Efficacy of Single-Dose and Triple-Dose Albendazole and Mebendazole against Soil-Transmitted Helminths and *Taenia* spp.: A Randomized Controlled Trial

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Abstract

**Background:** The control of soil-transmitted helminth (STH) infections currently relies on the large-scale administration of single-dose oral albendazole or mebendazole. However, these treatment regimens have limited efficacy against hookworm and *Trichuris trichiura* in terms of cure rates (CR), whereas fecal egg reduction rates (ERR) are generally high for all common STH species. We compared the efficacy of single-dose versus triple-dose treatment against hookworm and other STHs in a community-based randomized controlled trial in the People’s Republic of China.

**Methodology/Principal findings:** The hookworm CR and fecal ERR were assessed in 314 individuals aged ≥5 years who submitted two stool samples before and 3–4 weeks after administration of single-dose oral albendazole (400 mg) or mebendazole (500 mg) or triple-dose albendazole (3 × 400 mg over 3 consecutive days) or mebendazole (3 × 500 mg over 3 consecutive days). Efficacy against *T. trichiura*, *Ascaris lumbricoides*, and *Taenia* spp. was also assessed. Albendazole cured significantly more hookworm infections than mebendazole in both treatment regimens (single dose: respective CRs 69% (95% confidence interval [CI]: 55–81%) and 29% (95% CI: 20–45%); triple dose: respective CRs 92% (95% CI: 81–98%) and 54% (95% CI: 46–71%)). ERRs followed the same pattern (single dose: 97% versus 84%; triple dose: 99.7% versus 96%). Triple-dose regimens outperformed single doses against *T. trichiura*; three doses of mebendazole – the most efficacious treatment tested – cured 71% (95% CI: 57–82%). Both single and triple doses of either drug were highly efficacious against *A. lumbricoides* (CR: 93–97%; ERR: all >99.9%). Triple dose regimens cured all *Taenia* spp. infections, whereas single dose applications cured only half of them.

**Conclusions/Significance:** Single-dose oral albendazole is more efficacious against hookworm than mebendazole. To achieve high CRs against both hookworm and *T. trichiura*, triple-dose regimens are warranted.

**Trial Registration:** www.controlled-trials.com ISRCTN47375023


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Introduction

Hundreds of millions of people are infected with the common soil-transmitted helminths (STHs), namely hookworms (*Ancylostoma duodenale* and *Necator americanus*), *Ascaris lumbricoides* and *Trichuris trichiura*, many by multiple species concurrently [1–5]. *Taenia* spp. infections are also widespread [6,7]. STHs and taeniasis/cysticercosis belong to the neglected tropical diseases (NTDs) and are responsible for mainly chronic and often inconspicuous morbidity [8,9]. Iron-deficiency anemia, malnutrition, and impaired physical and cognitive development have all been attributed to STH infections [1,3,10]. *Taenia solium* cysticercosis is a major cause of epilepsy and other neurological disorders in developing countries [11,12].

The current strategy for STH control in highly endemic areas focuses on morbidity control through large-scale administration of single-dose anthelmintics to at-risk populations, particularly school-aged children [9,13,14]. Due to the zoonotic nature of
of pregnancy are not eligible for treatment [13]. Children below the age of 1 year and pregnant women in the first trimester dose of 400 mg and 500 mg, respectively [13,18,21]. Childrenmates. Albendazole [19] and mebendazole [20] display a broad – albendazole and mebendazole – both benzimidazole carba-
tasiasis/cysticercosis, its control must also include the veterinary
teristics) or ivermectin (against lymphatic filariasis) [9,22–24]. Surpris-
ingly though, only few clinical trials compared the efficacy of
of hookworm, high efficacy (in terms of cure rate [CR]) of both drugs against A.
lumbricoides, and disappointing efficacy of either drug against T.
[A18]. Few data are available regarding ERRs.
The aim of this randomized controlled trial was to assess the
efficacy of standard single-dose versus triple-dose oral albendazole
and mebendazole against hookworm and other STH infections in a
highly endemic but virtually benzimidazole-naïve population in the
People’s Republic of China (P.R. China).

