

Original Research Article

Identification of the adequate frequency for Praziquantel 600 mg mass administration in Schistosomiasis high transmission areas in Senegal River Basin.

ABSTRACT

Introduction: Urinary and intestinal schistosomiasis remains a major cause of morbidity and mortality in various countries, especially in Sub-Saharan Africa. However, the importance of periodic administration of *Praziquantel 600 mg* has been confirmed by the WHO. In the Senegal River Delta, intensity and transmission rates remain high despite several yearly mass treatment campaigns.

Place and Duration of Study: This study was carried out in Richard Toll (Saint-Lois, Senegal) from February 2013 to November 2015.

Aim: The objective of this study was to determine the adequate frequency of mass administration of *praziquantel 600 mg* in the high transmission areas of Senegal River Basin.

Methods: Four villages were randomly divided into two groups (control and study group) comprised of two villages each: a control group of two and an action group. The study population consisted of children of school age (5 to 14 year old) identified in the selected villages. A first mass administration operation was carried out in the 4 villages in order to ensure an identical starting point in the entire study population all of them. Six (06) months later, a first baseline survey provided the prevalence of schistosomiasis in the 4 villages. It was followed by a second mass administration operation in the study group two intervention villages only. A second survey was performed after six months to compare the effects of a bi annual mass administration with that those of an annual mass administration.

Results: In respect to of *Schistosoma haematobium*, prevalence was statistically lower after intervention: 10.8% against 35% ($p < 10^{-3}$). The same effect was noted for in respect of *Schistosoma mansoni*: 7.9% against 23.8% ($p = < 10^{-3}$). The prevalence of *Schistosoma haematobium* at 6 months after the second drug administration was 0.0% while that of *Schistosoma mansoni* was.....survey carried out 6 months after the second mass administration campaign showed a zero prevalence of *Schistosoma haematobium* in the intervention villages. In the control villages, the prevalence rate was still high after the mass administration campaign (indicate values). Our results show that a biannual administration

31 of this molecule reduced by 100% the prevalence of *S. haematobium* and by more than 75%
32 that of *S. mansoni*.

33 **Conclusion:** This research suggests that, in order to eliminate schistosomiasis for
34 elimination of schistosomiasis in the high transmission areas of the Senegal River Basin,
35 praziquantel 600 mg mass administration could must be renewed every 6 month months.

36 **Keywords:** Schistosomiasis, Praziquantel mass drug administration frequency, Senegal River
37 Basin.

38 1. INTRODUCTION

39 Urinary and intestinal schistosomiasis remain a major cause of morbidity and mortality in
40 various countries, especially in Sub-Saharan Africa. [1]. However, there has been a spectacular
41 drop in their respective levels of prevalence in many countries over the past few years. For
42 example, in China and Egypt, sustained efforts based on the use of *Praziquantel* (PZQ) have
43 led to a 90% reduction and Morocco has eradicated urinary schistosomiasis in 2005 [2].
44 These encouraging results based on mass drug administration of the population at risk with
45 praziquantel have led the WHO to maintain chemoprevention with this molecule among its
46 main strategies against these two parasitic diseases [3]. Indeed, PZQ is a drug of choice in
47 tackling the infections caused by the involved parasites because it entails minimal side
48 effects, is highly effective and affordable [4]. However, surveys carried out in various
49 ecological areas with very diverse epidemiological features have shown that mass treatment
50 of affected populations does not prevent re-infection and a return to initial levels of infection
51 within 8 to 12 months [5]. It has also been demonstrated that re-administration at regular
52 intervals makes it possible to reduce the intensity of reinfestation and parasite load and also
53 to maintain a low level of infection even where reinfection has been quick [5]. Hence, the
54 need to consider an adequate periodicity for mass administration towards the an eradication
55 of these diseases is a necessity. The importance of periodic administration has been
56 confirmed by the WHO [6]. The current directives prescribe a mass treatment every 12
57 months in high risk areas (prevalence rate equal to or higher than 50%) and every 24 months
58 in moderate risk areas (10% to 40% prevalence rate) [7]. However, it must be noted that
59 these directives are not complied with in many countries as the original prevalence rates is
60 often obtained 6 to 12 months after the interventions and, worse, that the prevalence rates go
61 back to the same levels 6 to 12 months after the interventions. That is why amendments were

