

Mass vaccination with a two-dose oral cholera vaccine in a refugee camp

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In refugee settings, the use of cholera vaccines is controversial since a mass vaccination campaign might disrupt other priority interventions. We therefore conducted a study to assess the feasibility of such a campaign using a two-dose oral cholera vaccine in a refugee camp. The campaign, using killed whole-cell/recombinant B-subunit cholera vaccine, was carried out in October 1997 among 44 000 south Sudanese refugees in Uganda. Outcome variables included the number of doses administered, the drop-out rate between the two rounds, the proportion of vaccine wasted, the speed of administration, the cost of the campaign, and the vaccine coverage. Overall, 63 220 doses of vaccine were administered. At best, 200 vaccine doses were administered per vaccination site and per hour. The direct cost of the campaign amounted to US\$ 14 655, not including the vaccine itself. Vaccine coverage, based on vaccination cards, was 83.0% and 75.9% for the first and second rounds, respectively. Mass vaccination of a large refugee population with an oral cholera vaccine therefore proved to be feasible. A pre-emptive vaccination strategy could be considered in stable refugee settings and in urban slums in high-risk areas. However, the potential cost of the vaccine and the absence of quickly accessible stockpiles are major drawbacks for its large-scale use.

Keywords: cholera vaccine; immunization programmes; feasibility studies; refugees; risk factors; Sudan; Uganda.

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Introduction

In refugee settings, overcrowding, poor sanitation, and inadequate water supplies increase the risk of outbreaks of cholera. Such outbreaks can last from 3 weeks to more than 3 months; attack rates range from 0.4% to 8%, and case-fatality ratios from 20% to 50% without treatment (1). Prevention of cholera in refugees relies on nonspecific public health measures such as provision of safe water in sufficient quantity, sanitation, and site planning to avoid overcrowding (2, 3). However, these measures are difficult to implement quickly and effectively in large communities, and plans to respond to an eventual cholera outbreak should be prepared well before the emergence of the first cases.

Orally administered cholera vaccines represent a potential new tool to prevent or control cholera outbreaks. The two-dose oral killed whole-cell/recombinant B-subunit (WC/rBS) cholera vaccine is

licensed in several countries for use with travellers. This vaccine consists of 10^{11} heat- or formalin-killed whole cells of *Vibrio cholerae* O1, Inaba and Ogawa serotypes, classical and El Tor biotypes, in combination with the purified recombinant B-subunit of cholera toxin (3). Field trials, conducted in Bangladesh (4, 5) and Peru (6), showed that this vaccine confers a high level of protection (85%) after the second dose, and still about 62% protection three years after, in vaccinees more than 5 years of age. Protection among children less than 5 years is high during the first 6 months and then decreases dramatically. No significant side-effects have been reported.

The use of two-dose oral cholera vaccine such as WC/rBS in complex emergencies and during the acute phase of population displacements is controversial. Indeed, the organization of a mass vaccination campaign against cholera might require heavy logistic support and disrupt other priority interventions such as provision of water, food, and shelter, or immunization against other diseases such as measles (7, 8).

We therefore conducted a feasibility study by organizing a mass vaccination campaign with WC/rBS cholera vaccine in field conditions of a refugee setting. The objectives of our study were (i) to evaluate the requirements for the organization of a mass vaccination campaign within a stable refugee population, the technical difficulties encountered in the administration of the vaccine, and the costs incurred; and (ii) to assess the results of this campaign, in terms of acceptability and vaccine coverage.

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Methods

Mass vaccination campaign

The vaccination campaign was carried out among the south Sudanese refugee population in Adjumani district, Northern Region, Uganda. Six settlement and transit sites, amounting to a target population of 43 963 individuals above 1 year of age, participated in the study.

A total of 100 000 doses of the WC/rBS cholera vaccine were donated by the US Army, and checked for quality by the producer (SBL Vaccine AB, Stockholm, Sweden), before being shipped to Uganda. The vaccine was administered with a buffer solution, prepared with safe water: for adults and children above 6 years of age, two sachets of sodium bicarbonate were mixed in 150 ml of water; for children aged 1–6 years, one sachet was mixed in 75 ml of water. The immunization schedule consisted of two doses, given at a 14-day interval. A specific vaccination card was distributed during the first round. Any person coming to the second round without a vaccination card was not given the vaccine. Apart from killed oral cholera, no other vaccine was offered to the refugees during this campaign.

