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Relationship between Pentavalent Rotavirus Vaccine and Intussusception: A Retrospective Study at a Single Center in Korea

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Purpose: Despite withdrawal of RotaShield® and the development of second generation live attenuated rotavirus vaccines, concerns remain regarding the relationship between rotavirus vaccine and intussusception. Nevertheless, since there is no study in Korea, we reviewed data from cases at Severance Children's Hospital to determine the association between rotavirus vaccine and intussusception.

Materials and Methods: Patients coded as intussusception and following a prescription of RotaTeq® from 2007 to 2013 were reviewed. We calculated comparative incidence figures (CIFs) and 95% confidence intervals (CIs) to compare the risk of intussusception in Korea with the risk in the United States. Expected cases within the four-week post-vaccination window were calculated by applying rates of intussusception from data compiled by the Health Insurance Review and Assessment Service (for a five-year period) to numbers of vaccinations.

Results: In total, 10530 doses of pentavalent rotavirus vaccine were administered. A total of 65 intussusception cases were diagnosed, although only two cases occurred within four weeks after vaccination. This was compared to six cases within 999123 doses in United States from April 2008 to March 2013 (CIF, 31.63; CI, 31.33–31.93). When we adjusted incidence rate differences for both countries, the CIF decreased to 7.05 (CI, 6.72–7.40). When we compared our identified cases with the expected cases from our hospital, there was no increased intussusception occurring within four weeks of vaccination.

Conclusion: We found no association between pentavalent rotavirus vaccine and intussusception. Therefore, rotavirus vaccination should be considered due to its benefits of preventing rotavirus-associated diseases.

Key Words: Pentavalent rotavirus vaccine, intussusception, Korea

INTRODUCTION

Rotavirus is the leading cause of acute gastroenteritis in infants and young children. It causes severe diarrhea and can lead to dehydration. Globally, it causes more than a half million deaths each year in children younger than five years. Also, it leads to two million hospitalizations and 25 million outpatient visits among children younger than five years worldwide.[1,2] Despite improvements in sanitation and hygiene, the incidence of rotavirus gastroenteritis has not markedly decreased, even in developed countries. This is the reason for the development of the rotavirus vaccine.

In August 1998, the RotaShield® (Wyeth, Delaware Valley, PA, USA) vaccine was first approved to prevent rotavirus gastroenteritis. Soon after its introduction, the risk of intussusception (IS) increased 20 to 30 times over the expected risk for children of this age group within two weeks following their first dose of the RotaShield® vaccine.[3-6] Based on the results of investigations, the US Centers for Disease Control and Prevention estimated that one or two additional cases of IS would be caused among each 10000 infants vaccinated with the RotaShield® vac-

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cine. In October 1999, RotaShield® was withdrawn from the market.

RotaTeq® (Merck, West Point, PA, USA), a pentavalent rotavirus vaccine, and Rotarix®, a monovalent rotavirus vaccine, were licensed in the United States in 2006 and 2008, respectively.[7,8] Because of the previous association between rotavirus vaccination and IS, large studies were done before licensing. No increased risk was found for IS after each vaccine.[9,10] In 2009, rotavirus vaccination was recommended by the World Health Organization for all infants.[11] Post-licensure studies of the association between vaccine and IS have been published in the United States, Australia, and Latin America. Studies from Australia, Brazil, and Mexico and one of three studies from United States have found an increased risk of IS.[10,12-19]

In Korea, a recent study has estimated the incidence of rotavirus-related gastroenteritis in children less than five years old to be 56.9 cases/1000 children.[20] Rotavirus gastroenteritis rarely causes mortality, although it causes significant morbidity in Korea. In Korea, RotaTeq® and Rotarix® were first used in 2007 and 2008, respectively. Even though it has not been included in the National Immunization Program (NIP), the rate of rotavirus vaccination has been increasing consistently, and in 2010, the rate had reached 60.8%. However, no studies have been conducted in Korea that prove or disprove the association between rotavirus vaccination and IS. The aim of this study was to evaluate the association between the rotavirus vaccine and IS in Korea.

