

Rotavirus vaccines WHO position paper

Summary

Rotaviruses (RVs) are globally the leading cause of severe, dehydrating diarrhoea in young children. Most children have been infected by these highly contagious viruses by the age of 5 years. The majority of severe rotavirus gastroenteritis (RVGE) episodes occurs in low-income countries and affects infants under one year of age. WHO estimates that in 2008 there were approximately 453 000 RVGE-associated child deaths. In most low income countries in Asia and Africa, the rotavirus epidemiology is characterized by episodes of relatively intense viral circulation against a background of year-round transmission. However, in high income countries in temperate climates, a distinct winter seasonality is typically observed.

Rotaviruses belong to the *Reoviridae* family. The outermost layer of these viruses contains the proteins VP7 and VP4 which stimulate the production of neutralizing antibodies. In human rotaviruses, at least 12 different VP7 antigens (G-types) and 15 different VP4 antigens (P-types) have been identified. Currently, 5 G-P combinations (G1P[8], G2P[4], G3P[8], G4P[8]) and G9P[8]) account for approximately 90% of all human rotavirus infections.

Rotaviruses damage the enterocyte lining of the small intestinal villi, leading to reduced absorptive capacity and diarrhoea. The wide clinical spectrum of rotavirus disease ranges from transient loose stools to severe diarrhoea and vomiting causing dehydration, electrolyte disturbances, shock and, in untreated cases, death. The cornerstones of treatment of severe RVGE are fluid replacement and zinc supplementation. An etiological diagnosis of rotavirus gastroenteritis requires laboratory confirmation.

Currently available vaccines are based on live, oral, attenuated rotavirus strains of human and/or animal origin that replicate in the human gut. Two rotavirus vaccines are marketed internationally: the monovalent (RV1) and the pentavalent (RV5). RV1 originates from a human strain, whereas RV5 contains 5 reassortants developed from rotaviruses of human and bovine origin.

A large number of randomized, controlled trials have shown that both RV1 and RV5 are 80%-90% efficacious against severe RVGE in countries with very low or low child and adult mortality, and 40% - 60% efficacious in countries with high child mortality and high or very high adult mortality. In most cases, vaccination in infancy provides protection against severe RVGE for at least 2 years. Breastfeeding and prematurity (<37 weeks' gestation) do not significantly impair the response to the rotavirus vaccines.

In large controlled trials, no differences were observed between the vaccine groups and the placebo groups in terms of serious adverse events. However, in some, but not all settings, post-marketing surveillance has detected a small increased risk of intussusception (about 1–2/100 000 infants vaccinated) shortly after the first dose. Still, the benefits that rotavirus vaccination provides, through prevention of severe diarrhoea and death from rotavirus infection, far exceed the risk of intussusception.

WHO recommendations: Rotavirus vaccines should be included in all national immunization programmes and considered a priority, particularly in countries with high RVGE-associated fatality rates, such as in south and south-eastern Asia and sub-Saharan Africa. The use of rotavirus vaccines should be part of a comprehensive strategy to control diarrhoeal diseases.

Plans for introduction of rotavirus vaccines should consider the epidemiology of the disease by age, the coverage and actual age at vaccination and also include an evaluation of the estimated public health impact and potential risks. It is important to establish the baseline incidence of intussusception. Proper planning and training of staff to conduct pharmacovigilance should take place before the vaccine is introduced. Also, caregivers should be adequately counselled to recognize danger signs of dehydration or intussusception.

The first dose of rotavirus vaccine should be administered as soon as possible after 6 weeks of age. RV1 should be administered in a 2-dose schedule at the time of DPT1 and DPT2, and RV5 in a 3-dose schedule at the time of the DTP1, DTP2, and DTP3 contacts. Both vaccines are given orally with an interval of at least 4 weeks between doses.

Infants should receive rotavirus vaccine together with DTP regardless of the time of vaccination. Rotavirus vaccination of healthy children aged over 2 years is not considered necessary. Rotavirus vaccinations can be administered simultaneously with other routine infant vaccines.

Apart from a very low risk of intussusception, the current rotavirus vaccines are safe and well tolerated. Major contraindications for rotavirus vaccination are severe allergic reaction after a previous dose and severe immunodeficiency. Precautions for use of rotavirus vaccination include a history of intussusception or intestinal malformations, chronic gastrointestinal disease, and severe acute illness. Vaccination should be postponed when the child has ongoing acute gastroenteritis or fever with moderate to severe illness.