Training in Infectious Diseases Modeling

A reflection on vaccination as a disease control measure

-Example of Rotavirus disease-

Participant's Guide

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Vaccination as a disease control measure
The example of Rotavirus disease-

Introduction

Since their identification in 1973, rotaviruses have been found to be one of the most important causes of gastroenteritis in both developed and developing countries with a big impact on morbidity and mortality especially in infants and young children.

By the end of this session, you will be able to:

1. Describe and give examples of information required about a disease prior to introduction of a vaccine
2. List the other issues involved in vaccine policy decisions
3. Reflect on factors that contribute to the success or failure of the use of vaccination as a measure for disease control in a particular context

PART I

Rotavirus is a double-stranded RNA virus, belonging to the family Reoviridae. The mode of transmission of rotavirus infection is primarily faecal-oral. The reservoir for persistence of rotavirus between the annual winter epidemics is unknown. However it is possible that healthy adults or partially immune children shed low levels of virus. The virus is stable in the environment, so a water-born reservoir is also possible.

At least 4 serotypes are clinically important in humans. Many serotypes are shared with animal viruses and these probably commonly exchange genetic material with human viruses ("reassortment").

Infants and young children most commonly have fever, vomiting and watery diarrhoea. Rotavirus enteritis can be associated with severe dehydration and death in young children. Natural rotavirus infection does not prevent re-infection in future but usually protects against severity of subsequent infections. Secondary symptomatic cases among adult family contacts can occur, although subclinical infections are more common. Illness caused by rotavirus is not distinguishable from that caused by other enteric viruses (cf. summary in annex 1.).

Q1. From what you know about rotavirus epidemiology, protection from natural rotavirus infection and knowing that a vaccine is available would you propose it as a control measure in your country? Why? What would be the aim of a vaccination programme: control, elimination, eradication?

Q2. What other information on the disease would you like to know in order to decide on the need for such a programme? Would it be easy to obtain in your country?

The most extensively evaluated candidate rotavirus vaccine consists of four live attenuated reassorted rotaviruses corresponding to the clinically important serotypes and produced in the 1990s. The clinical efficacy and safety of this vaccine has been studied in three multicentre trials in the US, a multicentre trial in Finland, and three single-site trials in Venezuela, Peru, and Brazil. US efficacy estimates showed a protection of 45% for rotaviral gastroenteritis, of 73% for physician intervention, of 80% for very severe rotaviral gastroenteritis, of 100% for dehydration and of 100% for hospital admission.

Q3. Based on the kind of protection showed by randomized control trials, what would be the aim of vaccinating children against rotavirus disease?

Q4. Besides disease burden, what other issues would you consider before developing a vaccine policy for your country?

Q5. Apart from the vaccinated, who would benefit the most from the campaign, who would be interested in its implementation?

Q6. Would you explore the acceptability of rotavirus vaccine before implementation and who would you target for this?

Q7. In your opinion, what factors, besides immunological failure, would contribute to the failure of vaccination as a control measure for rotavirus disease?

Assuming all randomised controlled trials conducted found no significant adverse effects associated with administration of the vaccine.

Q8. Would you consider it safe enough to be used? Are there more safety issues to be addressed once you implement the vaccination programme?

Q9. Once the programme is implemented, would the detection of adverse effects not found in early trials prompt you to take any decision(s) regarding the programme? What actions would you consider?

Part II.

Recent advances in molecular biotechnology have contributed to further confirming what has been known for two decades: 4 globally common rotavirus serotypes represent >95% of the rotavirus strains in circulation. But in addition to this, a much greater strain diversity has been identified, some emerging strains were so far thought to be rare. Recent studies also identified globally or regionally common serotype antigens not covered by the reassortant vaccines that have undergone efficacy trials.

Q10. As mentioned above, the tetravalent vaccine targeted four main serotypes and was tested in different populations: in the US, Finland, Venezuela, Peru, and Brazil. In your opinion, would there be consequences to introducing it in a population where the distribution of the serotypes differs? How would the use of rotavirus vaccine affect epidemiology of the disease?

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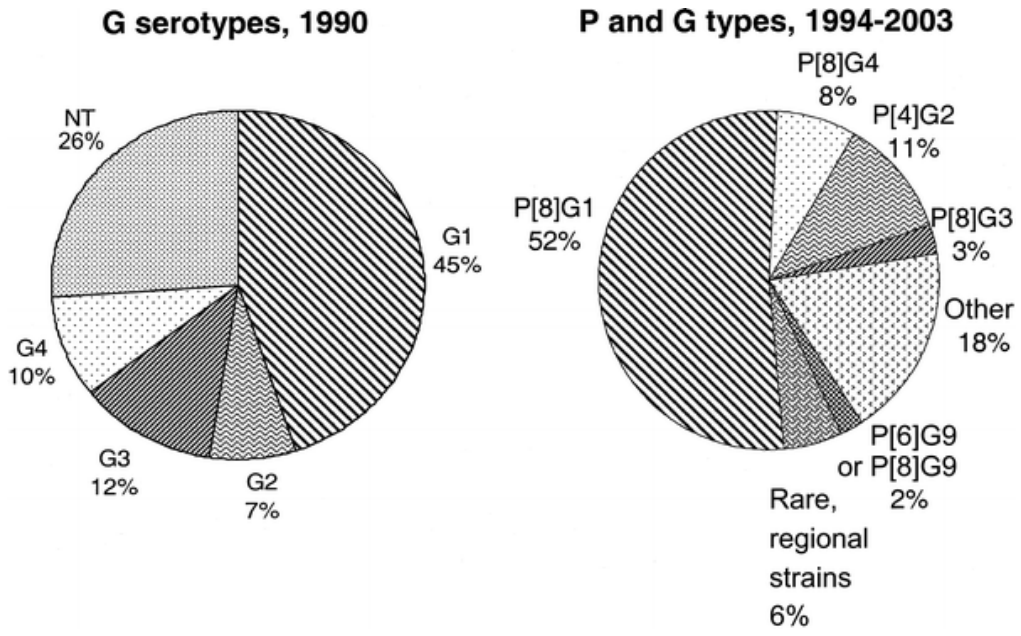

