Use of Oral Cholera Vaccine in Humanitarian Emergencies

Introduction

Humanitarian emergencies frequently result in mass population movements and resettlement in temporary locations, characterized by overcrowding, economic and environmental degradation, impoverishment, scarcity of safe water, poor sanitation and waste management, absence of shelter, poor nutritional status as a result of food shortages, and poor access to health care. These risk factors place populations affected by a humanitarian emergency at risk of high morbidity and mortality from infectious diseases. In areas where *V. cholerae* is endemic, the risk of cholera transmission is particularly high and requires rapid and effective interventions to avoid major and devastating outbreaks such as the ones that affected the Democratic Republic of the Congo in 1994[1] and Zimbabwe in 2008-9[2].

1. Cholera Prevention and Control in Humanitarian Emergencies

Cholera prevention and control should be a priority whenever an emergency occurs in an area in which the disease is endemic. The mainstay of control measures to be implemented during emergencies should remain (i) implementing interventions to improve water and sanitation, (ii) providing appropriate treatment to people with cholera and (iii) mobilizing communities. All of these interventions must also be supported by epidemiological surveillance (see Box in the Annexes).

Given the availability of 2 WHO-prequalified Oral Cholera Vaccines (OCV), Dukoral® and Shanchol®, and data on their efficacy, field effectiveness, feasibility and acceptance in cholera-affected populations, immunization with these vaccines should be considered by local health authorities in conjunction with other prevention and control strategies in areas at risk for cholera to help prevent potential outbreaks or the spread of current outbreaks to new areas.

Vaccination should not disrupt the provision of other high-priority health interventions to control or prevent cholera. Vaccines provide immediate, short-term protection that can be implemented while the interventions to improve access to safe water and sanitation are also put into place.

If implemented, vaccination should cover as many people as possible who are eligible to receive the vaccine, and should be conducted as quickly as possible. In the event that the number of available vaccine doses is limited, priority should be given to those population groups most likely to be severely affected (e.g. children under 5 in endemic settings, people living in areas with limited access to health care) and/or most exposed (people with no access to WaSH).

The feasibility and impact of vaccination should be documented and the results widely disseminated.

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[1] Goma Epidemiology Group. Public health impact of Rwandan refugee crisis: what happened in Goma, Zaire, in July, 1994. The Lancet. 1995, 345:339-344

[2] Mason P R. Zimbabwe experiences the worst epidemic of cholera in Africa. *J Infect Developing Countries* 2009; 3(2):148-151

2. Oral Cholera Vaccines

Both WHO-prequalified OCV are whole-cell, killed vaccines of *V. cholerae* O1. Shanchol® also includes the O139 serogroup and, unlike Dukoral®, does not contain the recombinant cholera toxin B subunit which makes it less expensive to produce and easier to administer.

Both vaccines have a 2-dose regimen (3 doses for Dukoral® in children aged 2–5 years), orally administered, and require a cold chain. They have proved to be safe and effective. In a recent trial in India, Shanchol® demonstrated 65% protection at five years in a population >1 year[3]. Dukoral® has been shown to provide 85% protection at 4–6 months of follow up and also confers significant short-term protection against Enterotoxigenic Escherichia coli (ETEC)[4]. See Table for vaccine schedules and administration in the Annexes.

3. Experience in use of OCV in mass-vaccination campaigns

OCVs have been used in mass-vaccination campaigns since 1997 as an additional tool for cholera control to supplement existing priority cholera control measures. Mass vaccination with OCVs acts directly, by protecting people receiving the vaccine, and indirectly, by reducing the risk of further contamination of the environment by those infected with *V. cholerae*. There is also evidence that OCVs confer significant herd protection[5].

Most mass vaccination campaigns with OCV have so far been pre-emptive and have taken place before any potential upsurge in cholera transmission or detection of outbreaks in targeted populations and areas at risk, including during humanitarian crises. On some occasions, mass vaccination campaigns with OCV have been organized on a reactive basis, as part of the response to a cholera outbreak which had already commenced, to reduce mortality and limit the spread of the disease.