Methods

The protocol for this trial and the supporting CONSORT
checklist are available as supporting information; see Protocol S1
and Checklist S1.

Study Area, Study Period, and Participants

The study was conducted between October and December 2008 in Nongyang, a village located in Menghai county, Yunnan province, P.R. China. Details of the study area, population and epidemiological characteristics, including the prevalence of STHs, Taenia spp., and intestinal protozoa, have been described before [3,27,28]. The local prevalence of each A. lumbricoides, hookworm, and T. trichiura exceeded 85% in a survey conducted in 2006 [3]. Upon completion of the 2006 survey, compound mebendazole (mebendazole 100 mg/tablet+levamisole hydrochloride 25 mg/tablet, 2 tablets per day for 3 consecutive days) was distributed to the village population. No further interventions took place until the present study.

Ethics

The study was approved by the Ethics Committee of Basel (no. 294/08) and the Academic Board of the National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention in Shanghai (no. 2008091701). The trial was registered with Current Controlled Trials (identifier: ISRCTN47375023). The study objectives and procedures were discussed with the village head, village committee, and local health care officials who informed the residents. Individuals who were interested to participate signed an informed consent form in Chinese (parents or legal guardians in case of minors aged 5–17 years). Upon study completion, albendazole was provided for treatment of study participants found to be infected at evaluation, drop-outs, sick individuals upon recovery, and pregnant women once beyond the first trimester.

Interventions, Trial Medication, and Outcome Measures

The trial was designed as a community-based open-label, outcome assessors-blinded randomized controlled trial with four arms: (i) single-dose albendazole (400 mg), (ii) single-dose mebendazole (500 mg), (iii) triple-dose albendazole (3×400 mg, given over 3 consecutive days), and (iv) triple-dose mebendazole (3×500 mg, given over 3 consecutive days). No placebo drugs were given to individuals assigned to single dose treatment (open label).

Albendazole (Zentel®; lot no 08060407) was commercially obtained from Sino-American Tianjin SmithKline and French Laboratories Ltd., a Chinese joint venture of GlaxoSmithKline Plc. Mebendazole (Vermox®, lot nos. 8CL4F00 and 7CL8900), produced by Johnson & Johnson/Janssen-Cilag S.p.A., was provided by the WHO regional office in Hanoi, Vietnam.

The primary outcome considered was CR against hookworm 3–4 weeks following dosing. Changes in hookworm infection intensity, as determined by ERR, and efficacy against A. lumbricoides and T. trichiura served as secondary outcomes. Additionally, the effects of all four treatment regimens on Taenia spp. were assessed.

Eligibility Criteria and Sample Size

Eligible for inclusion were all residents of Nongyang aged 5 years and above. The following exclusion criteria were applied: presence of diagnosed or perceived chronic disease or other conditions likely to interfere with anthelminthic treatment (e.g., hypersensitivity to anthelmintics), pregnancy (verbally assessed at enrolment and again before treatment), recent history of anthelminthic treatment, and participation in other trials (within 1 month).

The intended sample size at enrolment was 370 individuals, based on the following assumptions: a total of 176 individuals (44 in each of the four treatment arms) would be needed to detect differences in the CR following different treatments for the cure of hookworm infections with 80% power using a 2-sided statistical test with an α-level of 0.05 and CRs of albendazole and mebendazole against hookworm infections of 75% and 45%. According to Keiser and Utzinger [18], the respective CRs are 78% and 23%; the higher estimate for the CR of mebendazole was employed in order to include a safety margin. The local prevalence of hookworm infections was assumed to be 60% and compliance was estimated to be 80%. Recruitment was to be stopped once 400 individuals had been enrolled.

Field and Laboratory Procedures

Families were contacted in batches of 20–30 (~80–120 potential participants) based on family registry numbers. Interested family members were invited to the local primary school for further information and enrolment. No monetary compensation was offered for participation. Participants answered a short questionnaire investigating demographic and health-related issues, and were given a stool collection container labeled with a unique identifier and their full name. The ability of all study participants to recognize their collection container was determined, and the importance of using the own receptacle emphasized. Each morning, filled containers were collected, and a new container...
handed out with the aim to obtain two stool samples from each participant.

