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Effectiveness of Semestrial Mass Administration of *Praziquantel* 600 mg in the Schistosomiasis High Transmission Areas of Senegal River Basin

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Authors' contributions

This work was carried out in collaboration between all authors. Authors AM, FB and TRC wrote the protocol, designed the study, performed the statistical analysis and wrote the first draft of the manuscript. Authors AM, FB and GO corrected the protocol and manuscript drafts. Authors AM, FB and BMRD corrected the manuscript after reviewer. All authors provided feedback on manuscript drafts and read and approved the final manuscript.

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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.

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Aim: The objective of this study was to determine the Effectiveness of semestrial mass administration of *Praziquantel* 600 mg in the *Schistosomiasis* 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. 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. 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 only. A second survey was performed after six months to compare the effects of bi annual mass administration with that of an annual mass administration.

Results: In respect to *Schistosoma haematobium*, prevalence was statistically lower after intervention: 10.8% versus 35% ($p < 10^{-3}$). The same effect was noted for *Schistosoma mansoni*: 7.9% versus 23.8% ($p = <10^{-3}$). The prevalence of *Schistosoma heamatobium* at 6 months after the second drug administration was 0.0% while that of *Schistosoma mansoni* was 5.8%. In the control villages, the prevalence rate was still high after the mass administration campaign: 36.6% versus 21.7% ($p = 0.011$) for *Schistosoma heamatobium and* 15% versus 10% ($p = 0.242$) *for Schistosoma mansoni*. 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, in order to eliminate schistosomiasis in high transmission areas of the Senegal River Basin, *praziquantel* 600 mg mass administration could be renewed every 6 months.

Keywords: Schistosomiasis; praziquantel mass drug administration frequency; Senegal River Basin.

1. INTRODUCTION

Urinary and intestinal *Schistosomiasis* remains a major cause of morbidity and mortality in various countries, especially in SubSaharan 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 the 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 theses directives are not complied with in many countries as the original prevalence rates is often obtained 6 to 12 months after the interventions. That is why amendments were made in 2012 suggesting the need for biannual mass treatment (every 6 months). Nevertheless, 5 to 6 years of preventive chemotherapy at the current frequency has showed the prevalence rates still 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.

The objective was to determine the Effectiveness of semestrial mass administration of *Praziquantel* 600 mg in the *Schistosomiasis* high transmission areas of 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 (Dagana Department in the Republic of 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 *Schistosomiasis* (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. 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]: $n = P\ (1\text{-}P)\ Z^2\alpha\ /\ i^2$ with P = average prevalence of *Schistosomiasis* estimated at 70%; *i* = desired accuracy set at 6% and Zα = 1,96 for α = 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 villages only. A second survey was performed after six months to compare the effects of a bi annual mass administration with that of an annual administration (Table 1).

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/10 mlof urine) was determined by a direct counting of *S. haematobium* eggs after filtration through Millipore paper of 10 ml of urine. The intensity of the infection was broken down into 3 classes of parasite density [10]: no infestation (no eggs in the 10 ml 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 village and one control village.

2.5 Ethical Approval

This study was given the ethical green light by the National Committee of Ethics and Health Research. The Ministry of Health of the Republic of Senegal also authorized it. 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

Table 1. Study plan

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

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 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 done using Fisher's F test (ANOVA) after checking its applicability. Where the conditions for its applicability were not met, Kruskal-Wallis or Man Whitney's tests were used.

3. RESULTS

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

In respect to *Schistosoma haematobium*, prevalence was statistically lower after intervention (6 months after the first drug administration): 10.8% versus 35% ($p < 10^{-3}$) (Table 3). The same trend was noted for *Schistosoma mansoni*: 7.9% versus 23.8% ($p = <10^{-3}$) (Table 4).

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 (21.7%) after the mass administration campaign (Table 5).

Regarding *S. mansoni*, the prevalence survey performed 6 months after the first mass drug administration campaign showed a 5.8% prevalence rate versus 32.5% in the 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 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 villages for both *S. haematobium* and *S. mansoni*.

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

Table 2. Study population

		Study 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

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	$p < 10^{-3}$	

Table 4. Overall prevalence of *Schistosoma mansoni* during the study periods

Time	Before treatment	After treatment	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 and control villages

Study 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

Table 6. Comparison of overall prevalence of *Schistosoma mansoni* in study and control villages

Study 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

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

Study 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

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

Study 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

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 in achieving millennium development goals, including poverty reduction. The various types of *Schistosomiasis* 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 combating 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* 600 mg 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]. "There is evidence that regular treatment with *praziquantel* prevents severe, hepatosplenic *Schistosomiasis* and subtle morbidity due to *Schistosomiasis* [12,7]. Yes, children will get re-infected, but then you come back with the MDA again and kill the new adult worms. Thus children are 'worm-free' for a sufficient period of time that they do not develop severe disease, and if done regularly MDA will decrease subtle morbidity, but in most transmission settings this will not lead to elimination" [11].

Previous studies have demonstrated clearly high risk of Schistosomes infections in people who live closer to the transmission sites [13]. Others observations fall in line with that of previous authors in studies involving other helminths infections [14].

The eradication of *Schistosomiasis* will probably require a combination of such approaches with the control of molluscs, an improvement of the environment and education for behaviour change. 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* [15]. This shows the need to combine strategies whose effectiveness is proven in order to effectively eliminate *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.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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