International Journal of Scientific Study

Review Article

A Review of Current Practices for Management of Rotavirus Infection in Children Under - 5 Years in Ghana

Osonuga A[1], Osonuga O.A[2], Emegoakor C[3]

1 School of Medical Sciences, University of cape Coast, Cape Coast, Ghana. **2** School of Medical Sciences, University of cape Coast, Cape Coast, Ghana. **3** Director of Health Services/Adjunt Lecturer of Pharmacology, Olabisi Onabanjo University, Ago-Iwoye, Ogun state, Nigeria**.**

Abstract

Rotavirus causes significant morbidity and mortality in children less than five years. Various strategies have been explored in the control and prevention of rotavirus acute gastroenteritis. The main stay of prevention is vaccination. This review seeks to compare environmental sanitation (as a single entity) with vaccination against rotavirus. Google scholar, PUBMED and Cochrane library were used to gather articles used for this review. Vaccination showed to significantly reduce mortality, morbidity and transmission rates of rotavirus. Vaccination should however be integrated into pre-existing protocols for managing diarrheal diseases in children.

Keywords: Vaccination, Rotavirus, Acute Diarrhea Disease

Introduction:

Human Rotavirus is one of the most common causes of acute gastroenteritis (AGE) among infants and children. It is a genus of double-stranded RNA virus in the family Reoviridae. It was discovered in 1973 and accounts for the death of nearly 450,000 infants and children most occurring in developing countries.[1] Nearly every child in the world has been infected with rotavirus at least once by age five.[2] The virus is transmitted through the fecal-oral route. There are seven species of this virus referred to as A,B,C.D,E,F and G with Rotavirus A being the most common specie also identified as a major cause of dehydrating gastroenteritis in infants and young children.[1,2]

AGE is still a major cause of morbidity and mortality in children less than 5 years in sub-Saharan African (including Ghana) and half the children presenting with AGE have shown positive cultures for rotavirus with mortalities as high as 23-43%. [3,4]
The extended programme on immunization was initiated in Ghana in 1978 to cover six antigens. In 1992 and 2002 yellow fever and the pentavalent vaccines were introduced respectively. Rotavirus vaccine was introduced as a result of the increasing mortality and morbidity associated with AGE (alongside the pneumococcal vaccine) in 2012 [4].
This review seeks to address the pathophysiology and pathogenesis of rotavirus gastroenteritis and the role of vaccination in prevention of the disease.

Structure of the Rotavirus:

The virus is made up of structural and non-structural proteins. The non-structural proteins are thought to be related to RNA synthesis and packaging in the virion.

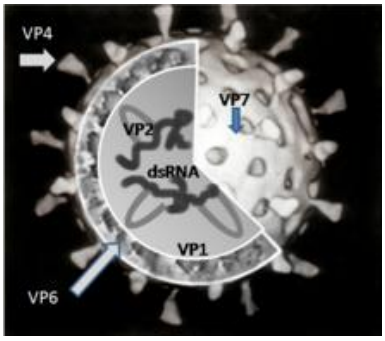

Fig 1.1: The structure of Rotavirus

The structural proteins are six and are briefly described below.

Viral protein (VP) 1 is an RNA polymerase enzyme,VP2 forms the core layer of the virion and binds the RNA genome. VP3 is part of the inner core of the virion and is an enzyme called guanylyltransferase. It is important for capping and post-translational modifications in the mRNA. VP4 is on the surface of the virion that protrudes as a spike (see fig 1.1 above) and it's important for the virus's virulence. VP6 forms the bulk of the capsid. It is highly antigenic and can be used to identify rotavirus species. This protein is used in laboratory tests for rotavirus A infections. VP7 is a glycoprotein that forms the outer surface of the virion. It has structural functions and determines the G-type of the strain. It is also involved in immunity to infection (along with VP4)

Pathogenesis of the Infection:

Rotaviruses replicate mainly in the gut, and infect enterocytes of the villi of the small intestine, leading to structural and functional changes of the epithelium. The triple protein coats make them resistant to the acidic pH of the stomach and the digestive enzymes in the gut.

The virus enters cells by receptor mediated endocytosis and forms a vesicle known as an endosome. Proteins in the third layer (VP7 and the VP4 spike) disrupt the membrane of the endosome, creating a difference in the calcium concentration. This causes the breakdown of VP7 trimers into single protein subunits, leaving the VP2 and VP6 protein coats around the viral dsRNA, forming a double-layered particle (DLP). The eleven dsRNA strands remain within the protection of the two protein shells and the viral RNA-dependent RNA polymerase creates mRNA transcripts of the double-stranded viral genome. By remaining in the core, the viral RNA evades innate host immune responses called RNA interference that are triggered by the presence of double-stranded RNA.

