The Introduction of Rotavirus Vaccines into South Africa

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Abstract

The massive impact of rotavirus-associated diarrhoea on the children of South Africa and Africa has long been acknowledged. Effective properly administered rotavirus vaccine could potentially prevent 170 000 – 210 000 childhood deaths per year or about one in 20 deaths in children under five years of age. While the rotavirus vaccines will not prevent all forms of diarrhoea in children it will prevent children from developing rotavirus-associated severe dehydrating diarrhoea that requires hospitalisation and avert deaths due to this common childhood pathogen.

SA Fam Pract 2006;48(6): 57-58

Introduction

Children are expected to have an average of one to three episodes of diarrhoea per year, with incidences rates as high as 10 per year for children in poor, less developed locales. [1] While most parents and practitioners consider diarrhoea a minor ailment rather than a deadly condition, diarrhoeal diseases are estimated to cause 20-25% mortality among children less than five years in the developing world.[1] The most important aetiological agents of diarrhoea are viral and bacterial, with rotavirus and enterotoxigenic E. coli frequently identified among children in developing countries and viral aetiologies playing a larger role in more developed countries with improved sanitation and access to clean water.[2, 3]

Prevalence

Rotavirus, an icosahedral, non-enveloped virus belonging to the *Reoviridae* family has a segmented genome of 11 distinct segments of dsRNA enclosed by three protein layers. In Africa alone, recent estimates consign 140 000 – 150 000 deaths per year due to rotavirus disease in children less than five years.[4] Rotavirus accounts for 20-25% of all deaths due to diarrhoea and 6% of all deaths among children younger than five years.[5, 6] Virtually every child will have at least one rotavirus infection in the first five years of life and because public health interventions to provide clean water and improved sanitation will not decrease the incidence of rotavirus disease, vaccines were developed as the primary prevention tool against severe dehydrating rotavirus diarrhoea.

Clinical

Rotavirus diarrhoea affects the young of human and animals, and viral particles are transmitted by the faecal-oral route, although indirect evidence also suggests that they may also be transmitted by the respiratory route.[6, 7] The incubation period is estimated at less than 48 hours and the virus attacks the mature enterocytes on the tips of the small intestinal villi. An infection usually begins with a sudden onset of vomiting lasting one to two days and watery diarrhea lasting for approximately five days. These symptoms are usually accompanied by several days of fever (37.9°C or greater) and dehydration.[6] Rotavirus infections are seasonal and occur in the cool, dry winter months in temperate zones i.e. in South Africa the rotavirus season runs from late March, early April to July or August.

The peak incidence of rotavirus infection in children in developing countries occurs between 6 and 11 months of age, while children in developed countries tend to become infected later i.e. during their second year of life. In neonates, rotavirus infections may often be asymptomatic but after 3 months of age rotavirus infections are more likely to be symptomatic and result in severe life-threatening dehydration.[8] Reinfection with rotavirus is common during childhood, however, the severity of the disease rapidly decreases after the first infection and no child experiences the severe form of the disease after the second rotavirus infection.[9]

Vaccines

Two live, attenuated rotavirus vaccine candidates have been developed and licensed by multinational pharmaceutical companies. RotaRix™, developed by GlaxoSmithKline Biologicals (Rixensart, Belgium), is a serotype G1P[8] human strain, based on the observation that natural rotavirus

infections protect children against subsequent severe dehydrating diarrhoea. Vaccine trials in Finland, Latin America and Asia have indicated 68-90% efficacy against severe rotavirus diarrhoea and 56-73% efficacy against any rotavirus diarrhoea.[10] In South Africa, two vaccine trials assessing interference with oral polio vaccine and optimum vaccine dose have been completed and an additional two trials assessing vaccine efficacy and safety in HIV-positive babies will be completed by the end of 2006 or beginning of 2007.

The GlaxoSmithKline rotavirus vaccine was licensed by the European Commission in February 2006 and an additional 35 licenses have been granted worldwide including Mexico, Brazil, Philippines, Singapore and Australia. Furthermore, Rotarix™ has been filed for approval in 75 countries, the United States and South Africa among these. Rotarix™ was registered in South Africa in July 2006 and is now available on a two dose schedule to children in the private sector. Recently, Brazil, Panama and Venezuela have included the rotavirus vaccine in their national official vaccination calendars and vaccination with Rotarix™ will be available free at public health clinics in these countries (GSK Press Release 05 May, 2006).

The second candidate, RotaTeq®, developed by Merck (Blue Bell, PA, USA), is a pentavalent bovine-human reassortant containing the surface proteins for serotypes G1, G2, G3, G4 and P[8] while retaining a bovine (WC3) genome backbone.[11] The vaccine has been based on the observation that candidate vaccines were successful in inducing protection against rotavirus in areas where the prevalent circulating strains was the same as that of the vaccine strain.[12] Vaccine trials have been conducted from 2001 to 2004 in 11 countries (the United States, Belgium, Costa Rica, Finland, Germany, Guatemala, Italy, Jamaica, Mexico, Sweden and Taiwan) and results show a 98% efficacy against severe rotavirus diarrhoea and 74% efficacy against any rotavirus diarrhoea.[13]

RotaTeq® was licensed by the American Food and Drug Administration in February 2006 and is the only rotavirus vaccine currently available to the American public. In addition, RotaTeq® has received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP), the Scientific Committee of the European Medicines Agency (EMEA) and the European Commission could grant marketing authorization for the vaccine anytime from July 2006 onwards (Sanofi Pasteur MSD Press Release 02 May, 2006). RotaTeq® has been filed for licensure in more than 50 countries including South Africa (ACIP Press Release 21 February, 2006). RotaTeq® has not yet been tested in an African setting but Merck is working with the Program for Appropriate Technology in Health (PATH) to conduct clinical studies in developing countries and at least one vaccine trial is planned to start by the end of 2006 (Merck Press Release 07 December, 2005).

Conclusion

The massive impact of rotavirus-associated diarrhoea on the children of South Africa and Africa has long been acknowledged.[14,15] It is, therefore, reassuring to know that an effective properly administered rotavirus vaccine could potentially prevent 170 000–210 000 childhood deaths per year or about one in 20 deaths in children under five years of age.[16] While the rotavirus vaccines will not prevent all forms of diarrhoea in children it will prevent children from developing rotavirus-associated severe dehydrating diarrhoea that requires hospitalization and avert deaths due to this common childhood pathogen.

This article has been peer reviewed

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