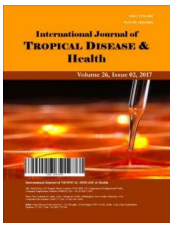

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Efficacy and Safety of Up-scaled Dosage of 60 mg/kg Praziquantel in Control of *Schistosoma mansoni* in School Going Children in Kirinyaga County, Kenya

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aim: The aim of this study was to determine efficacy, safety and morbidity of increased dosage of praziquantel (PZQ) of 60 mg/kg compared to the standard dosage of 40 mg/kg of PZQ in the treatment of *S. mansoni* in school going children in Kirinyaga County, Kenya.
Background: Chemotherapy with PZQ has been the core treatment strategy for schistosomiasis. Due to recent concerns on tolerance and resistance to praziquantel, efficacy studies of up-scaled

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dosage are warranted. Socio-economic activities in Kirinyaga County exposes the community to fresh water snails that harbour the schistosome parasite. Various studies have reported the increased prevalence and high infection intensity in the area despite ongoing mass drug administration (MDA) interventions.

Methods: Study area was in Kirinyaga County, Kenya where the prevalence of schistosomiasis in school going children was first determined. A sample size of 192 subjects of 4-17 year old infected with *S. mansoni* were randomly allocated in Group A (40 mg/kg) and Group B (60 mg/kg). Stool samples were examined by Kato Katz technique to determine baseline infection intensity. Cure rate and egg reduction rate were also determined at 21 days post-treatment in both groups. Comparison of the frequency and severity of adverse events (AE) at 4 and 24 hrs post-treatment were also determined. Peripheral blood was collected to study disease morbidity by measuring haemoglobin (Hb) and eosinophil levels.

Results: Prevalence of *S. mansoni* infection was 52.8%. Baseline intensity of infection was 40% representing light infection while 41.58% and 18.42% representing modereate and heavy infections respectively. Cure rates at 21 days post-treatment were 92% for 40 mg/kg while that of 60 mg/kg was at 94%, a slight variation which did not represent any significant difference between the two treatment groups ($p>0.05$). Mean haemoglobin levels for male and female at 21 days post-treatment were 11.26 g/dl and 11.34 g/dl respectively representing a non-significant difference ($p>0.05$). Eosinophil levels implied a significant decrease after treatment in both treatment groups although no difference was observed between the treatment groups ($p>0.05$). Adverse events recorded in the 60 and 40 mg/kg groups showed that mild abdominal pain was the most frequent AE for the 2 dosages while anoxia was the least occurring AE at 4 hrs and 24 hrs post-treatment.

Conclusion: The upscaled dosage of 60 mg/kg PZQ offers substantial cure to *S. mansoni* infected individuals. Efficacy tests in comparison with 40 mg/kg showed the difference in cure rates to be insignificant. The 60 mg/kg dosage was also associated with slightly higher mild adverse events.

Keywords: Schistosomiasis; praziquantel; S. mansoni; cure rate; egg reduction rate; adverse events.

1. INTRODUCTION

Schistosomiasis is a water-borne parasitic disease that affects more than 249 million people [1] 97% of which are on the African continent [2,3] with a global disease burden calculated at 24-56 million disability-adjusted life-years lost [4]. It is caused by human schistosome, a parasitic flatworm of the genus Schistosoma. Two major schistosome species are responsible for causing human Schistosomiasis in Kenya. These are: *S. haematobium*, and *S. mansoni*. Contamination of open water with human excreta containing the parasite's eggs initiates human to-snail transmission when miracidia released from hatching eggs penetrate into the appropriate fresh water snails species, which serve as intermediate hosts. Schistosome infections may lead to permanent damage to organs, increased morbidity and tragic effects on childhood development, and reduction in adult productivity. The severe infection has also resulted to death [5].

