

# Trachoma mass treatment with azithromycin 1.5% eye drops in Cameroon: feasibility, tolerance and effectiveness

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## **ABSTRACT**

### **Background/aims:**

An epidemiological study carried out in 2006 indicated the existence of a high prevalence of blinding trachoma in the Kolofata Health District, Far North Region, Cameroon. As a result, the national blindness control program of Cameroon instituted a trachoma elimination programme using the SAFE strategy.

### **Methods:**

A campaign to treat the entire district population with azithromycin 1.5% eye drops was undertaken in February, 2008. To measure the effectiveness of treatment on the prevalence of active trachoma, two epidemiological studies were conducted on a representative sample of children aged between 1 and 10 years. The first study was performed just prior to the treatment campaign and the second study was performed one year later.

### **Results:**

The prevalence of active forms of trachoma (TF + TF/TI) dropped from 31.5% (95%CI 26.4-37.5) before treatment to 6.3% (95%CI 4.1-9.6) one year after treatment; a reduction of nearly 80%. There were no reports of serious or systemic side effects. Tolerance was excellent. No treatment was interrupted.

### **Conclusion:**

Mass treatment with azithromycin 1.5% eye drops is therefore feasible, well tolerated, and effective.

## **INTRODUCTION**

Prevention of blindness and visual impairment is one of the public health priorities of the Cameroon Republic. The National Blindness Prevention Programme and a Vision 2020 plan were established as a result of this policy of prevention. A study to evaluate the prevalence of active and scarring trachoma, conducted in December 2006 in the Kolofata Health District (Fig 1), signalled the presence of endemic trachoma with significant blinding potential [1]. The National Program of Prevention of Blindness decided to plan a elimination program by implementing the SAFE strategy [2] and addressing the "A" (antibiotic) component, a mass treatment by azithromycin 1.5% eye drops of the entire population of the district.

The objective of this study was to assess the feasibility, tolerance and effectiveness of a topical treatment with azithromycin 1.5% eye drops, used for the first time on a large scale to reduce the prevalence of active forms of trachoma in a population.

## **METHODS**

### **Mass treatment campaign**

In accordance with the WHO recommendations [3], the trachoma control programme in the Kolofata Health District called for one mass treatment

campaign per year for three years. The treatment plan received authorisation from the Cameroon Ministry of Public Health in February 2008. The first campaign began on 23 February 2008 and ended on 10 March 2008.

The target population was all 115,274 residents of the Kolofata Health District [4].

A total of 120,000 complete treatments (720,000 single doses) of azithromycin 1.5%, donated by Théa Laboratories, were sent by air from Europe to Yaoundé, Cameroon and by train from Yaoundé to Kolofata.

A door-to-door strategy was used. In each compound (group of shelters housing an extended family), a local community health worker, helped by a literate second-level community health worker, performed a census of the entire population of the neighbourhood or village assigned to the local community health worker. One census form was completed for each compound.

Over the following days, an effort was made to treat the entire population of the district with azithromycin 1.5% eye drops, one drop in each eye in the morning and evening for three consecutive days (6 doses). Informed consent was systematically requested of parents of minors and indicated by signature or fingerprint. Questionnaires designed to document side effects or symptoms of intolerance to the eye drops were administered and collected daily by ophthalmologic nurses.

In all, 250 local community health workers, 23 second-level community health workers, 1 head nurse for each of the 7 health centres, 2 District Health Service logisticians, and 4 ophthalmologic nurses from the non-governmental organisation Ophtalmo Sans Frontières were involved in the campaign. The Kolofata District Medical Officer and an expert from the National Centre of Ophthalmology of the Quinze Vingts, Paris, coordinated and supervised all activities related to training, logistics, education, and treatment.

### **The studies**

Two descriptive cross-sectional studies were conducted in the Kolofata Health District, the first 15 days prior to treatment in February 2008 and the second one year after treatment in January 2009. These studies were performed in order to measure the effectiveness of treatment on the prevalence of active forms of trachoma in the population. TF and TF/TI forms among children aged between 1 and 10 years were used as indicators. The standard WHO protocol for trachoma prevalence surveys was used [5].

The population studied was chosen at random and was based on the exhaustive list of villages and demographic statistics gathered in 2006 for the national census [4].

Assuming a prevalence of less than 5% following the third year of mass treatment, it was necessary to include 2,400 children in the study to obtain a

precision of approximately 1.5% at a bilateral alpha threshold of 5% and a cluster effect of 4 [6]. This would also allow conclusions to be drawn, in accordance with WHO recommendations, concerning the interruption of transmission [3]. As a result, 2,400 children aged between 1 and 10 years were divided into 40 clusters, with 60 children per cluster. The WHO simplified grading system was used for the recognition and registering of cases of trachoma [7].

