Am. J. Trop. Med. Hyg., 90(4), 2014, pp. 634–637
doi:10.4269/ajtmh.13-0252

Short Report: Dosing of Praziquantel by Height in Sub-Saharan African Adults

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Abstract. The cornerstone of schistosomiasis control is mass praziquantel treatment in high prevalence areas. Adults are an important target population, given increasing recognition of the burden of male and female genital schistosomiasis. However, use of weighing scales to calculate praziquantel dosing in rural areas can be challenging. For school-age children, the World Health Organization (WHO) has approved a dose pole to simplify praziquantel dosing based on height. We modified the pediatric dose pole by adding two height categories and incorporating a simple overweight/obesity adjustment, for simplified mass treatment of adults in sub-Saharan Africa. Using the rural Zimbabwean Demographic and Health Survey data, we show that the modified dose pole with body mass index adjustment would result in > 98% of adults receiving an acceptable dose (30–60 mg/kg), with only 1.4% and 0.3% receiving an inadequate dose (< 30 mg/kg) or high dose (> 60 mg/kg), respectively. An adult dose pole may provide a more feasible alternative to weighing scales in community-based praziquantel treatment programs.

INTRODUCTION

The cornerstone of schistosomiasis control is mass praziquantel treatment in areas of high prevalence. The World Health Organization (WHO) recommends annual treatment of all school-age children and adults considered to be at risk in areas with > 50% prevalence, and treatment every 2 years in areas with 10–50% prevalence.[1] Given the challenges of using a weighing scale in rural households, praziquantel dosing for children has been simplified by use of a vertical "dose pole" that uses height as a surrogate for weight to estimate the correct dose of praziquantel for each child.[2,3] This dose pole has recently been modified for preschool-age children, a vulnerable target group previously excluded from mass drug administration (MDA) programs.[4,5]

Adults are generally dosed according to body weight, despite the logistical challenge of accurate weight measurement in rural areas of developing countries. Use of a dose pole, as for children, would simplify mass treatment of adults in rural communities. Including adults in control strategies is important, particularly in the context of morbidity reduction among women who are at risk of female genital schistosomiasis associated with human immunodeficiency virus (HIV) acquisition.[6–8] Males are also an important target group in MDA strategies, given the growing understanding of male genital schistosomiasis.[8]

We therefore set out to develop and validate a variant of the WHO praziquantel dose pole for the mass treatment of adults. Dosing adults based on height, rather than weight, in the context of the emerging obesity epidemic in developing countries risks underdosing with praziquantel. We therefore also evaluated a simple adjustment for overweight and obesity that could be used in community-based treatment programs.

MATERIALS AND METHODS

We first modified the WHO pediatric dose pole[1] to make it more suitable for adult use. The modified dose pole included two additional height/dose intervals corresponding to the median heights of adults in the original categories to correct for potential underdosing of heavy adults in these groups. The new height cut-offs of 156 cm and 164 cm allow for the dosing of 3.5 tablets and 4.5 tablets, respectively. The theoretical dose administered using each of the two poles was calculated by dividing the dosage corresponding to each adult's height category by his or her respective weight. An optimal dose of praziquantel was defined as 40–60 mg/kg, with an acceptable dose defined as 30–60 mg/kg.[2,3,9] We reasoned that adults could easily be classified as overweight or obese by fieldworkers using a pictogram (Figure 1).[10,11] Adults with body mass index (BMI) > 25 kg/m^2 were estimated to require an additional 25% of the average adult dose (2,400 mg), translating to one extra 600 mg tablet (Montresor A, WHO; personal communication).

Data from the 2005–06 Zimbabwe Demographic and Health Survey (DHS) were then used as a model for adults in sub-Saharan Africa to validate the modified dose pole compared with the original pediatric dose pole. The proportion of adults who would receive theoretical doses in the following categories was determined: inadequate (< 30 mg/kg), acceptable (30–40 mg/kg), optimal (40–60 mg/kg), and high (> 60 mg/kg). Stata 12.0 (StataCorp LP, College Station, TX) was used to perform χ^2 analysis to compare accuracy of the original pediatric dose pole with the modified dose pole in determining the correct dose of praziquantel, with and without BMI correction.