Schistosomiasis control has been attempted in several ways: chemotherapy, vector elimination, improved sanitation and health education [6]. Chemotherapy has become the key tool in the global strategy against Schistosomiasis [7]. Although there is no vaccine, the disease can be treated and controlled with anti-schistosomal drugs which include PZQ oxamniquine, hycanthone and niridazole. Praziquantel (PZQ) is an isoquinoline derivative and is the drug of choice for all species of Schistosoma as an effective antischistosomal drug. It is the least expensive, easiest to use and most readily available of all [8]. It is also extremely effective against all schistosome species that are known to infect humans and is well-tolerated, making it suitable for mass treatment campaigns particularly in school-age children deworming programme which target a high-risk group for infection, and the most heavily infected segment of the population [9,10].

In 2014, WHO announced a 'roadmap' for the elimination of schistosomiasis as a public health problem in multiple African countries by 2020 and globally by 2025. This, in turn, inspired a global alliance of 22 partners including the WHO, The Bill and Melinda Gates Foundation, World Bank and major pharmaceutical companies to announce through the 2012 'London Declaration' a sustained program to 'control' schistosomiasis

by 2020 (http://unitingtocombatntds.org). Praziquantel use has increased over the years, not only in intensity but also in frequency. The acceptable dose of PZQ for treatment of *S. mansoni* ranges between 30 to 60 mg/Kg with an optimum dose ranging between 40 to 60 mg/kg. The dosage of below 30 mg/Kg is termed as sub-curative while that of above 60 mg/kg is overdose [11,12]. The WHO recommended treatment dose of PZQ is 40 mg/kg. Even though the efficacy of the drug at this dose is high, reported cure rates commonly range from 60 to 95%. A high proportion of infected population occurs in endemic areas like Kirinyaga County, Kenya where the major economic activity is irrigation farming. This exposes the community to fresh water snails that harbour the infectious schistosome parasite. Current treatment and control measures in Kenya target only school children which aim at curing or reducing the morbidity of Schistosomiasis. Infected school-age children are often physically and intellectually compromised by concurrent anaemia, attention deficits, learning disabilities, school absenteeism and higher dropout rates [13,14]. Continuous annual MDA of PZQ has been taking place in Kirinyaga County. Despite these interventions, the prevalence of Schistosomiasis has increased over the years from 47% in 2011 [15] to 53% in 2015 [16]. In addition, there is concern that continued PZQ use will likely result to drug resistance or reduced susceptibility due to drug pressure. This is evident in a study in Egypt where low cure rates in response to the standard dose of 40 mg/kg began to appear 10-15 years after mass scale treatment [17]. Studies to establish the efficacy and safety of up-scaled dosage to 60 mg/kg PZQ in Kirinyaga County are therefore justified.

2. MATERIALS AND METHODS

2.1 Ethical Concerns and Biosafety Issues

The proposed study was approved by the KEMRI Scientific Review Unit(SERU) approval number KEMRI/SER/CBRD/0162/3398. The study was conducted according to applicable regulatory requirements as per the Helsinki declaration and the KEMRI Scientific and Ethics Review Unit (SERU) approval. In addition to this, the study was carried out in compliance with the protocol, and Good Clinical Practice were observed. At the beginning of the study, meetings were organised with parents, teachers and earmarked communities whereby detailed information was provided by the research team about the aims, procedures, benefits and potential risks of the study. The study was explained to children before they were randomly selected and invited to participate. They received an information sheet and a consent form, which they were asked to return the following day with a signature of their parent/guardian and individual assent of less 4-17 years of age. Participation in the study was on voluntary terms and that an individual was free to withdraw from the study at any time. The selected children were registered and their age, sex and participation at the last MDA recorded.

2.2 Study Design

The study involved school going children and involved collection of samples for randomised controlled groups to determine if higher doses of PZQ 60 mg/kg would improve treatment efficacy of *S. mansoni* with an adequate safety profile, in comparison with the standard dosage of PZQ 40 mg/kg in school going children.