MATERIALS AND METHODS

We reviewed the medical records of children below 12 months of age who the visited the outpatient clinic and emergency room of Severance Children's Hospital from January 1, 2005, to December 31, 2013. Confirmed IS cases were identified retrospectively by searching hospital databases using ICD-9-CM codes. Each case was confirmed with ultrasonography by an expert radiologist. We collected information regarding the vaccination schedule of all patients. As our hospital started to use only pentavalent rotavirus vaccine in November 2007, we analyzed the data of the RotaTeq® vaccine only. We defined the risk window to constitute four weeks after the vaccination day, because rotavirus vaccination-associated IS is known to occur within one month after vaccination, especially following the first dose.[3]

We first compared the pre-vaccination and post-vaccination times of patients with IS. The observation period was divided into two-month intervals. Standard Poisson-based methods were used, and 95% confidence intervals (CIs) were calculated.

Then, we compared our vaccine-associated IS cases in our study with those from the United States data, which were part of the Vaccine Safety Datalink project.[19] We used comparative incidence figures (CIFs) and 95% CIs calculated by Byar's method. Based on the difference in the incidence of IS in the two compared countries, we adjusted the CIFs accordingly.[21,22]

Lastly, we compared the observed number of cases with expected numbers. The relative risk was obtained by dividing the number of observed excess by the number of expected cases. The number of expected cases of IS in the risk window period was calculated by multiplying the child-time at risk post vaccination by the estimated background incidence of IS. The former was obtained by identifying the number of children who had received the RotaTeq® vaccine during the period of observation from our hospital's database. Calculations were made separately for each dose of the vaccine. The annual incidence of IS in our hospital was estimated by dividing the number of cases of IS by the number of children younger than 12 months old.

We calculated the ratio of observed to expected incidence (standardized incidence ratio), which provides an estimated relative risk under the assumption of constant relative risk.

Table 2. Total RotaTeq® Vaccinations Administered and the Number of Vaccinations Given One, Two, or Three Doses

Total	10530
Dose 1	4206
Dose 2	3446
Dose 3	2878

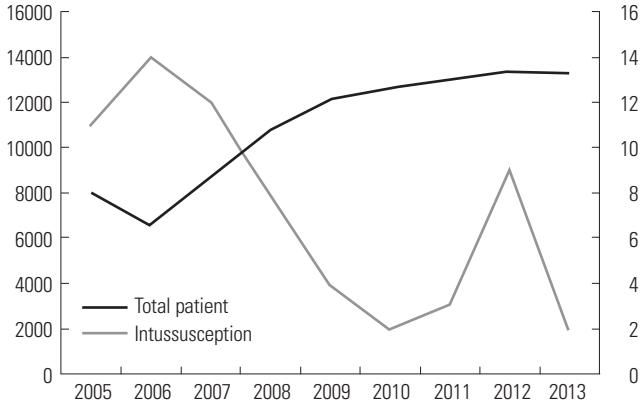

Fig. 1. Plot showing a trend for the total infants below 12 months of age who visited our hospital (black line), and total diagnosed and treated intussusception infants below 12 months of age in our hospital (gray line) between 2005 and 2013. The tendency of intussusception decreased across most of the years studied. The reason for the increased number of intussusceptions in 2012 remains unclear.

Table 1. Total RotaTeq® Doses Administered and Total Infants Vaccinated during the Study Period

	2007	2008	2009	2010	2011	2012	2013	Total
Total doses	52	983	1650	1718	1974	2045	2108	10530
Total infants	47	466	644	724	731	781	813	4206

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Standard poisson-based methods were used, which produced 95% CIs for these relative risks. IBM SPSS statistics, version 20 (SPSS Inc., Chicago, IL, USA) were used to conduct all the analysis.

This study was approved by the Institutional Review Board of Severance Hospital, Yonsei University College of Medicine, Seoul, Korea (IRB number: 4-2016-0314).

