

INFECTION

Mass vaccination is feasible in response to cholera epidemics

Amit Saha and Firdausi Qadri

Cholera is a public health problem worldwide, with prevalence increasing over the past decade. A safe and affordable oral cholera vaccine is now available, and a study in Guinea has demonstrated that a cholera vaccination programme can be conducted with success in high-risk areas at the beginning of a cholera epidemic.

Saha, A. & Qadri, F. *Nat. Rev. Gastroenterol. Hepatol.* **10**, 700–701 (2013); published online 19 November 2013; doi:10.1038/nrgastro.2013.217

Cholera is a worldwide problem, particularly in populations beset by poverty and at risk of outbreaks and epidemics. It is an ancient disease, but has increased in prevalence in the past decade, specifically in certain regions in South East Asia and Africa, as well as in Haiti.¹ Cholera is spread by person to person transmission, through the faecal–oral route; disruption of water supply, poor sanitation infrastructure, poor living conditions as well as cultural and genetic factors predispose populations to the rapid spread of the disease.²

“...immunization against cholera in epidemic and endemic settings is becoming more popular...”

Improving factors such as water supply and sanitation has been understood to be important for the control of cholera for a long time. These infrastructural improvements require financial resources as well as dedication from governments who have financial constraints that are often difficult to overcome. Immunization against cholera to control the disease has not been implemented in many countries at high risk. However, with the availability of a safe, affordable and easy to use oral cholera vaccine, immunization against cholera in epidemic and endemic settings is becoming more popular to prevent infections, transmission and severe disease.³ A WHO stockpile of oral cholera vaccine has already been initiated.⁴ The acceptability, affordability, global vaccine availability and capacity

to implement vaccination strategies in developing countries need proof and documentation. Ciglenecki *et al.*⁵ evaluated the feasibility of a mass vaccination programme in Boffa and Forecariah on the western coast of Guinea, Africa.

Cholera is endemic in Guinea, and various districts have faced major outbreaks of the disease since 1994, which have accounted for large numbers of cases and case fatality ranging from 3.6–8.6%.⁶ Peaks of epidemics are observed annually in the rainy season between July and August.⁶ A devastating cholera epidemic was ongoing in neighbouring Sierra Leone in 2012, and an unexpected and untimely outbreak of the disease was observed in two districts in Guinea in February of the same year. These factors prompted mass vaccination with the affordable oral cholera vaccine Shanchol™ (Shantha Biotechnics, Hyderabad, India) in an attempt to control the epidemic. Thus, the cholera-prone areas of Boffa and Forecariah were selected for vaccination; individuals >12 months old received two doses of Shanchol™ at an interval of 2–3 weeks.⁵ The vaccine was shipped under cold chain conditions directly from the manufacturer in India or from the Medecins sans Frontières stock in Kampala, Uganda. The two-dose vaccine was targeted to 209,000 people at high risk of contracting cholera living in the two districts. 287 vaccination sites with 43 teams were involved in the programme.⁵ Shanchol™ requires cold chain management;⁷ however, over the course of the day the vaccine was kept at ambient temperature and then stored again in the cold. Vaccination was carried

“The study yet again confirms the safety of the oral cholera vaccine...”

out between April and June 2012, with only a few weeks between inception of plans and actual vaccination.

Vaccine coverage in the study for at least one dose was 92% in Boffa and 71% in Forecariah district. For two doses, the coverage was 68% in Boffa and 51% in Forecariah. Vaccine wastage rate was <1% and each team on average vaccinated 703 persons daily. A record number of 172,544 doses of the vaccine were delivered in a period of 5 weeks, enabling completion of the programme before the start of the cholera season. The vaccine was found to be safe with only 46 adverse events reported.⁵ The study yet again confirms the safety of the oral cholera vaccine as studies in Kolkata, India, and Bangladesh have shown earlier.^{7,8}

This feasibility study used Shanchol™ as a truly public health tool, and stringent conditions were not used for selection of participants, maintenance of cold chain storage or for monitoring of adverse events. There was no exclusion criteria for pregnancy, immunocompromised health conditions or nutritional status and the vaccine was given to all participants >12 months of age.⁵

Health economics studies showed low costs for delivery of one dose of vaccine (~US\$1), with the vaccine cost at US\$1.85 per dose.⁵ The campaign was over-resourced with over-sized vaccination teams. To overcome these expenses during a routine vaccination programme, government staff who are involved in vaccinations could be included in the campaign. Vaccination cards for follow-up and surveillance would also be useful. Ciglenecki *et al.*⁵ suggest that simplification of the vaccine vial presentation and packaging could reduce the time needed for vaccination and potentially enable storage of vaccines at ambient temperature. Furthermore, the authors of the study suggest the use of single dose vaccines for mass vaccination studies. In endemic settings, baseline immune responses and memory to the pathogen already exist in the population. Therefore, a single dose of cholera vaccine might act as booster dose eliminating the

need for the second dose, saving costs and more importantly improving its delivery to large numbers of people within a very short time, especially during epidemics.

