SHORT COMMENTARY

Rotavirus Vaccine Trial in Jamaica

CDC Christie[1], ND Duncan[2]

ABSTRACT

Worldwide, rotaviruses have been a significant cause of dehydrating gastroenteritis. This contributed to increased infant morbidity and mortality in Jamaica. We enrolled 1804 Jamaican infants in the international randomized, placebo-controlled, pentavalent (G1, G2, G3, G4 and P1) rotavirus vaccine trial. This pentavalent vaccine was found to significantly reduce rotavirus gastroenteritis attributable emergency room visits and hospitalizations, without increasing the rates of intussusception, or other serious adverse events in Jamaican infants. It is recommended that the rotavirus vaccine be included in Jamaica's National Immunization Programme in accordance with recommendations from the World Health Organization.

Keywords: Children, gastroenteritis, Jamaica, rotavirus vaccine

Prueba de la Vacuna Contra el Rotavirus en Jamaica

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RESUMEN

A nivel mundial, los rotavirus han sido una de las causas fundamentales de la gastroenteritis deshidratante, contribuyendo por ende a la morbilidad y mortalidad infantil en Jamaica. En este estudio se enrolaron 1804 infantes jamaicanos en una prueba internacional de vacuna contra el rotavirus pentavalente (G1, G2, G3, G4 y P1), randomizada, con control placebo. Se halló que la vacuna pentavalente reducía de manera significativa las hospitalizaciones y visitas a la sala de emergencia por causas atribuibles al rotavirus, sin aumentar las tasas de invaginación, u otros serios eventos adversos en los niños jamaicanos. Se recomienda que la vacuna del rotavirus sea incluida en el Programa de Inmunización Nacional de Jamaica, de conformidad con las recomendaciones de la Organización de Mundial de la Salud.

Keywords: Niños, gastroenteritis, Jamaica, vacuna del rotavirus

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BACKGROUND

The significant worldwide infant morbidity and mortality from rotavirus gastroenteritis made the development of a safe and effective vaccine a public health priority. A rhesus rotavirus tetravalent vaccine (RRV-TV) previously in use in the United States of America was withdrawn from the market in 1999 when it was shown to be associated with an increased incidence of infant intussusception. The pentavalent human-bovine reassortant rotavirus vaccine, RotaTeq™, contained vaccine serotypes (G1, G2, G3, G4 and P1) which had specificity against the serotypes that are responsible for the majority of rotavirus infections worldwide.

Purpose

In celebration of Jamaica's 50th anniversary of political independence from Great Britain, we summarize herein,

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several research collaborative manuscripts on the impact of rotavirus gastroenteritis in Jamaica and also involvement in an international rotavirus vaccine trial.

Rotavirus Gastroenteritis in Jamaica

In Jamaica, a Caribbean middle-income developing island, with population of 2.8 million and annual birth cohort of 50 000, the attributable burden of rotavirus illness has been significant. Rotaviruses were identified as the major cause of infantile diarrhoea by Dowe *et al*, occurring in 19% of 1020 cases of gastroenteritis in a hospital-based study sponsored by the World Health Organization (1). The National Sentinel Surveillance System (NSSS) had been established by the Ministry of Health in Jamaica in 1976. Each year, about 15 000 to 30 000 diarrhoeal cases were being reported in Jamaican children aged less than five years, with 700 to 900 hospitalizations and 3 to 18 reported deaths. During 1998 to 2003, active surveillance showed that acute gastroenteritis occurred during the cooler months of the year, in children aged less than three years and deaths were relatively rare (2−3 per year). In 2003, the Jamaican Ministry of Health formally reported an unusually severe epidemic which occurred during the summer months involving older children and young infants, with significantly increased case-reporting from the community, increased hospital admissions and increased deaths, with 12 occurring during the short period of June to July (2). Eight of the 12 deaths were directly attributable to diarrhoea and occurred in children aged four months to three years. All of the infants had watery diarrhoea and vomiting lasting for one to five days. This outbreak was uncommon in that it involved older children (aged > 3 years) and it occurred in the summer. Seventy-six per cent of stools were found to be positive for rotaviruses, which expressed the common serotypes, including G1[P8], G9[P8], G2[P-nontypable], G2[P8] and G-nontypable[P8] (2, 3).

The United States Centers for Diseases Control and Prevention (CDC) opined that environmental exposures were the most likely cause of the outbreak, with heavy rains in the earlier months and subsequent flooding most likely causing faecal contamination (2). The CDC also indicated that the deaths associated with acute gastroenteritis might have been attributable to inappropriate case management, as certain children received anti-emetic and anti-diarrhoeal injections, which are not part of the standard diarrhoea management (2). After that period, annual seasonal epidemics of infant gastroenteritis due to the rotavirus were continuing in Jamaica, with 21 total reported deaths in 2003 and 23 deaths in 2004; there was also a summer peak seen in sentinel sites in 2005.