RESULTS

From January 1, 2005 to December 31, 2013, a total of 63915 children below 12 months of age visited our hospital. From November 1, 2007 to December 31, 2013, a total of 10530 doses of RotaTeq® vaccine were prescribed to 4206 infants (Tables 1 and 2). In the same period, 65 cases of IS were identified and treated in children below 12 months of age (Fig. 1, Table 3). There was a total of 12 cases diagnosed as IS after RotaTeq® administration. Ten of these were diagnosed more than four weeks after vaccination for rotavirus and could not be defined as rotavirus vaccination-associated IS. Two cases were identified within four weeks of RotaTeq® administration. No cases of IS were found after the first dose of RotaTeq® in our hospital. Both cases were treated by manual reduction.

When we calculated the incidence over the observation period, divided into two-month intervals, we observed a periodic increase in incidence; however, the overall pattern was a decline in incidents. When we compared the incident rate using standard poisson-based methods, a decrease in the risk ratio by 0.51 was observed, and there were no increased risks of IS on post-vaccination status, compared with pre-vaccination status (Fig. 2, Table 4).

Table 3. Number of Total Visited Infants, IS Diagnosed Infants, and IS Diagnosed Infants during Risk Window Period

	2005	2006	2007	2008	2009	2010	2011	2012	2013	Total
Total infants	3798	9939	5902	6816	6669	7326	7519	7894	8052	63915
Total infants with IS	11	14	12	8	4	2	3	9	2	65
Total infants with IS during the risk window period	-	-	0	0	0	0	1	0	1	2

IS, intussusception.