made in 2012 to suggesting the need for biannual mass treatment that mass treatment be implemented twice a year (every 6 months). Nevertheless, 5 to 6 years of preventive chemotherapy at the current frequency has showed the prevalence rates still remain high where, after 5 to 6 years of preventive chemotherapy at the current frequency, the prevalence rates remain high [8]. In the Senegal River Delta (BFS), intensity and transmission rates remain high despite several yearly mass treatment campaigns [6]. Our view is that the yearly mass administration campaigns might not be adequate for the goal of eradicating schistosomiasis and that mass treatment every 6 months might provide better results. To support that view, we have carried out this study comparing the prevalence rates of bilharziosis in various sites within a high transmission ecological area where mass treatment was performed at different intervals. The objective was to determine the adequate frequency of mass administration of praziquantel 600mg in the Senegal River Basin by performing mass drug administration at different intervals.

2. METHODS

2.1. Duration and Place of Study

The study was carried out from February 2013 to November 2015 in the Richard Toll Health District in the Département de Dagana (Senegal) on the left bank of the Senegal River. Richard Toll is located about 100 km east of Saint Louis and 374 km from Dakar. The 2014 population survey estimated its population at 60 127 inhabitants.

2.2. Sample Design and Sample Size

This is a prospective controlled study with a descriptive aim, carried out over a 3 year period. The area studied consists of 4 villages randomly selected in the area of Richard Toll where transmission is high. The selection was made taking into account the following criteria: presence of a permanent water source within 5 km; high prevalence of bilharziosis (urinary and intestinal) according to data collected by the health district and the presence of a public or coranic school. The 4 villages finally selected were: Didiéry, Keur Mbaye, Sandiéry and Gueum Yalla. These villages were randomly divided into two groups: a control group of two and a study group an intervention group. The study population consisted of children of school age (5 to 14 year old) identified in the selected villages. The minimum population size required for random sampling was estimated at 224 individuals based on the following

formula: $n = P (1-P) Z^2 \alpha / i^2$ with P = average prevalence of bilharziose estimated at 70% ; i = desired accuracy set at 6% and $Z\alpha = 1,96$ for $\alpha = 5 \%$. The sample was rounded off at 240, meaning 60 children per village.

2.3. Survey Procedures

After selecting the villages, a first mass administration operation was carried out in the 4 villages in order to ensure an identical starting point in all of them. Six (06) months later, a first baseline survey provided the prevalence of schistosomiasis in the 4 villages. It was followed by a second mass administration operation in the two study intervention villages only. A second survey was performed after six months to compare the effects of a bi annual mass administration with those that of an annual administration (table 1).

Table 1. Study plan

Activities Sampled Villages	PZQ mass administration	Morbidity survey	PZQ mass administration	Morbidity survey
Study Intervention villages (02)	X	X	X	X
Control villages (2)	X	X		X

2.4. Data collection

Individual sheets were used for demographic data as well as faeces and urine analysis to establish the prevalence and infestation rates of bilharziosis (urinary and intestinal. For urinary bilharziosis, the parasite load (in average number of eggs/10ml of urine) was determined by a direct counting of *S. haematobium* eggs after filtration through Millipore paper of 10ml of urine. The intensity of the infection was broken down into 3 classes of parasite density [10]: no infestation (no eggs in the 10ml of urine), low infestation (< 50 eggs/10 ml) and massive infestation (≥ 50 eggs/10 ml). For intestinal bilharziosis, the parasite load was determined using the Kato-katz technique whereby the number of *Schistosoma mansoni* eggs per gram of faeces is multiplied 24. Four classes of parasite density were determined [10]: no infestation (no eggs in the faeces), low infestation (1- 99 eggs/g), moderate infestation (100 - 399 eggs/g) and massive infestation (≥ 400 eggs/g). The

prevalence was correlated to the provision or not of Information, Education and Communication (IEC) sessions on the disease. These sessions were held in one study action village and one control village.

2.5. Ethical approval

This study has been was given the ethical green light by the national ethical committee (Comité National d’Ethique et de Recherche en Santé). The Ministry of Health of the Republic of Senegal has also authorized it. On site, In the study site, information and advocacy sessions were held, with the support of health authorities at all levels in order to obtain the informed consent of village chiefs, parents and guardians of the children involved and school authorities. Also, as per the directives of the WHO, the local health authorities organized the mass administration operations.

