Should Deworming Be Included in Antenatal Packages in Hookworm-endemic Areas of Developing Countries?

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ABSTRACT

Background: WHO recommends antenatal (after the first trimester) deworming for pregnant women who live in areas where the prevalence of hookworm infection exceeds 20-30%. However, deworming has not been included in antenatal care packages in most developing countries.

Methods: A review of articles publishing original data identified primarily through Medline was conducted using subject heading terms and text words for "deworming", "pregnant women", "hookworm", "anthelminthic", "anthelmintic", "albendazole", "mebendazole", "pregnancy" and their combinations. Bibliographies of retrieved articles were scanned to identify any additional relevant documents.

Results: Five articles examined the benefits of antenatal deworming. All provided evidence favourable to deworming, in terms of both maternal and infant outcomes. Comparison of outcome measures could be improved with a more standardized approach to outcome ascertainment and reporting.

Conclusion: The evidence base for the inclusion of deworming in antenatal care packages in hookworm-endemic areas is mostly observational in nature. Future research should be directed towards 1) strengthening the evidence base with empirical data from randomized controlled trials, and 2) furthering our understanding related to government uptake of the WHO policy on deworming.

MeSH terms: Hookworm infections; pregnancy; benzimidazole; developing countries

Nutritional iron deficiency is probably the main cause of anemia in pregnancy; however intestinal parasite (worm) infections, especially hookworm infections, contribute to anemia by causing blood loss and by affecting the supply of nutrients necessary for erythropoiesis. Hookworm infections are considered to be a leading cause of pathological blood loss in tropical and subtropical countries.[1] At any one time, one third of all pregnant women in developing countries are estimated to be infected with hookworms.[2] In 1996, the World Health Organization[3] recommended that deworming (using albendazole, levamisole, mebendazole or pyrantel) be given to pregnant women after the first trimester in areas where the prevalence of hookworm infection exceeds 20-30%. This recommendation was based primarily on expert opinion and published accounts of research in non-pregnant populations. However, despite this recommendation, routine deworming within government-sponsored antenatal care programs remains infrequent in most developing countries. Our objective, therefore, was to review published evidence from research conducted in pregnant populations in order to document the specific benefits and/or risks of antenatal deworming.

METHODS

A Medline search was carried out to identify reports of original data published from January 1966 to February 2006 using subject heading terms and text words for "deworming", "pregnant women", "hookworm", "anthelminthic", "anthelmintic", "albendazole", "mebendazole", "pregnancy" and their combinations. The search made no restriction to language of publication, but only papers published in English, French or Spanish were read fully. No other restrictions were made. Further references not captured by this search were sought from the bibliographies of the retrieved articles.

RESULTS

A total of five studies have examined the benefits of antenatal deworming in developing countries (Table I). Three were observational studies (two investigating mebendazole – both in Sri Lanka[4,5] – and

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TABLE I

Studies Examining the Benefits of Deworming in Antenatal Care in Developing Countries and Their Main Results

Study, Date, Location	Study Design	Deworming Drug	Sample Size	Deworming-attributable Result
Atukorala et al., 1994, Sri Lanka[4]	Non-randomized effectiveness trial	Anthelminthic (probably mebendazole)	115	Increase in women's iron status
de Silva et al., 1999, Sri Lanka[5]	Cross-sectional survey	Mebendazole	7087	Decrease in proportions of stillbirths, perinatal deaths and very low birthweight babies
Abel et al., 2000, India[7]	Pre-post experimental community-based study	Mebendazole	828	Decrease in prevalence of anemia; increase in mean hemoglobin in second and third trimesters
Torlesse and Hodges, 2001, Sierra Leone[8]	Randomized placebo-controlled factorial trial	Albendazole	125 (4 arms)	Decrease in hemoglobin lowest in albendazole group; effects of albendazole and iron-folate supplements additive
Christian et al., 2004, Nepal[6]	Non-randomized community-based study	Albendazole	3325	Decrease in severe anemia in third trimester; increase in birthweight and decrease in 6-month infant mortality after 2 doses

* Based on Medline Search 1966-2006

one, albendazole – in Nepal[6]); one was a pre-post experimental study (mebendazole – in India)[7]; and one was a randomized controlled trial of albendazole (in Sierra Leone)[8].

One of the first studies to investigate micronutrient supplementation and deworming in pregnant women was reported in 1994 in Sri Lanka among 115 pregnant women working on a tea plantation.[4] The government of Sri Lanka had included deworming in addition to iron-folate supplementation as a routine component of its antenatal care program. In the program, pregnant women received iron and folate in their first trimester and were offered a single dose of mebendazole in their second trimester. An evaluation of this program found that receiving the combination of mebendazole with iron-folate supplementation was more effective in improving women's iron status during pregnancy than receiving iron-folate supplementation alone. One limitation of this study was that its sample size was small.

In 1996, again in Sri Lanka, the effect of mebendazole treatment during pregnancy on birth outcome was investigated through a cross-sectional study.[5] The reported combined proportions of stillbirths and perinatal deaths (1.9% vs. 3.3%) were significantly lower in the mebendazole group, as was the proportion of very low birthweight babies (<1500 g) (1.1% vs. 2.3%). The sample size was very large (N=7,087). The information about mebendazole intake had been assessed by a questionnaire administered to the mothers on the second (for vaginal deliveries) or third day (for cesarean sections) post-partum. Although several biases could have been operating (recall bias, report bias, selection bias), this study provided meaningful evidence of the potential benefits of deworming during pregnancy. An even greater effect might have been demonstrated if the analysis had included a comparison of all low birthweight infants (<2500 g), but these data were not published.