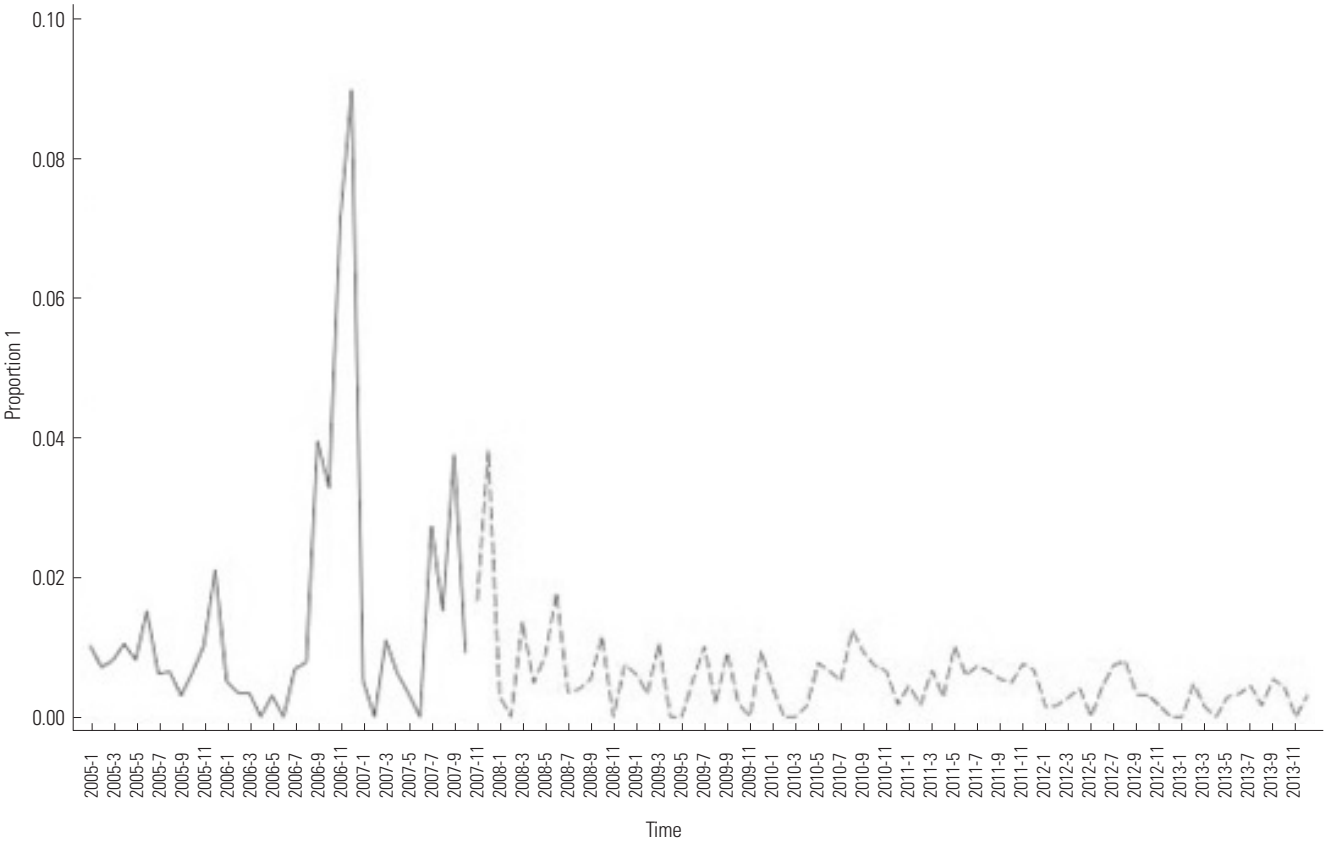

Fig. 2. Number of incidents over the observation period divided into two-month intervals. A periodic increase in incidents is seen; however, the overall pattern is a decline in incidence. The incidence rate was calculated using standard poisson-based methods, and a decrease in the risk ratio by 0.51 was observed.

Since there were only two cases of rotavirus vaccination determined among the total cases identified as IS, we compared our data with the United States for the same type of rotavirus vaccination to identify whether pentavalent rotavirus vaccination increases the risk of IS (Table 5).[19] Compared with the six cases among 999123 doses in United States from April 2008 to March 2013, the calculated CIF was 31.63 (CI, 31.33–31.93). However, after taking into consideration the difference in the background incidence rate of IS between the two countries,[22] the incidence rate was determined to be seven times higher in Korea than in the US.

Rather than comparing this pattern with that of another country, we decided to compare these results within our hospital. The expected case per vaccination was calculated using the background rate. Based on the assumption that IS is not associated with rotavirus vaccination, we calculated the relative risk and 95% CI (Table 6). The results for our hospital showed that the rotavirus vaccine caused no increasing risk of IS.

To aid our understanding of the outcome of this study, we examined the rotavirus antigen test results from 2005 to 2013 in our hospital (Table 7). A decreasing pattern for the rate of positive rotavirus antigen tests was observed.

DISCUSSION

Generally, natural rotavirus infection is not believed to cause IS.[23-26] However, the first-developed live oral tetravalent rotavi-

Table 4. Number of Infants Diagnosed with IS at our Facility and the Number of Infants Younger Than 12 Months Who Have Visited Our Facility

	2005	2006	2007	2008	2009	2010	2011	2012	2013	Total
IS	34	38	60	45	31	37	44	25	20	334
Infants visiting	3798	9939	5902	6816	6669	7326	7519	7894	8052	63915

IS, intussusception.

Table 5. Results from Our Facility Compared to Those from the VSD Project Conducted in the United States, Which Investigated Pentavalent Vaccine-Associated IS

	United States	Severance Hospital
Observed periods (yrs)	4.58	6.17
Total vaccinations	999123	10530
IS new cases	6	2
Calculated crude IS incidence rate (100000 PY)	0.6005267	18.993352
CIF 1 (95% CI)		31.63 (31.33–31.93)
CIF 2 (95% CI)		7.05 (6.72–7.40)

VSD, Vaccine Safety Datalink; IS, intussusception; CIF, comparative incidence figure; CI, confidence interval.
When we used CIFs, the rotavirus vaccine-associated IS rate at our facility was 31.63 times higher than that of the United States report. However, after taking into consideration the difference in the background incidence rate of IS between the two countries, the incidence rate was seven times higher in our hospital. However, one thing that needs to be considered here is that our data, which are from a single center study, are smaller compared to the United States data. Also, given that our facility is a tertiary medical center, the number of patients diagnosed and treated for IS may be much higher than the number of patients who visit for the sole purpose of receiving vaccinations. These factors could have contributed to such discrepancy.