Overall, more than 1.6 million doses of WHO pre-qualified OCV have been deployed in mass vaccination campaigns since 1997. Pre-emptive campaigns have been conducted in endemic settings in Beira, Mozambique (2003/04), and Zanzibar (2009). Pre-emptive use in refugee camps and post-crisis situations have been reported from Uganda (1997), Darfur, Sudan (2004), Aceh, Indonesia (2005), Haiti (2012), South Sudan (2013) and Thailand (2013).

Reactive mass vaccination campaigns were also organized as part of the response to a cholera outbreak in the Federated States of Micronesia (2000), Mayotte, France (2000), Marshall Islands (2000), Guinea (2012) and Solomon Islands (2012).

4. Decision-making tool for use of vaccines during humanitarian emergencies

With the support of SAGE, WHO has developed a decision-making tool to help decision-makers determine whether or not the delivery of one or more vaccines during the acute phase of an

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[3] Bhattacharya SK et al. 5 year effi cacy of a bivalent killed whole-cell oral cholera vaccine in Kolkata, India: a cluster-randomised, double-blind, placebo-controlled trial. *Lancet Infect Dis* 2013; 13: 1050–56

[4] Jelinek T, Kollaritsch H. Vaccination with Dukoral against travelers' diarrhea (ETEC) and cholera. *Expert Rev Vaccines.* 2008 Jul;7(5):561-7

[5] Ali M, Emch M, Von Seidlein L, Yunus M, Sack D, Rao M, Holmgren J, Clemens J. Herd Immunity Conferred by Killed Oral Cholera Vaccines in Bangladesh: A Reanalysis. *The Lancet,* 2005, 366(9479): 44-49

emergency would result in an overall saving of lives and a reduction in the burden of disease among the population[6]. The decision should be based on the assessment of the epidemiological risk posed by each Vaccine Preventable Disease (VPD) within a given context, and the properties of each vaccine to be considered for intervention, including the capacity to organize a mass campaign. Careful consideration should also be given to key ethical principles and contextual issues influencing the decision-making process.

Specifically for cholera, the decision to organize a mass campaign with OCV should be guided by:

1. A risk assessment for a cholera outbreak and the identification of areas / populations most at risk for outbreaks.
2. An assessment of whether key public health priorities for cholera control are or can be implemented in a timely manner, combined with an analysis of the capacity to contain a possible outbreak.
3. An assessment of the feasibility of an immunization campaign using OCV without disrupting the provision of other high-priority health interventions.

The biggest challenges for implementing an OCV mass vaccination campaign include:

- The availability of doses of vaccines to cover the target population (including registration of the vaccine in the country).
- Time required for the vaccines to reach beneficiaries from the producer
- Access to the target population (infrastructure, climate, security)
- Population stability to ensure administration and completion of the 2 doses
- Logistics (transport, cold chain, etc.) of a sufficient scale to support the volume of vaccines
- The availability of human and financial resources to conduct the campaign

See [7] for further details on the organization of a mass vaccination campaign with OCV.

5. Vaccination of deployed staff with OCV

Cholera affects mainly the most vulnerable populations who are living in situations that lack access to safe water and sanitation.

Primary prevention is possible by observing a few simple rules of good hygiene and safe water and food preparation. These include scrupulous washing of hands with safe water and soap, especially before food preparation and eating, thorough cooking of food, and consumption while hot ("boil it, peel it or leave it"), boiling or treatment of drinking water, and use of sanitary facilities.

Vaccination recommendations for staff before deployment should be based on risk assessment. Staff deployed should first be advised about the risks, and should be briefed on primary prevention. They can receive the OCV when available, if they wish, providing there is time to receive the 2 doses and ensure protection prior to departure (the 2 doses should be administered at a minimum of one week interval ; the protection starts one week after the second dose).

