Efficacy of current drugs against soil-transmitted helminth infections: systematic review and meta-analysis

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CRD summary
This review concluded that albendazole, mebendazole and pyrantel pamoate are effective for the treatment of Ascaris lumbricoides, and that albendazole is efficacious for hookworm infection. The authors’ conclusion may not be reliable given the quality of, and significant differences between, the included studies and potential publication bias.

Authors’ objectives
To assess the efficacy of currently recommended single-dose oral regimens of albendazole, mebendazole, levamisole and pyrantel pamoate for the treatment of infections with Ascaris lumbricoides (A. lumbricoides), hookworm and Trichuris trichiura (T. trichiura).

Searching
PubMed (1996 onwards), ISI Web of Science (1960 onwards), ScienceDirect (1960 onwards), the Cochrane CENTRAL Register and the World Health Organization library database (1960 onwards) were searched to August 2007; the keywords were reported. Additional studies were sought through the bibliographies of relevant studies. There were no restrictions on the basis of language or year of publication.

Study selection
Placebo-controlled randomised controlled trials (RCTs) of single-dose drug administration with currently recommended doses of albendazole, mebendazole, levamisole and pyrantel pamoate for the treatment of infections with A. lumbricoides, hookworm or T. trichiura were eligible for inclusion. The included studies assessed the following currently recommended single-dose regimens: albendazole (400 mg), mebendazole (500 mg) and pyrantel pamoate (10 mg/kg). No eligible trials of levamisole were identified.

The included studies were in both adults and children. The intensity of infection varied between the studies. Drug efficacy was assessed by different diagnostic methods, usually between 2 and 7 weeks after drug treatment.

The primary outcome was the cure rate, specified as the percentage of individuals who became helminth egg negative after treatment with an anthelminthic drug. To assess safety adverse events data, where present, were also collected.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Each study was allocated a score from 0 (lowest) to 5 (highest) using the Jadad scale. Study quality was assessed on the basis of randomisation methods, description of withdrawals and drop-outs, and blinding.

The authors did not state how the validity assessment was performed.

Data extraction
Relative risk (RRs) and 95% confidence intervals (CIs), and p-values, were calculated for each study.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
The pooled RR and corresponding CIs were calculated using random-effects meta-analysis.
Statistical heterogeneity was assessed using the Cochrane Q statistic and $I^2$ statistic. Publication bias was assessed using Egger's test and Begg's test.

**Results of the review**

Twenty studies were included: nine were double-blind, two single-blind, two non-blinded, and no information was provided for seven.

Fourteen studies assessed albendazole, of which 2 RCTs were of the highest quality (score 5) and two nearly so (score 4); the other 10 studies were of varying quality (score 1 to 3). There was significant heterogeneity between the studies and the results of the Egger and/or Begg's tests indicated publication bias. For the treatment of *A. lumbricoides* there were 557 individuals (10 RCTs), for *T. trichiura* 735 individuals (9 RCTs), and for hookworm infection 742 individuals (14 RCTs). The pooled RRs for albendazole treatment against the various infections, relative to placebo, were as follows: 0.12 (95% CI: 0.07, 0.21, p<0.001) for *A. lumbricoides* infection, 0.72 (95% CI: 0.61, 0.87, p=0.001) for *T. trichiura* infection and 0.28 (95% CI: 0.19, 0.41, p=0.001) for hookworm infection (both species).

Six studies assessed mebendazole, of which one RCT was of the highest quality (score 5); the other 5 studies were of varying quality (score 2 to 3). For all infections there was significant heterogeneity between the studies. For the treatment of *A. lumbricoides* there were 309 individuals, for *T. trichiura* 685 individuals (3 RCTs), and for hookworm infection 853 individuals (6 RCTs). The pooled RRs for mebendazole treatment against the various infections, relative to placebo, were as follows: 0.05 (95% CI: 0.03, 0.09, p<0.001) for *A. lumbricoides* infection, 0.64 (95% CI: 0.49, 0.84, p=0.001) for *T. trichiura* infection and 0.85 (95% CI: 0.73, 0.99; p=0.01) for hookworm infection (both species).

Four studies assessed pyrantel pamoate; all RCTs were of varying quality (score 1 to 3). The pooled RR for pyrantel pamoate treatment, relative to placebo, was 0.12 (95% CI: 0.07, 0.21, p<0.001) against *A. lumbricoides* infection (3 RCT, 131 individuals) and 0.69 (95% CI: 0.58, 0.81, p<0.001) against hookworm infection (both species).

No placebo-controlled RCTs were identified that assessed levamisole at the currently recommended dose.

**Authors' conclusions**

Single-dose albendazole, mebendazole and pyrantel pamoate show high cure rates against *A. lumbricoides*. Albendazole was more efficacious than either mebendazole or pyrantel pamoate in the treatment of hookworm infection. Single doses of current anthelminthics are not satisfactory for the treatment of *T. trichiura*.

**CRD commentary**

The review addressed a clear question and undertook a comprehensive search for studies, with no restriction placed on language. It is not clear how many of the authors were involved in the study selection, quality assessment and data extraction processes. The methodological quality of the included studies was assessed and incorporated into the discussion of the results. The authors drew conclusions about the superiority of some drugs over others, despite all being compared against placebo (i.e. no direct comparisons were included). The quality of most of the included studies was poor to moderate. There was significant heterogeneity between the studies and substantial publication bias was also evident for some analyses, thus the conclusions should be treated with caution.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that further research based on well-designed, adequately powered and rigorously implemented trials is needed for current anthelminthic drugs. They also stated that novel anthelminthic drugs to complement current therapies, and ideally with different mechanisms of action, need to be developed.

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