

Feasibility of a mass vaccination campaign using a two-dose oral cholera vaccine in an urban cholera-endemic setting in Mozambique[☆]

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Abstract

We conducted a study to assess the feasibility and the potential vaccine coverage of a mass vaccination campaign using a two-dose oral cholera vaccine in an urban endemic neighbourhood of Beira, Mozambique. The campaign was conducted from December 2003 to January 2004. Overall 98,152 doses were administered, and vaccine coverage of the target population was 58.6% and 53.6% for the first and second rounds, respectively. The direct cost of the campaign, which excludes the price of the vaccine, amounted to slightly over \$90,000, resulting in the cost per fully vaccinated person of \$2.09, which is relatively high. However, in endemic settings where outbreaks are likely to occur, integrating cholera vaccination into the routine activities of the public health system could reduce such costs.

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1. Introduction

Considerable progress has been made during the last two decades in the development of new-generation oral vaccines

against cholera [1]. These are licensed in many countries and used mainly by travellers from industrialized countries visiting endemic areas. Oral cholera vaccination may complement usually recommended control measures in areas with high endemicity. However, a recent WHO meeting of experts recommended that demonstration projects be first undertaken [2]. Indeed, demonstration projects using oral cholera vaccines are essential to determine whether and under which circumstances cholera vaccination may help countries in their fight against the disease. Although Sub-Saharan African countries account for a significant proportion of the cholera cases reported worldwide [1]. Feasibility and cost of a mass

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oral cholera vaccination campaign have not been explored in the region, apart from a study undertaken in a refugee setting in Uganda [3]. Such information will be crucial for informed decision-making, by governments of cholera-affected countries and international organizations regarding the utilization of vaccination for cholera control.

Mozambique experienced major epidemics occurring successively from 1997 onwards, and cholera control activities typically focus on case management, water chlorination campaigns, and dissemination of hygiene messages. With improved case management, case fatality ratio have decreased to below 1%, but remain high in the most severely affected or isolated areas [4]. In addition, response to cholera outbreaks is expensive and disrupt other essential health care activities. Orally administered cholera vaccines represent a potential new tool to prevent or control cholera outbreaks. The two-dose oral killed rBS-WC vaccine is well tolerated and provides significant protection against cholera. Field trials conducted in Bangladesh [5,6] and in Peru [7], showed that this vaccine confers a high level of protection: 85% after the second dose and still about 62% protection two years later, in adult vaccinees. Protection among children less than 5 years is high during the first 6 months and then decreases dramatically.

A demonstration project, using the two-dose killed oral cholera vaccine was conducted in Beira, Mozambique. The objectives were: (i) to evaluate the requirements for the organization of a mass vaccination campaign within an urban African setting, the technical difficulties encountered in the administration of the vaccine and the costs incurred; (ii) to assess the results of this campaign, in terms of acceptability and vaccine coverage; and (iii) to assess the effectiveness of the vaccination. This paper reports on the feasibility, the acceptability and vaccine coverage only. The results on vaccine effectiveness are reported elsewhere [8].

2. Materials and method

2.1. Study site and population

The port city of Beira, in the Sofala province, is the second largest city in Mozambique (Fig. 1). Beira was built on swampy ground at the mouth of the Pungwe River and has a population of approximately 450,000, divided into 22 neighbourhoods (*bairros*). Many areas of Beira are located below sea level. Cholera is endemic in Beira with high seasonal variations. Cases usually occur during the rainy season from January to June. The characteristic marshy areas with brackish water, periodic flooding during the rainy season, common practice of defecation in open areas, presence of non-tight latrines, and drainage of municipal waste into the embankments perpetuate the risk for cholera [4]. The *bairro* of Esturro, a densely populated neighbourhood in the centre of Beira was selected for the demonstration project. It is facing all the cholera risk factors typical for the area