Stool samples were forwarded to a nearby laboratory and processed on the collection day. First, samples were visually inspected for adult *A. lumbricoides* and *Taenia* spp. proglottids. Second, two 41.7 mg Kato-Katz thick smears [29] were prepared from each sample. Depending on the ambient temperature and considering over-clearance of hookworm eggs, slides were read within 30–90 min of preparation [30]. At least 5% of the daily diagnoses were cross-checked by the principal investigator.

**Procedures for the evaluation of the treatment efficacy**

**Diagnoses** were cross-checked by the principal investigator.**Within 30–90 min of preparation [30]. At least 5% of the daily diagnoses were cross-checked by the principal investigator.**

**Efficacy Against Hookworm and Other STHs**

A single dose of albendazole cured 69% (95% CI: 55–81%) of the hookworm infections, while single-dose mebendazole only cured 31% (95% CI: 20–45%), significantly less (Table 2 and 3). Triple doses of either drug were significantly more efficacious than single-dose regimens, but the difference between the two drugs persisted: triple-dose albendazole cured significantly more hookworm infections (92%, 95% CI: 81–98%) than triple-dose mebendazole (58%, 95% CI: 46–71%).

Triple-dose mebendazole exhibited the highest reduction in *T. trichura* prevalence (CR: 71%), followed by triple-dose albendazole (56%). Single-dose applications were found to be significantly less efficacious (mebendazole: 40%, albendazole: 34%). In both cases, the differences between drug-specific CRs were not statistically significant. As expected, both albendazole and mebendazole cleared most of the *A. lumbricoides* infections with observed CRs ranging between 93% and 97%. The efficacies of albendazole and mebendazole were comparable. Triple-dose treatment tended to be slightly more efficacious than single-dose treatment, but the difference was not statistically significant. For *Taenia* spp., a single dose of either drug cured about one half of the infections; triple-dose administration cured all infections.

**Adverse Events**

Thirteen study participants (4.1%) reported between one and five adverse events following drug administration, mostly in the morning of the third drug distribution day (about 12 hours after administration of the drugs).
the administration of the second dose, if given) and upon active questioning. Four of these individuals were treated with a single dose (3 with mebendazole, 1 with albendazole) while the remaining nine were treated with triple mebendazole (n = 5) or triple albendazole (n = 4). One symptom was reported by nine individuals, two symptoms by two individuals (1 treated with triple albendazole, 1 with triple mebendazole), three symptoms by one individual (triple mebendazole) and five symptoms by one individual (triple mebendazole). Adverse events included headache (n = 3; all mebendazole), abdominal cramps (n = 3; 2 mebendazole, 1 albendazole) and the closely related “full stomach” (n = 2; mebendazole), and waist pain (n = 1; albendazole). Two individuals each reported vomiting, including production of *A. lumbricoides* worms (1 albendazole, 1 mebendazole), diarrhea (2 mebendazole), fatigue (1 albendazole, 1 mebendazole), and chills (2 mebendazole). Vertigo (albendazole), throat pain (albendazole), fever (mebendazole), and a swollen face (mebendazole) were each reported once. None of the study participants requested medical interventions as adverse events were mild and self-limiting. More women than men reported adverse events (ten women among whom four treated with albendazole and six treated with mebendazole versus three men; *P* = 0.046) but there was no significant association between the report of adverse events and age, drug, or number of treatments according to the Fisher’s exact test.

**Figure 1. Participation and drop-out at various stages in a trial assessing the efficacy of anthelmintic drugs.** Participation and causes for drop-out at various stages in a randomized controlled trial assessing the efficacy of single-dose versus triple-dose albendazole and mebendazole against STH infections and *Taenia* spp. in a Bulang ethnic minority community in Yunnan province, P.R. China in late 2008. doi:10.1371/journal.pone.0025003.g001
This randomized controlled trial comparing the efficacy of single and triple dose albendazole and mebendazole confirmed that single oral albendazole is more efficacious than mebendazole against hookworm infections [18,32]. It also corroborated that triple-dose regimens result in significantly higher CRs than recommended and widely used single-dose regimens [13,33]. A single dose of mebendazole only cured 31% of the hookworm infections, while the highest CR, after triple albendazole, was 92%. Even triple administration of mebendazole was less efficacious than a single dose of albendazole. Keiser and Utzinger’s meta-analysis [18] estimated a CR of only 15% after single-dose mebendazole, and a value comparable to that found in the present study after single-dose albendazole (present study: 69%, meta-analysis: 72%). With regard to ERRs, all four drug regimens resulted in significant reductions among those infected at baseline. A triple dose of mebendazole was significantly more efficacious than a single dose.