2.3 Study Site

The study was primarily conducted in Mianya Primary school (0°38'08.9"S 37°19'25.1"E) in Kirinyaga County central Kenya where *S. mansoni*, the causative agent of Schistosomiasis is endemic. Inhabitants of the study area are mainly subsistence farmers and fishermen. These communities depend on irrigation scheme water for domestic and social economic needs. The study area was selected based on preliminary evidence of water contact activities such as; rice farming, water collection for domestic use, bathing and swimming. The population in Mwea is estimated at 176,261 (Kenya Population Census, 2009) and *S. mansoni* prevalence is at approx. 53% [16].

2.4 Study Population

The study was conducted on school going children from Mianya Primary school in Kirinyaga County, Kenya - within the Mwea rice irrigation scheme - aged between 4 and 17 years. This group was chosen because school age children are heavily susceptible to infection by *S. mansoni* because of the school locality and water contact activities. They would therefore be the most appropriate to receive an increased dosage of PZQ and consequently determine the safety profile of the up-scaled dosage in this age group.

2.5 Sample Size

The sample size calculation was determined according to the equation for determining the sample size below [18]. The sample size required at each site was computed at approximately 80 patients per treatment group assuming the cure rate of the standard dose (40 mg/kg) is 60% and cure rates of PZQ at 60 mg/kg is 80% at 95% confidence, totalling to 160 study subjects. However, considering a drop out of about 20% due to loss to follow-up or medical grounds, this will result to 192 study participants.

2.6 Inclusion Criteria

The following individuals were selected for the study:- *Schistosoma mansoni* infected individuals of either sex aged between 4 -17 years harbouring at least 100 eggs per gram (epg) with written informed consent and were able and willing to be examined on follow-up visits who provided stool samples. Those who had satisfied the inclusion criteria were further tested for the following exclusion criteria.

2.7 Exclusion Criteria

Children of less than 4 years, with previous history of adverse reaction associated with PZQ, history of acute or chronic severe disease, use of any other medication that may affect the results of the trial (e.g. antibiotics) within the past week, History of treatment in the past 30 days with PZQ. The WHO and pharmaceutical sector consider treatment with PZQ as being safe for children as young as four years of age, below this age limit is not yet fully endorsed for 'off-label' use of PZQ in national control programmes settings [14,19]. Signs and symptoms of clinical malaria were determined and those considered to have clinical malaria were referred for treatment at a nearby clinic and excluded from the study.

2.8 Baseline Laboratory and Clinical Procedures

Stool: At baseline, each participant recruited in the study provided a stool sample where duplicate Kato Katz slides (2 slides) [20] was prepared in the field (using the 41.7 mg faecal template) from each stool sample. The prepared Kato slides in the field were subjected to quantitative microscopic examination for *S. mansoni* ova identification.

Blood: Venous blood sample of 3 ml was obtained from each school child for Hb level and eosinophil count. Hemoglobin reading of 11 g/L was considered as anaemia and that of 7 g/L as severe anaemia.

Weight: was measured at baseline using digital electronic balance.

2.9 Treatment with PZQ and Sample Collection

Two random groups were recruited and categorised into current treatment group (Group A) and up-scaled treatment group (Group B). Each individual of either group was diagnosed for *S. mansoni* by Kato-Katz technique at baseline. Those who fulfilled the inclusion and exclusion criteria for enrolment in the trial were randomised to receive treatment with PZQ within 7 days (+/-1 day). Those found to harbour the parasite in the first group (current treatment group) were treated with 40 mg/kg PZQ. In the second group (up-scaled), the infected individuals received 60 mg/kg PZQ. Appendix I, table 7 contains the dose chart of 40 mg/kg vs. 60 mg/kg. Efficacy of the 40 mg/kg versus 60 mg/kg PZQ was determined during follow up.The intensity of infection at Day 0 and Day 21 of patients given PZQ 60 mg/kg or 40 mg/kg was compared. The intensity of infection for positive individuals was categorised as light, moderate and heavy infections according to WHO [21] whereby; light (1–100 eggs per gram of faeces); moderate (101–400 epg) and heavy (>400 epg). Participants with positive *Schistosoma spp.* diagnosis who do not fulfill the inclusion and exclusion criteria was treated with the standard treatment of a single dose of PZQ 40 mg/kg. Patients diagnosed with other soil transmitted helminthes were treated with Albendazole after 21 days post-treatment.