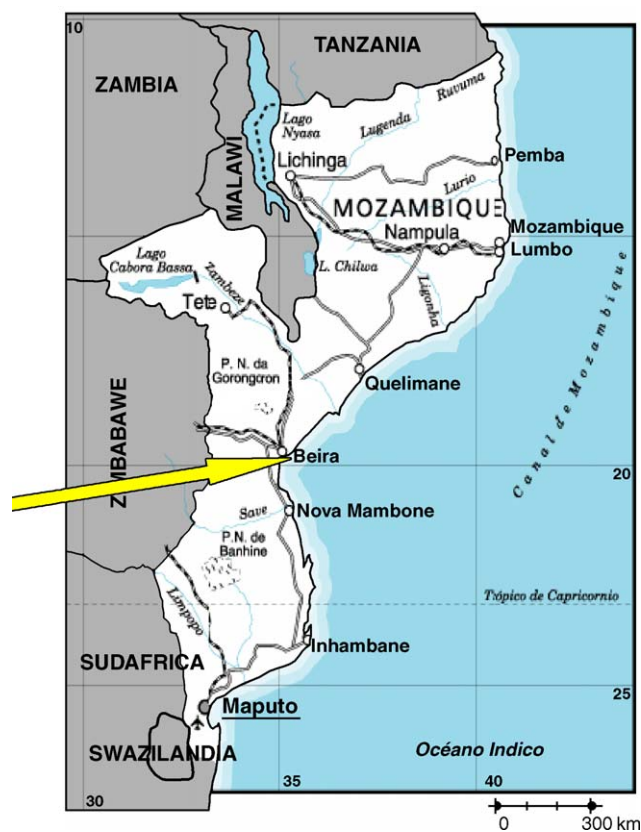


Fig. 1. Map of Mozambique.

and reported annual attack rates of up to 20 cases per 1000 population.

2.2. Vaccine

Each dose of the rBS-WC vaccine (Dukoral™, SBL Vaccine AB, Sweden) consists of 1 mg of a recombinant cholera B subunit, and 2.5×10^{10} of each of the following *Vibrio cholerae* O1 strains: Inaba classic, Inaba El Tor and Ogawa classic [9]. The vaccine was supplied as single dose 3 ml vials. Since the vaccine is acid labile, each dose was provided with a sachet of sodium hydrogen carbonate. Buffer solution was prepared by dissolving the sachet in 150 ml of water. The full dose of vaccine was mixed with 40, 75 or 150 ml of buffer solution, for persons 2–4 years, 5–11 years, and over 11 years, respectively.

Due to the precarious conditions of Beira's water distribution system, water used for the preparation of the buffer solution was drawn from the main reservoir of the municipality and stored in a flexible water tank located near the vaccine storage facility. The tank was refilled every 4 days by water trucking. Water temperature and chlorine level were monitored daily.

2.3. Mass vaccination campaign

Although residents of Esturro were selected as the target population, non-Esturro residents requesting vaccination

were not denied access and were vaccinated as well. A formal census of Esturro residents was conducted in October 2003 and enumerated a total population of 21,818 persons. All healthy, non-pregnant residents of Esturro who were 2 years of age and older were invited to participate in the mass vaccination campaign. During the census, 1177 were under 2 years of age and an estimated 5% (1091) were excluded for potential pregnancy, leaving a target population of 19,550.

One month before the campaign, meetings were organised to inform community leaders about the vaccine, the campaign and the feasibility study, obtain their approval, and solicit their support. Prior to and through-out the mass vaccination, an information campaign was conducted within Esturro, using posters and banners, local newspapers, radio and television. Further, a door-to-door awareness campaign was conducted during the second vaccination round. The two doses of vaccine were given at a 14-days interval. The volume of vaccine ingested by each individual was recorded. No replacement dose was given unless the content of the cup was entirely spilt. A vaccination card, issued during the first round, had to be presented when seeking the second dose of vaccine.

2.4. Feasibility

All information from the vaccination cards (name, age, address, vaccination date, volume ingested) was recorded on registration sheets and double entered in real time into a custom-made entry program using FoxPro software (Microsoft, Seattle, USA). The number of doses delivered during each round was also recorded. Vaccine wastage was estimated by comparing the number of doses delivered with the number of vials actually used. Time spent on vaccination was estimated based on the number of doses administered per outpost per day.

2.5. Cost incurred

The following expenses were taken into account for the analysis of the cost of the campaign: (i) before the campaign: transport of the vaccine from the European producer up to the field, customs clearance and storage; (ii) during the campaign: supplies and salaries of local personnel. Salaries of international collaborators and expenses related to the feasibility itself (e.g. vaccine coverage survey) were excluded. A simulation of the cost per fully immunised person was carried out using a price per dose of vaccine in the range of US\$ 0–3. The drop-out proportion between the two rounds and the vaccine waste observed during the campaign, as well as a 25% reserve stock, were all taken into account in the simulation.