RESULTS

The DHS data comprised 5,614 rural Zimbabwean adults between 15 and 49 years of age. Their mean height was 160 cm (range 131–191) and mean weight 57.2 kg (range 30.0–117.5), with 10.1%, 70.5%, 15.2%, and 4.2% of adults categorized as underweight (BMI < 18.5 kg/m^2), normal weight

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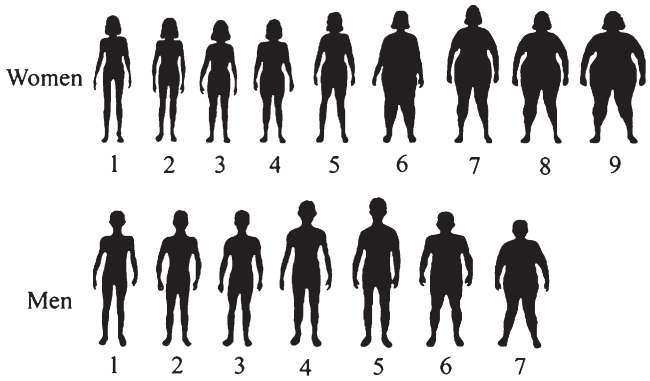
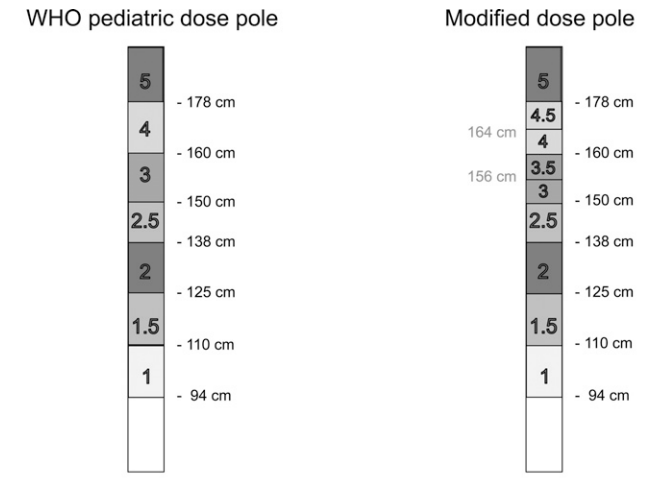


FIGURE 1. Body shape pictogram. Pictogram developed originally by Stunkard and others[11] to evaluate body in shape Danish men and women, and subsequently adapted and validated in other populations.[10] The optimal sensitivity and specificity for obesity in a Caucasian population uses the sixth figure for both men and women as the cut-off point[19]; however, the optimal cut-off for overweight was not assessed. To our knowledge, no study to date has evaluated use of this pictogram to categorize body-mass index in sub-Saharan African populations. Reprinted from[10] with permission from Elsevier.

(18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (≥ 30 kg/m^2), respectively.

Using the WHO pediatric dose pole to determine the number of tablets administered, 15.0%, 52.9%, 32.0%, and 0.1% of adults would receive an inadequate, acceptable, optimal, or high dose, respectively (Figures 2 and 3). Correcting for BMI by providing an additional 600 mg tablet to all adults classified as overweight or obese, resulted in a significant improvement of this model ($P < 0.001$, χ^2), with 3.8%, 58.4%, 37.7%, and 0.1% receiving an inadequate, acceptable, optimal, or high dose, respectively (Figures 2 and 3).

Using our modified WHO dose pole to determine the number of tablets administered, 8.7%, 45.3%, 45.7%, and 0.3% of adults would receive an inadequate, acceptable, optimal, or high dose, respectively (Figures 2 and 3). Correcting for BMI by providing an additional 600 mg tablet to all adults classified as overweight or obese, resulted in a significant improvement of this model ($P < 0.001$, χ^2), with 1.4%, 43.3%, 55.0%, and 0.3% receiving an inadequate, acceptable, optimal, or high dose, respectively (Figures 2 and 3). Of note, the new model was significantly better than the original WHO dose pole, both with and without BMI correction ($P < 0.001$, χ^2).



	(-) BMI corr	(+) BMI corr
Inadequate	15.0%	3.8%
Acceptable	52.9%	58.4%
Optimal	32.0%	37.7%
Excessive	0.12%	0.12%

	(-) BMI corr	(+) BMI corr
Inadequate	8.7%	1.4%
Acceptable	45.3%	43.3%
Optimal	45.7%	55.0%
Excessive	0.34%	0.34%

FIGURE 2. Dose pole models for praziquantel administration. Original World Health Organization (WHO) pediatric dose pole with height categories and corresponding number of 600 mg tablets to administer (left). Modified dose pole for adults with additional half-tablet categories and new height cut-offs in red (right). The tables below each pole show the percentage of adults who would have received an inadequate dose (< 30 mg/kg), acceptable dose (30–40 mg/kg), optimal dose (40–60 mg/kg), and high dose (> 60 mg/kg) of praziquantel.

