The impact of deworming on child mortality in programmatic conditions

Awasthi S, Peto R, Read S, Richards SM, Pande V, Bundy D; DEVTA (Deworming and Enhanced Vitamin A) team. (King George's Medical University, Lucknow, Uttar Pradesh, India; Clinical Trial Service Unit and Epidemiological Studies Unit [CTSU], University of Oxford, Oxford, UK; Human Development Network, The World Bank, Washington, DC, USA.) Population deworming every 6 months with albendazole in 1 million preschool children in North India: DEVTA, a cluster-randomised trial. *Lancet* 2013;**381:**1478–86.

SUMMARY

The DEVTA was a factorial trial of albendazole and vitamin A (retinol) that covered nearly 2 million preschool children. The trial was published in two parts and the first part dealt with vitamin A. The second part dealt with the effect of deworming on mortality among preschool children in rural areas of seven districts near Lucknow in Uttar Pradesh, between 1999 and 2004. The trial primarily aimed to assess the effects of a widely practicable periodic deworming regimen on mortality at ages 1–6 years. Another aim of this trial was to assess the feasibility of the Integrated Child Development Scheme (ICDS) to deliver antihelminthics inexpensively and sustainably at an operational scale in rural preschool children. This cluster-randomized study was done in 72 rural administrative blocks (8511 *anganwadi* centres [AWCs]) where the ICDS system was functional. The neighbouring blocks (clusters), in groups of four, were randomly allocated using a factorial design to: (i) usual care; (ii) 6-monthly vitamin A; (iii) 6-monthly albendazole; or (iv) both. AWC workers were trained to administer mass treatment on the chosen day and were monitored by the project and state government staff. Annually, one AWC per block (randomly selected by Oxford) was visited by a team of one phlebotomist, two field workers and one driver. It surveyed 30 preschool children (six per year of age) selected by the AWC workers. Data were collected on adverse effects of mass treatment, blood and stool sample for calculation of retinol assay, and helminth egg assay. Primary outcome (i.e. death) was measured by 18 full-time monitors (literate but not medically trained), each covered four neighbouring blocks (approximately 500 AWCs) during the 6-month period. Monitors identified and visited households with death in an under 10-year-old child in the past year. Age, sex, name, parental names and likely cause of death using simple verbal autopsy were recorded. During the third year of the study, monitors further undertook house-to-house surveys in every AWC to identify any missed deaths. Duplicate entries were eliminated manually and by computer. Child mortality was expressed for each block as the mean number of child deaths recorded per study AWC. Average child deaths/AWC (total: 72 block values) were regressed on albendazole allocation, retinol allocation, for interaction term and for infant deaths. The overall compliance was 86%. There was little non-study antihelminthic treatment except mebendazole treatment of children with obvious worm infestation by AWC workers in all age groups. Nearly 2% were lost to follow-up in both intervention and control groups. Weight, height and haemoglobin levels were not significantly improved by albendazole. However, the albendazole group did show an increase of 0.5 kg weight among the children who were infected with worms. Overall child mortality was 5% lower in the albendazole group compared to that in the control group. This study suggests that in villages with functioning ICDS AWC, delivery costs for simple preschool interventions could be as low as those for school-based health interventions. In spite of good compliance for 5 years and despite halving the prevalence of worm infection, this study failed to document any significant evidence of deworming on child survival (mortality RR 0.95, 95% CI 0.89–1.02). Although the confidence interval does not exclude mortality reduction of about 10%, such an effect is unlikely since there was no significant increase in weight gain—the proxy for better nutrition and postulated mechanism for mortality reduction. Overall, the present study shows that in a lightly infected rural population, routine deworming of preschool children would have little effect on mortality.

COMMENT

Since resources and funds are limited in developing countries, the interventions used in government programmes need to be cost-effective. The DEVTA was a large cluster-randomized trial to study the effect of twice-yearly vitamin A supplementation and albendazole on preschool child mortality. The magnitude of the trial can be gauged from the fact that the effective sample size was twice that of all previous trials combined. The overall compliance in this community-based trial was high (86%). The trial considered unbiased assessment of outcome (mortality at 1–6 years of age) and appropriate analysis (as 36 clusters *v.* 36 clusters). This was a mammoth trial that failed to achieve the pre-specified objective of lowering mortality but provided evidence that a large-scale community-based intervention is feasible in villages with functioning ICDS AWCs.

In the methodology section, the authors mentioned that mass treatment was given to children aged 6–72 months. However, at all other places, the age group mentioned was 12–72 months, presumably the first instance is a typographical error. For children between 1 and 2 years of age, the dose of albendazole suspension is 10 ml (200 mg) as a single dose.[1] However, in this trial, chewable tablets (400 mg albendazole) were administered to all children (independent of age), which is a cause for concern. How did a toddler chew a tablet?

