazole + ivermectin was perhaps superior to the other treatments, including the standard albendazole monotherapy, with regard to both cure and egg reduction rates. Indeed, no other monotherapy or combination of drugs has achieved better cure and egg reduction rates for trichuriasis than the albendazole + ivermectin combination.

The diethylcarbamazine treatment was inferior to the other treatments against ascariasis with respect to the infection rate on day 180 and egg counts on days 180 and 360. The infection rate in this treatment on day 360 was not markedly

different from that seen in the other treatments because of reinfection. With regard to trichuriasis, both the infection rates and the egg counts were lowest in the albendazole + ivermectin treatment, while the ivermectin treatment was superior to the albendazole treatment as regards both long-term infection rates and egg counts.

In areas where lymphatic filariasis and soil-transmitted helminthiases are public health problems the use of the albendazole + ivermectin may provide opportunities to integrate or combine interventions for both categories of parasite: the combination treatment has been reported to enhance the suppression of microfilaraemia attributable to *Wuchereria bancrofti* and *Brugia malayi* (*11*, *12*). Moreover, this treatment has been reported to control infections of *Strongyloides stercoralis* and infestations of the human itch mite, *Sarcoptes scabiei* (*13*).

The superior efficacy of albendazole + ivermectin against both lymphatic filariasis and trichuriasis suggests that the combination can be a useful tool in the integrated or combined control of these parasitoses. ■

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Résumé

Comparaison de l'efficacité de doses uniques d'albendazole, d'ivermectine et de diéthylcarbamazine seuls ou en association contre *Ascaris* et *Trichuris* spp.

Objectif Déterminer l'efficacité de doses uniques d'albendazole, d'ivermectine, de diéthylcarbamazine et d'associations albendazole + ivermectine et albendazole + diéthylcarbamazine contre les helminthiases intestinales courantes dues à *Ascaris* et *Trichuris* spp.

Méthodes Lors d'un essai contrôlé randomisé contre placebo, des enfants infectés ont été répartis par tirage au sort dans des groupes de traitement par albendazole + placebo, ivermectine + placebo, diéthylcarbamazine + placebo, albendazole + ivermectine ou albendazole + diéthylcarbamazine. Le diagnostic parasitologique qualitatif et quantitatif a été effectué par la méthode de Kato-Katz. On a utilisé le test du chi-carré pour déterminer le niveau de signification des taux de guérison, l'analyse de variance sur des mesures répétées pour la comparaison des numérations moyennes d'œufs en valeurs logarithmiques, la méthode de Newman-Keuls pour les tests comparatifs multiples, et la méthode de régression logistique pour comparer les taux d'infection 180 et 360 jours après le traitement.

Résultats L'albendazole, l'ivermectine et les associations ont donné des taux de guérison et des taux de réduction du nombre d'œufs significativement plus élevés que ceux obtenus avec la diéthylcarbamazine en ce qui concerne l'ascaridiase. Contre la trichocéphalose, l'association albendazole + ivermectine a donné des taux de guérison et de réduction du nombre d'œufs significativement plus élevés qu'avec les autres traitements ; les taux d'infection étaient plus faibles 180 et 360 jours après le traitement.

Conclusion Etant donné la supériorité de l'association albendazole + ivermectine à la fois contre la filariose lymphatique et contre la trichocéphalose, il peut s'agir là d'un outil adapté pour la lutte intégrée ou simultanée contre ces deux problèmes de santé publique.

Resumen

Comparación de la eficacia de las dosis únicas de albendazol, ivermectina y dietilcarbamazina, por separado o combinados, contra *Ascaris* y *Trichuris* spp.

Objetivo Determinar la eficacia de las dosis únicas de albendazol, ivermectina y dietilcarbamazina y de las combinaciones de albendazol + ivermectina y albendazol + dietilcarbamazina contra las helmintiasis intestinales comunes causadas por *Ascaris* y *Trichuris* spp.

Métodos En un ensayo aleatorizado controlado mediante placebo, los niños infectados fueron asignados al azar a recibir tratamiento con albendazol + placebo, ivermectina + placebo, dietilcarbamazina + placebo, albendazol + ivermectina, o albendazol + dietilcarbamazina. Se utilizó el método de Kato-Katz para efectuar un diagnóstico parasitológico cualitativo y cuantitativo. El grado de significación de las tasas de curación se determinó mediante la prueba de ji cuadrado; la comparación de las medias del logaritmo del recuento de huevos se basó en el análisis de la varianza de mediciones repetidas; para las pruebas de comparación múltiple se usó el procedimiento de Newman-Keuls, y la comparación de las tasas de infección al cabo de 180 y 360 días del tratamiento se realizó mediante análisis de regresión logística.

Resultados En el caso de las ascariasis, el albendazol, la ivermectina y las combinaciones medicamentosas consiguieron tasas de curación y de reducción del número de huevos significativamente mayores que la dietilcarbamazina. En cuanto a la tricuriasis, las tasas de curación y la reducción del número de huevos conseguidas con albendazol + ivermectina superaron de forma significativa las de los otros tratamientos: las tasas de infección fueron inferiores a los 180 y los 360 días del tratamiento.

Conclusión Dada la superioridad de la combinación albendazol + ivermectina tanto contra la filariasis linfática como contra la tricuriasis, dicha alternativa parece un instrumento apropiado para combatir de forma integrada o combinada esos dos problemas de salud pública.

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