DISCUSSION

Schistosomiasis affects over 240 million people worldwide, especially in developing countries with poor access to clean water and adequate sanitation.[12] Although praziquantel is an effective and low-cost medication that is suitable for MDA, only 10% of people in need of treatment in 2011 had access to it.[12] The development of the WHO pediatric dose pole has helped to address this treatment gap by facilitating dosing by height instead of weight; however, its use is limited to treating school-age children in endemic areas. More recently, a dose pole modification was proposed that includes new height categories corresponding to dosing for preschool-age children, an important target population previously excluded from MDA programs.[4,5]

We propose here an additional modification to the original dose pole to provide a more accurate means of calculating the dose of praziquantel by height for adults in rural areas of endemicity. Adding two height categories to the original pole enables dosing of half-tablets, reducing the proportion of adults receiving inadequate praziquantel doses (from 15% to 8.7%), and increasing the proportion receiving optimal dosing (from 32% to 46%); very few adults (< 1%) with either pole received too high a dose (> 60 mg/kg). Using the modified pole, without correction for BMI, 91% of adults received an acceptable (30–60 mg/kg) dose of praziquantel.

Given the emerging obesity epidemic in countries undergoing the nutrition transition,[13,14] it is important that a modified dose pole can accommodate supplementary dosing for overweight and obese adults. A simple pictogram, such as that developed originally in Denmark by Stunkard and others,[11] but validated[10,15] or modified[16] for other populations, would enable fieldworkers to visually assess body shape and increase the dose of praziquantel in those judged to be overweight or obese. With BMI correction, we found that both dose poles allowed improved dosing compared with no BMI correction. However, the modified pole with BMI correction performed better than the original WHO pediatric dose pole in this population of rural Zimbabwean adults. Overall, > 98% of adults would have received an acceptable dose in the 30–60 mg/kg range using the modified pole; the proportion of adults receiving an inadequate dose was reduced to 1.4%, whereas the proportion receiving a high dose remained very low (0.3%).

Underdosing is of particular concern in schistosomiasis control programs because it may lead to partial or inadequate treatment. Modifying the pediatric dose pole for adult use and applying a BMI correction led to very few adults receiving

