Published in final edited form as:
Trans R Soc Trop Med Hyg. 2007 November ; 101(11): 1120–1123. doi:10.1016/j.trstmh.2007.07.004.

Field testing of the WHO dose pole for administration of praziquantel in treatment of opisthorchiasis in Lao PDR

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Summary

In 2001, the World Health Organization developed a dose pole, which employs height measurements for the estimation of the dose of praziquantel. In the present study, conducted during a mass treatment campaign for the control of opisthorchiasis on 232 individuals in Nala Village, Keo Udom District, the performances of the dose pole in estimating dosages of praziquantel, was compared with a bathroom scale, whereas a digital scale was used as golden standard. Results showed that the bathroom scale performed significantly better than the dose pole in delivering dosages of 40-50 mg/kg for opisthorchiasis treatment (70.7% vs. 44.8%). Furthermore, the dose pole performed significantly better for children than adults. The reason of the poor performance of the dose pole among adults is likely to be due to the high percentage (19.4%) of overweight individuals in the adult population of the village. It was concluded that the WHO dose pole is not recommended for the distribution of praziquantel for opisthorchiasis treatment to populations where overweight is common.

Keywords

Praziquantel; WHO dose pole; drug administration; opisthorchiasis; schistosomiasis

1 Introduction

Praziquantel is the recommended drug for treating schistosomiasis (WHO, 2002) and foodborne trematode infections (WHO, 1995). For treatment of opisthorchiasis a dose of 40 mg/kg is considered optimal (WHO, 1995), but a dose range between 40 and 50 mg/kg is acceptable (Pungpak et al., 1985). A dose range of 40-60 mg/kg is the currently recommended dose for treatment of schistosomiasis (WHO, 2002).

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Conflicts of interest:
The authors have no conflict of interest concerning the work reported in this paper

Ethical approval:
Not required

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The administration of praziquantel is simple, being per oral and according to body weight. However, weight scales are often found to be in-accurate, expensive and difficult to maintain. In response to these problems, WHO developed a dose pole, which estimates the number of tablets needed to provide 40-60 mg/kg based on individual height measurements (WHO, 2002). The dose pole was successfully tested on data from more than 25000 children and adults from 11 African countries (Montresor et al., 2001) and 11 Asian countries (Montresor et al., 2005). The aim of the present study was to test whether the WHO dose pole could replace the scales presently used for opisthorchiasis control programs in Lao PDR.

2 Material and methods

The study was conducted in the village of Nala, Keo Udom district in Vientiane province as part of an ongoing mass treatment campaign conducted by the Ministry of Health.

The number of praziquantel tablets needed for treatment of each individual in the village was estimated with a bathroom scale and subsequently the performance of the dose pole was tested on 232 individuals (mean age of 26 years and an age range of 4 to 65 years of which 53% were females) by using a dose pole, which was placed vertically up against a wall and read by trained staff.

The number of tablets estimated by each of the two methods was then compared with the golden standard provided by a digital scale. The following eight weight intervals corresponding to the number of praziquantel (600 mg) tablets were used: 13-16 kg = 1 tablet, 17-24 kg = 1.5 tablet, 25-31 kg = 2 tablets, 32-38 kg = 2.5 tablets, 39-46 kg = 3 tablets, 47-54 kg = 3.5 tablets, 55-60 kg = 4 tablets and 60 + = 5 tablets. The height intervals and the corresponding number of praziquantel tablets used, according to the WHO standard for the dose pole were as follows: 94-110 cm = 1 tablet, 111-125 cm = 1.5 tablets, 126-138 cm = 2 tablets, 139-150 cm = 2.5 tablets, 151-160 cm = 3 tablets, 161-178 cm = 4 tablets, 179 + = 5 tablets.

For both methods, people were categorized as receiving one of the following doses by dividing the total number of mg provided to each individual by the weight registered by the digital scale: < 30 mg/kg, 30 ≤ x < 40mg/kg, 40 ≤ x < 50mg/kg, 50 ≤ x < 60mg/kg and ≥ 60 mg/kg.

For the calculation of an estimated Body Mass Index (BMI=weight/height^2), the height was calculated by the middle point of the dose pole interval attributed to each individual (i.e. if a person was assigned 3 tablets it was assumed that the height was 156 cm, corresponding to the middle point of the 151-160 cm interval). The estimated BMI thresholds of 23 and 27.5 Kg/m^2 were utilized to classify the weight status of the individuals respectively as “overweight” and “obese” as recommended for Asian populations by the WHO Expert Consultation (WHO, 2004).

Data were analyzed using the software STATA 8.0. Chi-square test was applied to compare to the number of people in the dose categories obtained by the two methods and for analysing the relationship between underdosing and overweight/obesity. Student’s *t*-test was

applied for assessing differences in dose ratio (actual dose based on either weight or height interval dosing and the true dose) comparing males and females as well as children (≤ 15 years) and adults (> 15 years).

