J Pediatr (Rio J). 2016;92(2):181–187

Jornal de Pediatria
www.jped.com.br

ORIGINAL ARTICLE

Hospital-based surveillance of intussusception among infants☆

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Received 14 November 2014; accepted 2 June 2015
Available online 21 January 2016

KEYWORDS
Rotavirus vaccines;
Intussusception;
Surveillance;
Brazil

Abstract
Objective: Intussusception surveillance was initiated after the nationwide introduction of live attenuated monovalent rotavirus vaccine (RV1). The objective is to assess the epidemiology of intussusception and compare the number of cases before and after the introduction of rotavirus vaccine.
Methods: Cases of intussusception occurring between March 2006 and January 2008 were identified through a prospective enhanced passive surveillance system established in sentinel state hospitals. Retrospective review of medical records was used to identify cases, which occurred in sentinel hospitals between January 2001 and February 2006.
Results: From 2001 to 2008, 331 intussusception cases were identified, 59.5% were male, with peak incidence among those 18–24 weeks of age. Overall <10% of cases were among infants 6–14 weeks of age (when the first dose of RV1 is administered). The most frequently observed signs or symptoms of intussusception included vomiting (89.4%), bloody stool (75.5%), and abdominal distention (71.8%). A majority (92.1%) of the case-patients required surgery for treatment; 31.8% of those who underwent surgery required bowel resection, and 13 (3.9%) died. Among the 21 hospitals that reported cases throughout the entire surveillance period (2001–2008), the number of intussusception events during 2007 ($n = 26$) and 2008 ($n = 19$) was not greater than the average annual number ($n = 31$, range 24–42) during baseline years 2001–2005.

☆ Please cite this article as: Fernandes EG, Leshem E, Patel M, Flannery B, Pellini AC, Veras MA, et al. Hospital-based surveillance of intussusception among infants. J Pediatr (Rio J). 2016;92:181–7.

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http://dx.doi.org/10.1016/j.jped.2015.06.008

Conclusions: Although this analysis did not identify an increase in intussusception cases during the two years after RV1 introduction, these results support the need for special epidemiologic methods to assess the potential link between rotavirus vaccine and this very rare adverse event.

PALAVRAS-CHAVE
Vacina contra rotavírus;
Intussuscepção;
Vigilância;
Brasil

Vigilância hospitalar de intussuscepção entre neonatos

Resumo
Objetivo: A vigilância da intussuscepção foi iniciada após a introdução da vacina monovalente viva atenuada contra rotavírus (RV1) em todo o país. O objetivo é avaliar a epidemiologia da intussuscepção e comparar a quantidade de casos antes e depois da introdução da vacina contra rotavírus.
Métodos: Os casos de intussuscepção entre março de 2006 e janeiro de 2008 foram identificados por meio de um sistema de vigilância passivo prospectivo aprimorado estabelecido em hospitais-sentinela estaduais. A análise retrospectiva de prontuários médicos foi utilizada para identificar os casos que ocorreram em hospitais-sentinela entre janeiro de 2001 e fevereiro de 2006.
Resultados: De 2001-2008, identificamos 331 casos de intussuscepção, 59,5% dos quais ocorreram em pacientes do sexo masculino, com pico de incidência entre aqueles com 18-24 semanas de idade. Em geral, < 10% dos casos ocorreram entre neonatos com 6-14 semanas de idade (quando a 1ª dose de RV1 é administrada). Os sinais ou sintomas de intussuscepção observados com mais frequência incluíam vômito (89,4%), fezes com sangue (75,5%) e distensão abdominal (71,8%). A maioria (92,1%) dos pacientes precisou de cirurgia para o tratamento; 31,8% dos que se submeteram à cirurgia precisaram de ressecção intestinal, e 13 (3,9%) vieram a óbito. Entre os 21 hospitais que relataram casos durante todo o período de vigilância (2001-2008), a quantidade de casos de intussuscepção em 2007 (n = 26) e 2008 (n = 19) não foi maior que a quantidade média anual (31, faixa de 24-42) durante os anos-base de 2001-2005.
Conclusões: Embora esta análise não tenha identificado um aumento nos casos de intussuscepção nos dois anos após a introdução da RV1, esses resultados justificam a necessidade de métodos epidemiológicos especiais para avaliar a possível associação entre a vacina contra rotavírus e esse evento adverso muito raro.

Introduction

Rotavirus is a leading cause of severe diarrhea, accounting for ~453,000 deaths annually among children <5 years of age worldwide.[1] The World Health Organization (WHO) has recommended global introduction of one of the two licensed rotavirus vaccines [RotaTeq or RV5 (Merck®, PA, USA) and Rotarix or RV1 (Rotarix®, GlaxoSmithKline Biologicals, Rixensart, Belgium)] in national immunization programs for preventing severe rotavirus disease.[2] In March 2006, the Brazilian Ministry of Health introduced RV1, a live attenuated monovalent vaccine derived from human G1P[8] strain, simultaneously in all 27 states, through its National Immunization Program (Programa Nacional de Imunização [PNI]).

A key issue for rotavirus vaccine immunization programs is the need for safety monitoring with regard to intussusception, a form of intestinal obstruction occurring at a background rate of approximately 50 per 100,000 infants.[3] An earlier rotavirus vaccine (Rotashield, Wyeth Vaccines, PA, USA) based on a different (rhesus) strain than the current WHO recommended vaccines was found to be associated with an increased risk of intussusception, with the vaccine causing roughly ten excess cases per 100,000 vaccinated infants.[4] Large clinical trials have not detected a risk of intussusception associated with either currently used vaccines[5,6]; however, post-licensure surveillance in Mexico and Australia has observed a small risk of intussusception after the initial dose.[7,8] In Mexico, an association was found between RV1 and intussusception, with the vaccine causing one to four excess cases of intussusception per 100,000 vaccinated infants.[8,9] In Australia, a possible temporal clustering of intussusception episodes was noted during the seven days after the initial dose of both RV1 and RV5, though there was no increase in overall risk at 12 months of age.[7] In Brazil, no increased risk was identified after the first dose, but a potential small risk was identified after the second dose of RV1 (excess of 1.5 cases per 100,000 vaccinated infants).[9] No definite increased risk of intussusception has been identified after use of RV5 in the United States, but an excess risk less than one in 65,000 vaccinated infants has not been excluded.[10] Marked declines in severe and fatal diarrhea were demonstrated in early adopter countries after the introduction of rotavirus vaccine.[11] Because the documented benefits of vaccination have far outweighed the low-level risk of intussusception observed in some settings, regulatory agencies have continued to recommend