Two teams shared the field work. Each team consisted of a census nurse and either an ophthalmologic nurse or an ophthalmologist. The same teams and the same ophthalmologist conducted the before-treatment study and the after-treatment study. A 4-day training session was held for the nurses. After these training sessions, the inter-observer variation was very satisfactory (Kappa 0.81-1.00). Data were compiled and analysed using EPIINFO 6 software. Estimated confidence intervals took into account the composition of sample clusters using the EpiTable Program from EPIINFO 6[8].

## **RESULTS**

### **Results of the mass treatment campaign using azithromycin 1.5% eye drops**

Each of the 250 local community health workers was assigned a village or neighbourhood of 400 to 500 residents. During the 15 days preceding the beginning of treatment, the local community health workers, helped by a literate second-level community health worker, conducted an exhaustive door-to-door census of all residents of the Kolofata Health District. The local community health workers then administered treatment by visiting each household morning and evening for three consecutive days.

Of 115,274 people counted in the census, community health workers administered azithromycin 1.5% eye drops, 1 drop in each eye in the morning and evening for three days, to 111,340 people (coverage 96.6%). The campaign covered the entire district and lasted 15 days. A total of 51,659 adults and 59,681 children under 15 years old were treated (52,866 males and 58,474 females). Two adults refused treatment for personal reasons not linked to the treatment.

Questionnaires concerning side effects of treatment were administered by ophthalmologic nurses during daily visits to assigned villages. Minor complaints were recorded (blurred vision lasting several minutes following instillation of eye drops or transient burning sensation in the eyes). No adult requested that treatment for themselves or their children be interrupted.

There were no reported serious or systemic side effects.

### **Age and sex distribution of study population of children aged between 1 and 10 years**

The number of children examined during the study relative to the number counted in the census is presented in Table 1.

**Table 1** Study participation

	Examined		Counted		% participation	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
<b>Children &gt; 1 year and &lt; 10 years</b>	2517	2404	2570	2411	97.9%	99.7%

**Table 2** Comparison of the distribution of children included in the study in 2008 and 2009 by age and sex

	Sample			
	Before treatment		After treatment	
	Number	%	Number	%
1-4 years	1391	55.3	1332	55.4
5-9 years	1126	44.7	1072	44.6
Male	1280	50.9	1236	51.4
Female	1237	49.1	1169	48.6
Total	2517	100	2404	100

Age and sex distributions were similar in the sample populations before and after treatment ( $p > 0.05$ ) (Table 2).

### **Prevalence of trachoma before and after treatment among children aged between 1 and 10 years**

The prevalence of TF in the study sample was estimated to be 24% (95%CI 20.7-27.5) before treatment and 5.8% (95%CI 4.1-8) after treatment (Table 3). The prevalence of TF/TI was estimated to be 7.5% (95%CI 5.7-10) before treatment and 0.5% (95%CI 0.13-1.6) after treatment (Table 3). The prevalence of active forms (TF + TF/TI) was estimated to be 31.5% (95%CI 26.4-37.5) before treatment and 6.3% (95%CI 4.5-8.6) after treatment (Table 3). The odds ratio for TF before and after treatment was 5.1 (4.2-6.2). The odds ratio was 14 (8.1-24) for TI forms and 6.7 (5.6-8.1) for TF + TF/TI forms.

**Table 3** Prevalence of active trachoma (TF, TF/TI and TF + TF/TI) before and after treatment among children aged between 1 and 10 years

	TF		TF/TFI		TF + TF/TFI	
	n	%	n	%	n	%
Before treatment	603	24% (95%CI : 20.7-27.5)	190	7.5% (95%CI : 5.7-10)	793	31,5% (95%CI : 26.4-37.5)
After treatment	140	5.8% (95%CI : 4.1 - 8)	14	0.5% (95%CI : 0.13 – 1.6)	154	6.4% (95%CI : 4.5 – 8.6)

## DISCUSSION

There are currently two ways of assessing the epidemiological situation in a trachoma endemic area, the nucleic acid amplification tests and the clinical grading. Because the WHO trachoma simplified grading system is currently the only WHO recommended system to assess the clinical trachoma prevalence and to monitor a trachoma control program in a community [9], we decided to use it to assess the feasibility, tolerance and effectiveness of a topical treatment with azithromycin 1.5% eye drops, used for the first time on a large scale to reduce the prevalence of active forms of trachoma in a population

### Feasibility of mass treatment with azithromycin 1.5% eye drops

A high coverage (96.6% of the census population) was obtained as a result of treatment having been administered directly by the health personnel who participated in the campaign. The campaign required the mobilisation of all the district's community health workers during a period of 15 days. Daily supervision in the field as well as high quality coordination by the health service authorities were also indispensable, as these prevented interruptions in the supply of eye drops and assured the daily collection of data relating to treatment coverage and side effects.

### Tolerance of mass treatment with azithromycin 1.5% eye drops

Apart from minor complaints which did not result in treatment interruption, treatment was accepted and well tolerated by both children and adults.

### Results of mass treatment with azithromycin 1.5% eye drops

The importance of the endemic trachoma in this district justified the mass treatment of the entire district population with azithromycin 1.5% eye drops as part of the SAFE strategy and in accordance with WHO recommendations [3].

