Rotavirus infection

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Abstract
Rotavirus gastroenteritis is a common cause of severe infection throughout the world, even in countries with good hygiene and sanitation measures. Rotavirus infection is characterised by sudden onset of watery diarrhoea, fever and vomiting. Although the infection is usually mild and self-limiting, it can lead to severe dehydration with electrolyte imbalances followed by death. Prevention of rotavirus infections can best be achieved through vaccination. The rotavirus vaccine has been shown to be a safe and effective vaccine. The World Health Organization recommends that rotavirus vaccination be incorporated into all national immunisation schedules.

Introduction
Rotavirus infections are a common cause of severe gastroenteritis in infants and young children worldwide. Most children will have had their first infection by the age of 3 years. In developing countries, most children are infected before 1 year of age. The World Health Organization (WHO) estimates that approximately 527,000 children under 5 years of age die annually from rotavirus infections. In this article we discuss rotavirus infection and focus on the prevention of rotavirus infection through vaccination.

Rotavirus
Rotavirus is a double stranded RNA virus in the family Reoviridae. Two structural viral proteins namely VP4, the protease cleaved protein (P protein) and VP7 the glycoprotein (G protein) are situated on the outer surface of the virus. These two proteins define the serotype of the virus and elicit distinct serotype specific neutralising antibodies. The gene segments that encode G protein and P protein can segregate independently and therefore a typing system consisting of P and G proteins has been developed. Fourteen rotavirus G serotypes have been identified. However, the P serotypes are more difficult to determine and molecular methods are used to define genetically distinct P proteins by nucleotide sequencing.

In the United States (US) the serotype G1 accounts for 75% of rotavirus infections and G1, G2, G3, G4 and G9 together account for 90% of infections in children younger than 5 years.

In a large placebo-controlled trial conducted in Malawi and South Africa, it was found that serotype G1 accounts for approximately 50% of infections in South Africa. Other serotypes causing infection in South Africa include G2, G8, G9 and G12.

Transmission of rotavirus
In South Africa, rotavirus infection peaks during winter to spring. Rotavirus is shed in high concentrations in the stools of an infected person. Virus is shed from two days before the onset of diarrhoea up to 10 days after the onset of symptoms. However, immunocompromised individuals including those infected with human immunodeficiency virus (HIV) shed virus in the stools for longer periods.

Transmission to susceptible individuals is primarily by faecal-oral spread through close person-to-person contact and by contact with contaminated toys or other surfaces. Rotavirus is very stable and may remain viable in the environment for weeks if not disinfected. Few infectious virions are needed to cause disease in a susceptible individual.

Rotavirus enters the body through the mouth. Viral replication occurs in the villous epithelium of the small intestine. Rotavirus also contains a nonstructural protein that acts as a viral enterotoxin. The enterotoxin plus the replication process destroys the epithelial surface resulting in blunted villi and extensive damage.

Rotavirus infection may lead to isotonic diarrhoea due to decreased intestinal absorption of sodium, glucose, and water and decreased levels of intestinal lactase, alkaline phosphatase and sucrase activity.

Clinical features of rotavirus infection
The incubation period is usually less than 48 hours. Although the clinical spectrum of disease ranges from asymptomatic infection to severe dehydration with electrolyte imbalance and death, the disease is characterised by the sudden onset of watery diarrhoea, fever and vomiting. In most children, the disease is mild. Vomiting usually lasts less than 24 hours and other gastrointestinal symptoms generally resolve within 3-7 days.

Children who are immunocompromised due to a congenital deficiency or because of a bone marrow or solid organ transplant, may experience severe or prolonged rotavirus gastroenteritis.
appears as though rotavirus infection is not more severe in HIV infected children compared with children not infected with HIV.2

Children can be infected with rotavirus several times.1,5 Recovery from the first rotavirus infection does not lead to permanent immunity. After the first natural infection1,5:

• 38% of children are protected against subsequent rotavirus infection
• 77% of children are protected against rotavirus diarrhoea
• 87% of children are protected against severe disease

Subsequent infections confer progressively greater protection against reinfection and infections are generally less severe than the first.1,5

Rotavirus infections are more likely to be severe in children aged 3–24 months.2 Rotavirus infection in infants younger than 3 months is often asymptomatic or mild.1 Maternal antibodies may protect infants less than 3 months of age.1,2 Adults can also contract rotavirus infections. Recurrent infections are usually asymptomatic or result in mild diarrhoea with vomiting and a low-grade fever.5

Individuals at increased risk of rotavirus infections are:5

• Children who attend daycare centres
• Hospitalised children
• Care takers and parents of children in daycare centres or in hospital
• Children and adults with immunodeficiency-related diseases

Treatment
Treatment of rotavirus gastroenteritis is supportive.9 Correcting dehydration and electrolyte imbalances can be achieved by administering oral rehydration solutions or by intravenous fluid administration if the dehydration is severe and the infant cannot take oral solutions.9

Prevention
Preventative measures include hand washing with soap, proper disposal of nappies and other infection control measures.9 However, rotavirus is a common cause of severe disease even in regions with high standards of health and good sanitation.2,4 Therefore, reduction of rotavirus infection is mainly through vaccination.2