In order to have the campaign organized under regular field conditions, the vaccination was carried out by two nongovernmental organizations (NGOs) operating in the camps. The study investigators were only present to advise NGO staff, supervise the vaccination process, and collect study data. An information campaign and social mobilization activities were conducted during the 2 weeks preceding the campaign.

The number of doses delivered and logistic and human resources requirements were collected on every vaccination day. The following expenses were taken into account for the analysis of the cost of the campaign: (i) before the campaign: transport of the vaccines from the European producer to Uganda and to the field, customs clearance, storage; (ii) during the campaign: material used and salaries of local personnel. The expenses related to the feasibility study itself (e.g. vaccine coverage survey) were all omitted.

A simulation of the cost per fully immunized person was carried out using a price per dose of vaccine in the range 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.

Vaccine coverage survey and acceptability

We carried out a vaccine coverage survey following the vaccination in the settlements. A sample of households was selected using a systematic random design, and all household members were included in the survey. Refugees who arrived in the camps after the beginning of the information campaign (15 September 1997) were excluded.

Data collected included family size, and the age, sex, and date of arrival in the camp of each

individual aged over 1 year. Cholera vaccination status was ascertained from the vaccination cards and by interview. Vaccine coverage for each vaccination round, drop-out proportion, and 95% confidence intervals were calculated. Vaccine coverage was also stratified by age, sex, and type of camp. In order to assess vaccine acceptability, a subsample was randomly taken from the adults selected for the vaccine coverage survey. Questions were asked about the taste of the vaccine and the occurrence of side-effects. Data entry and analysis were performed using Epi Info software (Centers for Disease Control and Prevention, Atlanta, GA, USA).

Results

Mass vaccination campaign

The 100 000 doses of vaccine received for the campaign occupied 5.5 m³ and weighed 958.3 kg. The buffer solution was conditioned in sachets of effervescent granulated sodium bicarbonate. The 197 250 sachets sent with the vaccines occupied 3.9 m³ and weighed 1085.7 kg. The vaccines were stored at 4–8 °C in the cold rooms of the Expanded Programme on Immunization (EPI), in Entebbe, Uganda. Before each round, the vaccines were shipped from Entebbe to the field by plane, since road transportation was not permitted for security reasons. Because of the lack of suitable cold-chain facilities outside the capital city, and because of the good thermostability of the vaccine, no cold chain was used during the shipment or during the campaign.

The vaccination campaign was carried out between 22 September and 26 October 1997. Fifteen vaccination sites were established, each run by a team with at least one health professional (nurse, midwife, or nursing aide), complemented by community health workers (CHWs) and other nonprofessional persons. The teams established the vaccination site, prepared and delivered the vaccine, monitored its ingestion, fetched water, cleaned the cups, and filled the specific cards and the tally sheets. For the fifteen sites, the human resources represented 114 persons: 19 nurses/midwives, 21 nursing aides, 44 CHWs, and 30 persons without qualifications.

Four vehicles were used to transport staff and material to the vaccination sites, as well as for supervision. At each vaccination site, the following material was used: jerrycans to fetch water from the borehole up to the vaccination site, buckets to store the water, measuring cups, cups for vaccine ingestion, basins to rinse the cups, chairs, tables, and benches.

Overall, 63 220 doses of vaccine were administered during the campaign (9925 to children aged 1–4 years), of which 35 613 doses were administered during the first round and 27 607 during the second (Table 1). The vaccination teams vaccinated between 250 and 1735 persons per day. During the busiest periods, each team could vaccinate up to 200 persons per hour. Based on the number of doses adminis-

tered, the drop-out rate between the two rounds was 22.5%, but was lower in transit (21.4%) than in settlement camps (23.3%) ($P < 0.0001$). The drop-out rate was higher among over-15-year-olds (27.1%) than among 5–14-year-olds (18.7%) and 1–4-year-olds (14.6%) ($P < 0.0001$). Drop-out was lower among males (22.0%) than females (23.0%) ($P = 0.02$).

A total of 69 750 doses were used during the campaign, giving a vaccine waste proportion of 9.4%. The waste proportions were 5.5% (37 700 doses used for 35 613 doses administered), and 13.9% (32 050 vs. 27 607) for the first and the second rounds, respectively. Overall, 13 610 litres of water were used during the two rounds, representing an average of 215 ml per administered dose.

