

Adverse events of albendazole due to mass drug administration

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Received: 19 April 2017

Accepted: 16 May 2017

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ABSTRACT

Background: Soil-transmitted helminths are mostly prevalent in developing countries due to poor sanitation and lack of adequate clean water. The present study examines adverse events (AEs) experienced following administration of albendazole to children (2-19 Years) at Uttarakhand on national de-worming day.

Methods: Children were given single doses of albendazole on national de-worming day. Some of children experienced adverse events and were admitted in hospital of Govt Medical college Haldwani (Uttarakhand). Data were collected and analyzed.

Results: Total twenty five children were admitted due to albendazole adverse events. Out of these 92% were female. Mean age of admitted children was 14.14 years with standard deviation 3.45. Mean onset of adverse events was 5.6 hours with standard deviation of 1.5 hours. All children were treated symptomatically and were discharged once they recovered. No fatality due to adverse events was observed. Average duration of stay in hospital was 3.4 days. Out of twenty five children 12% children reported four or more adverse events, 40% children reported three adverse events and 48% reported two adverse events. Out AEs, 33% AEs were mild, 19% AEs were moderate, 31% AEs were severe and 17% AEs were serious. Abdominal pain was reported by 76%, headache by 44%, loss of consciousness by 32%, vomiting by 28%, nausea by 16%, convulsions by 12%, rashes by 8%, fever by 8%, and breathlessness by 14% and vertigo by 4%.

Conclusions: The adverse events were mild to serious but transient, but all of them recovered after hospitalization. Therefore, it is imperative that mass drug administration programmes put in place surveillance measures in order to ensure timely detection, management and reporting of potential life threatening AEs.

Keywords: Albendazole, Adverse events, De-worming programme, Mass drug administration

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.¹⁻³ *Taenia spp.* infections are also widespread.^{4,5} STHs and taeniasis/cysticercosis belong to the neglected tropical diseases and are responsible for mainly chronic and often inconspicuous morbidity.^{6,7} Iron-deficiency anemia, malnutrition, and impaired physical and cognitive development have all been attributed to STH infections.^{3,8} *Taenia solium* cysticercosis is a major cause of epilepsy and other neurological disorders in developing countries.⁹

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 children.^{10,11} Due to the zoonotic nature of taeniasis/cysticercosis, its control must also include the veterinary sector.^{4,12,13} At present, only four drugs are recommended by the World Health Organization for treating STH infections.^{10,14} The global STH control relies on two of them-albendazole and mebendazole-both benzimidazole carbamates. Albendazole and mebendazole display a broad spectrum of activity and are administered orally, usually at a single dose of 400mg and 500mg, respectively.^{10,14-17} Children below the age of 1 year and pregnant women in the first trimester of pregnancy are not eligible for treatment.¹⁰

Albendazole and mebendazole have been extensively used worldwide for more than 30 years, both as stand-alone treatments and, more recently, in combination with other drugs, e.g., praziquantel (against schistosomiasis and food-borne trematodiasis) or ivermectin (against lymphatic filariasis).⁷ Justification for the indiscriminate use of either drug is derived from high egg reduction rates achieved with both albendazole and mebendazole, and the assumption that morbidity is a function of infection intensity.¹⁸ However, a recent meta-analysis of randomized placebo-controlled single-dose drug efficacy trials pointed to a marked superiority of albendazole over mebendazole against hookworm, high efficacy in terms of cure rate of both drugs against *A. lumbricoides*, and disappointing efficacy of either drug against *T. trichiura*.¹⁴

The new de-worming initiative of the Indian Health Ministry aims to de-worm all pre-school and school-age children between the ages of 1-19 years. Starting from the National De-worming Day on 10th February 2015, albendazole tablets are being given to all targeted children; half tablet to 1-2 years children and one full tablet for 2-19 years. The children who are left out are being covered by a mop-up round to be carried out till next four days. In the year 2016, also children were given albendazole on national De-worming Day (10 Feb 2016) in state of Utrkhand. Some of children experienced serious adverse events like Convulsions/ loss of consciousness / breathlessness due to albendazole and were admitted in hospital of Govt Medical College Haldwani. Due to above some of children and parents were apprehensive, and children having mild AEs like nausea /headache/ rashes were also admitted in hospital. This hospital based study was carried out to study adverse events of albendazole in children due to mass drug administration for de-worming programme.

METHODS

This cross-sectional hospital based study was carried out in admitted children at hospital of Govt Medical College Haldwani due to adverse events (AEs) due to albendazole administration for national de-worming programme. This study was carried out from 11 February 2016 to 25 February 2016. Patients were referred from School/ Primary Health Center/Community Health Center. Oral informed consent was obtained from the study participants or their parents. A structured questionnaire was designed to study the adverse events of albendazole in admitted children. Questionnaire included (name, age, sex, onset of adverse events, clinical symptoms, outcome). Questionnaire was administered by investigator to all the admitted children or their parents in language they understand. Approval was taken from ethical committee of Govt Medical College Haldwani to carry out the study in admitted children. AEs were classified as defined in the WHO guidelines whereby mild AEs were defined as undesirable experiences associated with use of the antihelmithics but not affecting

daily activities (e.g. playing) whereas moderate AEs were defined as those affecting performance of daily activities. Severe AEs were defined as those requiring total rest and/or medication while serious AEs were defined as those that were life-threatening requiring admission to hospital.¹⁹ Data were collected and analyzed in Microsoft Excel.