The number of *T. trichiura* infections in each treatment arm was significantly, though only moderately reduced, in line with previous findings [18,33,34]. As expected, triple doses resulted in higher CRs than a single dose regardless of the drug. Worryingly, the highest CR observed was only 71% following triple-dose mebendazole. Single and triple doses of mebendazole resulted in higher ERRs than the respective number of albendazole administrations. With regard to *A. lumbricoides* infections, high CRs were observed for both drugs even at a single dose;

### Table 1. Demographic characteristics of the participants in a trial assessing the efficacy of anthelminthic drugs.

<table>
<thead>
<tr>
<th></th>
<th>Total n (%)</th>
<th>Single-dose albendazole</th>
<th>Single-dose mebendazole</th>
<th>Triple-dose albendazole</th>
<th>Triple-dose mebendazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total n (%)</td>
<td>314 (100)</td>
<td>82 (100)</td>
<td>81 (100)</td>
<td>68 (100)</td>
<td>83 (100)</td>
</tr>
<tr>
<td>Sex: Female n (%)</td>
<td>151 (48.1)</td>
<td>35 (42.7)</td>
<td>39 (48.2)</td>
<td>36 (52.9)</td>
<td>41 (49.4)</td>
</tr>
<tr>
<td>Age n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5–14 years</td>
<td>42 (13.4)</td>
<td>9 (11.0)</td>
<td>8 (9.9)</td>
<td>14 (20.6)</td>
<td>11 (13.3)</td>
</tr>
<tr>
<td>15–24 years</td>
<td>88 (28.0)</td>
<td>26 (31.7)</td>
<td>20 (24.7)</td>
<td>19 (27.9)</td>
<td>23 (27.7)</td>
</tr>
<tr>
<td>25+ years</td>
<td>184 (58.6)</td>
<td>47 (57.3)</td>
<td>53 (65.4)</td>
<td>35 (51.5)</td>
<td>49 (59.0)</td>
</tr>
<tr>
<td>Parasite n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hookworm (95% CI)</td>
<td>228 (72.6; 67.7–77.5)</td>
<td>55 (67.1)</td>
<td>58 (71.6)</td>
<td>50 (73.5)</td>
<td>65 (78.3)</td>
</tr>
<tr>
<td>Ascaris lumbricoides (95% CI)</td>
<td>284 (90.4; 87.2–93.7)</td>
<td>78 (95.1)</td>
<td>71 (87.7)</td>
<td>63 (92.6)</td>
<td>72 (86.7)</td>
</tr>
<tr>
<td>Trichuris trichiura (95% CI)</td>
<td>234 (74.5; 69.7–79.3)</td>
<td>65 (79.3)</td>
<td>63 (77.8)</td>
<td>48 (70.6)</td>
<td>58 (69.9)</td>
</tr>
<tr>
<td>Taenia spp. (95% CI)</td>
<td>33 (10.5; 7.1–13.9)</td>
<td>10 (12.2)</td>
<td>6 (7.4)</td>
<td>7 (10.3)</td>
<td>10 (12.0)</td>
</tr>
</tbody>
</table>

Demographic characteristics and baseline helminth prevalence of the study participants in a randomized controlled trial assessing the efficacy of single-dose and triple-dose albendazole versus mebendazole against STH infections and *Taenia* spp. in a Bulang ethnic minority community in Yunnan province, P.R. China, stratified by treatment arm.

### Table 2. Prevalences and cure rates in a trial assessing the efficacy of anthelminthic drugs (hookworm and *Ascaris lumbricoides*).