Cost incurred

The overall cost of organizing the campaign was US\$ 14 655, without taking into account the price of storage, since the EPI programme accepted to store the vaccine at no charge (Table 2). The local staff received an incentive of US\$ 3 per person per day. The cost of air freight between Stockholm and Entebbe was included with taxes and insurance.

If we assume a reserve stock of 25% for the vaccine, the amount of vaccine needed to fully immunize 27 607 individuals was 87 188 doses. Taking into account the cost of organizing the campaign, the cost per fully immunized individual would have ranged from US\$ 0.53 for a free-of-charge vaccine, to US\$ 3.69 for a vaccine at US\$ 1 per dose, and to US\$ 10.01 if the dose cost US\$ 3 (Fig. 1).

Vaccine coverage survey and acceptability

The vaccine coverage survey was conducted between 4 and 7 November 1997. Two of the six settlements could not be accessed for security reasons, and so the survey was conducted in only four camps. A total of 1040 individuals from 216 families were included; the median family size was 4 (range, 1–25) and the sex ratio of males to females was 0.87 (483/557).

Based on vaccination cards, the first- and second-dose vaccine coverage was 83.0% and 75.9%, respectively (Table 1). Excluded from the analysis were 43 persons (4.1%) with missing information. The drop-out rate between the two rounds was 9.5% (95% confidence interval, 7.9–11.4). The vaccine coverage did not differ by sex or age group. Based on the interview results, the first- and second-dose vaccine coverage was 94.7% and 87.0%, respectively (Table 1).

Among 144 randomly selected adults who received at least one dose of the vaccine, 138 (95.8%) liked its taste, and 128 (88.9%) reported no side-effects following its ingestion. Minor and nonspecific complaints, including itching (six persons), headache (four persons), weakness, joint pain, etc., were reported by 16 persons (11.1%).

Table 1. Number of doses of WC/rBS administered and vaccine coverage by source of information during the first and second rounds, Adjumani district, Uganda, 1997

	No. of doses	% coverage from	
		immunization cards	interviews
First round	35 613	83.0 (80.9–84.9) ^a	94.7(93.4–95.8)
Second round	27 607	75.9 (73.5–78.0)	87.0 (85.0–88.7)

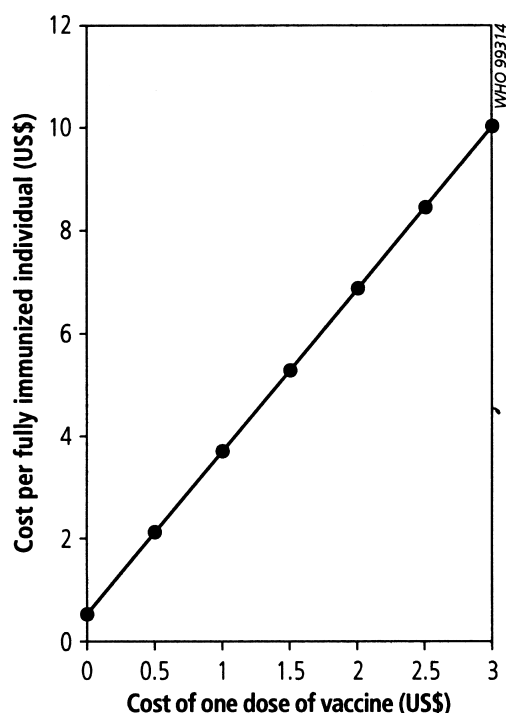
^a Figures in parentheses are 95% confidence intervals.

Table 2. Costs of a mass vaccination campaign with a two-dose oral cholera vaccine in a refugee camp, Adjumani district, Uganda, 1997

	Cost (US\$)
Airfreight between Stockholm and Entebbe	4 421 ^a
Customs clearance	1 600
Storage	Free of charge
Transport between Entebbe and Adjumani	3 239
Vaccination cards	2 890
Material for vaccine administration	225
Material for data collection	80
Local personnel salaries	2 200
Total	14 655

^a Estimated cost.

Fig. 1. Costs of a mass vaccination campaign with a two-dose oral cholera vaccine in a refugee camp, Adjumani district, Uganda, 1997



Discussion

Based on our results, mass vaccination of a refugee population with a two-dose oral cholera vaccine proved to be feasible. The WC/rBS vaccine was well accepted by the beneficiaries, and high vaccine coverage was achieved. Since the role of the investigators was limited to data collection, we believe that this campaign was conducted under realistic field conditions. In addition, the conditions in Adjumani camps are similar to those in most stable refugee settings; thus our findings probably apply to other refugee situations in sub-Saharan Africa.

