

Intussusception in southern Indian children: lack of association with diarrheal disease and oral polio vaccine immunization

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Background: Intussusception is the most common cause of intestinal obstruction in young children and has been reported as a complication of a recently withdrawn tetravalent reassortant rotavirus vaccine.

Methods: We studied the history, clinical presentation, management and outcome of intussusception presenting to a tertiary care hospital in southern India over a 10-year period, in order to assess potential association with diarrheal disease and immunization. **Results:** Data from 137 index cases and 280 control subjects indicated that the risk of diarrheal disease or oral polio vaccine administration in the month prior to presentation was similar in the index cases and controls. Mean time to presentation to hospital after developing symptoms was 1.8 days, and 77.3% of patients required surgery, with 47.4% undergoing intestinal resection. Mortality was 0.006%. **Conclusions:** No association could be demonstrated between gastroenteritis or oral poliovirus vaccine immunization and intussusception in southern Indian children. These children presented later and required operative intervention more frequently than has been reported in other studies, but had a good outcome with low mortality. [*Indian J Gastroenterol* 2003;22:82-84]

Key words: Rotavirus, vaccine

Intestinal intussusception (ISS) is the most common cause of intestinal obstruction in children aged 2 years or below.¹ The cause of this condition in this age group remains unclear,² though infectious agents (bacterial and viral), gender, and environmental or developmental factors have all been implicated.^{1,3} Of various infectious agents, adenoviruses have been most frequently implicated, but rotavirus, picornaviruses, and herpesvirus also have been suspected.^{1,4,5,6}

A live tetravalent rotavirus vaccine, *RotaShield* (Wyeth; Madison, NJ, USA) or RRV-TV, was introduced in the United States in 1998, but was withdrawn from the market in 1999 after reports of ISS in vaccinees.⁷ Recent analysis of epidemiological data following *RotaShield* vaccination revealed an increased risk of ISS 3 to 14 days following first or second doses of the vaccine.⁸

Prior to the reports with the *RotaShield* vaccine, data on association of rotavirus with ISS in children were limited and variable. One Japanese study found rotavirus infection in 11 of 30 infants with ISS;^{9,10} however, several other studies have failed to identify rotavirus as an etiologic agent in such patients.^{6,11,12} Following the withdrawal of the rotavirus vaccine, concerns were also raised that other oral vaccines, including the oral polio vaccine (OPV), could be associated with ISS. Analysis of data from the UK, Canada and the US and a publication based on data from the UK concluded that there was no evidence to indicate a relationship between OPV and intussusception.^{13,14}

We carried out a retrospective study of the history, clinical presentation, management and outcome of intussusception presenting to a tertiary care hospital in southern India over a 10-year period, in order to assess potential association with diarrheal disease and immunization, and to determine whether appropriate, timely management resulted in favorable outcome.

Methods

Christian Medical College Hospital, Vellore is an 1800-bed tertiary-care hospital that serves an urban population of 400,000 and a rural population of 200,000. We identified all cases diagnosed as intussusception (International Classification of Diseases Code 560.0) in children below the age of 5 years between January 1991 and December 2000. All out-patient and in-patient records for these patients were reviewed to confirm the diagnosis and assess prior illness, history of immunization, duration of symptoms, presentation, investigative and surgical findings, treatment and outcome. Where complete details were not available in the records, letters were sent to the families of the patients asking them to visit the hospital for review or to send records by mail.

We then carried out a case-control evaluation to determine whether there was a relationship between prior diarrheal illness or vaccination with OPV and the risk of intussusception within one month of administration of the vaccine. Two children who presented to the out-

patient department or to the accident and emergency department with a condition other than intussusception, requiring admission, in the same month as the index child were matched for age, sex, socio-economic status of parents and geographic area. The date of diagnosis in each child was used as the index date from which the time from the last vaccination was computed.

A total of 165 children under 5 years of age were diagnosed to have intussusception in the period reviewed. It was possible to obtain information by retrospective chart review, mail questionnaires, or telephonic or personal interviews, from 137 cases and 280 matched control subjects. For each patient and control, information on diarrheal illness was collected only from the records, because of the expected lack of accuracy of recall over a 10-year period. Since immunization histories were always not available in the in-patient records, we requested for documents related to immunization, in the form of immunization clinic records, well-baby clinic records or doctors' certificates. Information on BCG vaccination was also collected using similar methods, as a control intervention.