Vaccination
The WHO recommends that the rotavirus vaccine should be included in all national immunisation programmes. The introduction of the vaccine is strongly recommended in countries where diarrhoeal diseases account for more than 10% of deaths in children aged less than 5 years.4

In South Africa, a live oral monovalent human rotavirus (RV1) vaccine is available (Rotarix®). It contains an attenuated human rotavirus strain RiX4414 that originated from a G1P1A[8] rotavirus strain.3,5

A large placebo-controlled trial was conducted in Malawi and South Africa to investigate the efficacy of the rotavirus vaccine (RV1) in African children during the first year of life.6 After completion of the vaccine series:

• the efficacy of RV1 in South African children was shown to be 76.9% (95% CI, 56-88.4%) in preventing severe rotavirus gastroenteritis.6,7

The vaccination course consists of 2 ORAL doses.1,4

• The first dose must be given between 6 weeks and 14 weeks of age.
• The second dose must be given between 14 and 24 weeks of age.

The interval between the two doses must be at least 4 weeks.

Each dose contains at least 10⁶ median cell culture infective units of virus.5,8

Due to the safety concerns resulting from the use of an older rotavirus vaccine (see below) the dosing schedule of RV1 must be strictly adhered to.1

The potential to transmit vaccine virus to other susceptible individuals has not been assessed.1,5

Adverse effects
No serious adverse reactions attributable to RV1 have been reported.6 Adverse effects occurring within 8 days of the vaccine in clinical trials included vomiting in 15–18%, diarrhoea in 9–24%, irritability in 13–62% and fever in 40–43%. However, the rate of these symptoms was similar in vaccinated and unvaccinated

The concern about intussusception
In 1998, a rhesus-human tetravalent rotavirus vaccine was licensed in the United States and recommended for routine use in infants. Evaluations undertaken before the product was licensed showed the product to be safe and effective. However, in less than a year the vaccine was withdrawn from the market following an association between the vaccine and intussusception within 2 weeks of the vaccine being administered. Intussusception occurs when the intestine folds in on itself causing an obstruction.3 This adverse event was seen primarily after the first dose and occurred mostly in infants older than 3 months.2

Safety and efficacy data on the newer rotavirus vaccines (RV1 and RV5 a live, oral pentavalent human-bovine reassortant rotavirus vaccine available overseas), have been closely monitored. In December 2008, the WHO Global Advisory Committee on Vaccine Safety (GACVS) concluded that RV1 and RV5 are safe vaccines and the risk of intussusception as seen with the withdrawn rotavirus vaccine can be ruled out.2
Points to remember

- Infants who contract rotavirus infections before or during the vaccine series should still begin or complete the vaccination course. The infant may not have been infected with the same serotype that the vaccine will protect against and initial infection may only provide partial immunity.
- If the infant vomits after receiving the vaccine, the vaccine should not be repeated. The infant should receive the remaining dose as scheduled if it was the first dose that was regurgitated. If it was the second dose that was regurgitated no further doses should be given.
- Premature infants can be vaccinated with the rotavirus vaccine according to the same precautions as full-term infants. As long as the infant's chronological age is between 6-14 weeks for the first dose and 14 and 24 weeks for the second dose and the infant is clinically stable.
- As vaccine virus is shed in the stools, good hygiene measures are recommended after changing the infant's nappy.
- Breastfeeding does not interfere with the efficacy of RV1.

In conclusion

Gastroenteritis caused by rotavirus occurs throughout the world. Rotavirus gastroenteritis is mostly a mild self-limiting infection. However, it can be a severe illness requiring hospitalisation and may lead to death. The best option we have for preventing rotavirus gastroenteritis is through vaccination. The RV1 has been shown to be effective in South African children without serious adverse effects. The increased risk of intussusception seen with an earlier rotavirus vaccine has not been seen with either the RV1 or RV5 rotavirus vaccine. The RV1 vaccine is an oral vaccine and comprises of a course of 2 doses that must be given at the specified ages time intervals.

References:

Children. Other adverse effects listed as common include loss of appetite, fatigue, flatulence, abdominal pain, regurgitation of food.

Contro-indications

RV1 is contra-indicated in
- Infants who have had an anaphylactic reaction to a previous dose or to any of the vaccine components.
- Infants with a known or suspected immunodeficiency. However, RV1 can be given to asymptomatic HIV positive infants.
- Infants with any history of chronic gastrointestinal diseases including any uncorrected congenital malformation of the gastrointestinal tract.

Precautions

- RV1 should generally not be administered to infants with acute moderate or severe gastroenteritis or other acute moderate or severe illnesses until the condition improves. However, in the event of a mild acute illness the infant can be vaccinated particularly if a delay in vaccination will result in the first dose being given over the maximum age limit of 15 weeks and 0 days for the first dose.
- Infants with a history of intussusception may be at a higher risk of a repeat episode. Although RV1 has not been associated with intussusception, there is no data available on the administration of a RV1 in these infants.

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