

Introduction

Cholera is an acute intestinal infection caused by the bacterium called *Vibrio cholerae*. Throughout the history, devastating outbreaks of cholera have resulted in millions of cases and hundreds of thousands of deaths. Young children living in endemic areas are most affected by the disease, but any age group may suffer.

Altogether 7 cholera pandemics have been reported. The latest one, which is still ongoing, started in Indonesia in 1961, reached the African continent in the 1970s and South America in 1991. As the pandemic is still ongoing, the number of countries affected continues to increase. The disease is now considered to be endemic in many countries.

Bacteriology

Vibrio cholerae is a motile, curved Gram-negative bacillus and differences in the O antigens have led to the description of more than 200 serogroups, only two of which have been found to cause cholera. Cholera epidemics are caused by enterotoxin producing *V. cholerae* of serogroups O1 and O139 ('Bengal' strain).

V. cholerae O1 causes the majority of outbreaks worldwide. Serogroup O139, first identified in Bangladesh in 1992, possesses the same virulence factors as O1, and creates a similar clinical picture. Currently, the presence of O139 has been detected only in South-East Asia.

V. cholerae is a non-invasive organism that colonizes the lining epithelium of the gut after penetrating the mucous layer. It affects the small intestine through its secreted cholera toxin. As a result, water is drawn from the intravascular and extracellular spaces of the body, and rapidly lost into the gut lumen.

Mode of transmission

Humans are the only known natural host for *V. cholerae*, and the disease is spread by faecal contamination of water and food. Thus cholera endemicity and epidemicity are closely linked to poor sanitation.

Clinical Features

Most persons infected with *V. cholerae* do not become ill, although the bacterium is present in their faeces for 7-14 days. When illness does occur, about 80-90% of episodes are of mild or moderate severity and are difficult to distinguish clinically from other types of acute diarrhoea. Less than 20% of infected persons develop typical cholera with profuse, watery diarrhoea. It is associated with rapid dehydration and occasionally hypovolemic shock, which may be life-threatening.

Case fatality ranges from 50% or more without treatment to less than 1% among adequately treated patients. The incubation period varies from few hours to five days, usually 2 to 3 days.

Resistance to first-line antibiotics (tetracycline and doxycycline), as well as resistance to multiple drugs, occurs frequently and has been associated with more severe illness and higher rates of secondary infection.

Epidemiology

Global Situation

Globally, the number of deaths from cholera rose from 4948 in 2009 to 7543 in 2010, an increase of 52% with an overall CFR of 2.38%. Of the 32 countries that reported deaths from cholera, 20 were on the African continent: these countries accounted for 3397 deaths and 45% of the global total. In the Americas, Haiti reported 3990 deaths, accounting for 53% of the global total.

In year 2010, a total of 13 819 cases were reported from 14 countries in Asia, which accounted for 4% of the global total.

Situation in Sri Lanka

Cholera is a notifiable disease in Sri Lanka. Last confirmed cholera case in Sri Lanka was reported to the epidemiology unit in 2003. Last outbreak of cholera reported in Sri Lanka, was confirmed as due to sero group O139.

Cholera vaccine

Several oral cholera vaccines have been developed and proved to be safe, immunogenic and effective. Only 2 of these are currently being marketed, only one of which has been prequalified by WHO. Both available vaccines are whole-cell killed vaccines, one with a recombinant B subunit, the other without it.

WHO has never recommended the use of the parenteral cholera vaccine because of its limited protective efficacy (45% for 3 months) and its unsuitability for public health purposes. The previously licensed oral, live, attenuated single-dose vaccine too (CVD 103-HgR) is no longer being produced.

Characteristics of the cholera vaccines

There are two types of inactivated oral cholera vaccines currently available.

◆ Monovalent oral cholera vaccine (WC/rBS)

This monovalent oral cholera vaccine consisting of killed whole-cell *V. cholerae* O1 in combination with a recombinant B-subunit of cholera toxin (WC/rBS) has been marketed since the early 1990s.