Results

Age distribution of the cases is shown in the Table. Intussusception was observed most commonly in the 3-6 month (29.1% of total cases) and 6-9 month (26.3%) age groups, with 73.7% occurring in the first year and 92.7% by 2 years of age. More boys (86/137; 62.8%) were affected. Of the 137 patients for whom data were available, 116 lived in Vellore district, within a distance of 60 kilometers from the hospital.

Mean duration of symptoms at the time of presentation was 1.8 days (median 2; range 6 hours to 8 days). The common sites of ISS were ileo-cecal (94; 68.6%), ileo-ileal (12; 9.2%), ceco-colic (12; 9.2%) and ileo-cecocolic (6; 4.6%). In 6 of 10 patients between the ages of two and five years, and in 3 patients below the age of two years, a Meckel's diverticulum was identified. In one patient each, a juvenile polyp and lymphoma were identified. In 6 (4.6%) patients, the ISS could be reduced externally. Hydrostatic reduction by barium en-

ema was successful in 26 patients (18.9%). Laparotomy without intestinal resection was done in 31 patients (29.9%), but 65 (47.4%) patients required intestinal resection.

One five-month-old child, who presented with signs of sepsis and aspiration pneumonia, underwent reduction of an ileo-ileo-cecal ISS, but developed septic shock the day after surgery and died on the second postoperative day. Two children who had undergone hydrostatic reduction developed recurrent ISS that required reduction at laparotomy.

There appeared to be no clustering of ISS by season, and there was no correlation with increased cases of gastroenteritis in the community (data not shown). Twelve (9.2%) children with ISS gave a history of diarrhea that could be clearly distinguished from the passage of bloody or currant jelly stools. Four children with ISS had been weaned in the week prior to presentation. Among control children, history of diarrhea was obtained in 31 (11.1%), but introduction of foods could not be assessed.

Overall, the relative risk for ISS in children who had diarrhea was 0.8 (95% CI 0.5-1.1). A clear history of OPV administration could be obtained in 91 (66.5%) cases and in 207 (73.9%) controls. The relative risk for ISS in children who had received OPV in the four weeks prior to presentation to hospital was 0.9 (95% CI 0.5-1.3). In each age group, the relative risk for both diarrhea and OPV administration was close to 1, indicating no increased risk (Table).

History of BCG vaccination, studied as a control intervention, was obtained in 83 (60.5%) cases and 176 (62.8%) controls ($p=ns$).

Discussion

In our study, the occurrence of ISS had no relationship with gastroenteritis, although previous studies have linked this condition with infective diarrhea and asymptomatic enteric infections.^{4,5,10} Similarly, our data indicate that children receiving OPV immunization were not at higher risk of developing ISS.

Interestingly, in some children solid foods had been introduced in the week prior to the development of ISS. In a model of ISS in Syrian hamsters, a change in diet increased the incidence of ISS significantly.¹⁵ The role of breast feeding could not be assessed in our study because many charts had incomplete feeding history; however, in other studies, breast feeding has been shown variably to increase or reduce the risk of ISS.^{16,17}

A striking feature of our data was the high rate (47.4%) of intestinal resection among children with ISS; this may be related to delay in seeking health care, although the time to presentation and subsequently to treatment could not be accurately evaluated. The mean

Table: Prior history of diarrhea or immunization with oral polio vaccine (OPV) in patients with ISS and controls

Age (mo)	Cases	Controls	Diarrhea		OPV	
			Cases	Controls	Cases	Controls
<3	3	7	0	1	2	6
3-6	40	83	3	6	32	72
6-9	36	72	3	9	12	27
9-12	22	44	3	5	4	6
12-15	14	28	1	3	5	15
15-18	6	13	1	2	1	2
18-24	6	12	0	3	4	9
>24	10	21	1	2	3	7
Total	137	280	12	31	63	144

time to presentation after development of symptoms in our study was 1.8 days, which is longer than has been described previously in studies from developed countries.^{18,19}

The difficulty of travel and the availability of other hospitals in Vellore and surrounding towns may prevent all patients with ISS from presenting to the hospital where this study was carried out. Our current study does not provide data on incidence of ISS for the Vellore district. However, a reporting system for communicable disease covering all health-care providers in this district has been established.²⁰ Using this system, it may be possible in future to obtain information on incidence of ISS and the risk factors involved in its causation.

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