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Short report

Early impact of rotavirus vaccination in a large paediatric hospital in the UK

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SUMMARY

The impact of routine rotavirus vaccination on community-acquired (CA) and healthcare-associated (HA) rotavirus gastroenteritis (RVGE) at a large paediatric hospital, UK, was investigated over a 13-year period. A total of 1644 hospitalized children aged 0–15 years tested positive for rotavirus between July 2002 and June 2015. Interrupted time-series analysis demonstrated that, post vaccine introduction (July 2013 to June 2015), CA- and HA-RVGE hospitalizations were 83% [95% confidence interval (CI): 72–90%) and 83% (95% CI: 66–92%] lower than expected, respectively. Rotavirus vaccination has rapidly reduced the hospital rotavirus disease burden among both CA- and HA-RVGE cases.

Introduction

Prior to the introduction of routine vaccination, rotavirus was the most frequent cause of severe gastroenteritis in children aged <5 years worldwide.[1] In the UK, rotavirus gastroenteritis (RVGE) was estimated to be responsible for 45% and 20% of acute gastroenteritis hospitalizations and emergency department attendances in children aged <5 years, respectively.[2] Rotavirus is also an important cause of healthcare-associated (HA) gastroenteritis; among children at a large paediatric hospital, UK, rotavirus was detected by reverse transcription–polymerase chain reaction (RT–PCR) in 43% of community-acquired (CA) and in 31% of HA gastroenteritis cases.[3]

Several European countries have introduced rotavirus vaccine into their childhood immunization programmes, with effectiveness against RVGE hospitalizations estimated at >80%.[4] In July 2013 the UK introduced the live-attenuated, two-dose oral monovalent rotavirus vaccine (Rotarix™, GlaxoSmithKline Biologicals S.A., Rixensart, Belgium) with doses given at two and three months of age.[5] Vaccine uptake for a completed course reached 89% by June 2015.[6] Early impact studies in the UK suggested a large reduction (77%) in

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Table I
Rotavirus gastroenteritis (RVGE) hospitalizations at Alder Hey among children 0–15 years of age, pre and post rotavirus vaccine introduction

Variable	Yearly mean no. of hospitalizations (range) pre vaccine introduction, July 2002 to June 2013[a]	No. of hospitalizations post vaccine introduction, July 2013 to June 2015		Risk ratio (95% CI)	Percentage decline in hospitalizations (95% CI)[b]	*P*-value
		Year 1	Year 2			
Overall	145 (109–191)	22	30	0.18 (0.11–0.30)	82 (70–89)	<0.001
Age (years)						
<2	111 (88–145)	17	16	0.16 (0.10–0.26)	84 (74–90)	<0.001
2–4	22 (15–32)	2	13	0.31 (0.14–0.62)	69 (38–86)	0.017
5–15	12 (6–20)	2	1	–	–	–
CA-RVGE	108 (83–150)	18	19	0.17 (0.10–0.28)	83 (72–90)	<0.001
HA-RVGE	37 (18–58)	4	11	0.17 (0.08–0.34)	83 (66–92)	<0.001

CI, confidence interval; CA, community-acquired; HA, healthcare-associated.
[a] Yearly means are based on a rotavirus year running July to June.
[b] Calculated as 1 − (risk ratio). Risk ratio was calculated using a negative binomial model adjusting for calendar month and rotavirus year.

laboratory-confirmed rotavirus infections in vaccine age-eligible infants.[7] However, no impact on HA infection has yet been described. Understanding the impact of rotavirus vaccination on both CA- and HA-RVGE cases may have implications for both hospital infection control and bed management policies, and will help inform the evidence base for continued immunization in the UK.

This retrospective investigation aimed to quantify the impact of rotavirus vaccination on HA- and CA-RVGE cases at the same children's hospital as our prospectively conducted study from the pre-vaccine period.[3]

Methods

Study setting

The study was conducted at Alder Hey Children's NHS Foundation Trust, Liverpool, UK (Alder Hey). Alder Hey provides primary, secondary, and tertiary care facilities for >200,000 children each year and has ~240 inpatient beds. General medicine, general surgery, and a range of specialist services including critical care, oncology, cardiology, and neurosurgery are provided; there is also a large emergency department.

Case definition

Children aged between 0 and 15 years who were admitted with RVGE between July 2002 and June 2015, or those in whom RVGE developed after hospitalization, were eligible for inclusion. Testing for rotavirus was conducted on clinician request throughout the study period with no age restriction. RVGE was defined as rotavirus antigen detected by immunochromatographic test or by enzyme immunoassay in a faecal specimen of a child with acute gastroenteritis. RVGE was considered HA if gastroenteritis developed ≥48 h after admission and there was no record of diarrhoea or vomiting on admission. Clinical and anonymized demographic data were collected for each participant, and included information on specimen date, admission date, age, and symptoms on admission. The pre-vaccine period was defined as July 2002 to June 2013 and the vaccine period was defined as July 2013 to June 2015.

Statistical analysis

To assess the impact of rotavirus vaccination on hospitalizations for CA- and HA-RVGE, an interrupted time-series methodology was used. First, monthly expected incidence of rotavirus hospitalizations was estimated by fitting a negative binomial regression model to pre-vaccine monthly incidence data, offset for total monthly admissions and adjusting for seasonality and secular trends using calendar month and rotavirus year (July to June), respectively.[8] This model was used to predict the counterfactual numbers of RVGE hospitalizations (in the absence of vaccination) for the vaccine period, where the impact of vaccination is expressed by the difference between the counterfactual expectation and observed number of hospitalizations. To quantify change in the number of RVGE hospitalizations by the introduction of the vaccine, a second model included a derived binary indicator variable for the post-vaccine period, enabling the computation of risk ratios (RR) and associated 95% confidence intervals (CI). This second model offset for total monthly admissions and adjusted for month and rotavirus year. Percentage change in incidence was calculated as $100\times(1-\mathrm{RR})$. The analysis was undertaken separately for CA- and HA-RVGE hospitalizations. To investigate the impact of routine vaccination on different age groups the analysis stratified overall RVGE hospitalizations by age group (<2 years and 2–4 years).

Demographic and clinical characteristics were compared between RVGE cases from the pre- and post-vaccine periods and between CA- and HA-RVGE cases. Continuous variables were tested by Student's *t*-test or Wilcoxon rank-sum test if not normally distributed and χ^2-test or Fisher's exact test for categorical variables. All data handling and statistical analyses were performed using R Version 3.1.2 (R Development Core Team, Vienna, Austria).

Ethical approval

Ethical approval was provided by NHS Research Ethics Committee, South Central-Berkshire (Reference: 14/SC/1140).

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