



Impact of rotavirus vaccination on child mortality, morbidity, and rotavirus-related hospitalizations in Bolivia



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ABSTRACT

Background: The public health impact of rotavirus vaccination in countries with high child mortality rates remains to be established. The RV1 rotavirus vaccine was introduced in Bolivia in August 2008. This study describes the trends in deaths, hospitalizations, and healthcare visits due to acute gastroenteritis (AGE) and in rotavirus-related hospitalizations, among children <5 years of age, during the pre- and post-vaccination periods.

Methods: Data were obtained from the National Health Information System to calculate vaccine coverage and AGE-related health indicators. Trend reductions in the main health indicators were examined using the pre-vaccine period as baseline. The effect of vaccination on the epidemiology of rotavirus-related AGE was assessed using data from the active surveillance hospitals.

Results: Compared with the 2001–2008 pre-vaccine baseline, the mean number of rotavirus-related hospitalizations was reduced by 40.8% (95% confidence interval (CI) 21.7–66.4%) among children <5 years of age in the post-vaccine period (2009–2013). Reductions were most pronounced in children <1 year of age, eligible for vaccination. The mean proportions of AGE-related deaths, AGE-related hospitalizations, and AGE-related healthcare visits during 2009–2014 were reduced by 52.5% (95% CI 47.4–56.3), 30.2% (95% CI 23.5–36.1), and 12.9% (95% CI 12.0–13.2), respectively. The greatest effect in reduction of AGE-related deaths was found during the months with seasonal peaks of rotavirus disease. Over the post-vaccine period, changes in rotavirus epidemiology were observed, manifested by variations in seasonality and by a shift in the mean age of those with rotavirus infection.

Conclusions: The significant decrease in main AGE-related health indicators in children <5 years of age after the introduction of rotavirus vaccine provides evidence of a substantial public health impact of rotavirus vaccination in Bolivia, as a measure for protecting children against AGE.

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Introduction

Globally, rotavirus is the leading cause of acute gastroenteritis (AGE) in children <5 years of age, causing 37% of hospitalizations annually and approximately 215 000 deaths per year (Tate et al., 2016). In 2009, the World Health Organization (WHO) recommended including rotavirus vaccination worldwide (WHO, 2009a).

Two live attenuated oral rotavirus vaccines are licensed and available globally: a human monovalent strain (RV1) (Rotarix, GlaxoSmithKline Biologicals) and a pentavalent bovine–human reassortant (RV5) (Rotateq, Merck) (WHO, 2009b). Currently, 81 countries have introduced rotavirus vaccines into their national immunization programs (Program for Appropriate Technology in Health, 2017). Similar to the results of vaccine efficacy clinical trials, vaccine effectiveness (VE) has been found to be lower in countries with greater levels of child mortality (Pringle et al., 2016; Gastanaduy et al., 2016a, 2016b). Nevertheless, post-introduction surveillance studies have demonstrated the impact of rotavirus vaccines on reducing the burden of AGE among children <5 years of age, both in developing and developed countries (Tate et al.,

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2013; Sanchez-Uribe et al., 2016; Enane et al., 2016; Ngabo et al., 2016).

Bolivia has been characterized as a country among those of the Latin America and Caribbean region displaying high child mortality rates (39 per 1000) (UNICEF et al., 2014). AGE is considered the second leading cause of mortality and morbidity among children <5 years of age. Rotavirus is the main pathogen associated with AGE, accounting for a high burden of the disease annually, representing almost half of hospital admissions (Smith et al., 2011). The country was one of the first Global Alliance for Vaccines and Immunization (GAVI) countries eligible for the introduction of RV1 vaccine, which was introduced into the National Immunization Program in August 2008. Since then, the performance of the rotavirus vaccine has been evaluated in two consecutive case-control studies, one in 2011 and the other in 2013. These showed effectiveness (using negative test controls) of 69% and 59%, respectively, against rotavirus-related hospitalizations, and 62% and 72%, respectively, against very severe disease (Pringle et al., 2016; Patel et al., 2013). The observed rotavirus VE was similar to that found in other studies performed in developing countries (Patel et al., 2016; Armah et al., 2016).

In this study, through a combination of active and passive surveillance, it was aimed to assess the impact of RV1 administration in Bolivia on the decline in rotavirus-related hospitalizations and main AGE-related health indicators during the period 2009–2014.