The most important logistic problem encountered was the bulkiness of the vaccines and buffer solution required for the campaign, which complicated storage and shipment to the field and to vaccination sites. On the other hand, since WC/rBS is considered to be stable for one month at 37 °C, a cold chain was not required, which in any case would have been difficult to organize.

The ca. 0.2 litres of water needed to vaccinate each individual should be available in any refugee situation, even during the acute phase of population displacement. However, emphasis should be placed on the quality of the water provided and the cleanliness of the containers used, so as to avoid contamination and spreading of diarrhoeal diseases.

The rate of vaccine administration, at best 200 doses delivered per hour with three operators and one supervisor, was low when compared with mass vaccination campaigns using injectable vaccines (9). This arose because of the time needed to prepare the vaccine, especially the buffer solution, and the time needed for children to drink the vaccine, particularly those under 2 years of age.

The vaccination campaign in the Adjumani refugee camps was organized in such a way as to minimize its impact on other health activities. Most of the staff were only involved in the campaign during the six days needed to conduct the two vaccination rounds. Moreover, vaccination was carried out during the weekends in order not to interfere with the regular functioning of health services. Therefore we believe that in a well-established refugee camp, the opportunity costs associated with such an operation are negligible with regard to its direct cost.

Since protection with WC/rBS is obtained one week after the second dose, our study showed that a minimum of 4–5 weeks is needed to achieve protection of a refugee community. Therefore, a reactive strategy that consists of launching a mass vaccination campaign once the cholera outbreak has already started is likely to have only a limited impact. This finding, obtained from a practical experiment, supports the conclusions of a recent cost-effectiveness study of cholera control strategies which underlined that only pre-emptive vaccination should be recommended in refugee settings (7).

Our study also demonstrated that significant human and logistic resources are needed to carry out a mass vaccination campaign with this type of cholera

vaccine. This suggests that the use of this vaccine during complex emergencies can be considered only in circumstances where the risk of outbreak is extreme, and where such resources are available. Indeed, the potential for cholera vaccination to disrupt priority relief operations would be high during the acute phase of displacement of a population.

Apart from refugee camps in the post-emergency phase, the lessons learned during the mass campaign in Adjumani could be applied to other African settings. Like refugees, inhabitants of large urban slums often live in environments characterized by overcrowding, poor hygiene and sanitation, lack of safe water, and limited access to health care. We believe that pre-emptive vaccination could be considered not only for refugees but also for urban slums, which harbour a fast-growing population of millions of people throughout the African continent and where the risk of cholera outbreak is high.

However, before recommending strategies based on pre-emptive vaccination of populations at risk with WC/rBS, issues related to vaccine cost and availability must be addressed. As demonstrated by our study, the main economic determinant of such a strategy would be the cost of the vaccine itself. The current vaccine price has been set for the traveller's market and is not affordable for large-scale use in developing countries. Furthermore, at present there is no sufficient stockpile of WC/rBS readily available to cover quickly the needs of any large preventive operation. A stockpile of at least 1 million doses should be established and maintained at the international level before the use of cholera vaccine could be recommended.

For all these reasons, more work is needed to develop a cholera vaccine both easy to use and effective that would be affordable for large-scale use. In this regard, it is interesting to mention that a two-dose oral killed cholera vaccine, produced in Viet Nam at low cost, has already been successfully evaluated (10). This vaccine does not require a buffer solution, which would further reduce the cost and simplify the logistics of its delivery. Its bivalent (O1 + O139) formula is now being field-tested in Viet Nam. If it proves to be effective, its use in refugee situations should be considered. ■

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Résumé

Vaccination de masse par deux doses de vaccin anticholérique oral dans un camp de réfugiés