[6] SAGE Working Group on Vaccination in Humanitarian Emergencies. Vaccination in Acute Humanitarian Emergencies: a Framework for Decision-Making. 2012.
[7] Oral cholera vaccines in mass immunization campaigns guidance for planning and use. http://whqlibdoc.who.int/publications/2010/9789241500432_eng.pdf

Annexes

Cholera control methods

Cholera control methods involve both curative and preventive activities. Like other diseases spread by the faecal-oral route, universal access to potable water and adequate sanitation remain the mainstay of preventing both endemic cholera and cholera outbreaks, i.e. in both the immediate and longer-term, and include: the development of piped water systems with water treatment facilities (chlorination), interventions at the household level (water filtration; water disinfection with chlorine, solar systems or heat (boiling), improved water storage containers), as well as the construction of sewerage systems and latrines.

Early detection and timely and effective case management of cholera cases, reduces the case fatality rate to less than 1%, even in difficult contexts such as complex humanitarian emergencies and crisis situations. Disease surveillance and early warning systems should be strengthened, including the diagnostic capacities of the laboratories. Rapid and appropriate rehydration with Oral Rehydration Solutions (ORS) and IV fluids for severe cases are the cornerstones of cholera patient management. Antibiotic therapy is also recommended for severe cases.

Health education campaigns, adapted to local culture and beliefs, shall promote the adoption of appropriate hygiene practices such as hand-washing with soap, safe preparation and storage of food and breastfeeding. Awareness campaigns during outbreaks will also encourage people with symptoms to seek immediate health care.

Implementation / reinforcement of food safety laws for restaurants, food vendors and food processing factories and banning of unsafe agricultural practices (e.g., use of sewerage water to irrigate crops) are also key to help control cholera.

Characteristics of WHO pre-qualified oral cholera vaccines

Characteristics	Oral cholera vaccines	
Trade name	Dukoral®	Shanchol®
Type of vaccine	Killed whole cell vaccine *V.cholerae* O1 serogroup + recombinant B subunit of cholera toxin (WC/rBS)	Killed bivalent (O1 and O139 serogroups) whole-cell vaccine suspension (BivWC)
Presentation (or packaging)	3 ml single dose vials and 5.6 g of effervescent granules of sodium bicarbonate buffer in a sachet	1.5ml single dose vials (in 3 ml glass vial with aluminium cap)
Age	From 2 years of age	From 1 year of age
Administration course	- Adults and children 6 years and older: 2 doses given orally 1-6 weeks apart – booster dose after 2 years. - Children 2-5 years: 3 doses given orally 1-6 weeks apart – booster dose after 6 months. - Fasting required 1 hour before and after vaccination.	- 2 doses given orally 2 weeks apart. - A period of +3 days is accepted for second dose. - No official recommendation on booster yet.
Buffer	Dilution in 150ml of water (75ml for children 2-5 years) mixed with buffer	- No buffer needed - Water may be offered following ingestion of the vaccine, but is not required.
Protection/ efficacy	- Earliest onset of protection 7 days after 2nd dose. - 85-90% protection at 6 months in all age groups and 62% at 1 year in adults	- Earliest onset of protection 7-10 days after 2nd dose. - 65% protection for at least 5 years in > 1 year of age
Adverse effects /contraindications	- No major adverse effects reported. - Currently not recommended for use in pregnancy - Can be given to HIV-infected persons.	- No major adverse effects reported. - Currently not recommended for use in pregnancy - Currently not recommended in HIV/AIDS or other immuno-compromised states
Shelf life, storage and cold chain	- 3 year shelf life at 2-8° C. - Stable for 1 month at 37 ° C . 2 weeks at < 27 ° C - Do not freeze	- 30 months shelf life at 2-8° C - Stable for 21 days at 37° C - Do not freeze - VVM of type 14