2.6. Data analysis

The data were collected in Excel format. Their univariate, bivariate and multivariate analysis was were performed using version 12 of the STATA software. The qualitative variables were described in terms of population and percentage of the data entered. The comparisons were made using Pearson’s Chi square test or Fisher’s exact test according to the applicability. The significance threshold of these tests was set at 5%. The quantitative variables were presented in terms of average and standard deviation. The bivariate and multivariate analysis were was done using Fisher’s F test (ANOVA) after checking it’s applicability. Where the conditions for its applicability were not met, Kruskal-Wallis or Man Withney’s tests were used.

3. RESULTS

Table 2. Study population

		Intervention villages		Control villages		Total
		First survey	Second survey	First survey	Second survey	
Gender	Male	58	60	60	60	238
	Female	62	60	60	60	242

Age	5 to 10 years	52	68	98	43	261
	> 10 years	68	52	22	77	219
Total		120	120	120	120	480

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139 The populations involved in the two surveys were similar irrespective in respect to of age and
 140 gender (sex ration = 0.9). No significant difference was noted (Table 2).

141 **Table 3. Overall prevalence of *Schistosoma heamatobium* in relation to intervention**

Time	Before intervention	After intervention	p (Fisher)	IC
Negative patients	156 (65%)	214 (89.2%)		18.96 – 41.34
Positive patients	84 (35%)	26 (10.8%)		6.87 – 14.72
Total	240	240	p <10⁻³	

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143 In respect to of *Schistosoma haematobium*, prevalence was statistically lower after
 144 intervention (6 months after the first drug administration second mass administration
 145 operation 6 months after the first one): 10.8% versus against 35% (p <10⁻³) (table 3). The
 146 same trend was noted for in respect of *Schistosoma mansoni*: 7.9% versus against 23.8% (p
 147 = <10⁻³) (tableau 4).

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149 **Tableau 4. Overall prevalence of *Schistosoma mansoni* during the study periods in**
 150 **relation to intervention**

Time	Before treatment intervention	After treatment intervention	p (Fisher)	IC
Negative patients	183 (76.2%)	221 (92.1%)		18.32 – 29.07
Positive patients	57 (23.8%)	19 (7.9%)		4.48 – 11.312
Total	240	240	$p < 10^{-3}$	

Table 5. Comparison of overall prevalence of *Schistosoma haematobium* in the study intervention villages and control villages

Intervention villages	First survey	Second survey	p (Fisher)
Negative patients	80 (66.7%)	120 (100%)	
Positive patients	40 (33.3%)	0 (0%)	
Total	120	120	$p < 10^{-3}$
Control villages			
Negative patients	76 (63.3%)	94 (78.3%)	
Positive patients	44 (36.6%)	26 (21.7%)	

Total	120	120	p = 0.011
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The prevalence survey carried out 6 months after the second mass drug administration campaign showed a zero (0.0%) prevalence of *Schistosoma heamatobium* in the intervention villages. In the control villages, the prevalence rate was still high (...Value) after the mass administration campaign (table 5).

Tableau 6. Comparison of overall prevalence of *Schistosoma mansoni* in intervention villages and control villages

Intervention villages	First survey	Second survey	p (Fisher)
Negative patients	81 (67.5%)	113 (94.2%)	
Positive patients	39 (32.5%)	07 (5.8%)	
Total	120	120	p <10⁻³
Control villages			
Negative patients	102 (85%)	108 (90%)	
Positive patients	18 (15%)	12 (10%)	
Total	120	120	p = 0.242

Regarding *S. mansoni*, the prevalence survey performed 6 months after the first mass drug administration campaign showed a 5.8% prevalence rate versus against 32.5% in the intervention villages ($p < 10^{-3}$) while no significant drop was recorded in the control villages ($p = 0.242$).

A multivariate logistic regression analysis established the protective effect of the biannual mass drug administration campaign in the intervention villages at 82% ($ORa = 0.18$, $p < 10^{-3}$) for urinary bilharziosis and 79% ($ORa = 0.21$, $p < 10^{-3}$) for intestinal bilhaziosis. IEC sessions generated a 98% ($ORa = 0.02$, $p < 10^{-3}$) protective effect.

The intensity of infestation presented in tables 7 and 8 showed that the decline in the percentage of low infestations and massive infestation is higher in intervention villages as well as for both *S. haematobium* and *S. mansoni*.