“For cholera vaccines, benefit can be achieved by both direct and indirect protection”

The study demonstrated that mass cholera vaccination can be conducted with success at the beginning of a cholera epidemic. Before the implementation of a mass cholera vaccination programme using oral cholera vaccines, practical issues need to be considered, such as selecting a target population, time of vaccination, cost, logistical challenges and official registration of the vaccine by national authorities. Funding for oral cholera vaccine stockpiles, which has now been obtained, is important for the timely implementation of large campaigns.⁴ The concept of herd protection will also have a vital role in increasing the effect of vaccination and reducing the cholera burden.⁹ Finally, the need for effective surveillance is of utmost importance for estimating the disease burden and assessing the efficacy of control strategies. Ciglenecki *et al.*⁵ did not

present effectiveness data but plan to do so later. However, it is difficult to conceive from the design of the study how these analyses will be performed, as people were vaccinated in two districts and there is no mention of a control population who could be analysed for surveillance. However, the cholera peak was reported to be at low levels in the vaccinated regions, which indirectly demonstrates the effectiveness of the vaccine. No immunological tests were carried out to determine the vaccine specific response in the Guinean population in different age groups.

In conclusion, the study provides evidence that Shanchol™ is safe and can be delivered at ambient temperature in a short interval of time to large numbers of people living in high-risk areas at the onset of a cholera epidemic. For cholera vaccines, benefit can be achieved by both direct and indirect protection,^{9,10} although it is not clear whether the study by Ciglenecki *et al.* is designed to determine herd protection.

International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B), Centre for Vaccine Sciences, 68 Shaheed Tajuddin Ahmed Sarani, Mohakhali, Dhaka 1212, Bangladesh (A. Saha, F. Qadri).

Correspondence to: F. Qadri
fqadri@icddr.org

Competing interests

The authors declare no competing interests.

1. Ali, M. *et al.* The global burden of cholera. *Bull. World Health Organ.* **90**, 209–218A (2012).
2. Schwartz, B. S. *et al.* Diarrheal epidemics in Dhaka, Bangladesh, during three consecutive floods: 1988, 1998, and 2004. *Am. J. Trop. Med. Hyg.* **74**, 1067–1073 (2006).
3. [No authors listed]. Cholera, 2011 [English, French]. *Wkly Epidemiol. Rec.* **87**, 289–304 (2012).
4. Martin, S., Costa, A. & Perea, W. Stockpiling oral cholera vaccine. *Bull. World Health Organ.* **90**, 714 (2012).
5. Ciglenecki, I. *et al.* Feasibility of mass vaccination campaign with oral cholera vaccines in response to an outbreak in Guinea. *PLoS Med.* **10**, e1001512 (2013).
6. WHO. Cholera country profile: Guinea. WHO [online], <http://www.who.int/cholera/countries/CountryProfileGuinea2013.pdf> (2013).
7. Mahalanabis, D. *et al.* A randomized, placebo-controlled trial of the bivalent killed, whole-cell, oral cholera vaccine in adults and children in a cholera endemic area in Kolkata, India. *PLoS ONE* **3**, e2323 (2008).
8. Saha, A. *et al.* Safety and immunogenicity study of a killed bivalent (O1 and O139) whole-cell oral cholera vaccine Shanchol, in Bangladeshi adults and children as young as 1 year of age. *Vaccine* **29**, 8285–8292 (2011).
9. Ali, M. *et al.* Herd immunity conferred by killed oral cholera vaccines in Bangladesh: a reanalysis. *Lancet* **366**, 44–49 (2005).
10. Khatib, A. M. *et al.* Effectiveness of an oral cholera vaccine in Zanzibar: findings from a mass vaccination campaign and observational cohort study. *Lancet Infect. Dis.* **12**, 837–844 (2012).