The adverse effects of albendazole and praziquantel in mass drug administration by trained schoolteachers

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SUMMARY

Eastern and Southern Africa Centre of International Parasite Control (ESACIPAC) conducted stool examinations for soil transmitted helminthiases (STH) and *Schistosoma mansoni*, among school children in Mwea Division, Central Kenya where both infections are endemic. Mass drug administrations (MDAs) were then conducted in 2004 and 2005 using schoolteachers trained on how to administer treatment, physically and psychologically prepare the children to take the medication, have them eat before treatment, handle minor and refer serious side effects to local health facilities. Local health workers were on standby to help manage severe side effects. This study examined side effects of the drugs and the teachers' preparedness to handle the children when such effects occurred. No serious side effects requiring referral to the health centre occurred and the minor ones observed were temporal.

In 2005 children in Mwea schools were treated with albendazole 400mg and praziquantel 40mg/kg body weight while those of Ndia, a neighboring division treated with only albendazole 400mg since there was low S.mansoni prevalence. Monitoring of side effects was done in two schools of Ndia and in three of Mwea through a questionnaire distributed to grade three pupils a week after treatment.

Of 73 pupils from Mwea, 49.7% reported incidences of stomachache, vomiting/nausea, headache and dizziness whereas 39.2% of 186 from Ndia experienced incidences of cough, stomachache and headache. This shows that more pupils from Mwea, (albendazole and praziquantel) than from Ndia (albendazole alone) experienced minor side effects.

These results show that both drugs have temporary, minor side effects, which can be managed by trained schoolteachers by ensuring that the school children do not swallow the drugs on an empty stomach and rest immediately after swallowing the drugs but should be closely monitored by health personnel. In this study, one trained schoolteacher could administer treatment to three hundred children in one day, which makes the approach cost effective and should be adopted nationally.

KEYWORDS: albendazole, praziquantel, soil transmitted helminthiasis, schistosomiasis

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Introduction

Soil-transmitted helminthiasis (STHs) and schistosomiasis infections are big burdens to school age children in large parts of the world [1] including Kenya [2]. They can interfere with the nutritional status [3] and the cognitive abilities of children [4]. Recently education sectors have been used for delivering medicines for parasite control because the school network is usually well established than the health system in developing countries [5].

A wide scale stool examination for intestinal parasites

was conducted followed by MDAs for de-worming of STHs and human schistosomes by trained school teachers in Mwea division, Central Kenya in March 2004. In the year 2005, the de-worming activity was expanded to the neighboring division, Ndia, which has low prevalence of schistosomiasis, less than 1%, (unpublished data). Albendazole (ALB) and praziquantel (PZQ) have been widely used for STH and schistosomiasis control [1]. However, though they are reported to be safe [6], it is important to monitor the events of side effects in the projects when widely used for MDA, as there are some reports of severe adverse effects (SAEs) of PZQ [2, 7, 8, 9]. In order to observe the kinds, the frequency, and the degree of the SAEs of these two medicines, a survey was conducted one week after the MDA using a questionnaire.

Materials and Methods

School setting

All primary schools in both Mwea and Ndia division were targeted for the de-worming programme. Mwea division, which has an irrigation scheme within it, had a prevalence of Schistosoma mansoni (Sm), Ascaris lumbricoides (Al), hookworm (Hw), and Trichuris trichuria (Tt) at 17.4%, 0.0%, 1.4%, and 2.9%, respectively following the results of sample schools. Ndia division, which does not have an irrigation scheme, had a prevalence of Sm, Al, Hw, and Tt was 0.6%, 1.3%, 20.9%, and 1.8%, respectively. [unpublished data] and treatment was done for STH only.

De-worming

Schoolteachers who were trained by staff from the district education office, the district medical office, and ESACIPAC administered tablets. The training session which lasted half a day introduced the teachers to the aims of the school health programme, the presence of worms in the area, characteristics of the de-worming drugs, their safety and storage, administration of the de-worming drugs, the need to physically and psychologically prepare each child to take the drugs and record keeping. The training also had a practical session on drug administration, during which the teachers practically administered the drugs to a selected number of pupils who would then not be treated on the scheduled de-worming day. Teachers were also asked to ensure that the school children did not take the drugs on an empty stomach by having them take some food before taking the drugs and also have some porridge to swallow the tablets with. Pupils of Ndia took 400mg of ALB tablet **(name of the tablets, unibazole)** and those in Mwea took 400mg of ALB and 40mg/kg of PZQ **(name of the tablets, prazitel®),** the dosage of which was adjusted by measuring height (WHO, 2002a). Two schools from Ndia (ALB) and three schools from Mwea (ALB + PZQ) were targeted for monitoring the adverse effects. It was the first time for the pupils in Ndia, but the second time for those in Mwea to take the tablets during MDA.

Questionnaire

A questionnaire sheet was distributed to the standard three pupils who were randomly selected one week after the administration of the medication. Under the guidance of the teachers, pupils were expected to fill the answers by themselves. Questions included: age, sex, and whether they had had headache, fever, cough, dizziness, diarrhea, stomachache, or vomiting/nausea immediately after taking the medication up to the following two days.

Statistical analysis

Continuous data between two groups were compared by t-test. Categorical data were compared between two groups using chi-square test with Yate's correction. The threshold for significant level was 0.05 of *p* value.