During the infection, rotavirus produces mRNA for both protein biosynthesis and gene replication. Most of the rotavirus proteins accumulate in viroplasm, where the RNA is replicated and the DLPs are assembled. Viroplasm is formed around the cell nucleus as early as two hours after virus infection, and consists of viral factories thought to be made by two viral nonstructural proteins: NSP5 and NSP2. Inhibition of NSP5 by RNA interference results in a sharp decrease in rotavirus replication. The DLPs migrate to the endoplasmic reticulum where they obtain their third, outer layer (formed by VP7 and VP4). The progeny viruses are released from the cell by lysis.[5]

Signs and Symptoms:

Rotavirus gastroenteritis can range from mild to severe disease. It is usually characterized by early onset vomiting, watery diarrhea for four to eight days, and low-grade fever. It has is an incubation period of about two days before symptoms appear. Dehydration occurs and is characterized by sunken eyes, increased skin recoil, impaired consciousness and circulatory shock. Dehydration is more common in rotavirus infection than in most of those caused by bacterial pathogens, and is the most common cause of death related to rotavirus infection. Rotavirus A infections can occur throughout life: the first usually produces symptoms, but subsequent infections are typically mild or asymptomatic. The most severe symptoms tend to occur in children six months to two years of age, the elderly, and those with compromised or absent immune system functions.

Diagnosis:

Presumptive diagnosis is made in any child less than five years with acute diarrhea especially in low resource centers. However definitive diagnosis in made on stool examination by enzyme-linked immunoassay (ELISA) for Rotavirus A. Polymerase chain reaction (RT-PCR and G and P typing PCR), polyacrylamide gel electrophoresis and electron microscopy are used for research purposes.

Treatment:

Treatment is based on severity of the presenting symptoms. Oral rehydration therapy (ORS) is administered based on the WHO protocol, after estimation of severity of dehydration [7].

Prevention:

Because improved sanitation does not decrease the prevalence of rotaviral disease, and the rate of hospitalizations remains high despite the use of oral rehydrating medicines, the primary public health intervention is vaccination.[10] The two vaccines against Rotavirus A infection that are both safe and effective in children include Rotarix by GlaxoSmithKline and RotaTeq by Merck. Both are taken orally and contain attenuated live virus.[4] In 2009, the immunization programmes.[5] The incidence and severity of rotavirus infections has declined significantly in countries that have acted on this recommendation.[12]

The Rotavirus vaccine was introduced in Ghana in 2012 when the morbidity and mortality rate for AGE became really high. The mortality rate however has reduced by 30% since the usage of the vaccines.[4] In Ghana the oral rotavirus vaccine is given twice; at six weeks and ten weeks, along with the pentavalent vaccine.

Methodology:

Google scholar, Cochrane library and PUBMED databases were used to search for articles relating to rotavirus infection. These were critically analyzed and their suitability for this review determined

Results:

From the databases, two strategies for controlling rotavirus infection were evaluated. These are improved sanitation and vaccination strategies.

Discussion:

Sanitation has been previously described as key in the control of infectious disease especially diarrhea diseases [12]. However, recent researchers have shown that sanitation alone has not significantly improved the control of rotavirus diarrhea disease. This has been attributed to the fact that enteric viruses are more resistant to common water treatment processes than their coliform counterparts. [2,13]

Mortality and hospitalization from AGE has significantly decreased since the advent of rotavirus vaccines. This is in agreement with reports by other workers [2-5]. It also provides some form of immunity for non-vaccinated individual by herd immunity thereby reducing the burden of the infection [12].

Despite the landmark achievements of the rotavirus vaccine, it was discovered to cause intussusception in children especially in those less than one year. Rotashield was subsequently withdrawn by the center for disease control in the United States [14]. In Ghana, rotarix is not given to children with previous history of intussusception, uncorrected congenital gut anomalies etc. It is however generally a safe vaccine[3].

Table 1.1: Comparison between Sanitation (Only) and Vaccination in the Management of Rotavirus Age.

Parameter	Sanitation	Vaccination
Involvement	Hand-washing, environmental sanitation, exclusive breastfeeding,	Rotarix oral live vaccines given at 6 and 10 weeks after birth
Mortality	Higher	Lower
Morbidity	Higher	Lower
Severity of symptoms	More severe	Milder
Effect on transmission of diarrhea diseases	Stops transmission of bacteria and parasitic infections but not rotavirus infection	Adequately controls rotavirus infection
Complications and contra-indications	None	Hypersensitivity to vaccine, intussusception

Conclusion:

Rotavirus infection and its attendant effects can be reduced by comprehensive, preventive strategies which includes vaccination alongside other modalities like breastfeeding, oral rehydration therapy, zinc treatment, environmental and water sanitation.

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Corresponding Author

Osonuga Ayokunle
School of Medical Sciences, University of Cape Coast, Cape Coast, Ghana.
E-mail: *overcomers2007@yahoo.com*