Individual stool samples were obtained and prepared for Kato Katz quantitative microscopic examination for *S. mansoni* ova. Blood samples were obtained by venipuncture in heparinised syringes after 21 days post-treatment for blood haemoglobin, eosinophil counts and biochemical analysis.

2.10 Determination of Efficacy of 60 mg/kg from 40 mg/kg PZQ

Two stool samples were collected from each participant from which thick smear was prepared from each stool specimen, using 42-mg plastic templates. The prepared Kato slides in the field were subjected to quantitative microscopic

examination for *S. mansoni* ova identification. The cure rate was described as being complete cure, to define negative stools for *Schistosoma* eggs and partial cure to describe reduced egg count with the two dosages after three weeks. Cure rate at 21 days after treatment for the PZQ 40 mg/kg and PZQ 60 mg/kg groups was estimated as the proportion of subjects with a negative result at 21 days after treatment. Egg reduction rate at 21 days after treatment for the 40 and 60 mg/kg groups was estimated through the following formula:

[1 - (epg2 / epg1) x 100]

Where: epg1 and epg2 are the geometric mean of log10 transformed (x+1) numbers of eggs per gram of faeces at the baseline and the Day 21 post-treatment respectively.

2.11 Determination of Morbidity

2.11.1 Anaemia determination

Whole blood was obtained in a Hemocue cuvette from each school child and examined for Hb by a digital hemoglobinometer (Hemocue). Children with Hb of less than 11 g/dL were considered anaemic (WHO, 2011).

2.11.2 Blood cell count

A thin smear blood film was prepared using a part of each venous blood sample from each child and stained with Giemsa as described by Cheesbrough [22]. Differential cell count was performed on 100 white blood cells in each film and the numbers of each type of white blood cells expressed as a percentage of the total 100 white blood cells. Eosinophilia was defined as eosinophils above 7% of white blood cells on the blood film (https://emedicine.medscape.com/article/2085133-overview#showall).

2.12 Determination of Safety (Adverse Events)

Occurrence and severity of adverse events at 4 hrs, Day 1 and 21 days after treatment was collected. To determine the safety of the up-scaled dosage, data was gathered on the occurrence of adverse events (AEs) on Day 0 at 4 hrs and Day 1 and Day 21 post-treatment. An AE was defined as any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal or investigational product, whether or not related to that product. Treatment with PZQ was done in the morning of Day 0 and the research team remained at the treatment centre until 18.00 hr. Participants administered with PZQ was observed for at least 4 hrs before leaving. All participants enrolled in the study were assessed after treatment for the following signs and symptoms: abdominal pain, nausea, vomiting, diarrhoea, anorexia, fever, headache, dizziness and allergic reaction. Each symptom was graded as described in Table 1. Each participant's data of adverse events included date and time of onset, duration, severity, seriousness and relationship to PZQ treatment. This was repeated on the following day (Day 1), that is, 24 hrs post-treatment to assess to see if they experience adverse events.

2.13 Statistical Analysis

Baseline characteristics were compared using Student's t-test and Chi-square. In the efficacy evaluation, cure rates were compared using Chi-square test. The egg reduction rate was assessed by determining geometric mean egg counts (GMECs) at baseline and day 21. Analysis of variance (ANOVA) was utilised to determine if there was a difference in the mean log egg counts between the two groups at baseline and day 21. For safety assessment,

Table 1. Severity grading for other Adverse Events post-treatment

Grade 1	**Mild.** Transient or mild discomfort (<48hs); no medical intervention/therapy required
Grade 2	**Moderate.** Mild to moderate limitation in activity – some assistance may be needed; no or mini al medication intervention/therapy required
Grade 3	**Severe.** Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalisation possible
Grade 4	**Life threatening.** Extreme limitation I activity, significant assistance required; significant medical intervention/therapy required, hospitalisation or hospice care probable

Chi-square test was used to determine if the prevalence of adverse events was significantly different between the treatment groups.