<table>
<thead>
<tr>
<th></th>
<th>Single-dose albendazole (n=82)</th>
<th>Single-dose mebendazole (n=81)</th>
<th>Triple-dose albendazole (n=68)</th>
<th>Triple-dose mebendazole (n=83)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hookworm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalence at baseline [% (n)]</td>
<td>67.1 (55)</td>
<td>71.6 (58)</td>
<td>73.5 (50)</td>
<td>78.3 (65)</td>
</tr>
<tr>
<td>Prevalence after treatment [% (n)]</td>
<td>20.7 (17)</td>
<td>50.6 (41)</td>
<td>5.9 (4)</td>
<td>36.1 (30)</td>
</tr>
<tr>
<td>New positives at evaluation</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Cure rate [% (95% CI)] excluding new positives at evaluation</td>
<td>69.1 (55.2–80.9)</td>
<td>31.0 (19.5–44.5)</td>
<td>92.0 (80.8–97.8)</td>
<td>58.5 (45.6–70.6)</td>
</tr>
<tr>
<td>Difference between drug-specific cure rates [% (95% CI)] Reference</td>
<td>38.1 (21.0–55.1)**</td>
<td>Reference</td>
<td>33.5 (19.4–47.7)**</td>
<td>Reference</td>
</tr>
<tr>
<td>Difference single- vs. triple-dose cure rates [% (95% CI)] Reference</td>
<td>22.9 (8.6–37.2)**</td>
<td>Reference</td>
<td>27.4 (10.5–44.3)**</td>
<td></td>
</tr>
</tbody>
</table>

| **Ascaris lumbricoides** |                               |                               |                               |                               |
| Prevalence at baseline [% (n)] | 95.1 (78) | 87.7 (71) | 92.6 (63) | 86.7 (72) |
| Prevalence after treatment [% (n)] | 3.7 (3) | 6.2 (5) | 2.9 (2) | 6.0 (5) |
| New positives at evaluation | 0 | 0 | 0 | 0 |
| Cure rate [% (95% CI)] excluding new positives at evaluation | 96.1 (89.1–99.2) | 93.0 (84.3–97.7) | 96.8 (89.0–99.6) | 93.1 (84.5–97.7) |
| Difference between drug-specific cure rates [% (95% CI)] Reference | 3.2 (–4.1–10.5) | Reference | 3.8 (–3.5–11.1) | Reference |
| Difference single- vs. triple-dose cure rates [% (95% CI)] Reference | 0.7 (–5.4–6.8) | Reference | 0.1 (–8.2–8.4) | Reference |

Cure rates following single-dose and triple-dose albendazole versus mebendazole against STH infections and *Taenia* spp., and comparisons between treatment arms.

* P value <0.05, ** P value <0.01, *** P value <0.001.

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**Discussion**

This randomized controlled trial comparing the efficacy of single and triple dose albendazole and mebendazole confirmed that single oral albendazole is more efficacious than mebendazole against hookworm infections [18,32]. It also corroborated that triple-dose regimens result in significantly higher CRs than recommended and widely used single-dose regimens [13,33]. A single dose of mebendazole only cured 31% of the hookworm infections, while the highest CR, after triple albendazole, was 92%. Even triple administration of mebendazole was less efficacious than a single dose of albendazole. Keiser and Utzinger’s meta-analysis [18] estimated a CR of only 15% after single-dose mebendazole, and a value comparable to that found in the present study after single-dose albendazole (present study: 69%, meta-analysis: 72%). With regard to ERRs, all four drug regimens resulted in significant reductions among those infected at baseline. A triple dose of mebendazole was significantly more efficacious than a single dose.

The number of *T. trichiura* infections in each treatment arm was significantly, though only moderately reduced, in line with previous findings [18,33,34]. As expected, triple doses resulted in higher CRs than a single dose regardless of the drug. Worryingly, the highest CR observed was only 71% following triple-dose mebendazole. Single and triple doses of mebendazole resulted in higher ERRs than the respective number of albendazole administrations. With regard to *A. lumbricoides* infections, high CRs were observed for both drugs even at a single dose;
observations that are in line with systematic reviews and meta-analysis [18,33].