Results

73 pupils in Mwea and 186 pupils in Ndia responded to the questionnaire. There was no significant difference between the two groups in age and sex. There were about fifty per cent (49.7%) incidences of adverse effects reported by pupils of Mwea and 39.2 % by pupils of Ndia. Among the pupils in the ALB group, the most frequent adverse effect was stomachache (13.4%), followed by headache (5.5%). Coughing which is not a side effect of taking the drugs and could have been due to any other cause was reported by (16.1%) of the pupils from Ndia. The most frequent adverse effect among the pupils in the other group was stomachache (30.1%), followed by vomiting/nausea (8.2%), headache (5.5%), and dizziness (5.5%).

Twenty-two (30.1%) from Mwea, and 25 (13.4%) from Ndia (p=0.002) reported incidences of stomachache when comparisons were made between the side effects of the two regimes. Six (8.2%) pupils from Mwea, and 3 (1.6%) from Ndia (p=0.017) reported incidences

Table 1 Adverse effects of treatment with ALB+PZQ and ALB among pupils in Mwea and Ndia Divisions, respectively

Variables	Percentage of respondents % Mwea	Ndia	p-value
	ALB +PZQ (n=73)	ALB alone (n=186)	
Sex: no boys/no girls	39/34	97/90	0.89
Mean age (SD, range)	11.4 (10.5, 7-15)	10.2 (2.0, 7-17)	0.13
Side/adverse effects:	**Number (%)**	**Number (%)**	
Nothing	44(60.3)	113(60.8)	1.00
Headache	4(5.5)	5(5.5)	0.28
Fever	0(0.0)	6(3.2)	0.19
Cough	0(0.0)	30(16.1)	0.00
Dizziness	4(5.5)	6(3.2)	0.48
Diarrhea	2(2.7)	6(3.2)	1.00
Stomachache	22(30.1)	25(13.4)	0.00
Vomiting/nausea	6(8.2)	3(1.6)	0.02

vomiting/nausea. All adverse effects were temporally and no severe ones were reported.

Discussion

The result of this study shows the frequencies of the adverse effects of the two drugs used in MDA among school children in an area of central Kenya. In Ndia Division,where only ALB was used cough was reported more frequently than in Mwea Division. Cough is a general reaction and can be associated with any drug especially in young children. Minor gastro-intestinal symptoms were however reported after administration of PZQ in Mwea but there were no major side effects associated with it. These two medicines are widely used in MDA for the control of STH and human schistosomes. ALB provides safe and highly effective therapy against infections with Al, Tt, and Hw administered in a single 400-mg oral dose for adults and children more than 2 years of age [10]. It has only limited solubility in water. After a 400-mg oral dose, ALB cannot be detected in plasma, due to low absorbance of the drug from the intestines [10]. The metabolites are excreted mainly in the urine. ALB is said to produce few side effects when used for short-term therapy of STHs. Transient abdominal pain, diarrhea, nausea, dizziness, and headache occur occasionally [6].

PZQ is used in MDA for schistosomiasis and is readily absorbed after oral administration, so that maximal levels in human plasma occur in 1 to 2 hours. Its plasma half-life is 0.8 to 2.0 hours, but this may be prolonged in patients with severe liver disease, including those with hepatosplenic schistosomiasis. About 70% of an oral dose of PZQ is recovered as metabolites in the urine within 24 hours. Abdominal discomfort, particularly pain and nausea, headache, dizziness, and drowsiness may occur shortly after taking PZQ; these direct effects are transient and dose-related. There is no pharmacokinetic interaction and no synergistic effect by the treatment between the two medicines [11,12].

After introduction of these two medicines in MDA, their side effects have been studied. When Olds [14] studied the side effects of ALB and PZQ among the children with S.mansoni in Western Kenya, abdominal pain, diarrhea, and bloody diarrhea were detected to have higher frequency among children who took PZQ with or without ALB. On the contrary, this study showed only few cases of diarrhea (2.7%), stomachache (30.1%) among the children with PZQ and ALB probably because emphasis was made on the need to take food before taking the medication. Jaoko [2] in a study in Southeastern Kenya reported that the main side effects were abdominal pain (36.3%), headache (35.3%), nausea (13.1%), dizziness (9.7%), and fever (7.8%). Berhe [7] also reported that abdominal cramp (86.9%), diarrhea with blood and/or mucus (49.5%), dizziness (31.2%), and vomiting (24.9%) were the most common treatment related symptoms in their study in Ethiopia.

The spectrums of the side effect 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. To the best of our knowledge, it was the first time for the pupils in Ndia to join a de-worming activity and it

maybe that some may have had difficulties swallow the tablets while others may have been scared to do so. They might not have had enough information of the needs of de-worming and adverse effects, which might have led to the high percentage of cough and stomachache in this group. On the other hand, it was the second round of de-worming activity for the pupils in Mwea, and they could take medicine more easily as they realized the reason and efficacy of the de-worming and adverse effects through the activity in the previous year and teachers of Mwea schools may have appreciated the need to administer the tablets to children when they had taken a meal. Stomachache and vomiting/nausea were seen more in Mwea, which means that these effects were really caused by PZQ alone.

Although there were no cases of severe adverse/ side effects, the district medical staff was stand-by at their workstations on the de-worming day in readiness for any emergency cases. Tablets have been administered by trained teachers in many projects and incase of severe side effects their efficacy may not be very good. It is important to monitor the adverse/ side effects, the type and the frequency and use the information gathered while training the schoolteachers and health staff in the communities, so that they can use such information to handle emergency cases.

Conclusions

This study shows that both ALB and PZQ have minor side effects, trained schoolteachers can however use the two drugs in MDA for control of S. mansoni and 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. The school children experienced minor side effects, which were temporal and required resting under a shade until they subsided. 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 severe side effects should they arise. This approach is cost effective and should be adopted for a national de-worming programme.

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