A community-based study was carried out in India.[7] The intervention group received an education program focussing on anemia, iron supplementation (60 mg elemental iron), and 100 mg mebendazole tablets taken twice daily for 3 days. It was reported that the control group received the usual government-sponsored prophylaxis program but this program was not described. (It is likely that it would not have included deworming.) Therefore, interpretation of these results is difficult. The authors reported a significant decrease in the prevalence of anemia and increased mean hemoglobin in both the second and third trimester in those receiving the education plus iron plus mebendazole intervention.

Subsequently, a randomized placebo-controlled trial was conducted in Sierra Leone to measure the impact of a single dose (400 mg) of albendazole and daily iron-folate supplements (36 mg iron and 5 mg folate) on hemoglobin concentration during pregnancy.[8] After controlling for baseline hemoglobin concentration (obtained during the first trimester), the mean benefit of deworming relative to the placebo group on the change between baseline and third trimester was 6.6 g/L hemoglobin. In addition, it was found that the combined effect of deworming and iron-folate supplements was additive. These findings suggested that deworming could be included in strategies to control anemia during pregnancy in Sierra Leone and in other developing countries. Unfortunately, this trial was limited by a small sample size (N=125; 4 arms; between 29 and 35 women per arm) and the lower than standard amount of elemental iron (i.e., 36 mg instead of 60 mg).[9]

Finally, within a micronutrient randomized trial conducted in 30 villages in Nepal, a 400 mg single dose of albendazole was offered to pregnant women at mid-gestation and again at late gestation.[6] Women receiving albendazole in the second trimester were found to have increased hemoglobin levels and a lower proportion of severe anemia in the third trimester. The birthweights of infants born to women who had received two doses of albendazole were higher by 59 g (compared to women who had not taken the albendazole). It was also reported that infant mortality at 6 months fell by 41%, however, this number must be used carefully because of small numbers. It is also important to add that these results, while adjusted for micronutrient supplement intake, were not randomized to intake of albendazole.

Two additional studies have examined adverse birth outcomes following the use of mebendazole during pregnancy.[10,11] These studies, in addition to the five mentioned above, did not find significantly more adverse outcomes in the dewormed group compared to the comparison group.

It should be noted that these reports provide different outcome measures and so

a rigorous and direct comparison of outcomes cannot be undertaken. Efforts to use standardized outcome measures would be helpful.

DISCUSSION

The results of this review provide evidence of the benefits of antenatal deworming both for the mothers and for the infants. In addition, there were no reports of increased proportions in adverse birth outcomes in infants of mothers who had been dewormed compared to mothers who had not. Therefore, cumulative evidence to date, which also includes policy statements from WHO based on several Informal Consultations over a number of years, with concurring policy uptake by other agencies such as Unicef, would suggest that there is convincing evidence for the inclusion of deworming in antenatal care packages (after the first trimester) in any country where hookworm infection is of public health importance.

The deworming drugs, albendazole and mebendazole, have several features that make them attractive to their inclusion within government-sponsored antenatal programs. First and foremost, they are inexpensive, at less than US$0.02 per tablet in most countries.[12] Iron supplementation, which has been estimated at US$21.39 per pregnant woman per year in South America, has been estimated to be significantly more expensive than deworming.[13] Additionally, areas participating in the Global Programme for the Elimination of Lymphatic Filariasis receive albendazole free of charge.[14] Finally, the distribution and administration of these deworming drugs is simplified by the fact that they are available in single dose format, and do not require weights for dosing.

At the present time, only Sri Lanka and Nepal have included deworming in their routine antenatal care programs. The weakness of the evidence base may have been one reason why uptake of this policy by other governments has been hindered. Future research, therefore, should be directed towards 1) strengthening the evidence base with empirical data from randomized controlled trials, and 2) furthering our understanding of barriers and of enabling factors related to government uptake of the WHO policy on deworming.

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RÉSUMÉ

Contexte : L'OMS recommande une vermifugation prénatale (après le premier trimestre) pour les femmes enceintes habitant des régions où la prévalence d'infections à ankylostomes dépasse 20 à 30 %. Cependant, la vermifugation n'est pas incluse dans les soins prénataux dans la plupart des pays en développement.

Méthodologie : Un examen des articles publiant des données originales, recensés principalement dans Medline, a été effectué à l'aide de balises et de mots-clés comme « deworming » (vermifugation) , « pregnant women » (femmes enceintes) , « hookworm » (ankylostome), « anthelminthic » (anthelminthique), « albendazole », « mebendazole », « pregnancy » (grossesse) et leurs combinaisons. Les bibliographies des articles recensés ont été examinées afin de recenser d'autres documents pertinents, le cas échéant.

Résultats : Cinq articles traitent des avantages de la vermifugation prénatale; tous présentent des données favorables à la vermifugation, pour les résultats concernant la mère et ceux concernant l'enfant. La comparaison des résultats pourrait être améliorée par le recours à une approche plus normalisée de la détermination et de la présentation des résultats.

Conclusion : La preuve en faveur de l'inclusion de la vermifugation dans les soins prénatals pour les femmes habitant dans des régions où il y a endémie d'ankylostomes est surtout fondée sur l'observation. D'autres recherches devraient être menées afin 1) de renforcer la preuve par des données empiriques découlant d'essais contrôlés randomisés et 2) d'approfondir notre compréhension en ce qui concerne l'adoption par le gouvernement de la politique de l'OMS sur la vermifugation.