Table 6. Expected Rate per Vaccination Calculated Using the Background Rate

Doses	No. of doses	No. of cases of IS		Relative risk	95% CI
		Observed	Expected		
All doses	10530	2	1.91	1.05	0.12–5.12
Dose 1	4206	0	0.63	-	
Dose 2	3446	2	0.62	3.21	0.36–15.65
Dose 3	2878	0	0.52	-	

IS, intussusception; CI, confidence interval.
Based on the assumption that IS is not associated with rotavirus vaccination, we calculated the relative risk and 95% CI for the total doses and for those who received the second dose. The results indicate that there is no association between the rotavirus vaccination and IS.

Table 7. Examination of the Rotavirus Antigen Test Results from 2005 to 2014 at Our Facility

	2005	2006	2007	2008	2009	2010	2011	2012	2013	Total
Rota Ag test	923	1047	1339	1251	1158	921	799	866	669	8973
Rota (+)	149	267	448	268	255	129	108	127	93	1844
Positive rate (%)	16.1	25.5	33.5	21.4	22.0	14.0	13.5	14.7	13.9	20.6

Rota, rotavirus; Ag, antigen.
A decreasing pattern of positive tests was observed.

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rus, RotaShield®, was withdrawn due to an increasing risk of IS. This is thought to be based on a difference in the viral strain used in that vaccine; however, its mechanisms are not fully understood yet.[27] Despite the fact that post-licensure studies showed no increased risk of IS after rotavirus vaccination, this matter is still the subject of debate. According to a recent study conducted in the United States, RotaTeq® was found to increase cases of IS by approximately 1.5 (95% CI, 0.2 to 3.2) per 100000 recipients after one dose, although no significant increase in risk was shown after the second and third doses.[28,29] In Mexico, the first dose of the rotavirus vaccine was associated with an increased risk of IS between 5.3 and 5.8 within seven days after vaccination. By contrast, in Brazil, a second dose of the vaccine increased the risk of IS by 1.9 to 2.6 within seven days after vaccination, while no increased risk of IS was seen after the first dose.[16] In Australia, two studies conducted showed opposite results. One found an increased risk of IS after both pentavalent and monovalent vaccination.[18] However, another showed no overall increased risk of IS after both types of vaccination.[17]

When we used CIFs, the rotavirus vaccine-associated IS rate at our facility was 31.63 times higher than that of the United States report. However, after taking into consideration the difference in the background incidence rate of IS between the two countries, the incidence rate was seven times higher in our hospital. However, one thing that needs to be considered here is that our data, which are from a single center study, are smaller compared to the United States data. Also, given that our facility is a tertiary medical center, the number of patients diagnosed and treated for IS may be much higher than the number of patients who visit for the sole purpose of receiving vaccinations. Nevertheless, when we compared the cases with the expected cases, there was no increased IS risk associated with pentavalent rotavirus vaccination during the window period of four weeks post-vaccination, compared to the background incidence rate. These factors could have contributed to such discrepancy. In fact, a decreasing tendency was observed. Also, a fewer number of patients tested positive for rotavirus antigen overall.

There are some limitations in this study. First, it was not based on nationwide data. Since the data were collected only in our hospital, the numbers of corresponding data were small. Despite the results that showed RotaTeq® does not increase the risk of IS, it is thought that the precision of the estimates was affected by the number of cases. Second, the incidence rate of natural IS in Korea is unknown. The trend of the incidence rate of IS in children below 12 months of age in our hospital showed a decreasing pattern, from 142 cases to 15 cases per 100000 children during the observation period. This is quite low compared with 47 cases in United States,[13] 81 cases in Australia,[30] 28.9 in Singapore,[31] 19.70–47.83 in Thailand,[32] and 38 in Switzerland.[33] There is one report from Jeonbuk Province in Korea showing 236 cases per 100000 children below 12 months of age,[22] although nationwide data are needed to fully understand and interpret the results of this study. Third, our data were collected by reviewing electronic medical records. There could have been some missing data regarding medical conditions that can foster IS. Rotavirus vaccination is not included currently in the NIP in Korea. This means that it is not covered by insurance as Korea has a National Health Insurance System. This makes it extremely difficult to assess rotavirus vaccination status of all children in the country. We are planning to expand our study by obtaining data from multiple centers and eventually from all of Korea. Lastly, this study only investigated the effects of a pentavalent vaccine. Our center uses RotaTeq only, and thus, we do not have any information on the effects of Rotarix®, which is a monovalent vaccine.

