Effect of administration of intestinal anthelmintic drugs on haemoglobin: systematic review of randomised controlled trials

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CRD summary
This review evaluated the efficacy of intestinal anthelmintic drugs on haemoglobin concentrations and concluded that the routine administration of these agents results in a modest increase in haemoglobin levels. This review was generally well conducted, but findings suggest that the size of the treatment effect may vary across different settings and populations.

Authors' objectives
To evaluate the effects of routine administration of intestinal anthelmintic drugs on haemoglobin (Hb) concentrations.

Searching
MEDLINE and the Cochrane Controlled Trials Register were searched from 1966 to 31 July 2006; the search terms were reported. Bibliographies of retrieved articles, reviews and books, abstracts, and proceedings of international conferences or meetings were checked for additional eligible studies. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) or quasi-randomised controlled studies were eligible for inclusion in the review.

Specific interventions included in the review
Studies evaluating the use of an intestinal anthelmintic drug were eligible for inclusion. When other micronutrients and drugs were given concomitantly, the study was eligible if the only difference between the intervention and control groups was the intestinal anthelmintic drug. A study was excluded if schistosoma treatment was provided only to the intervention group, or only in case of simultaneous schistosoma and helminth infection. Most of the included studies evaluated albendazole; other studies evaluated mebendazole and bephenium. The doses and regimens varied across the studies. Control patients received placebo. In some of the included studies, iron and praziquantel were given concomitantly.

Participants included in the review
Inclusion criteria relating to the participants were not specified. The participants in the included studies varied considerably, with ages ranging from 6 months to 66 years. Most studies were of pre-schoolchildren and schoolchildren from developing countries (South Asia and Africa); other studies were of non-pregnant or pregnant adult women. One study enrolled patients of any age. Several studies were conducted in areas endemic for malaria or for schistosoma.

Outcomes assessed in the review
The primary outcome was the change in Hb, both in patients treated with an intestinal anthelmintic drug and in the control group. Studies were eligible provided that pre-intervention, post-intervention and change variances were reported.

How were decisions on the relevance of primary studies made?
Two reviewers selected the studies, but the paper did not state whether they made their selections independently or not.

Assessment of study quality
Validity was assessed in relation to concealment of allocation, attrition bias, drop-outs and blinding. The authors did not state how many reviewers performed the validity assessment.
Data extraction
Two reviewers extracted the data. Authors were contacted, where necessary, to obtain additional information. Where standard deviations (SD) for the change in Hb were not reported, these were estimated using four different reported methods.

Methods of synthesis
How were the studies combined?
Both fixed-effect and random-effect models were used to calculate the pooled weighted mean difference (WMD) and 95% confidence intervals (CIs). Publication bias was visualised using funnel plots and tested by Egger's and Begg's methods.

How were differences between studies investigated?
Statistical heterogeneity was assessed through the chi-squared and I-squared tests.

Pre-specified stratified analyses were carried out for age, country (developing or developed), endemicity for malaria or schistosoma, pre-intervention worm load, methodological quality, compliance monitoring, number of anthelmintic courses, co-administration of iron and baseline Hb concentrations. Univariate and multivariate meta-regression were also performed to investigate the contribution of these variables to heterogeneity. The analysis was repeated after excluding each study in turn and after using different methods to estimate the SDs.

Results of the review
Fourteen RCTs (7,829 patients) were included in the review.
Allocation concealment was judged adequate in 5 studies. Six trials had less than 10% loss at follow-up and six were double-blind.

Treatment with intestinal anthelmintic drug was associated with a statistically significant increase in Hb levels compared with the control (pooled WMD 1.71 g/L, 95% CI: 0.70, 2.73, p<0.001); there was evidence of statistical heterogeneity for this outcome (p<0.001; I-squared 61%). The effect of the intervention was larger, homogeneous, and remained statistically significant when the analysis was limited to studies reporting the SD for the change in Hb (WMD 2.55 g/L, 95% CI: 1.52, 3.57, p<0.001).

There was no evidence of publication bias according to the funnel plot and to Egger's (p=0.11) and Begg's (p=0.11) methods. The stratified analysis showed a significant effect on Hb levels when adult patients were included (WMD 2.85 g/L, 95% CI: 1.00, 4.70, p=0.002) or when iron was co-administered (WMD 1.92 g/L, 95% CI: 0.22, 3.62, p=0.027). The exclusion of individual studies in the sensitivity analysis had no impact on the results.

The authors estimated that at the Hb cut-offs recommended by the World Health Organization the prevalence of anaemia could be slightly reduced (with reductions ranging from 1 to 12.4% in adults and from 4.4 to 21.0% in children). The lower the Hb cut-off used the higher the reduction observed.

Authors' conclusions
Treatment with intestinal anthelmintic agents results in modest increases in Hb concentrations, which can mean a lower rate of anaemia among populations with a relatively high prevalence of intestinal helminthiasis.

CRD commentary
This review addressed a well-defined question in terms of the interventions, outcomes and study design; inclusion criteria for the study participants were not specified clearly. Two relevant databases were searched and efforts were made to find further published and unpublished studies, thus reducing the potential for publication bias. Publication bias was evaluated and no evidence of it was found. No language restrictions were applied, which limits the possibility of language bias. Two independent reviewers extracted the data, but it was unclear whether the study selection and......
quality assessment processes were also performed in duplicate.

Statistical heterogeneity was assessed and, although significant heterogeneity was found for the change in Hb, the studies generally showed the same direction of treatment effect. Various potential sources of differences between the studies were investigated. This review was generally well conducted, but the significant heterogeneity suggests that the size of the treatment effect may vary across different settings and populations.

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

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

**Research:** The authors stated that additional studies are needed to assess the safety of routine administration of anthelmintics and to determine whether concomitant iron supplementation can improve the results.

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