3 Results

Considering any dose below 40 mg/kg as being sub-curative for opisthorchiasis treatment, the number of sub-curative treatments, using the WHO dose pole (49.6%) exceeded that using bathroom scale (27.1%) at a statistically significant level ($p<0.05$). The optimal dose range of 40 to 50 mg/kg was achieved in 70.7% of the cases using the bathroom scale and in only 44.8 % of the cases using the dose pole. Over-dosing, i.e. a dose of above 50 mg/kg, occurred at a statistically significantly higher level ($p<0.01$) in the dose pole (5.6%) than in the bathroom scale (2.2%). Severe under-dosing, i.e. a dose below <30 mg/kg, was observed in 11.2% of the subjects when using the dose pole as compared to none when using the bathroom scale.

To better interpret the low performances of the dose pole, the doses provided in different groups of age were analyzed (Table 1). The dose pole performed significantly better ($p<0.001$) among children (<15 years) than among adults (> 15 years). Extending this, the dose pole was significantly better when used on adult men (>15 years) than when used on adult women ($p<0.05$). This difference reflects that under-dosing among adults, especially women, is more frequent than among children. In order to further investigate the reasons of under-dosing, the estimated BMI of each individual was calculated: 19.4% of the adult populations in the sample under investigation were “overweight” or “obese”. All the individuals who were under-dosed by the dose pole were in the category of overweight/obese and this elevated BMI was strongly statistically associated with underdosing ($p= 0.00$).

Figure 1 shows the height for weight distribution in the population. In the height categories 3 (151-160cm) and 4 (161-178cm), the range of weights was 38-85 kg, and 40-94 kg, respectively.

4 Discussion

The introduction of a dose pole is considered a major progress in wide-scale drug delivery programs (WHO, 2002). The WHO dose pole has the advantage of being user-friendly, requiring limited maintenance and no calibration. The dose pole thus represents a major step forward in praziquantel treatment of large populations.

The performances of the dose pole in estimating the correct dose of praziquantel was significantly lower in this study that in any other studies previously conducted during distribution campaigns for schistosomiasis, where the number of individuals receiving dosages under 30 mg/kg was less than 1% (Montresor et al., 2001, 2002, 2005). The conclusions from the present study should not challenge the overall validity of the dose pole approach to drug delivery. However, the findings simply point to the fact that the performances of the dose poles should be evaluated before adopting it as a method for drug delivery, especially on adult populations. The height for weight relationship in the present

Lao population differed markedly from those African and other Asian populations on which the dose pole has been used with good results.

A similar failure in providing adequate dose by height in population where overweight was common, was addressed during the development of the tablet pole for ivermectin treatment (Alexander et al., 1993). It was proposed to identify overweight individuals by visual appearance and to offer them increased dose of ivermectin, but this idea was discharged because it was considered too complex.

Regarding the possibility to develop an alternative pole in delivering appropriate doses to a Lao population, we do not consider this option feasible because of the high variability of the weight in each category of the height. Figure 1 shows the range of weights in the height intervals, some including a variation of over 125%. This variation makes it impossible to define valid height intervals in the population considered. As an example there are individuals weighing between 40 and 95 kg in the 4th height interval (160-178 cm) and for this reason it would be impossible to assign tablets to these intervals without providing serious underdosing or overdosing to parts of the population identified by the interval.

Using too low doses raises the issue of development of resistance to the drug. Although never demonstrated in the case of fluke infections and praziquantel, the possibility should definitively be kept in mind (Denhoff, 1998). On the contrary, a dose of 60-80 mg/kg is unlikely to be of concern, since praziquantel is known to be well tolerated (WHO, 1995), and daily dosages of 100 mg/kg for 10 days have been safely used for treatment of neurocysticercosis (Bittencourt et al., 1990).

The presence of overweight/obese individuals also resulted in a poor performance of estimating the correct number of tablet using the weight interval. Since the maximum number of tablets provided using the weight interval is 5 (for all individuals above 60 kg) any individual weighing more than 75 kg would receive a dose below 40 mg/kg. To solve this problem it would be sufficient to include the number of tablets needed to treat individuals over 75 Kg and over 100 Kg.

In conclusion, the WHO dose pole remains the most practical way to distribute praziquantel among children and interestingly in this age group, the tool obtained good performances. When drug distribution is being conducted among adult populations where overweight is common, the dose pole is not recommended. In such populations the bathroom scale provides better estimations of the needed doses.

Acknowledgements

The authors would like to thank the staff at the Center of Malariology, Parasitology and Entomology, Ministry of Health, Vientiane for their assistance and support. We also wish to thank the staff at the Provincial Malaria Center in Keo Udom district, Vientiane province, for their kind assistance.

