

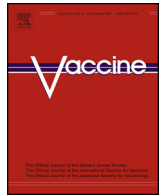


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Impact of non-routine rotavirus vaccination on hospitalizations for diarrhoea and rotavirus infections in Spain

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ABSTRACT

This study shows hospital discharges related to all-cause diarrhoea and rotavirus infection in children up to five years of age from 2005 to 2009 in Spain. Rotavirus vaccines have been available in Spain since late 2006 and early 2007. They are neither funded nor reimbursed by the National Health Care System. However, they are recommended by the Spanish Association of Pediatricians and prescribed by paediatricians. The vaccination coverage was 17% in 2007, 35% in 2008 and 38% in 2009. Among a total of 111,738 hospitalizations recorded, 24% ($N=26,500$) were coded as rotavirus and 14% ($N=16,217$) as diarrhoea of undetermined aetiology. The overall annual incidence of hospitalization was 991,235 and 144 per 100,000 children up to five years of age for all-causes diarrhoea, rotavirus infection and diarrhoea of undetermined aetiology respectively. The annual rate significantly decreased during the study period.

Hospitalization rates for all-cause diarrhoea, rotavirus infection and diarrhoea of undetermined aetiology in children under five years of age in 2009 were 35, 37 and 36% lower than in the period 2005–2006, before rotavirus vaccine introduction. This decrease was greater in children <12 months of age: 42% for all-cause diarrhoea and 43% for rotavirus and diarrhoea of undetermined aetiology.

The use of rotavirus vaccines, with relatively low vaccination coverage, in Spain has been shown to decrease hospitalizations for rotavirus gastroenteritis and all-cause diarrhoea during the study period.

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1. Introduction

Rotavirus infection is one of the leading causes of diarrhoea in young children worldwide. Although mortality is not high in developed countries, it is an important cause of morbidity. There are more than 3.6 million cases per year in children up to five years old in Europe, and it accounts for a large number of hospitalizations, especially in very young children [1–3].

Rotavirus vaccines have been available in Spain since August 2006 (Rotarix[®]) and January 2007 (RotaTeq[®]). They are neither funded nor reimbursed by the National Health Care System. However they are recommended by the Spanish Association of Pediatricians and prescribed by paediatricians. Parents pay the full cost of vaccination. The estimated vaccination coverage is calculated using the number of doses distributed by region, and on

the assumption that all children receive the complete vaccination schedule. It increased from 17% in 2007, to 35% in 2008 and 38% in 2009. During the 2007–2009 period, 47% of doses distributed were Rotarix[®] and 53% RotaTeq[®] (distribution data provided by IMS Health).

The Spanish centralized hospital discharge database includes approximately 98% of admissions to hospitals of the National Health Care System, which covers almost all the Spanish population. The database provides a complete record of all hospitalizations and, in general, is not subject to the limitations of outpatient surveillance systems. This database uses standardized diagnosis code lists that allow secular trend analysis of incident disease for a given population. It has been used for research purposes including epidemiological studies on rotavirus and other infectious diseases [4–8].

This epidemiological retrospective study was designed to provide population-based estimates of the burden of hospitalization for all-cause diarrhoea and rotavirus infection in children ≤ 5 years of age during a five year period (2005–09), and to assess the impact of non-routine rotavirus vaccination which started in late 2007.

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2. Methods

This retrospective study used the national information system for hospital data (Conjunto Mínimo Básico de Datos; CMBD), maintained by the Ministry of Health, which includes an estimated 98% of admissions to public hospitals. Compulsory health insurance covers an estimated 99.5% of the Spanish population [9–11].

Hospital discharge data for all children up to five years of age, with diarrhoea listed as primary or secondary cause of hospitalization, were analyzed for the period covering 1 January 2005 to 31 December 2009. The 9th International Classification of Diseases ICD-9-CM (CIE-9-MC) codes were selected: for bacterial and parasitic diarrhoea (001-005, 006-007, 008.0-008.5 excluding localized salmonella infections 003.2, and amebiasis 006.3-006.6); viral diarrhoea (008.6-008.8, including rotavirus 008.61); diarrhoea of undetermined aetiology (009.0-009.3) and non-infectious diarrhoea (558.9 and 787.91). Diarrhoea of undetermined aetiology was included because rotavirus infection is not a reportable disease in Spain. Therefore specific diagnostic tests for rotavirus may not have been ordered at the hospital as the result would not significantly alter the selected treatment. For each case, data were gathered on age, sex, average length of hospitalization, diagnosis and outcome.

3. Statistics

The average number of hospitalizations per year, the annual incidence of hospital admissions and the average length of stay in the hospital (ALOS) were calculated. Differences in proportions were assessed by the Chi-square test, and confidence intervals (95% CI) were calculated. ANOVA was used for comparisons by age group. The post hoc Bonferroni correction was used to adjust statistical significance for multiple comparisons. Poisson regression was used to assess differences in the hospitalization rate during the study period, and between pre- and post-vaccination periods. In all tests, the significance level used was $p < 0.05$. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS/PASW for windows, version 19.0; Chicago, IL, USA) and STATA 11 (StataCorp LP TX, USA).