Methods

Study design and setting

This was a retrospective study conducted from January 2001 to December 2014 (pre-vaccine period 2001–2008, post vaccine period 2009–2014). Sentinel surveillance for rotavirus-related AGE was conducted at eight pediatric hospitals: Hospital del Niño Ovidio Aliaga and Hospital Materno Infantil in the city of La Paz, Hospital Boliviano Holandés and Hospital Los Andes in the city of El Alto, Hospital Albina Patiño and Hospital German Urquidi in the city of Cochabamba, Hospital San Martín de Porres in the rural community of Cochabamba region, and Hospital Mario Ortiz in the city of Santa Cruz. During the study period, all of these hospitals except the Hospital San Martín de Porres (which was included after vaccine introduction) participated in the rotavirus surveillance network. Surveillance sites were located across three main geographic regions of Bolivia, where the majority of the population is located, and covered populations of different socio-economic status. The study protocol was approved by the National Bioethics Committee. Rotavirus surveillance among children <5 years of age hospitalized with AGE has been in existence since 2001 at the Institute of Molecular Biology and Biotechnology of the Universidad Mayor de San Andrés. In 2006, this surveillance network became part of the established National Rotavirus Surveillance at the Ministry of Health.

Specimen collection, storage, and laboratory testing

A suspected case of rotavirus AGE was defined as a child <5 years of age who was hospitalized for the treatment of acute watery diarrhea (≥ 3 looser than normal stools in a 24-h period during the illness, and onset of diarrhea ≤ 7 days at presentation). Stool samples were collected within 48 h of hospitalization and tested for group A rotavirus using a commercially available enzyme immunoassay within 24 h of stool collection (ProSpecT; Oxoid, Cambridge, UK).

Vaccine coverage

Annual data (2009–2014) for the national coverage of each dose of RV1 vaccine and pentavalent vaccine were collected prospectively from the records of the National System of Health Information and Epidemiological Surveillance of the Bolivian Ministry of Health (Sistema Nacional de Información en Salud y Vigilancia Epidemiológica, SNIS-VE).

Rotavirus-related hospitalizations

For the years 2001–2013, monthly data for AGE- and rotavirus-related hospitalizations were obtained from the Rotavirus Surveillance Program. The monthly proportion of rotavirus-related hospitalizations was obtained by using the number of rotavirus-positive hospitalizations as the numerator and the number of AGE-related hospitalizations as the denominator. To calculate the total number of rotavirus-related hospitalizations, the proportion of rotavirus-related hospitalizations was extrapolated to the total number of AGE-related hospitalizations, obtained from the SNIS-VE and adjusted for the month of the year and for age.

AGE-related deaths

The numbers of all-cause and AGE-related deaths among children <5 years of age were collected monthly from the SNIS-VE data for the period 2001–2014. The proportion of AGE-related deaths was obtained by using the number of AGE-related deaths as the numerator and all-cause deaths as the denominator.

AGE-related hospitalizations

The numbers of all-cause and AGE-related hospitalizations among children <5 years of age were collected monthly from the SNIS-VE data for the period 2001–2013. Data were not available for 2014. The proportion of AGE-related hospitalizations was calculated by using the monthly number of AGE-related hospitalizations as the numerator and all-cause hospitalizations as the denominator.

AGE-related healthcare visits

The number of AGE-related healthcare visits during the years 2001–2014 was obtained from the SNIS-VE. The proportion of AGE-related healthcare visits was obtained by using the monthly number of AGE-related healthcare visits in children <5 years of age as the numerator and all-cause healthcare visits as the denominator. Pre-vaccine baseline included 2001–2006. SNIS-VE data from 2007 and 2008 were excluded from the analysis due to inconsistencies (low quality and lack of data).

Statistical analysis

For all analyses, 2008 was considered a pre-vaccine year, since rotavirus vaccine was introduced after the rotavirus main season and due to very low vaccine coverage observed from August to December 2008. The numbers of rotavirus-related hospitalizations and AGE-related deaths were adjusted to the population growth factor using the National Census of Housing and Population. Trends in AGE-related mortality, AGE-related hospitalizations, AGE-related healthcare visits, and rotavirus-related hospitalizations among children <5 years of age, before and after rotavirus vaccine introduction, were examined by time series analysis. The time series analysis was performed through exponential smoothing using the Holt–Winters procedure, in order to capture the trend

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