Les vaccins contre le choléra administrés par voie orale représentent de nouveaux moyens de lutte contre les épidémies. Dans les populations réfugiées ou déplacées, l'utilisation de ces vaccins est controversée dans la mesure où une campagne de masse contre le choléra risque, dans ce contexte, de désorganiser d'autres interventions prioritaires. Nous présentons ici une étude sur la faisabilité d'une telle campagne dans un camp de réfugiés de grande taille. La campagne de vaccination a été réalisée en octobre 1997 parmi 44 000 réfugiés du Sud-Soudan en Ouganda. Deux doses de vaccin tué germes entiers sous unité B recombinante ont été administrées. L'étude a mesuré la quantité de vaccin utilisée, la proportion d'abandons entre les deux tours, la quantité de vaccin perdue, la rapidité d'administration, le coût direct de la campagne et la couverture vaccinale estimée à partir d'une enquête transversale par échantillonnage systématique. Au total, 63 220 doses de vaccin ont été administrées. La proportion de perte était de 9,4%. Au mieux, chaque équipe de vaccination a pu vacciner 200 personnes par heure. Les coûts directs de la campagne se montaient à US \$14 655, coût du

vaccin non compris. A US \$1 la dose, le coût par individu complètement vacciné s'élèverait à US \$3,7. Mesurée sur une carte, la couverture vaccinale était respectivement de 83,0 et 75,9% pour le premier et le second tour. Cette étude montre que la vaccination de masse d'un grand nombre de réfugiés avec un vaccin anticholérique oral est réalisable. Le principal problème logistique rencontré était le volume représenté par le vaccin et la solution tampon à transporter et à manipuler. Le vaccin a été bien accepté par les bénéficiaires, malgré quelques difficultés d'administration chez les très jeunes enfants. Une vaccination préventive dans les camps de réfugiés stables et les zones urbaines défavorisées pourrait être envisagée lorsqu'il existe un risque élevé d'épidémie de choléra. Cependant, le coût potentiel de ce vaccin et le fait qu'il n'existe pas aujourd'hui de stock de vaccin suffisant et rapidement mobilisable font qu'il est difficile de recommander une telle stratégie. A ce stade, il importe de souligner les perspectives intéressantes offertes par le vaccin tué bivalent (O1 + O139). Ce vaccin est en cours d'évaluation au Viet Nam où il pourrait être produit localement à faible coût.

Resumen

Vacunación masiva con dos dosis de una vacuna anticolérica oral en un campamento de refugiados

Las vacunas orales contra el cólera son una nueva arma potencial contra las epidemias de esa enfermedad. En las poblaciones refugiadas desplazadas, el recurso a dichas vacunas es una decisión controvertida, ya que al lanzar una campaña masiva contra el cólera se corre el riesgo de desarticular otras intervenciones prioritarias en esas circunstancias. Presentamos aquí un estudio de la viabilidad de una iniciativa de vacunación de esa índole en un campamento de refugiados de grandes dimensiones. Dicha campaña se llevó a cabo en octubre de 1997 entre 44 000 refugiados del sur del Sudán llegados a Uganda. Se administraron dos dosis de la vacuna inactivada de células enteras y subunidad B recombinante (WC/rBS). Se determinaron la cantidad de vacuna utilizada, la proporción de abandonos entre las dos tandas, la cantidad de vacuna perdida, la rapidez de administración, el costo directo de la campaña y la cobertura vacunal estimada a partir de una encuesta transversal por muestreo sistemático. En total se administraron 63 220 dosis de vacuna. La proporción de pérdidas fue del 9,4%. Cada equipo de vacunación pudo vacunar como máximo a 200 personas por hora. Los costos directos de la campaña se elevaron a US\$ 14 655, excluida la vacuna. Partiendo de un precio

de US\$ 1 por dosis, el costo por individuo completamente vacunado habría sido de US\$ 3,7. La cobertura vacunal determinada cartográficamente fue del 83,0% y el 75,9%, respectivamente, para la primera y la segunda tandas. Este estudio demuestra la viabilidad de la inmunización masiva de una importante población de refugiados con una vacuna oral contra el cólera. El principal problema logístico surgido guarda relación con el volumen de la vacuna y la solución amortiguadora que había que transportar y manejar. La vacuna WC/rBS fue bien aceptada por los destinatarios, pese a que en el caso de los niños de muy corta edad hubo algunos problemas de administración. Podría preverse una vacunación preventiva en los campamentos de refugiados estables y en zonas urbanas desfavorecidas en las situaciones de riesgo elevado de epidemia de cólera. No obstante, el costo potencial de la vacuna WC/rBS y el hecho de que las existencias de la misma no son ni suficientes ni rápidamente movilizables hacen poco recomendable una estrategia de esa naturaleza. Por el momento, es importante subrayar las interesantes perspectivas abiertas por la vacuna bivalente (O1+O139) inactivada que se está evaluando en Viet Nam, donde podría fabricarse localmente a bajo costo.

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