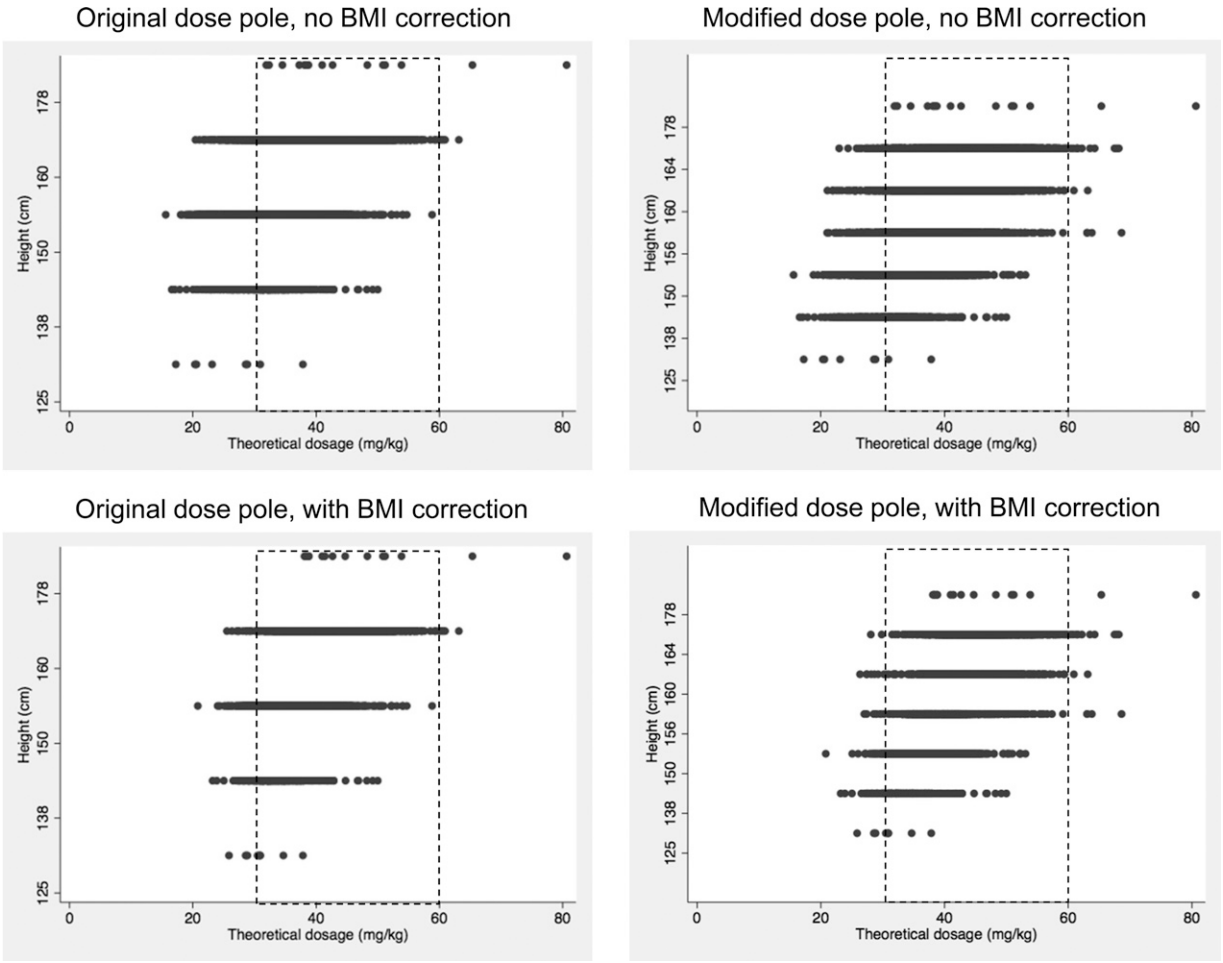


FIGURE 3. Dosing range of praziquantel in rural Zimabwean adults. Range of theoretical dose received by rural Zimbabwean adults based on their height category as determined by the original World Health Organization (WHO) dose pole (left), which has three height categories, and the modified dose pole (right), which has five height categories, without body mass index (BMI) correction (upper panels) and with BMI correction (lower panels). The dashed lines indicate the acceptable dose range of praziquantel (30–60 mg/kg).

an inadequate dose. The number of adults who would receive a high dose (> 60 mg/kg) with this new strategy remained low (3 adults/1,000); even at this dose, praziquantel is generally well tolerated because daily doses of 100 mg/kg are safely administered for 10 days for the treatment of neurocysticercosis. However, there are potential side-effects at high dose, including abdominal pain, nausea, fatigue, dizziness, and headache, in addition to the unnecessary increased costs to MDA programs associated with overdosing of praziquantel.

Previous field-testing of the WHO dose pole for administering praziquantel to treat opisthorchiasis in a village in Lao People's Democratic Republic (PDR) with a high proportion (19.4%) of overweight adults, concluded that the dose pole performed poorly when compared with digital scales as the gold standard.[17] A similar limitation in determining the dose of ivermectin among a population in northern Nigeria that included a high proportion of overweight individuals has been reported.[18] From the rural Zimbabwean DHS data used in our study, the percentage of overweight (15.2%) and obese (4.2%) adults is lower than in these previous studies; there is therefore a need to validate this modified dose pole in settings with a different prevalence of overweight. We propose that a pictogram,[10,11] instead of a subjective visual assessment, should be used to identify adults who require an additional 600 mg tablet for overweight or obesity. A pictogram has the advantage of being feasible for use in communities with low literacy and avoids the need for complex dose corrections by fieldworkers. The cut-off point providing the best sensitivity and specificity for obesity has been defined in Caucasian populations using this pictogram (Figure 1)[19]; however, to our knowledge, this analysis has not been undertaken in African populations, and the optimal cut-off for overweight has not been evaluated in any population. Modified figure-rating scales using photographs of Caucasian volunteers provide overweight and obese categorization[20]; however, we are not aware of a scale using photographs of black Africans. Therefore, further work may be required to develop a field tool that optimally identifies adults requiring additional praziquantel dosing in developing countries.

There are potential disadvantages to introducing a new dose pole for adults. Currently, paper copies of the pediatric dose pole are included in boxes of praziquantel donated for MDA programs; introducing additional poles would increase printing costs and may cause confusion to fieldworkers. Additionally, dose poles were introduced to minimize the need to divide praziquantel tablets, which complicates dosing and

can lead to wastage. However, given the recent development of a preschool-age dosing pole,[5] policymakers may wish to consider redesigning these materials so that all three poles could be included in MDA boxes, together with a simple pictogram on the adult pole to facilitate dosing of overweight and obese adults. Although dividing tablets is more complicated, we show here that use of half-tablets would increase the number of adults receiving an optimal dose of praziquantel. Furthermore, the preschool-age pole requires division of tablets, therefore a similar change in adult dosing may be feasible.

In conclusion, we have modified the WHO praziquantel dose pole for adult use and added an overweight/obesity adjustment to provide a more feasible alternative to weighing scales in estimating appropriate doses for adults during praziquantel MDA programs in developing countries. We show that the modified pole with BMI correction would reduce inadequate dosing and increase optimal dosing of praziquantel in rural Zimbabwean adults, compared with the current pole. Given the large burden of disease among adults, simplifying mass treatment for school-age and preschool-age children, may be an important step in improving control of schistosomiasis.

Received May 8, 2013. Accepted for publication January 5, 2014.

Published online March 3, 2014.

Financial support: AJP is funded by the Wellcome Trust [093768/Z/10/Z].

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