Attention was paid to enhance the sensitivity of STH diagnosis by examining multiple Kato-Katz thick smears before and after drug administration [3,35,36]. The low number of “new” infections found at treatment evaluation (Table 2 and table 3) indicates that a high sensitivity had been achieved despite the rather low density of hookworm and T. trichiura eggs. Because of the low T. trichiura prevalence and since the study was not designed to evaluate treatment efficacy against this parasite, the respective results should be interpreted with caution. The conventional indicator for the successful cure of T. trichiura infections – i.e., recovery of the scolex – is no definitive proof whenever individuals harbor several worms, and is difficult to perform outside an institutional setting. We focused on the presence of proglottids and eggs.

An open-label trial design was adhered to due to the complexities and high cost for implementing a double-blind trial in a field setting. We are confident that this did not negatively impact on the validity of the results since outcome assessors were blinded. One individual assigned to the triple albendazole group switched to the single-dose group, and in two instances the drug assignment was changed between members of the same family due to an initial mix-up. We used logistic regression to assess if our results were sensitive to the potential effect modifiers age and sex.

Table 3. Prevalences and cure rates in a trial assessing the efficacy of anthelminthic drugs (Trichuris trichiura and Taenia spp.).

<table>
<thead>
<tr>
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<th>Single-dose albendazole (n=82)</th>
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<th>Triple-dose albendazole (n=68)</th>
<th>Triple-dose mebendazole (n=83)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trichuris trichiura</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalence at baseline [% (n)]</td>
<td>79.3 (65)</td>
<td>77.8 (63)</td>
<td>70.6 (48)</td>
<td>69.9 (58)</td>
</tr>
<tr>
<td>Prevalence after treatment [% (n)]</td>
<td>53.7 (44)</td>
<td>49.4 (40)</td>
<td>32.4 (22)</td>
<td>25.3 (21)</td>
</tr>
<tr>
<td>New positives at evaluation</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Cure rate [% (95% CI)] excluding new positives at evaluation</td>
<td>33.8 (22.6–46.6)</td>
<td>39.7 (27.6–52.8)</td>
<td>56.2 (41.2–70.5)</td>
<td>70.7 (57.3–81.9)</td>
</tr>
<tr>
<td>Difference between drug-specific cure rates [% (95% CI)]</td>
<td>–5.8 (–22.5–10.8)</td>
<td>Reference</td>
<td>–14.4 (–32.7–3.8)</td>
<td>Reference</td>
</tr>
<tr>
<td>Difference single- vs. triple-dose cure rates [% (95% CI)]</td>
<td>Reference</td>
<td>Reference</td>
<td>22.4 (4.3–40.5)**</td>
<td>31.0 (14.2–47.8)**</td>
</tr>
</tbody>
</table>

**Taenia spp.**

|                  |                                |                                |                               |                               |
| Prevalence at baseline [% (n)] | 12.2 (10)                      | 7.4 (6)                        | 10.3 (7)                      | 12.0 (10)                     |
| Prevalence after treatment [% (n)] | 7.3 (6)                        | 4.9 (4)                        | 0 (0)                         | 1.2 (1)                       |
| New positives at evaluation | 1                              | 1                              | 0                             | 1                             |
| Cure rate [% (95% CI)] excluding new positives at evaluation | 50.0 (18.7–81.2)              | 50.0 (11.8–88.2)              | 100 (59.0–100)                | 100 (69.2–100)                |
| Difference between drug-specific cure rates [% (95% CI)] | 0 (NA)                         | Reference                     | 0 (NA)                        | Reference                     |
| Difference single- vs. triple-dose cure rates [% (95% CI)] | Reference                      | Reference                      | 50.0 (19.0–80.1)*             | 50.0 (10.0–90.0)*             |

Cure rates following single-dose and triple-dose albendazole versus mebendazole against STH infections and Taenia spp., and comparisons between treatment arms. * P value <0.05, ** P value <0.01, *** P value <0.001.

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Table 4. Infection intensity and egg reduction rates in a trial assessing the efficacy of anthelminthic drugs (geometric mean).