The Ministry of Health has also reported that public health education of healthcare providers, parents and caregivers regarding the use of oral rehydration therapy can reduce the severity and mortality from diarrhoea during outbreaks of acute gastroenteritis (4).

The Rotavirus Vaccine Trial in Jamaica

The international placebo controlled, Rotavirus Safety and Efficacy Trial (REST) was conducted in 70 321 subjects from 356 centres in 11 countries and the rotavirus gastroenteritis attributable emergency room visits and hospitalizations were reduced by 95% (5). The primary purpose of this study conducted in Jamaica as part of this multinational mega-trial was to assess the safety of RotaTeq™ with respect to serious adverse experiences, particularly intussusception (5−8). We also examined the effectiveness of RotaTeq™ to reduce the healthcare utilization, including emergency department visits and hospitalizations, for rotavirus gastroenteritis in Jamaica, especially during the 1993 community outbreak, which overlapped the vaccine trial (5−8).

According to Christie *et al*, 1804 infants, six to twelve weeks of age, were enrolled in the trial from the University Hospital of the West Indies (7). The infants were from low-middle income families of primarily African heritage and received > 1 dose of rotavirus vaccine, or placebo in a 1:1 ratio. During the first year, there were two hospitalizations and 11 emergency room visits attributable to rotavirus gastroenteritis involving any serotype among 831 evaluable vaccine recipients and 809 evaluable placebo recipients, respectively, resulting in a rate reduction of 82.2% (95% CI, 15 [1, 98%]). All eight evaluable G1-4 rotavirus-attributable events that occurred two or more weeks after the third dose of the vaccine occurred in the placebo group, with a rate reduction of 100% (95% CI 41, 100%). Among the 1802 subjects that were included in the safety analysis, intussuseption was confirmed in one vaccine recipient 115 days after the third dose and in three placebo recipients. Four deaths occurred, one in a vaccine recipient and three in placebo recipients and none of the deaths were considered to be vaccine related.

CONCLUSIONS

Christie *et al* concluded that the pentavalent rotavirus vaccine reduced emergency room visits and hospitalizations which were attributable to rotavirus gastroenteritis without increasing the risk of intussusception or other serious adverse events in a resource limited country, such as Jamaica. This vaccine has now been recommended by the World Health Organization for inclusion into the immunization schedules of all countries throughout the world since April 2009 in order to reduce the worldwide burden from this infection. Already, several countries have reported significant reduction in illnesses and deaths as a result of implementing these guidelines.

REFERENCES

1. Dowe G, King SD, Maitland PB, Swaby-Ellis DE. Laboratory investigations on rotavirus in infantile gastroenteritis in Jamaica. Trans R Soc Trop Med Hyg 1988; **82:** 155–9.
2. Ashley D. Outbreak of severe rotavirus gastroenteritis among children: Jamaica, 2003. MMWR Morb Mortal Wkly Rep 2003; **52:** 1103–05.

3. Fischer TK, Ashley D, Kerin T, Reynolds-Hedmann E, Gentsch J, Widdowson MA. Rotavirus antigenemia in patients with acute gastroenteritis. J Infect Dis 2005; **192:** 913–19.
4. Walker GJ, Ashley DE, Hayes RJ. The quality of care is related to death rates: hospital inpatient management of infants with acute gastroenteritis in Jamaica. Am J Public Health 1988; **78:** 149–52.
5. Vesikari T, Matson DO, Dennehy P, Van Damme P, Santosham M, Rodriguez Z et al. Safety and efficacy of a pentavalent human bovine (WC3) reassortant rotavirus vaccine. N Engl J Med 2006; **354:** 23–33.
6. CDC Christie, ND Duncan, KT Thame, Smith HD. New rotavirus vaccines for infant gastroenteritis arriving soon [Editorial]. West Indian Med J 2006; **55:** 1−3.
7. Christie CDC, Duncan ND, Thame KA, Onorato MT, Smith HD, Malcolm LG et al. Pentavalent rotavirus vaccine in developing countries: Safety and healthcare resource utilization. Pediatrics 2010; **126:** e1499–e1506. Epub Nov 29, 2010. DOI: 10.1542/peds.2010−1240.
8. Vesikari T, Itzler R, Matson D, Santosham M, Christie CDC, Coia M et al. Efficacy of a pentavalent rotavirus vaccine in reducing rotavirus-associated healthcare utilization across three regions and eleven countries. Int J Infect Dis 2007; **11** (**Suppl 2**)**:** S28−35.