3. RESULTS

3.1 Prevalence and Intensity of Infection of *S. mansoni*

The study had a total of 192 pre-primary and primary schools going children of ages 4 -17 years. Of the infected population, 48.95% were boys while 51.05% were girls. The mean age of participants with *S. mansoni* was 10.5±3.1 years and the mean egg per gram (epg) was 252.1. The point prevalence of schistosomiasis of the school children after screening was 52.8%. The overall infection intensity was categorised as low infection (1-100 epg) 76 (40%); moderate infection (101-400 epg) 79 (41.58%) and heavy infection (>400 epg) 35 (18.42%) as observed on Fig. 1. The baseline mean egg count among positive children was 270.65±62.58 for 40 mg/kg and 233.56±34.89 for 60 mg/kg and mean Hb levels were 10.96±0.15 and 11.19±0.10 g/dl respectively as shown in Table 2.

3.2 Efficacy and Morbidity of 40 mg/kg and 60 mg/kg PZQ

There was a significant reduction of *S. mansoni* infections in both treatment groups as observed in Table 4. Parasitological cure rates at Day 21 post-treatment was 92% for 40 mg/kg and 94% for 60 mg/kg as observed in Table 3. There was no significant difference observed in cure rates after treatment in sex and age group in both treatment groups ($p>0.05$). The cure rate of PZQ in relation to infection intensity differed significantly. A higher cure rate in light and moderate infected participants was observed when compared to heavy infected participants. There was no significant difference in egg reduction rate at day 21 post-treatment for both 40 mg/kg and 60 mg/kg groups as observed in Fig. 1. The percentage reduction rate was 96% for both 40 mg/kg and 60 mg/kg respectively. Hemoglobin levels at 21 days post-treatment were 11.26 and 11.34 g/dl respectively but the difference was not significant. Prevalence of anaemia among the two dose groups showed no significant difference at baseline and after treatment as observed in Table 5.

Eosinophil levels showed a significant decrease after treatment in both treatment groups although no difference was observed between the treatment groups. In addition, there was a huge reduction of eosinophil levels in both treatment groups, eosinophilia (eosinophils ≥7%) was still high at 88% after treatment in both treatment groups as shown in Table 3.