2.6. Vaccine coverage and acceptability

Vaccine coverage and the drop-out proportion between the two rounds were estimated through a survey conducted immediately after the campaign. The sampling frame used

census data collected from September to October 2003, that estimated the number of individuals residing in the target area at 21,818, and included data on age and sex of each household member, as well as each household address linked to a Geographic Positioning System (GPS) point. A random sample of 1084 individuals was selected from the census register. Households of the selected individuals were located using GPS.

Cholera vaccination status was ascertained from the vaccination card. Vaccine coverage for each vaccination round, drop-out proportion, and 95% confidence intervals were calculated. Vaccine coverage was also stratified by age and sex. To evaluate the clinical acceptability of the vaccine, a second list of 381 individuals over 14 years of age was randomly selected. Individuals were asked about the taste of vaccine, the occurrence of side-effects, as well as the possible reasons for non-vaccination. Data was compiled using Epi-Info 6.04b [10] and analysed using SPSS 11.5 [11].

2.7. Ethics

The ethical review boards of the International Vaccine Institute, Seoul, Korea, and of the World Health Organization, Geneva, Switzerland approved the study protocol, which was also presented to the national review board of the Government of Mozambique. Informed consent was obtained at the community level through meetings with community leaders and at the individual level, by a signature or thumbprint, just before vaccine administration.

3. Results

3.1. Feasibility of the mass vaccination campaign

A total of 115,600 doses of rBS-WC vaccine and the corresponding buffer sachets were packed together resulting in a total volume of 9 m³ and weight of 3310 kg. The vaccine was transported in EPI cool-boxes by air from Stockholm, Sweden to Beira via Nairobi, Kenya. In Beira, vaccines and buffer were stored between 4 and 8 °C in a cold room facility. EPI cool-boxes were used for daily transportation of the vaccine to the vaccination sites.

The two rounds of vaccination were conducted prior to the start of the 2004 rainy season, during school holidays. The first round was from 11 to 20 December 2003. The second round was from 5 to 12 January 2004. Vaccine outposts were set up in churches and schools within Esturro. Each outpost was opened daily, from 8 am to 3 pm, 6 days a week, from Monday to Saturday. Each outpost had one supervisor (nurse or midwife), and 15–23 team members, depending on the attendance expected for each site. The teams set-up the vaccination site, informed potential vaccinees in the waiting area, prepared the buffer solution, delivered the vaccine, fetched water, cleaned the cups, and filled in the cards and registration sheets. In total, 213 persons were involved, with

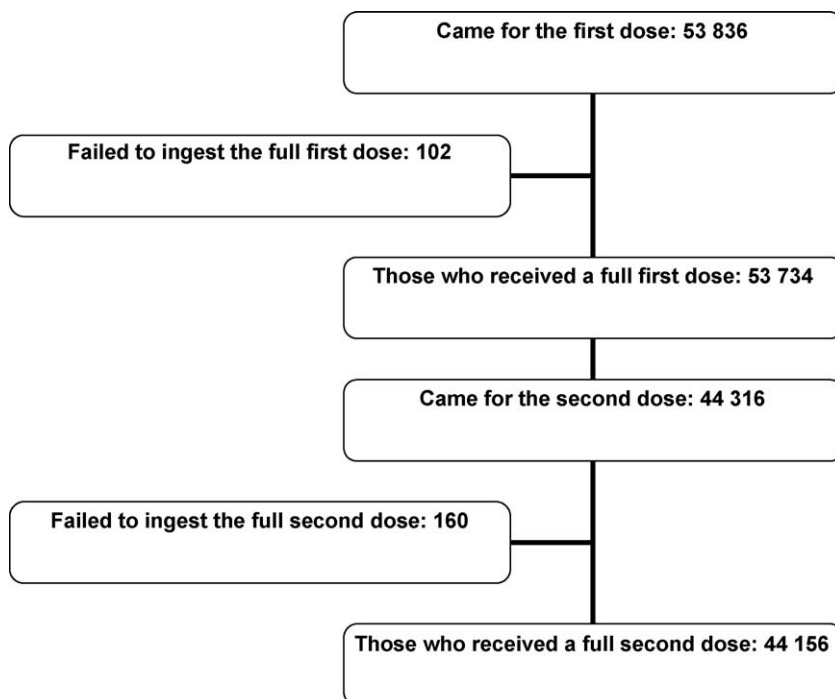


Fig. 2. Cholera mass vaccination campaign in the Esturro Neighbourhood, Beira, Mozambique, December 2003 to January 2004.

an average of 21 persons per outpost, and an overall activity of 4050 person-days. Six vehicles were used for supervision and to transport staff and supplies to vaccination outposts.

