Severe intussusception after administration of anti-rotavirus vaccine: case series

A. Pugi [1,2], M.C. Lenti [1,2], V. Maggini [1,2], N. Lombardi [1,2], E. Gallo [1,2], R. Bonaiuti [1,2], E. Lucenteforte [1,2], M. Moschini [1,2], A.M. Calvani [3], F. Mannelli [4], L. Innocenti [4], M. Parrilli [5], M. Rossi [2,6], A. Mugelli [1,2], A. Vannacci [1,2]

[1] Dept. of Neurosciences, Psychology, Drug Research and Child Health (NEUROFARBA), University of Florence
[2] Tuscan Regional Centre of Pharmacovigilance of Florence
[3] Hospital Pharmacy, Meyer Children's Hospital, Florence
[4] Emergency Dept., Meyer Children's Hospital, Tuscan Regional Centre of Pharmacovigilance of Florence, Florence
[5] Pharmacovigilance Unit, ASL 10, Firenze
[6] Unit of Pharmacology, University Hospital of Siena

Background
Rotaviruses are the major cause of gastroenteritis among children of less than 5 years of age and of acute diarrhea in infants. The first rotavirus vaccine was introduced in 1998 but was subsequently withdrawn because of association with intussusceptions. The rotavirus vaccine licensed in 2006 (Rotarix®) is a live attenuated vaccine derived from the human 89-12 strain belonging to G1Ptype, and contains at least 10 median Cell Culture Infective Dose of live, attenuated rotavirus. Post-marketing safety studies assessed rare adverse events (rates <1 in 50.000), such as intussusceptions. Here we report 4 cases of intussusception that may represent an observed value higher than expected, considering an administration of vaccine lower than 7100 doses/year, although the actual exposure to the vaccine and the background intussusception incidence in Italy are unknown.

Description
From February 2012 to April 2013 four ADR reports of anti-rotavirus vaccine (Rotarix®) induced severe intussusception were reported to the Tuscan Centre of Pharmacovigilance. They occurred in four healthy male infants, born at term. The reactions occurred after the first dose in all cases (within 6 days) and all required hospitalization. Clinical manifestations comprised vomiting, melena and abdominal pain. Intussusception was generally diagnosed with ultrasound scan and barium enema, that in one case completely resolved the medical occurrence. In the other three cases surgical interventions were performed with good clinical outcomes. Babies did not assume other medications, but in two cases immunization with Rotarix® was concomitant with the administration of Infanrix Hexa® (DTaP-IPV-HepB/Hib) and Prevenar13® (Pneumococcal polysaccharide conjugate vaccine).

Discussion
The cases reported, even if at a preliminary level, suggest that the actual incidence of the syndrome may be higher than expected. Evaluation of the safety of rotavirus vaccines, particularly with respect to the risk of intussusception, is recommended for countries planning to introduce rotavirus vaccines into the National Immunisation Program. However, as prospective studies are costly, require time to conduct and may be difficult to perform in some settings, retrospective studies and healthcare professionals with spontaneous surveillance could be efficacious methods to monitor this medical occurrence.

CDC. Intussusception Among Recipients of Rotavirus Vaccine - United States, 1998-1999
MMWR. July 16, 1999 / 48(27);577-581
Lloyd-Johnsen C et al. Retrospective hospital based surveillance of intussusception in children in a sentinel paediatric hospital: Benefits and pitfalls for use in post-marketing surveillance of rotavirus vaccines. Vaccine. 2012;30 Suppl 1:A190-5