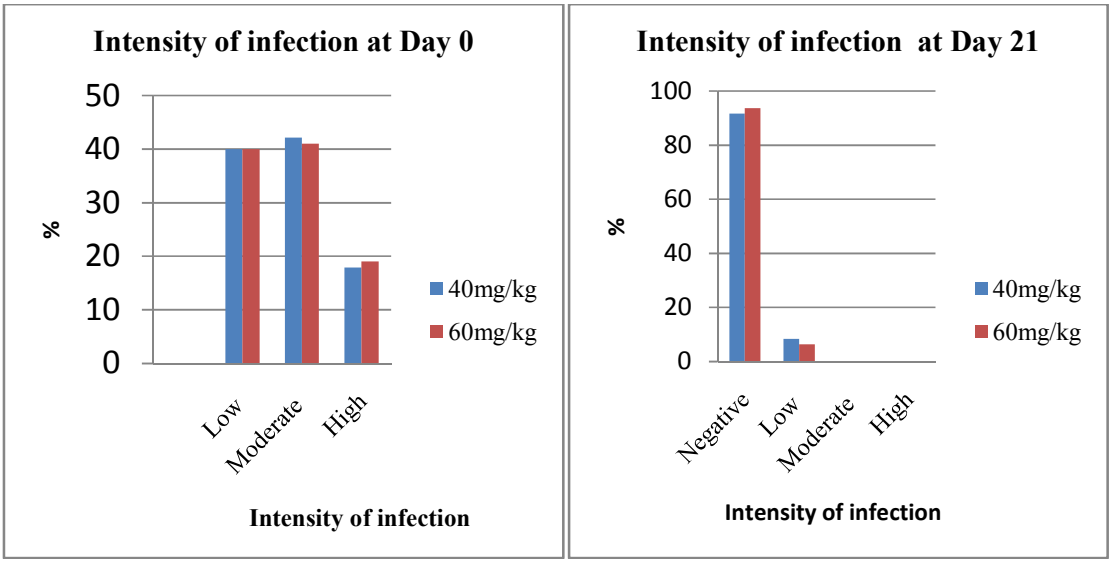

Fig. 1. Intensity of infection at baseline and 21 days post reatment. Low infection (1-100 epg); moderate infection (101-400 epg) and heavy infection (>400 epg)

Table 2. Baseline assessment of 40 and 60 mg/kg PZQ

Parameters		40 mg/kg	60 mg/kg	P value*
Sex	Male	48	45	0.16
	Female	47	50	
EPG mean±SEM		270.65±62.58	233.56±34.89	0.33
Geometric EPG (CI 95%)		2.01 (1.08 – 3.71)	1.98 (1.08 – 3.23)	0.33
Hemoglobin mean±SEM		10.96±0.15	11.19±0.10	0.052
Anaemia		44%	42%	
Eosinophil count		12.67±0.45	13.11±0.36	0.39
Eosinophilia (<7%)		96%	100%	

*n: number of children; EPG: egg per gram of stool; SEM: standard error of the mean; CI: confidence interval; *Level of significance was set at 0.05*

Table 3. Day 21 post-treatment assessment of 40 and 60 mg/kg PZQ

Parameters	40 mg/kg	60 mg/kg	P value*
EPG mean±SEM	1.89±0.81	1.58±0.78	0.7
Cure rate	92%	94%	
Egg reduction rate	96%	96%	
Geometric EPG (CI 95%)	0.08 (0.00 – 1.78)	0.08 (0.00 – 1.78)	0.7
Hemoglobin mean±SEM	11.26±0.13	11.34±0.09	0.062
Anaemia	37.9%	37.9%	
Eosinophil count mean±SEM	12.67±0.45	10.05±0.27	0.25
Eosinophilia (<7%)	88%	88%	

*n: number of children; EPG: egg per gram of stool; SEM: standard error of the mean; CI: confidence interval; *Level of significance was set at 0.05*

Table 4. Efficacy of PZQ at 40 and 60 mg/kg

Group	Pretreatment EPG mean ±SEM	Post-treatment EPG mean ±SEM	P* value	CI (95%)
A (40 mg/kg) n=95	270.65±62.58	1.89±0.81	0.0001	145.46 - 392.05
B (60 mg/kg) n=95	233.56±34.89	1.58±0.78	0.0001	163.78 – 300.18

*n: number of children; EPG: egg per gram of stool; SEM: standard error of the mean; CI: confidence interval; *Level of significance was set at 0.05*

3.3 Safety of 40 mg/kg and 60 mg/kg PZQ

Most frequent adverse events observed in the treatment groups were abdominal pain, headache and nausea whereas the least occurring were anorexia, fever and allergic reaction. No significant differrence in the adverse events was observed between the treatment groups, however the cumulative adverse events (Subjects with at least one adverse event) was higher in 60 mg/kg than 40 mg/kg (Tables 5 and 6).

4. DISCUSSION

In the present study, we have established that the prevalence of 53.2% of *S. mansoni* infection determined in the study is considered high according to WHO classification [21]. This confirms the previous findings that the area is highly endemic to *S. mansoni* [16]. The socio-economic demographics of this region explains why despite the ongoing mass drug administration (MDA) interventions, prevalence has not reduced. This can also be attributed to the decline in susceptibility of the parasite to the drug, exclusion of adult population treatment in ongoing MDA which may result to high re-infection rate. However, it was noted that majority of the participants had low to moderate infection rate which accounted to over 80% of the overall infection intensity.

