

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 Subsaharan 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: 4 villages were randomly divided into two groups: 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 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 intervention villages only. A second survey was performed after six months to compare the effects of a bi annual mass administration with those of an annual administration.

Results: In respect of *Schistosoma haematobium*, prevalence was statistically lower after intervention: 10.8% against 35% ($p < 10^{-3}$). The same was noted in respect of *Schistosoma mansoni*: 7.9% against 23.8% ($p = < 10^{-3}$). The prevalence 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. 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*.

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 months.

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

1. INTRODUCTION

Urinary and intestinal schistosomiasis remain a major cause of morbidity and mortality in various countries, especially in Sub-Saharan Africa. [1]. However, there has been a spectacular drop in their respective levels of prevalence in many countries over the past few years. For example, in China and Egypt, sustained efforts based on the use of *Praziquantel* (PZQ) have led to a 90% reduction and Morocco has eradicated urinary schistosomiasis in 2005 [2]. These encouraging results based on mass drug administration of the population at risk with *praziquantel* have led the WHO to maintain chemoprevention with this molecule among its main strategies against these two parasitic diseases [3]. Indeed, PZQ is a drug of choice in tackling the infections caused by the involved parasites because it entails minimal side effects, is highly effective and affordable [4]. However, surveys carried out in various ecological areas with very diverse epidemiological features have shown that mass treatment of affected populations does not prevent re-infection and a return to initial levels of infection within 8 to 12 months [5]. It has also been demonstrated that re-administration at regular intervals makes it possible to reduce the intensity of reinfestation and parasite load and also to maintain a low level of infection even where reinfection has been quick [5]. Hence, the need to consider an adequate periodicity for mass administration towards an eradication of these diseases is a necessity. The importance of periodic administration has been confirmed by the WHO [6]. The current directives prescribe a mass treatment every 12 months in high risk areas (prevalence rate equal to or higher than 50%) and every 24 months in moderate risk areas (10% to 40% prevalence rate) [7]. However, it must be noted that these directives are not complied with in many countries and, worse, that the prevalence rates go back to the same levels 6 to 12 months after the interventions. That is why amendments were made in 2012 to suggest that mass treatment be implemented twice a year (every 6 months) 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.

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 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: [9] : $n = \frac{P(1-P)Z^2\alpha}{i^2}$ 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 intervention villages only. A second survey was performed after six months to compare the effects of a bi annual mass administration with those of an annual administration (table 1).

Table 1. Study plan

Activities Villages	PZQ mass administration	Morbidity survey	PZQ mass administration	Morbidity survey
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 action village and one control village.

2.5. Ethical approval

This study has been 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, 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 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 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	

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

Table 3. Overall prevalence of *Schistosoma haematobium* 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	$p < 10^{-3}$	

In respect of *Schistosoma haematobium*, prevalence was statistically lower after intervention (second mass administration operation 6 months after the first one): 10.8% against 35% ($p < 10^{-3}$) (table 3). The same was noted in respect of *Schistosoma mansoni*: 7.9% against 23.8% ($p = < 10^{-3}$) (tableau 4).

Tableau 4. Overall prevalence of *Schistosoma mansoni* in relation to intervention

Time	Before intervention	After 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 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	$p = 0.011$

The prevalence 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 (table 5).

154 **Tableau 6. Comparison of overall prevalence of *Schistosoma mansoni* in intervention**
 155 **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	$p = 0.242$

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

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

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

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

Intervention villages	First survey	Second survey	p (Fisher)
Low infestation	35 (29.2%)	00 (0%)	
Massive infestation	05 (4.2%)	00 (0%)	
No infestation	80 (66.6%)	120 (100%)	
Total	120	120	$p < 10^{-3}$
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	$p = 0.0926$

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

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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

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

180

181 4. Discussion

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

189 In its latest guidebook on combatting soil-transmitted helminth infections [8], the WHO insist
 190 that mass administration of effective drugs, periodically carried out on school age children
 191 could contribute to achieving of millennium development goals, including poverty reduction.
 192 The various types of schistosomiasis most frequently affect school age children and expose
 193 them serious long term complications. Implementing this strategy using praziquantel, an
 194 effective drug, is therefore one of the ways of combatting them. However, some limitations
 195 have been identified. Indeed, the WHO prescribe mass administration every 12 months in
 196 high risk areas (prevalence rate of 50% or more) and every 24 months in moderate risk areas
 197 (prevalence rate between 10% and 49%) [7]. But assessments carried out 8 to 10 months after
 198 mass administration operations show prevalence rates almost unchanged due to reinfestation
 199 [5]. In the same document [7], it is indicated that the strategy should be assessed after 4 or 5
 200 years to adjust the administration frequency. The data collected in Richard Toll suggest that
 201 after years of annual mass administration, the prevalence levels remain high. Based on that
 202 observation, our study measured the impact of a biannual administration of praziquantel to
 203 children of school age on the prevalence of schistosomiasis compared to the current strategy
 204 (annual administration). Our results show that a biannual administration of this molecule
 205 reduced by 100% the prevalence of *S. haematobium* and by more than 75% that of *S.*
 206 *mansoni*. This clearly demonstrates the usefulness of this new approach. Various studies are
 207 currently experimenting biannual administration to ascertain the usefulness of this new
 208 strategy, notably in Côte d'Ivoire, Mozambique and Tanzania [11]. The eradication of these
 209 diseases will probably require a combination of such approaches as the control of molluscs,
 210 an improvement of the environment and education for behaviour change. In our study, we
 211 also analysed the addition of Information, Education and Communication sessions on
 212 schistosomiasis in the strategy. The data collected indicate a 98% protective effect.

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 month.

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