Figure 1. Findings from typing studies conducted during 1987–1991 that used G serotype–specific monoclonal antibodies (left panel; data are adapted from Woods et al.) or that used G-serotyping and P-genotyping or G- and P-genotyping (right panel). The "other" category in the chart of P and G types refers to strains that were nontypeable (NT) for P type, G type, or P and G type, or were mixed infections of common P or G types.

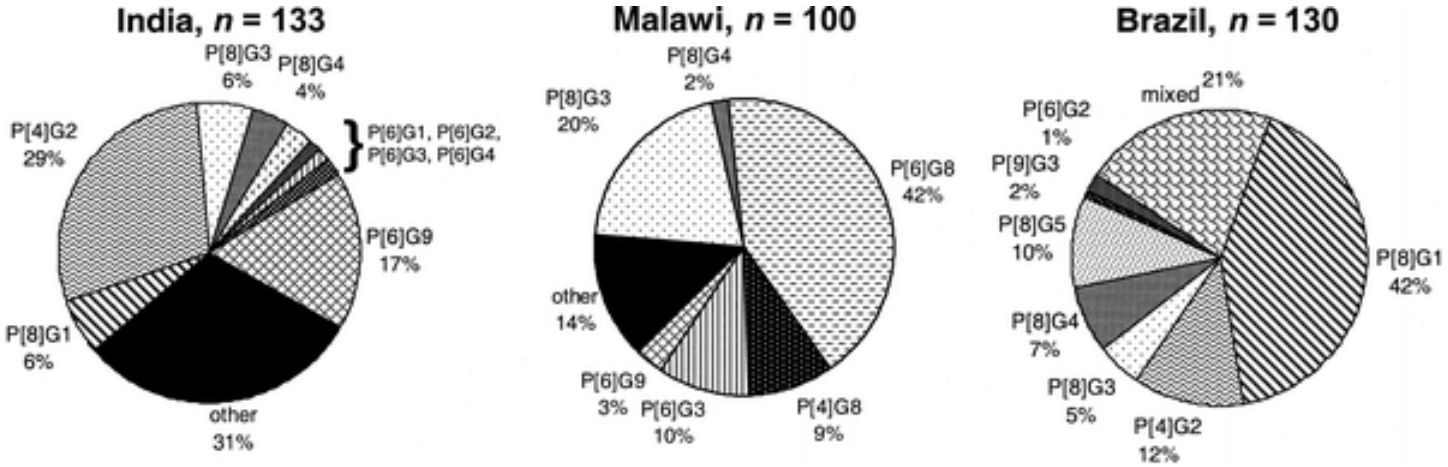

Figure 2. Examples of regionally important strains from India (n=133) [41, 42], Malawi (n=100) [53], and Brazil (n=130) [40]

Annex 1.

Rapid clinical overview – Rotavirus infections[1]

Agent 70 nm rotavirus, Reoviridae family
Symptoms & signs Sporadic, seasonal, often severe gastroenteritis: fever, vomiting and watery diarrhoea. Occasionally associated with severe dehydration and death in young children.
Incubation period: 24-72 hours **Period of communicability**: during the acute stage and later while virus shedding continues. Symptoms last for an average 4-6 days. Virus survives for long periods on hard surfaces, contaminated water or hands. It is relatively resistant to common used disinfectants but is inactivated by chlorine.
Diagnostic criteria (clinical and/or laboratory) Diagnosis is based on demonstration of rotavirus antigen in stool specimens or rectal swabs. False positive ELISA reactions are common in newborn.
Natural history – treated and untreated Rotavirus is more associated with more severe diarrhoea than other enteric pathogens. In temperate climate, rotavirus diarrhoea occurs in seasonal peaks during cooler months. Globally among children under 5 years of age, rotavirus may account for 30-40% of hospitalisations and deaths due to diarrhea, or 6% of all childhood deaths.
Treatment and/or prophylaxis No specific treatment known. Oral rehydration therapy is adequate in most of the cases. Parenteral rehydration needed in case of vascular collapse or uncontrolled vomiting. An oral, live, pentavalent vaccine is available for administration to infants between 6 weeks and 1 year in 2 or 3 doses, with a minimum interval between doses of a least 4 weeks.
Transmission Mainly faecal-oral with possible contact or respiratory spread. May be present in contaminated water. Very low infective dose (~10 virions)
Susceptibility; high risk groups Susceptibility greatest between 6-24 months of age. By age 3, most individuals have been infected with rotavirus. After primary infection with rotavirus, mild or asymptomatic infection in subsequent seasons is not uncommon. Thus, natural infection does not confer lifelong immunity against mild rotavirus disease.

[1] Heyman DL, Control of Communicable Diseases Manual, 18th edition, American Public Health Association