Each 3.0 ml liquid vaccine dose vial contains heat and formalin inactivated Inaba, Ogawa, classic and El Tor strains of *V. cholerae* O1, 2.5×10^{10} vibrios of each, combined with 1.0 mg rCTB.

◆ Bivalent oral cholera vaccines

Bivalent oral cholera vaccines Shanchol and mORCVAX are based on serogroups O1 and O139. Unlike monovalent vaccine, these vaccines do not contain the bacterial toxin B subunit and will therefore not protect against ETEC.

Indications

- ◆ Vaccination against cholera is indicated for protection of the population at risk as, preschool-aged children, school-aged children, pregnant women and immunocompromized individuals during outbreaks.
- ◆ For immunization of travellers to highly endemic areas. Recommended to take 2 weeks before departure.

WHO recommends that immunization with currently available cholera vaccines be used in conjunction with the usually recommended control measures in areas where cholera is endemic as well as in areas at risk of outbreaks. Vaccination should not be the mainstay of control measures.

Efficacy

◆ Monovalent oral cholera vaccine (WC/rBS)

Inactivated oral cholera vaccine is well tolerated and confers high level (85 -90%) protection for 6 months after the second immunization in all vaccinees aged > 2 years. The level of protection is still about 50% 3 years after immunization in vaccinees who were aged > 5 years at the time of vaccination.

◆ Bivalent oral cholera vaccines

Bivalent oral cholera vaccines are considered safe and immunogenic against both O1 and O139 infection. This bivalent oral cholera vaccines provide relatively less short-term protection than monovalent vaccine against classical cholera,

but at 2 years and 3 years of follow up the protection was equal to, or better than with monovalent vaccines.

Immunization Schedule

◆ Monovalent oral cholera vaccine (WC/rBS)

Primary immunization consists of 2 oral doses given >7 days apart (but <6 weeks apart) for adults and children aged ≥ 6 years.

Children aged 2–5 years should receive 3 doses >7 days apart (but <6 weeks apart).

If the interval between the primary immunization doses is delayed for >6 weeks, primary immunization should be restarted.

Protection may be expected about 1 week after the last scheduled dose.

Provided there is continued risk of *V. cholerae* infection, one booster dose is recommended by the manufacturer after 2 years for adults and children aged ≥ 6 years. If the interval between the primary series and booster immunization is >2 years, primary immunization must be repeated.

For children aged 2–5 years one booster dose is recommended every 6 months, and if the interval between primary immunization and the booster is >6 months, primary immunization must be repeated.

◆ Bivalent oral cholera vaccines

According to the manufacturer, bivalent cholera vaccines should be administered orally in 2 liquid doses 14 days apart for individuals aged ≥ 1 year. A booster dose is recommended after 2 years.

Dosage & Administration

◆ Monovalent oral cholera vaccine (WC/rBS)

The vaccine is intended for oral use. Vaccine is provided in 3 ml single-dose vials together with the bicarbonate buffer (effervescent granules in sachets). Vaccine and buffer are mixed in 150 ml of water for persons aged >5 years and in 75 ml of water for children aged 2–5 years. Food and drink should be avoided 1 hour before and 1 hour after vaccination.

The inactivated oral cholera vaccine can be given at the same time as other travel vaccines.

◆ Bivalent oral cholera vaccines

The vaccine is intended for oral use. 1.5 ml single dose vials available.

Storage

The recommended storage temperature for both vaccines is +2⁰ C to +8⁰ C . Do not freeze. Protect from light.

Cautions and contraindications

Except for possible hypersensitivity to any of the components, no contraindications are known for oral cholera vaccines. It is well tolerated by HIV-positive and immunocompromised individuals.

This vaccine has been proved to be safe even in pregnancy and during breastfeeding.

Postpone administration during either an acute febrile illness or acute gastrointestinal illness with persistent diarrhoea or vomiting, until recovered.

Adverse Events

Occasional mild gastrointestinal disturbances were reported following oral cholera vaccination.

Sources

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