During the first round, 53,836 doses of vaccine were administered, and 44,316 during the second round, totalling 98,152 doses (Fig. 2). On average, each team was able to vaccinate 609 persons per day (93 persons per hour). During the busiest periods, each team was able to vaccinate up to 212 persons per hour. A total of 98,679 doses were used during the campaign, indicating a vaccine wastage of 527 doses (1%). Overall 27,500l of water were used during the two rounds, representing 280 ml per administered dose.

3.2. Cost incurred

The overall cost of organizing the campaign was \$92,287 (Table 1). Of this amount the cost of shipping the vaccine from

Table 1
Cost of mass vaccination campaign with a two-dose oral cholera vaccine Beira, Mozambique, 2003–2004

	Cost (\$)	Total (%)
Vaccine	Free of charge	0.0
Airfreight between Stockholm and Nairobi	6,608	7.2
Regional transport between Nairobi and Beira	28,236	30.6
Insurance fees	900	1.0
Vaccine storage	1,835	1.9
Local transportation in Beira	3,439	3.7
Vaccination cards	4,717	5.1
Supplies for vaccine administration	8,869	9.6
Staff salaries (vaccination campaign)	30,973	33.6
Awareness campaign	9,710	10.5
Total	92,287	100.0

the manufacturer to Beira was evaluated to \$34,844 while the staff salaries accounted for \$30,973 (respectively, 37.8 and 33.6% of the total delivery cost). If we assume a reserve stock of 25% for the vaccine, the amount of vaccine to fully immunise 44,156 individuals was 123,349 doses. Taking into account the cost of organizing the campaign, the cost per fully immunized individual would have ranged from \$2.09 for a free-of-charge vaccine, to \$4.88 for a vaccine at \$1 per dose, and to \$10.47 if the dose costs \$3.

3.3. Vaccine coverage survey and acceptability

The vaccine coverage survey was conducted between 22 January and 7 February 2004. Of the 1084 interviewees, 73 (6.7%) with missing information were excluded from the

Table 2
Vaccine coverage according to vaccination cards, by gender and age. Cholera mass vaccination campaign in the Esturro Neighbourhood, Beira, Mozambique, 2003–2004

	Vaccine coverage ^a (95% CI)	
	First dose	Second dose
Gender		
Males	56.8 (52.6–61.0)	51.7 (47.4–55.9)
Females	60.9 (56.6–65.1)	55.6 (51.2–59.9)
Age groups		
2–4	63.5 (57.9–68.8)	58.7 (52.4–63.6)
5–14	66.1 (61.2–70.7)	62.1 (57.1–66.8)
15 and over	46.1 (41.1–51.1)	40.8 (35.9–45.8)
Overall	58.6 (55.6–61.5)	53.6 (50.3–56.3)

^a Percentage.

analysis. Using the vaccination cards for confirmation of the vaccination status, the first and second dose coverage were 58.6% (95%CI: 55.6–65.1) and 53.6% (95%CI: 50.3–56.3), respectively (Table 2). The drop-out proportion between the two rounds was 8.5% (95%CI: 6.4–11.1). Vaccine coverage did not differ by gender but was significantly lower among the over-15-year-old as compared to children aged 5–14 (40.8 and 62.1%, respectively, OR = 0.4 [CI = 0.3–0.6]).

Of the 381 individuals who were interviewed for acceptability, 190 (49.9%) said they received one or two doses, while 191 (50.1%) declared they had not received any dose of the vaccine. Among vaccinated individuals, 13 (7%) thought that the vaccine had a bad taste, and 184 (96%) reported no side-effects following its ingestion. Minor and non-specific complaints, including nausea, abdominal pain or weakness were reported by six persons. Among the non-vaccinated individuals, 111 (58%) did not take the vaccine because they were travelling and 50 (26%) said they were busy. Other reasons being reported: pregnancy (10), refusal (7), long waiting time (6), taking medication (5).

