Schistosomiasis in African infants and preschool children: let them now be treated!


**The burden of schistosomiasis (SCH) in children and infants**

Until recently, a paucity of information fueled the debate of whether national neglected tropical disease control programs should treat young children with praziquantel (PZQ). International dialogue was driven by uncertainty regarding the distribution and prevalence of SCH in children under 5, and whether targeting them with preventative chemotherapy should be considered by international policy. Compelling data suggest that SCH in young children causes severe morbidity and irreversible developmental damage. This prompted the World Health Organization (WHO) to call for improved diagnoses and treatment for this group. The recommendation triggered investigations on drug efficacy and safety, along with efforts aimed at promoting drug access and equitable delivery.

**Praziquantel safety**

Despite the widely acknowledged safety of PZQ for preventative chemotherapy, its safety in children under 5 was not well understood. To address this knowledge gap a seminal study was conducted in children under 5 comparing the efficacy of PZQ syrup, Epiquantel, with conventional PZQ tablets. Results suggested that Epiquantel offered no significant health benefit, bulky packaging presented logistical storage problems, and the ad-hoc production of the syrup made it more expensive and limited its availability. Therefore final recommendations concluded that crushed or broken PZQ tablets could be safely administered and should be distributed during Expanded Programme of Immunization campaigns.

**SCH mapping and treatment needs in young children**

To address the knowledge gaps pertaining to the burden of SCH in young children and infants, a cohort study in Uganda evaluated the heath-related needs for PZQ treatment, and how often treatment should be administered. Prevalence rates were assessed using the Kato-Katz method, urine circulating cathodic antigen dip-sticks and blood antigen ELISA detection kits. Results indicated a high disease burden among pre-school children, as over 50% of infants over 3-months of age had active infections and were also considered at severe risk of re-infection. Among the children in the study cohort, the average age of infection was between 3.25 and 3.75 years old. A high transmission among this age group was likely due to their high risk of daily water contact, known to be an ecological niche for SCH parasites. Furthermore, this study found that prevalence mapping of SCH by circulating cathodic antigen dip-stick could be a useful tool, as it was more effective than a single stool microscopy and was not significantly impacted by treatment history or intestinal helminth co-infection.

**New SCH detection methods**

It is unclear whether classic SCH markers such as fecal or urine sample egg counts are appropriate markers for SCH morbidity in young children and infants, and whether these sampling methods are applicable for field tests for this age group. Nevertheless, studies reported that pre-school children display certain clinical indicators of infection including upper and lower urinary tract damage, blood presence in stool samples, liver and spleen damage, and liver fibrosis and periportal thickening. Two
novel SCH detection methods in young children are described. First, Betson et al used fecal occult blood (FOB) rapid diagnostic tests in an attempt to uncover novel SCH diagnostic methods. Strong positive associations between S. mansoni infection and FOB rapid diagnostic tests, maintained over a 12-month study period, suggested that FOB rapid diagnostic tests could play an important role detecting baseline and post-MDA levels of infant intestinal morbidity. Other studies testing Albumin-HemoCue photometers found they could effectively be used as markers of pathology in school children. By measuring albumin levels in urine samples in Malawi, this method showed strong associations with S. haematobium infection and microhaematuria in young children, and serology suggested adequate sensitivity and specificity.

**SCH cure rates using PZQ in young children**
While PZQ has been shown to adequately treat SCH in young children, cure rates among populations suffering from persistent and chronic infection suggest that more aggressive treatment may be required. The standard 40mg/kg dose currently administered does not seem sufficient to elicit full parasitological cure. Despite an overall cure rate of over half of study participants, treating children with PZQ showed a significant difference between those with a history of treatment (41.7% cure rate) and those who had never been treated (77.6% cure rate), providing evidence that cure rate was lower among those with a treatment history and among children under 3 years old. However, treating children with higher doses of PZQ have yielded promising results in another study and increasing cure rates up to 91% when administering 60mg/kg.

**PZQ donations and formulations for SCH free young children**
Until 2007, there was low PZQ availability due to the skepticism of organizations, inflated prices and low donor contributions. However the London Declaration on Neglected Tropical Diseases altered the landscape. WHO took a cardinal step in setting up a clear strategy of scaling up of preventive chemotherapy. These led to Merck to increase their existing PZQ donation to 250 million tablets each year. Merck also committed to addressing the treatment needs of infants and preschool children by developing an appropriate new paediatric formulation. For this purpose, a public-private partnership was established to develop appropriate formulation, and current preclinical tests are projected to enter clinical development by 2014. Children are the priority target of the control programs. Scaling up PZQ treatment in this group however has to be closely monitored, and securely embedded within a strong public health platform such as EPI.

**Editor Comment**
Young children and infants represent a sizeable proportion of the population in Africa and are the most vulnerable and neglected group. The evidence demonstrating levels of morbidity and mortality due to schistosomiasis infection overwhelmingly justify the need for PZQ treatment for this age group. Although efforts have been made to develop age-specific PZQ formulation, the national programs should not wait until the paediatric formulation available for wide use to target this group of young children, as the crushed PZQ tablets are perfectly safe and effective as the authors described. However, caution must be taken and stringent supervision must be given when proceeding with the crushed PZQ tablet approach to minimize the potential side effects. The community drug distributors used in the NTD programs may not be the ideal approach. Better trained health workers and nurses to deliver such treatments would be needed. As authors discussed, existing EPI system will be a good platform. In addition, vitamin A supplementation program for children under 5 years old exists in many African countries, which is normally coupled with deworming with albendazole/mebendazole. This also provides an excellent platform to include PZQ treatment.
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