The study was conducted in Kirinyaga County which is characterised by low socio-economic status and poor hygiene conditions such as lack of clean water supply, latrines and sewage disposal facilities. The target group was school going children who come from families with river water contact activities such as; rice farming, river water collection for domestic use, bathing and swimming.

Table 5. Severity of adverse events of 40 mg/Kg and 60 mg/Kg at 4 hrs post-treatment

Parameter	40 mg/kg n = 95				60 mg/kg n = 95				P value*
	Total n (%)	Mild n	Mod n	Severe n	Total n (%)	Mild n	Mod n	Severe n	
Nausea	34 (36)	14	9	11	36 (38)	18	15	3	
Fever	2 (2)	2	0	0	2 (3)	2	1	0	
Headache	36 (38)	18	14	4	34 (38)	22	7	5	
Allergic reaction	2 (2)	2	0	0	4 (4)	2	1	1	
Abdominal Pain	41 (43)	27	12	2	42 (44)	26	10	6	
Vomiting	6 (6)	4	2	0	10 (11)	6	2	2	
Diarrhoea	24 (23)	15	8	1	22 (23)	13	9	0	
Anoxia	1 (1)	1	0	0	2 (2)	1	1	0	
Drowsiness	9 (9)	8	1	0	11(12)	8	1	2	
Cumulative adverse events		68%			72%				0.15

*n: number of patients with adverse events after 4 hrs post-treatment; * Level of significance was set at 0.05.*

Table 6. Severity of adverse events of 40 mg/Kg and 60 mg/Kg at 24 hrs post-treatment

Parameter	40 mg/kg n = 95				60 mg/kg n = 95				P value*
	Total n (%)	Mild n	Mod n	Severe	Total n (%)	Mild n	Mod n	Severe n	
Nausea	28 (29)	18	10	0	35 (37)	18	15	3	
Fever	12 (13)	6	4	2	11 (12)	2	1	0	
Headache	40 (42)	28	7	5	38 (40)	22	7	5	
Allergic reaction	12 (13)	10	2	0	16 (17)	2	1	1	
Abdominal Pain	38 (40)	24	10	4	39 (41)	26	10	6	
Vomiting	4 (4)	4	0	0	8 (8)	6	2	2	
Diarrhoea	22 (23)	13	7	2	21(22)	13	9	0	
Anoxia	6 (6)	4	2	0	9 (9)	1	1	0	
Drowsiness	9 (9)	9	0	0	11(12)	8	1	2	
Cumulative adverse events		53%			59%				0.17

*n: number of patients with adverse events after 24 hrs post-treatment; * Level of significance was set at 0.05.*

Participants administered with up-scaled dosage of 60 mg/kg PZQ had a cure rate of 94% and egg reduction rate of 96%. Participants administered with the standard dose of 40 mg/kg had a cure rate of 92% while the egg reduction rate remained at 96%. Both treatment groups were shown to be within the usual range of between 63 and 95% [23,24].

Low Hb levels were recorded at baseline and wererelative to the intensity of infection. The baseline Hb levels for both 40 mg/kg and 60 mg/kg treatment groups of 11.66 g/dl and 11.19 g/dl respectively and post-treatment levels of 11.26 g/dl and 11.34 g/dl respectively showed there was no observed difference. There was a reduction of participants with anaemia in both treatment groups. *Schistosoma mansoni* infection has been shown to cause significant loss of blood and iron leading to anaemia. Treatment with both dosages of PZQ which led to a significant reduction in infection may be attributed to the reduced anaemic status. Baseline eosinophil count established over 96% eosinophilia of the study participants. There was a significant reduction of eosinophils after treatment in both treatment groups where eosinophilia reduced to 88% in both treatment groups with no significant difference observed between the groups ($p>0.05$). The high eosinophil levels may be due to immunological cell response to *S. mansoni* infection where they play important role in host defence against helminth infections. The exact roles of

eosinophils in schistosomiasis regarding immunopathology remains unclear but it is believed that eosinophils participate in Ab-dependent protective immune and acute schistosomiasis patients have increased levels of circulating eosinophils [25].