<table>
<thead>
<tr>
<th></th>
<th>Single-dose albendazole</th>
<th>Single-dose mebendazole</th>
<th>Triple-dose albendazole</th>
<th>Triple-dose mebendazole</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hookworm [n]</strong></td>
<td>55</td>
<td>58</td>
<td>50</td>
<td>65</td>
</tr>
<tr>
<td>EPG at baseline (geometric mean)</td>
<td>69</td>
<td>73</td>
<td>90</td>
<td>86</td>
</tr>
<tr>
<td>EPG after treatment (geometric mean)</td>
<td>2</td>
<td>12</td>
<td>0.3</td>
<td>3</td>
</tr>
<tr>
<td>ERR, difference in geometric mean [%; (95% CI)]</td>
<td>97.3 (95.2–98.7)**</td>
<td>83.6 (72.9–90.3)**</td>
<td>99.7 (99.1–99.9)**</td>
<td>96.4 (93.3–98.2)**</td>
</tr>
<tr>
<td><strong>Ascaris lumbricoides [n]</strong></td>
<td>78</td>
<td>71</td>
<td>63</td>
<td>72</td>
</tr>
<tr>
<td>EPG at baseline (geometric mean)</td>
<td>8,442</td>
<td>7,855</td>
<td>6,485</td>
<td>8,435</td>
</tr>
<tr>
<td>EPG after treatment (geometric mean)</td>
<td>0.1</td>
<td>0.5</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>ERR, difference in geometric mean [%; (95% CI)]</td>
<td>&gt;99.9 (&gt;99.9–100)*</td>
<td>&gt;99.9 (&gt;99.9–100)</td>
<td>&gt;99.9 (&gt;99.9–100)</td>
<td>&gt;99.9 (&gt;99.9–100)*</td>
</tr>
<tr>
<td><strong>Trichuris trichiura [n]</strong></td>
<td>65</td>
<td>63</td>
<td>48</td>
<td>58</td>
</tr>
<tr>
<td>EPG at baseline (geometric mean)</td>
<td>58</td>
<td>47</td>
<td>68</td>
<td>55</td>
</tr>
<tr>
<td>EPG after treatment (geometric mean)</td>
<td>14</td>
<td>8</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>ERR, difference in geometric mean [%; (95% CI)]</td>
<td>76.7 (62.6–86.1)**</td>
<td>82.5 (71.0–89.6)**</td>
<td>94.0 (89.4–96.8)**</td>
<td>97.3 (94.9–98.8)**</td>
</tr>
</tbody>
</table>

Infection intensities among those infected at baseline expressed as EPG and ERR following single-dose and triple-dose albendazole versus mebendazole against STH infections, and comparisons between treatment arms. Different letters (a, b, c) designate significant differences of ERR between treatment arms, defined by non-overlapping 95% confidence limits (calculated by bootstrap resampling).

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and also as a continuous variable (in years). None of the analyses showed noteworthy differences between the crude and adjusted models with respect to the point estimates or CIs of the odds ratios. The sole exception was the treatment regimen (single dose versus triple dose) for which adjustment for sex and age showed stronger effects for both drugs in the case of Trichuris trichiura.

In populations primarily parasitized by A. lumbricoides and/or hookworm infections, single or – in case of a high prevalence or high-intensity hookworm infections – triple-dose albendazole might suffice. Mebendazole treatment with one or better three doses should be adopted in areas with a high prevalence of T. trichiura (and possibly A. lumbricoides), but a lower number of hookworm infections. In areas where all three species are co-endemic, alternation between albendazole and mebendazole as well as co-administration of different anthelmintic drugs should be considered.

 Supporting Information

Protocol S1 Trial protocol.

Checklist S1 CONSORT checklist.

Figure S1 Frequency distribution of baseline EPGs and changes following treatment.

Data S1 Raw data of the trial.
Efficacy of Anthelmintic Drugs

Conceived and designed the experiments: PS JU J-Y JC A. Performed the experiments: PS JU J-Y JH. Analyzed the data: PS JU JH. Contributed reagents/materials/analysis tools: PS JU J-Y JH. Wrote the paper: PS JU JH.

Codes S1 Codes to raw data of the trial.

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References