4. Results

A total of 111,738 all-cause diarrhoea hospital discharges in children <5 years of age were reported during the five year study period: 991 hospitalizations per 100,000 children <5 years of age. Twenty-four percent, 26,500 admissions, were coded as rotavirus (ICD 9CM code 008.61) and 15%, 16,217 admissions, as diarrhoea of undetermined aetiology (ICD 9CM codes 009.0-009.3). This corresponds to an annual incidence of hospitalization of 235 and 144 per 100,000 children <5 years of age respectively (Table 1). The remaining 61% were coded as bacterial (35.3%) and parasitic diarrhoea (1.1%), viral diarrhoea other than rotavirus (2.5%) and non-infectious diarrhoea (22%).

Mean age (SD) was 12 months (SD 11) and 56% were male. The average length of stay in hospital was five days (SD 9) for all-cause diarrhoea, six days (SD10) for rotavirus and four days (SD 7) for diarrhoea of undetermined aetiology. These figures did not change significantly during the study period. Diarrhoea was reported as the primary cause of hospitalization in 75% of the cases. The remaining 25% were acute respiratory infection (rhino-pharyngitis, bronchiolitis, pneumonia), acute urinary infection and febrile convulsions.

Table 1 shows the number and hospitalization rate for all-cause diarrhoea, rotavirus and diarrhoea of undetermined aetiology by age group. Eighty-seven percent of hospitalizations for rotavirus diarrhoea were children <24 months of age. The highest incidence of hospitalization is shown in the first year of life: hospitalization rate per 100,000 children <12 months of age was 2312 (95% CI: 2292–2332) for all-cause diarrhoea, 692 (95% CI: 681–703) for rotavirus infection and 317 (95% CI: 309–324) for diarrhoea of undetermined aetiology.

Hospitalization rates in 2008 and 2009 were lower than in the 2005–2006 period in children <24 months of age, especially in children <12 months of age. Rates for all-cause diarrhoea decreased significantly during the study period from 1138 (95% CI: 1123–1152) hospitalizations per 100,000 in 2005 to 748 (95% CI: 738–759; $p < 0.001$) in 2009. Hospitalizations for rotavirus infection decreased from 300 (95% CI: 292–307) per 100,000 in 2005 to 174 (95% CI: 168–179; $p < 0.001$) in 2009 and hospitalizations for

Table 1
Hospitalization rates related to all-cause diarrhoea, rotavirus and diarrhoea of undetermined aetiology by age group in Spain (2005–2009).

Age group (months)	All-cause diarrhoea		Rotavirus		Diarrhoea of undetermined aetiology	
	N	Hospitalization rate* (per 100,000) CI (95%)	N	Hospitalization rate* (per 100,000) CI (95%)	N	Hospitalization rate* (per 100,000) CI (95%)
<12	50,644	2312.7 (2292.8–2332.6)	15,160	692.3 (681.3–703.3)	6944	317.1 (309.7–324.6)
12–23	33,127	1433.9 (1418.6–1449.2)	7826	338.8 (331.3–346.2)	4895	211.88 (206.0–217.8)
24–35	14,690	644.9 (634.5–655.3)	2369	104.0 (99.8–108.2)	2261	99.3 (95.2–103.4)
36–47	7670	338.9 (331.3–346.4)	754	33.3 (30.9–35.7)	1250	55.2 (52.2–58.39)
48–59	5607	251.5 (244.9–258.1)	391	17.5 (15.8–19.3)	867	38.9 (36.3–41.5)
Total (<5 years)	111,738	991.4 (985.6–997.2)	26,500	235.1 (232.3–238.0)	16,217	143.9 (141.7–146.1)

* Statistically significant differences ($p < 0.05$) per age group. ANOVA. The post hoc Bonferroni correction was used to adjust statistical significance for multiple comparisons.

Table 2
Reduction in hospitalization rates related to all-cause diarrhoea by age group following introduction of rotavirus vaccines use in Spain.

Age (months)	All-cause diarrhoea				
	Hospitalization rate period 2005–2006 (per 100,000) CI (95%)	Hospitalization rate 2008 (per 100,000) CI (95%)	Decrease (%)	Hospitalization rate 2009 (per 100,000) CI (95%)	Decrease (%)
<12	2741.3 (2706.2–2776.4)	2025.2 (1984.1–2066.2)	26.1*	1583.7 (1548.6–1618.9)	42.2*
12–23	1649.9 (1623.2–1676.5)	1252.2 (1220.7–1283.8)	24.1*	1085.2 (1056.3–1114.1)	34.2*
24–35	743.3 (725.2–761.5)	546.1 (525.1–567.1)	26.5*	539.6 (519.0–560.2)	27.4*
36–47	389.5 (376.3–402.7)	295.7 (280.2–311.2)	24.1*	294.7 (279.4–310.0)	24.3*
48–59	282.8 (271.5–294.1)	213.3 (200.0–226.5)	24.6*	228.2 (214.7–241.7)	19.3*
Total (<5 years)	1155.7 (1145.5–1165.8)	859.1 (847.3–871.0)	25.7*	748.9 (738.1–759.8)	35.2*

* Statistically significant differences ($p < 0.05$)

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