Funding:

None

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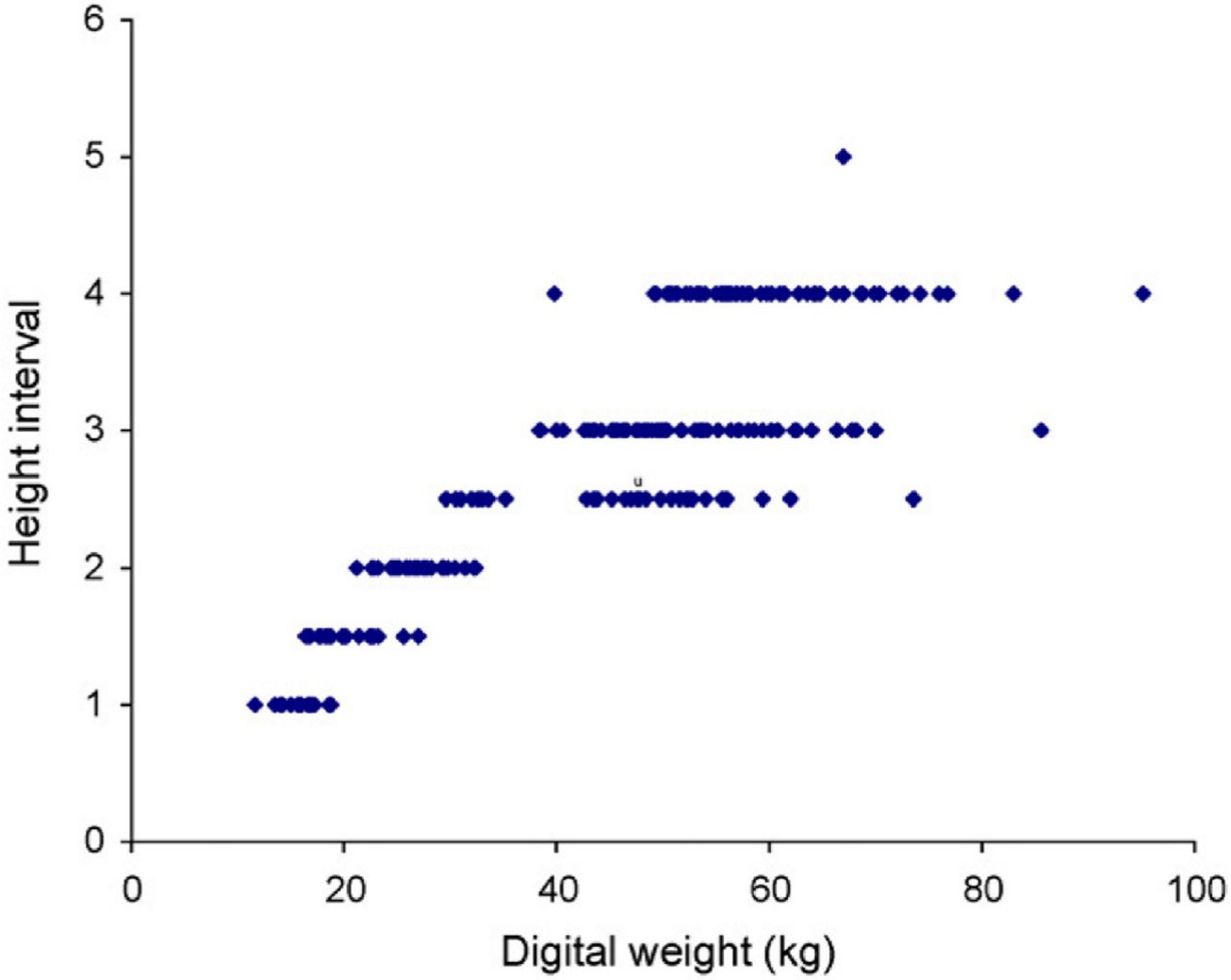

Figure 1.

Height for weight distribution among study subjects. Heights were recorded as the middle point of each person's measured height interval.

* 1=94-110 cm, 1.5=111-125 cm; 2=126-138 cm; 2.5=139-150 cm; 3=151-160; 4=161-178 cm; 5=179 +

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Table 1

Performance of WHO dose pole in estimating the dosages of praziquantel in children and in adults.

	Dose provided by WHO pole mg / kg	
Dose	**Children (age ≤ 15 years)**	**Adults (age >15 years)**
Minimal dose administered	31 mg / kg	21 mg / kg
Maximum dose administered	57 mg / kg	60 mg / kg
Average dose administered	45 mg / kg	37 mg / kg
< 30mg/kg	0	26 (18.7)
≥ 30&< 40mg/kg	23 (24.7)	65(46.8)
≥ 40&<50mg/kg	57 (61.3)	47(33.8)
≥ 50&<60mg/kg	13 (14.0)	0
≥ 60 mg/kg	0	1 (0.7)
Total cases	93	139