The reduction of the prevalence of active trachoma among children is likely to be mainly a result of the mass treatment with azithromycin 1.5% eye drops. Between the first study conducted in 2006 and the study conducted prior to the first treatment in 2008, there was no significant reduction of trachoma prevalence, which might have been due to a "secular trend" effect. Between

February 2008 and January 2009, the application of the other components of the SAFE strategy consisted of the construction of a borehole water pump to provide safe water in each of three villages and the undertaking of numerous educational activities to promote individual and collective hygiene, but it seems unlikely that these other interventions alone could have produced so large a reduction in trachoma prevalence in so short a time.

### **Relative effectiveness of azithromycin 1.5% eye drops and oral azithromycin**

The most common drugs currently used in trachoma mass treatment campaigns are azithromycin 20 mg/kg taken orally and tetracycline 1% eye ointment.

In Niger from 2002 to 2005, a mass treatment campaign using oral azithromycin was conducted in 2 districts with 72 villages. The prevalence of TF among children decreased from 62.3% and 49.5% to 7.6% and 6.7% in three years [10], a reduction of 89% in one village and 85% in the other. No study was conducted within the 3 year interval. In Mali from 2002 to 2005, a mass treatment campaign using oral azithromycin was conducted in 7 districts. The prevalence of TF/TI among children decreased from 33% to 2.5% in 3 years [11], a reduction of 92.4%.

Since prevalence rates 1 year after treatment with oral azithromycin are unknown, it is not yet possible to conclude with certainty that mass treatment with azithromycin 1.5% eye drops can be considered at least as effective as treatment with oral azithromycin. Confirmation must await results of studies planned for 2010 and eventually 2011 following the third of three consecutive annual treatment campaigns.

A clinical trial showed that azithromycin 1.5% twice a day for 3 days has a similar efficacy to a single oral 20 mg/kg dose of azithromycin for the treatment of active trachoma in children 2 months after treatment [12]. There are no publications on the relative effectiveness of tetracycline 1% eye ointment and azithromycin 1.5% eye drops on active trachoma.

### **Potential advantages of topical azithromycin over topical tetracycline and oral azithromycin**

In 1997, a working paper pointing out the need for a topical treatment was presented at the WHO Alliance for the Global Elimination of Blinding Trachoma by the Year 2020 (GET2020) meeting [13]. This paper also listed the potential advantages of topical azithromycin over topical tetracycline and oral azithromycin.

In children with active trachoma, topical tetracycline ointment can be difficult to apply, and compliance is poor. The ointment may cause discomfort and blurred vision. Many children who are asymptomatic may not continue the topical

treatment, and parents may not be motivated to continue such therapy. The lack of compliance with topical tetracycline ointment may account for the failure to control trachoma as a major cause of blindness worldwide [14]

Cases of entropion trichiasis detected during the investigating teams' visits to the villages were referred to the ophthalmologic service of the Kolofata District Hospital for free surgery. The same was true of cases detected by community health workers during treatment and education campaigns. From January 2007 through December 2008, nearly 1,000 eyelids affected by entropion trichiasis were surgically repaired.

Following encouraging results from the first mass treatment campaign with azithromycin 1.5% eye drops, two additional mass treatment campaigns were planned. The second campaign took place in February 2009. A third study to track the evolution of active trachoma prevalence among children is planned for January 2010 prior to the proposed third mass treatment campaign.

To reinforce and perpetuate the reduction of trachoma prevalence and to advance towards elimination of blinding trachoma in this area, the other 3 components of the SAFE strategy must also be reinforced as recommended by the (GET 2020) [2]. Furthermore, it would be advisable to proceed to a rapid evaluation of the prevalence of trachoma in the North and Far North Regions in order to understand the geographic extent of the trachoma endemic in Cameroon. If the endemic is widespread, the success of this first trachoma treatment campaign should be extended to the entire North and Far North Regions of Cameroon.

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## Figures

Figure 1 Map of Cameroon

## Tables

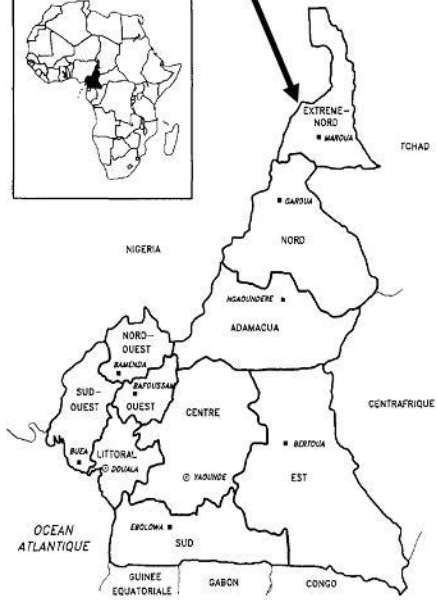
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# CAMEROON

**Kolofata**





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