Many studies examining whether IS is associated with rotavirus vaccination are being conducted, and no consensus has been reached yet. However, the fact that rotavirus-associated morbidity has decreased has been established in many countries is why we need to weigh the risks against benefits.

Rotavirus vaccines are still not included in the Korean NIP. As mentioned previously, there are rare mortalities, but considerable morbidities, still associated with rotavirus gastroenteritis. Rotavirus has strong infectivity and can spread to more than 50 children in one minute. To cover rotavirus vaccination within the NIP, stronger evidence regarding the safety and effectiveness of this vaccination is needed. Towards this, a large study should be conducted to determine the association between rotavirus vaccination and IS.

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REFERENCES

1. Tate JE, Burton AH, Boschi-Pinto C, Steele AD, Duque J, Parashar UD; WHO-coordinated Global Rotavirus Surveillance Network. 2008 estimate of worldwide rotavirus-associated mortality in children younger than 5 years before the introduction of universal rotavirus vaccination programmes: a systematic review and meta-analysis. Lancet Infect Dis 2012;12:136-41.
2. Kang HY, Kim KH, Kim JH, Kim HM, Kim J, Kim MS, et al. Economic evaluation of the national immunization program of rotavirus vaccination for children in Korea. Asia Pac J Public Health 2013; 25:145-58.
3. Murphy TV, Gargiullo PM, Massoudi MS, Nelson DB, Jumaan AO, Okoro CA, et al. Intussusception among infants given an oral rotavirus vaccine. N Engl J Med 2001;344:564-72.
4. Murphy TV, Smith PJ, Gargiullo PM, Schwartz B. The first rotavirus vaccine and intussusception: epidemiological studies and policy decisions. J Infect Dis 2003;187:1309-13.
5. Kramarz P, France EK, Destefano F, Black SB, Shinefield H, Ward JI, et al. Population-based study of rotavirus vaccination and in-