Table 7. Comparison of intensity of infestation by *S. haematobium* in intervention villages and control villages

Intervention villages	First survey	Second survey	p (Fisher)
Low infestation	35 (29.2%)	00 (0%)	p <10 ⁻³
Massive infestation	05 (4.2%)	00 (0%)	
No infestation	80 (66.6%)	120 (100%)	
Total	120	120	
Control villages			
Low infestation	43 (35.8%)	25 (20.8%)	

Massive infestation	01 (0.8%)	01 (0.8%)	
No infestation	76 (63.3%)	94 (78.4%)	
Total	120	120	p = 0.0926

Table 8. Comparison of intensity of infestation by *S. mansoni* in intervention villages and control villages

Intervention villages	First survey	Second survey	p (Fisher)
Low infestation	12 (10%)	01 (0.8%)	
Moderate infestation	19 (15.8%)	05 (4.2%)	
Massive infestation	08 (6.7%)	01 (0.8%)	
No infestation	81 (67.5%)	113 (94.2%)	
Total	120	120	p < 0.0025
Control villages			
Low infestation	12 (10%)	09 (7.5%)	

Moderate infestation	05 (4.2%)	03 (2.5%)	
Massive infestation	01 (0.8%)	00 (0%)	
No infestation	102 (85%)	108 (90%)	
Total	120	120	p = 0.145

For moderate infestation by *S. mansoni*, the impact is very low in control villages compared to **intervention** villages (table 8).

4. Discussion

In spite of **many** decades of interventions, urinary and intestinal schistosomiasis remain endemic and still constitute major causes of mortality and morbidity in many countries, especially in sub-Saharan Africa. Having drawn little attention for so long, they belong in the group of neglected tropical diseases. But the significant progresses achieved in the prevention of infectious diseases such as malaria make it possible to envisage their possible elimination in some regions. This has led the international community to give more attention to Neglected Tropical Diseases, including schistosomiasis.

In its latest guidebook on combating soil-transmitted helminth infections [8], the WHO insist that mass administration of effective drugs, periodically carried out on school age children could contribute **to in** achieving **of** millennium development goals, including poverty reduction. The various types of schistosomiasis **most** frequently affect school age children and expose them **to** serious long term complications. Implementing this strategy using praziquantel, an effective drug, is therefore one of the ways of combatting them. However, some limitations have been identified. Indeed, the WHO prescribe mass administration every 12 months in high risk areas (prevalence rate of 50% or more) and every 24 months in moderate risk areas (prevalence rate between 10% and 49%) [7]. But assessments carried out 8 to 10 months after mass administration operations show prevalence rates almost unchanged

due to reinfestation [5]. In the same document [7], it is indicated that the strategy should be assessed after 4 or 5 years to adjust the administration frequency. The data collected in Richard Toll suggest that after years of annual mass administration, the prevalence levels remain high. Based on that observation, our study measured the impact of a biannual administration of praziquantel to children of school age on the prevalence of schistosomiasis compared to the current strategy (annual administration). Our results show that a biannual administration of this molecule reduced by 100% the prevalence of *S. haematobium* and by more than 75% that of *S. mansoni*. This clearly demonstrates the usefulness of this new approach. Various studies are currently experimenting biannual administration to ascertain the usefulness of this new strategy, notably in Côte d'Ivoire, Mozambique and Tanzania [11]. The eradication of these diseases will probably require a combination of such approaches **as with** the control of molluscs, an improvement of the environment and education for behaviour change. In our study, we also analysed the addition of Information, Education and Communication sessions on schistosomiasis in the strategy. The data collected indicate a 98% protective effect. **The other should read publications on research work done in Cameroon on praziquantel impact on schistosomiasis eg: Nkengazong et al., 2010, 2013; Tcheum heunte et al., 200...etc) in order to have more introduction and discussion informations**

A study carried out in Uganda showed that acceptance of mass administration is easier in populations which have some knowledge of the mode of transmission and prevention of schistosomiasis [12]. This shows the need to combine strategies whose effectiveness is proven in order to effectively combat schistosomiasis.

5. CONCLUSION

This research suggests that, for elimination of schistosomiasis in the high transmission areas of Senegal River Basin, *praziquantel 600 mg* mass administration must be renewed every 6 **mounth month**.

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