Adverse events (AE) in both treatment groups showed high prevalence which were generally mild. The occurrence of these AE may be explained by drug effects in the body, however, it can also be attributed to parasitic infections. [26]. Most of the participants (40%) in both treatment groups experienced lower abdominal pain as the major adverse event. Other events were transient and mild but none reported severe reactions that required special treatment with most of them clearing after 24 hrs after drug administration. This is in agreement with other studies conducted among school children in other endemic regions in Kenya which concluded that abdominal pain to be the most frequently reported AE after treatment with PZQ [27,28]. Other frequently observed AE includes headache and nausea which have previously been reported by Li et al. [26]. In comparing the cumulative adverse events between the groups, a higher proportion (74%) of participants in the 60 mg/kg group experienced at least one or more adverse events compared to the standard dose (68%). Administration of larger doses of praziquantel has been attributed to higher reports of adverse events [1].

5. CONCLUSION

This study concludes that the up-scaled dosage of 60 mg/kg PZQ in mass chemotherapy campaigns of *S. mansoni* treatment offers no significant advantage over the WHO recommended 40 mg/kg. Morbidity markers in both dosages showed a significant reduction in eosinophil. No significant difference was observed in Hb levels post-treatment in both dosages. This study observed that the high prevalence of schistosomiasis in Kirinyaga County, Kenya amid continuous MDA programmes for only school children in the region possess a potential risk of developing PZQ resistance.

6. RECCOMENDATION

We recommend the continued use of 40 mg/kg dosage given the treatment with 60 mg/kg did not translate into a significant advantage in efficacy in this study. Given that Kirinyaga county has been under Kenya National School-Based Deworming Programme since 2009, the prevalence of schistosomiasis has not reduced. This trend warants for drastic public health and enviromental intervention measures such as vector/snail control, basic sanitation, clean water supply and health education. Since these MDA programmes target only school children, these leaves most of the adult population untreated thereby resulting into high reinfection rates. We, therefore, recommend entire community MDA treatment.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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APPENDIX I

Table 7. Number of praziquantel tablet to be given to subjects under the 40 mg/kg and 60

40 mg/kg regimen		60mg/kg regimen	
(kg)	**Number of tablets**	**(kg)**	**Number of tablets**
13-15	1	10	1
16-18	$1^1/_4$	10-12.5	$1^1/_4$
19-22	$1^1/_2$	12.6-15	$1^1/_4$
23-25	$1^3/_4$	15.1-17.5	$1^1/_2$
26-29	2	17.6-20	$1^3/_4$
30-33	$2^1/_4$	20.1-22.5	2
34-37	$2^1/_2$	22.6-25	$2^1/_4$
38-40	$2^3/_4$	25.1-27.5	$2^3/_4$
41-44	3	27.6-30	3
45-48	$3^1/_4$	30.1-32.5	$3^1/_4$
49-52	$3^1/_2$	32.6-35	$3^1/_2$
53-55	$3^3/_4$	35.1-37.5	$3^3/_4$
56-59	4	37.6-40	4
60-63	$4^1/_4$	40.1-42.5	$4^1/_4$
64-66	$4^1/_2$	42.6-45	$4^1/_2$
67-70	$4^3/_4$	45.6-47.5	$4^3/_4$
71-75	5	47.6-50	5
		50.1-52.5	$5^1/_4$
		52.6-55	$5^1/_2$
		55.1-57.5	$5^3/_4$
		57.6-60	6

In this table, 13-15 means 13.0 kg to 15.9 kg. The same applies to other weight ranges

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