tussusception. Pediatr Infect Dis J 2001;20:410-6.
6. Centers for Disease Control and Prevention (CDC). Withdrawal of rotavirus vaccine recommendation. MMWR Morb Mortal Wkly Rep 1999;48:1007.
7. Parashar UD, Alexander JP, Glass RI; Advisory Committee on Immunization Practices (ACIP), Centers for Disease Control and Prevention (CDC). Prevention of rotavirus gastroenteritis among infants and children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2006; 55:1-13.
8. Cortese MM, Parashar UD; Centers for Disease Control and Prevention (CDC). Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2009; 58:1-25.
9. Ruiz-Palacios GM, Pérez-Schael I, Velázquez FR, Abate H, Breuer T, Clemens SC, et al. Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. N Engl J Med 2006;354:11-22.
10. Velázquez FR, Colindres RE, Grajales C, Hernández MT, Mercadillo MG, Torres FJ, et al. Postmarketing surveillance of intussusception following mass introduction of the attenuated human rotavirus vaccine in Mexico. Pediatr Infect Dis J 2012;31:736-44.
11. Rotavirus vaccines: an update. Wkly Epidemiol Rec 2009;84:533-40.
12. Haber P, Patel M, Pan Y, Baggs J, Haber M, Museru O, et al. Intussusception after rotavirus vaccines reported to US VAERS, 2006-2012. Pediatrics 2013;131:1042-9.
13. Shui IM, Baggs J, Patel M, Parashar UD, Rett M, Belongia EA, et al. Risk of intussusception following administration of a pentavalent rotavirus vaccine in US infants. JAMA 2012;307:598-604.
14. Zickafoose JS, Benneyworth BD, Riebschleger MP, Espinosa CM, Davis MM. Hospitalizations for intussusception before and after the reintroduction of rotavirus vaccine in the United States. Arch Pediatr Adolesc Med 2012;166:350-5.
15. Yen C, Tate JE, Steiner CA, Cortese MM, Patel MM, Parashar UD. Trends in intussusception hospitalizations among US infants before and after implementation of the rotavirus vaccination program, 2000-2009. J Infect Dis 2012;206:41-8.
16. Patel MM, López-Collada VR, Bulhões MM, De Oliveira LH, Bautista Márquez A, Flannery B, et al. Intussusception risk and health benefits of rotavirus vaccination in Mexico and Brazil. N Engl J Med 2011;364:2283-92.
17. Buttery JP, Danchin MH, Lee KJ, Carlin JB, McIntyre PB, Elliott EJ, et al. Intussusception following rotavirus vaccine administration: post-marketing surveillance in the National Immunization Program in Australia. Vaccine 2011;29:3061-6.
18. Carlin JB, Macartney KK, Lee KJ, Quinn HE, Buttery J, Lopert R, et al. Intussusception risk and disease prevention associated with rotavirus vaccines in Australia's National Immunization Program. Clin Infect Dis 2013;57:1427-34.
19. Weintraub ES, Baggs J, Duffy J, Vellozzi C, Belongia EA, Irving S, et al. Risk of intussusception after monovalent rotavirus vaccination. N Engl J Med 2014;370:513-9.
20. Kim JS, Bae CW, Lee KY, Park MS, Choi YY, Kim KN, et al. Immunogenicity, reactogenicity and safety of a human rotavirus vaccine (RIX4414) in Korean infants: a randomized, double-blind, placebo-controlled, phase IV study. Hum Vaccin Immunother 2012;8:806-12.
21. Tate JE, Simonsen L, Viboud C, Steiner C, Patel MM, Curns AT, et al. Trends in intussusception hospitalizations among US infants, 1993-2004: implications for monitoring the safety of the new rotavirus vaccination program. Pediatrics 2008;121:e1125-32.
22. Jo DS, Nyambat B, Kim JS, Jang YT, Ng TL, Bock HL, et al. Population-based incidence and burden of childhood intussusception in Jeonbuk Province, South Korea. Int J Infect Dis 2009;13:e383-8.
23. Konno T, Suzuki H, Kutsuzawa T, Imai A, Katsushima N, Sakamoto M, et al. Human rotavirus infection in infants and young children with intussusception. J Med Virol 1978;2:265-69.
24. Nicolas JC, Ingrand D, Fortier B, Bricout F. A one-year virological survey of acute intussusception in childhood. J Med Virol 1982;9: 267-71.
25. Mulcahy DL, Kamath KR, de Silva LM, Hodges S, Carter IW, Cloonan MJ. A two-part study of the aetiological role of rotavirus in intussusception. J Med Virol 1982;9:51-5.
26. Rennels MB, Parashar UD, Holman RC, Le CT, Chang HG, Glass RI. Lack of an apparent association between intussusception and wild or vaccine rotavirus infection. Pediatr Infect Dis J 1998;17: 924-5.
27. Nakagomi T. Rotavirus infection and intussusception: a view from retrospect. Microbiol Immunol 2000;44:619-28.
28. Yih WK, Lieu TA, Kulldorff M, Martin D, McMahill-Walraven CN, Platt R, et al. Intussusception risk after rotavirus vaccination in U.S. infants. N Engl J Med 2014;370:503-12.
29. Noel G, Minodier P, Merrot T. Intussusception risk after rotavirus vaccination in U.S. infants. N Engl J Med 2014;370:1766.
30. Justice F, Carlin J, Bines J. Changing epidemiology of intussusception in Australia. J Paediatr Child Health 2005;41:475-8.
31. Phua KB, Lee BW, Quak SH, Jacobsen A, Teo H, Vadivelu-Pechai K, et al. Incidence of intussusception in Singaporean children aged less than 2 years: a hospital-based prospective study. BMC Pediatr 2013;13:161.
32. Khumjui C, Doung-ngern P, Sermgew T, Smitsuwan P, Jiraphongsa C. Incidence of intussusception among children 0-5 years of age in Thailand, 2001-2006. Vaccine 2009;27 Suppl 5:F116-9.
33. Buettcher M, Baer G, Bonhoeffer J, Schaad UB, Heininger U. Three-year surveillance of intussusception in children in Switzerland. Pediatrics 2007;120:473-80.

https://doi.org/10.3349/ymj.2017.58.3.631