RESULTS

Total twenty five children were admitted due to albendazole adverse events. Out of these 2 (8%) were male and 23 (92%) were female. Mean age of admitted children was 14.14 years with standard deviation 3.45 and range was 3.5 years to 18 years. Mean onset of symptoms was 5.6 hours with standard deviation of 1.5 hours. All children were treated symptomatically and were discharged once they recovered. No fatality due to adverse events was observed. Average duration of stay in hospital was 3.4 days. Out of twenty five children 3 (12%) children reported four or more adverse events, 10 (40%) children reported three adverse events and 12 (48%) reported two adverse events. Total sixty four adverse events were reported. Out AEs, 33% AEs were mild ,19% AEs were moderate, 31%AEs were severe and 17% AEs were serious (Figure 1).

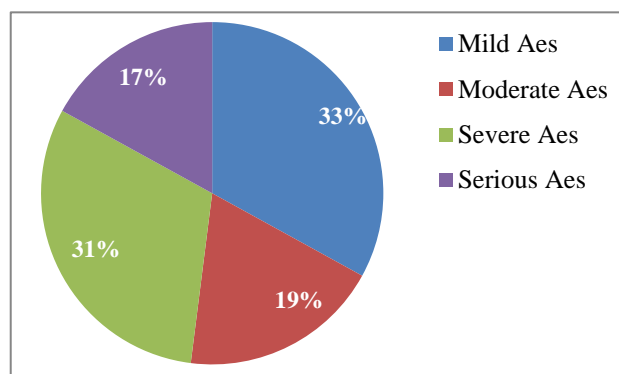


Figure 1: Nature of adverse events (Aes).

Table 1: Adverse events due to Albendazole Mass drug administration.

Type of adverse event	Frequency	Percentage
Abdominal pain	19	76%
Headache	11	44%
Loss of consciousness	8	32%
Vomiting	7	28%
Nausea	4	16%
Convulsions	3	12%
Rashes	2	8%
Fever	2	8%
Breathlessness	1	4%
Vertigo	1	4%

Abdominal pain was reported by 19 (76%), headache by 11 (44%), loss of consciousness by 8 (32%), vomiting by

7 (28%), nausea by 4 (16%), convulsions by 3 (12%), rashes by 2 (8%), fever by 2 (8%), breathlessness by 1 (4%) and vertigo by 1 (4%) (Table 1).

DISCUSSION

The spectrums of the adverse events of drugs are not always same between different ethnic groups, and it can be influenced by the genetic factors and even the temporary conditions of children at the de-worming activity. The result of this study shows the frequencies of the adverse effects of the albendazole used in national de-worming programme among children in an area Utrakhand. In mass de-worming programme in Central Kenya with albendazole cough was reported more frequently. Cough is a general reaction and can be associated with any drug especially in young children.²⁰ In our study cough was not reported at all as AEs. Albendazole provides safe and highly effective therapy against worm infestation.²¹ It has only limited solubility in water. After a 400mg oral dose, albendazole cannot be detected in plasma, due to low absorbance of the drug from the intestines.²² The metabolites are excreted mainly in the urine. Albendazole is said to produce few adverse events when used for short-term therapy of worm infestations. Transient abdominal pain, diarrhea, nausea, dizziness, and headache occur occasionally.²³ Indeed, a review by Horton, reported that incidences of side effects associated with albendazole at the doses used for the treatment of intestinal helminths are very low, mild and self-limiting with only gastrointestinal side effects occurring with an overall frequency of just greater than 1%.²⁴ Similar adverse events were also reported in our study. However in our study some of children reported serious adverse events like loss of consciousness, convulsions but all of them recovered after hospitalization and in none of children convulsion and loss of consciousness was observed during hospital stay. The reasons for the variations in proportions of adverse events experienced after antihelminthic treatment could probably be due to dissimilar intensities of parasites as well as differences in socio-economic status, types of foods and environmental conditions associated with the diverse populations. Mass use of praziquantel in areas where cysticercosis is endemic can trigger seizures in persons with latent brain cysts a potential concern for mass deworming campaigns involving albendazole. A case of unmasking of neurocysticercosis was reported in Peru due to albendazole administration.^{23,25} Those designing or executing deworming programs should carefully consider the possibility of this complication. Therefore, it is imperative that mass drug administration programmes put in place surveillance measures in order to ensure timely detection, management and reporting of potential life threatening AEs.

CONCLUSIONS

This study shows that albendazole have mild as well as serious adverse events. Trained school teachers can

however use the albendazole in MDA for control of STHs since schools provide an efficient and effective channel to reach large portions of the population within a short time, which makes a programme cost effective. However, the health/medical personnel should be involved in the programme so that they can give moral support and be on standby to handle any serious adverse events should they arise. This approach is cost effective and should be adopted for a national deworming programme. Therefore, it is imperative that mass drug administration programmes put in place surveillance measures in order to ensure timely detection, management and reporting of potential life threatening AEs.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Agrawal P, Srivastava B, Bhardwaj R, Gaur S. Adverse events of albendazole due to mass drug administration. *Int J Basic Clin Pharmacol* 2017;6:1674-7.