4. Discussion

This was the first demonstration project aimed at gaining evidence on the use of oral cholera vaccines in an endemic setting in Africa. Mass vaccination using the two-dose oral killed cholera vaccine proved to be feasible in this highly cholera-endemic urban area in Mozambique which required considerable logistical support and thorough planning and preparation. However, the size of the target population (approximately 20,000), was far short of the actual target of a real campaign aimed at stopping cholera in Beira city (500,000). Currently, most of the African population lives in poor suburbs of mega-cities of several million inhabitants. Considering cholera control in such needy environments, would involve addressing problems on a much larger scale than the demonstration project in Esturro.

Nearly 100,000 doses of vaccine were administered during two rounds of immunization conducted within one month. The rate at which the vaccination were given was, at most, 609 doses per day (93 dose per hour), less than that reported during mass vaccination campaign conducted in Vietnam using a two doses oral cholera vaccine [12], and less than that recorded during mass vaccination campaigns using needles (i.e. measles or meningitis), during which, an average of 350 individuals were vaccinated per hour [13]. The difference can be attributed to the time needed to provide information regarding the vaccine, to drink the vaccine, especially in younger children and to record the vaccination.

Although enhanced by the sound and transparent information strategy being adopted and targeting the community leaders and politicians, as well as the general population of Beira and Esturro residents, the vaccination campaign in Beira resulted in a two-dose vaccine coverage of 54%,

much lower than that achieved in previous mass oral cholera vaccination projects [12,14]. An early challenge in conducting this campaign was finding a non-refugee setting with a population size appropriate for the available number of vaccines. Beira city with its annual occurrence of cholera and its large outbreak in 1998 was the most suitable for a mass vaccination campaign. However, in view of the large population size of the city (500,000) and the limited availability of vaccines, and following discussions with community representatives, a smaller target area was selected within Beira, taking into account high incidence of cholera in previous years. However, the exclusion of non-Esturro residents from vaccinations was not acceptable for the community. The vaccine was therefore administered to all those who came to the vaccination outposts on a first-come first-served basis. As more and more people came from other areas of Beira, access to vaccine outposts for Esturro residents became increasingly difficult as the campaign progressed. The availability of the vaccine for all Beira residents was therefore a limiting factor in maximizing vaccine coverage in Esturro.

An important finding from the Esturro survey was the lower vaccine coverage among adults. An effective approach for obtaining a more complete coverage in future mass vaccination campaigns might require targeting adults through providing possibilities for vaccination outside working hours to increase their participation. When questioned regarding the reasons for non-participation during the vaccine coverage survey, more than half of the non-vaccinated residents declared that they were travelling at the time of the campaign. Trips were related to the Christmas celebrations and preparation of agricultural areas before the start of the rainy season. Although it is important to schedule mass vaccination activities prior to the cholera season, it is also important to take into consideration community activities in order to maximize participation.

The cost of the campaign was relatively high. The project aimed at ensuring an efficient process for the mass vaccination campaign and vaccination teams were therefore staffed generously. Expenses could be reduced through the integration of cholera vaccination in the public health system activities. In contrast, there were few options for decreasing the transport costs of the vaccine to the field site. Due to the risk of breaking the cold chain, an airplane was chartered for transporting the vaccines from Nairobi to Beira. Because of the high volume of storage capacities needed to safely store the vaccine, the absence of a safe cold chain could jeopardize future mass vaccination campaigns in certain settings. For this project, the vaccine was provided free of charge. However, vaccine and vaccine delivery costs are likely to be the main constraints to a wider use of cholera vaccination campaigns.

This study was, to our knowledge, the first large-scale project using the two-dose killed oral cholera vaccine in a real life situation. Logistics were challenging partly due to the fact that the implementation of the campaign needed to

be documented in order to gain evidence on the use of such vaccines in an endemic setting. Future mass vaccination campaigns outside a research setting can be simplified but will always require thorough planning and preparation. A key question for public health decision makers is where and when this vaccine should be used. Given the relatively short immunological protection and the relatively high cost, it would currently not be appropriate for routine vaccination programs in resource poor settings.

Lessons learned on the importance of timing, targeting adults, and emphasizing the need for two doses will be useful for planning future campaigns using the killed oral cholera vaccine. Cost of vaccine remains a key issue, especially when considering large implementation of cholera immunization in countries where cholera is endemic, while keeping in mind that the cost of the vaccine is dependent on the quantities of vaccines produced. Governments and donors should provide funding for prevention of, and preparedness for cholera outbreaks.

Pre-emptive vaccinations can not only save costs related to emergency responses to control outbreaks, but more importantly prevent unnecessary suffering.

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