Rotavirus Genotype Distribution after Vaccine Introduction, Rio de Janeiro, Brazil

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Brazil introduced rotavirus vaccination in March 2006. We studied 133 rotavirus-positive fecal samples collected from February 2005 through December 2007. Genotype 1 (G1) P[8] vaccine, Rotarix (GlaxoSmithKline, Rixensart, Belgium), was included in the Brazilian Expanded Immunization Program and, after March 2006, became available to the whole birth cohort. Rio de Janeiro is the second largest Brazilian city; vaccine coverage was 43.3% in 2006 and 74.4% in 2007. Although Rotarix was highly efficacious for preventing severe rotavirus gastroenteritis in phase III trials carried out in Latin America and Europe, it appears to be less effective in preventing diarrhea caused by G2P[4] rotavirus strains, which do not share the VP7 or VP4 surface antigen with the vaccine strain (2).

Initial studies carried out in northeastern Brazil after rotavirus vaccine introduction demonstrated the predominance of rotavirus 1 (G1) P[8] in vaccinated populations (3–5). The recently developed attenuated 1 (G1) P[8] vaccine, Rotarix (GlaxoSmithKline, Rixensart, Belgium), was included in the Brazilian Expanded Immunization Program and, after March 2006, became available to the whole birth cohort. Rio de Janeiro is the second largest Brazilian city; vaccine coverage was 43.3% in 2006 and 74.4% in 2007. Although Rotarix was highly efficacious for preventing severe rotavirus gastroenteritis in phase III trials carried out in Latin America and Europe, it appears to be less effective in preventing diarrhea caused by G2P[4] rotavirus strains, which do not share either the VP7 or the VP4 surface antigen with the vaccine strain (2).

From February 2005 through December 2007, fecal samples were collected from 464 hospitalized children from birth to 5 years of age who exhibited gastroenteritis and dehydration and required intravenous fluid replacement. The study was conducted in Salles Netto Municipal Hospital, a pediatric unit in Rio de Janeiro.

Most children studied (390 [84%]) were not eligible for full vaccination; they either were born before January 1, 2006, or were <4 months of age. Nevertheless, 39 (8.4%) had been vaccinated with 2 doses of Rotarix, and 35 (7.5%) did not receive the vaccine.

Samples were collected after written consent was given by the parents. This study was approved by the Oswaldo Cruz Foundation Ethical Research Committee (protocol no. 311/06).

Polyacrylamide gel electrophoresis and a combined enzyme immunoassay for rotavirus A strains and adenoviruses were used to detect RV-A. Most samples were G- and P-type through seminested reverse transcription–PCR, as described (11). Seventeen RV-A–positive samples were P-type through partial genome sequencing. This method was also used to G-type 1 sample. These strains could not be typed through PCR. All samples that were P-typed through sequencing were P[8]. The only sample G-typed through sequencing was G9.

RV-A strains were detected in 133 (29%) of 464 samples. Genotype distribution showed a different profile for each year: 45% G9P[8], 30% G3P[8], 14% G1P[8], and 1.4% G2P[4] in 2005; 41% G2P[4], 18% G3P[8], and 15% G9P[8] in 2006; and 96% G2P[4] in 2007 (Table).

In the 18 months from July 2006 through December 2007, almost all RV-A–positive samples (35/36, 97%) showed G2P[4] specificity, which suggests a shift in geno-
type distribution, characterized by an increase in G2P[4] detection since 2006. When the pre- and postvaccination periods were compared, these changes in genotype distribution were found to be accompanied by a significant reduction in the detection rate of RV-A from 38% (73/193) in 2005 to 24% (26/109) in 2007 (p = 0.012 by χ² test). Vaccination rates in the RV-A–positive and –negative groups (considering only children eligible for full vaccination) were 29% (4/14) and 58% (35/60), respectively (odds ratio 0.29; 95% confidence interval 0.07–1.15; p = 0.043 by Fisher exact test, 1-sided. The 4 RV-A–positive vaccinated children were infected with G2P[4] genotype.

Conclusions
The first studies that assessed the RV-A genotype distribution after the introduction of Rotarix were carried out in northeastern Brazil (3–5). They offered the hypothesis that vaccination with the monovalent G1P[8] vaccine possibly created conditions in which RV-A G2P[4] could acquire selective advantage over P[8] genotypes (5). Nevertheless, a temporal periodicity, within the ≈10-year cyclic pattern of G2P[4] occurrence in Brazil, should be considered to explain the increased detection of this genotype since 2006. This periodicity could coincide with RV-A vaccine introduction and the consequent reduction of circulation of non-G2 strains.

G2P[4] RV-A was not detected from 2000 to 2004 in Rio de Janeiro (2–6); it was identified in 2005 (1.4%) and reemerged in 2006 (41%). Similarly, in northern Brazil, RV-A G2P[4] was detected in 2005 after a period of absence (A. Linhares, pers. comm.). When other Latin American countries are considered, an outbreak of RV-A gastroenteritis with a high rate of G2P[4] detection was recently described in Honduras (12). According to Patel et al. (13), ongoing surveillance in El Salvador, Guatemala, and Honduras showed that G2P[4] was the predominant circulating strain in 2006 (68%–81%). In Argentina, this genotype was also circulating in 2006 (J. Stupka, pers. comm.). RV-A with short electropherotype, characterized as G2P[4], was detected at high frequency in 2005 in Paraguay, after a 6-year absence (14). In these South American countries that border Brazil, there are no RV-A immunization campaigns, and G2P[4] was detected before introduction of Rotarix in Brazil.


Our data also suggest a significant reduction in the rate of RV-A detection between the pre- and postvaccination periods. The comparison of vaccination rates between RV-A–positive and –negative children, even with a small sample size, suggests that vaccinated children have a reduced risk for severe RV-A diarrhea.

This survey is among the first to evaluate the effects of Rotarix in Brazil, the first Latin American country to introduce universal rotavirus vaccination. We believe that the emergence of strains that may escape protection can be a challenge to the RV-A immunization program in Brazil and needs to be continuously monitored.

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References


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