Besides these minor ones, there are some major methodological issues too. A Cochrane review by Taylor-Robinson *et al.* published in 2012 found no effect of deworming on weight gain.[2] This review included three studies with a positive effect of deworming on weight gain. Of these studies, two were reported from areas with a high prevalence of worm infestation.[3,4] The baseline prevalence of worm infestation in the present study area has not been mentioned. The authors have provided some data on mid-study prevalence of worm infestation, which was low. Probably, a higher prevalence and heavy load of worm infestation would have shown a larger effect of deworming on child growth.

The proposed mechanism for decrease in mortality was mentioned in the present study as deworming leading to improvement of nutritional status (weight/height), but this is not supported by most other studies. Further, selection of child mortality in the 1–5 years age group seems inappropriate as high prevalence of worm infestation occurs in the schoolgoing age group.[5] Since micronutrients could be a limiting factor for catch-up growth, the effect of deworming on nutritional status needed to be studied along with micronutrient supplementation.[6]

Baseline comparability was not assessed (prevalence of worm infestation, nutrition, immunization, socioeconomic factors and child mortality). The authors also do not comment about baseline child mortality (primary outcome). From the third year of the study, anthropometry and faecal eggs were measured annually in children who were selected by the AWC workers. The possibility of selection bias cannot be ruled out. The authors have mentioned

the total number of deaths (primary outcome) but they have not given desegregated deaths in the intervention and control groups. To provide for a clear denominator, they could have given the estimated number of children in subgroups at each stage.

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Reducing maternal deaths in India: Will good emergency obstetric care be useful?

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SUMMARY

Maternal mortality is high in West Africa. In many places, a large number of women die giving birth in hospitals. Hence, access to as well as quality of emergency obstetric care (EmOC) services in hospitals need to improve to reduce maternal deaths. This study assessed the effect of a multifaceted intervention by promoting maternity death reviews and onsite training in EmOC in referral hospitals with high maternal mortality rates in Senegal and Mali.

The study was a stratified, cluster-randomized controlled trial. Forty-six referral hospitals with more than 800 deliveries per year were enrolled in the study, stratified by country and hospital type. A system of data collection was set up in all hospitals in the intervention and control clusters. Baseline data collection was done for a period of 1 year followed by implementation of the intervention for the next 2 years and then, collection of post-intervention data for 1 year. The intervention consisted of an initial interactive workshop and quarterly educational outreach visits focused on maternal death reviews and implementation of best practices.

The primary outcome was reduction of risk of hospital-based mortality. Patients were the unit of analysis. More than 95 000 patients were included in the analysis in each of the intervention and control clusters. Analysis was by intention-to-treat using generalized estimating equations extension of the logistic regression model to account for clustering of women within hospitals. Mortality reduction in intervention hospitals was significantly higher than that in control hospitals (odds ratio [OR] 0.85, 95% CI 0.73–0.98, p=0.0299), but this effect was limited to capital and district hospitals, which mainly acted as first-level referral hospitals in this trial. There was no effect in second-level referral (regional) hospitals outside the capitals (OR 1.02, 95% CI 0.79–1.31, p=0.89). The effect of intervention on three secondary outcomes was also assessed—resource availability in each hospital, medical practice for EmOC and perinatal mortality. A significant positive change was seen in all secondary outcomes. The trial confirmed that large-scale implementation of maternal death reviews and training in EmOC reduced hospital-based maternal mortality in low-income countries.

COMMENT

Maternal mortality remains a major challenge to health systems worldwide. Efforts are being made to reduce maternal mortality ratio (MMR), which is also emphasized in the Millennium Development Goal 5, the target for which is a 75% reduction in the MMR from 1990 to 2015.[1]

Every two minutes, a woman dies of pregnancy-related complications. Almost 99% of maternal deaths occur in developing countries; most could have been prevented with proven interventions. Although MMR has declined globally by 47%, from 1990 to 2010, disparity exists within and across countries and regions. One-third of all maternal deaths occur in just two countries—India and Nigeria.[2] The complications leading to maternal deaths can often be managed with a health system that provides skilled personnel and facilities to handle emergencies and postpartum care.[3] It is important that all births are attended by skilled health professionals, as timely management and treatment can make the difference between life and death.[4] Hence, EmOC is critical for reducing maternal deaths.

Maternal mortality remains one of the most daunting health challenges for India. A key contributing factor to this situation is the lack of skills among rural general doctors and medical officers in the primary healthcare system to provide high-quality EmOC and medical termination of pregnancy services.[5] Poor quality of EmOC services in India has also been reported in different studies.[6,7] The Ministry of Health and Family Welfare has