Diarrhoea in children: aetiology and clinical aspects

Diarrea nei bambini: eziologia ed aspetti clinici

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INTRODUCTION

Rotavirus is a very common cause of acute diarrhoea in infant and young children throughout both the developing and developed world, occurring more frequently during the winter [1]. Person-to-person transmission is principally via faecal-oral contamination and exposure. The debilitating nature of rotavirus is reflected in the fact that an estimated one-third of all nosocomial paediatric diarrhoea cases globally can be attributed to this viral agent [2]. In the developed world the actual number of rotavirus infections with associated diarrhoea may well be much greater because severity appears diminished, resulting from immunological tolerance evolving from repeat exposures [3-5]. In developing countries, where young children are often already immunologically compromised in relation to poor nutritional status, severe, debilitating diarrhoea and associated fatalities are frequently attributed to this enteric viral pathogen [6-8]. Persistent and recurrent acute diarrhoea frequently caused by rotavirus infection is one of the three main causes of morbidity and mortality worldwide, accounting for an estimated annual five million deaths among infants under 5 years, particularly in developing countries [9]. Given the importance of rotavirus infection for the epidemiology of acute childhood diarrhoea and the fact that improved hygiene conditions have failed to decrease the incidence of rotavirus-associated diarrhoea, a vaccine against rotavirus has been intensely researched. However, the first vaccine was withdrawn from the market only a few months after becoming commercially available due to an association with intestinal intussusception [9-13]. Another safer, efficacious vaccine against rotavirus is already available in several countries. However, more data on the impact of rotavirus infection on the epidemiology of acute diarrhoea in children, especially in the most severe cases, are required to support massive vaccination [14-16]. Clinical presentation of rotaviral disease ranges from asymptomatic to severe dehydration pictures, albeit generally characterized by abdominal pain, vomit, fever and watery diarrhoea, with incubation ranging from 24 to 72 hours.

The aim of this retrospective study was to determine the prevalence and clinical aspects of rotavirus infection in a group of children under five years of age affected by acute diarrhoea.

PATIENTS AND METHODS

In all, 402 children (180 male and 222 female) under five years of age (mean age 25 months, range 2 months-5 years, 83% under four years of age) with acute diarrhoea were examined between February 2003 and December 2006 in the Paediatric Department, Sondrio Hospital, Italy. Relevant clinical information was collected by means of a standard questionnaire, including age, sex, clinical status (fever, vomiting, and dehydration status), and duration of diarrhoea. Diarrhoea was defined as the passage of three or more loose stools within the previous 24 hours. Dehydration was classified as absent, mild, moderate and severe according to standard criteria [19].
Faecal samples were collected after natural evacuation. Stools were divided into two fractions: one was tested for the presence of rotavirus using a commercially available enzyme immunoassay kit (Rotaclone, Meridian Diagnostic, Cincinnati, USA).

The second aliquot was processed by routine microbiological and biochemical tests from BioMerieux (Paris, France; API 20E) to identify Salmonella species, Shigella species and Yersinia enterocolitica. Salmonella and shigella strains were selected from SS agar, XLD agar and VB agar (Difco, Le Pont de Claix, France). Yersinia enterocolitica strains were identified by means of a polyvalent serum (Yersinia enterocolitica polyvalent) and four monovalent sera: 03, 05, 08 and 09 (Probac test, Germany). Rotavirus-associated illness was diagnosed only in patients who had rotavirus antigens detected in the stools and negative stool cultures.

## RESULTS

During the study period, 402 patients affected by acute diarrhoea were admitted to the paediatric clinic, Sondrio Hospital, Italy. Most of the patients (310/402, 77.1%) were infected by rotavirus, while of the remaining 82 (22.9%) 40 were infected by Salmonella species. In 42 no bacterial agent was evidenced by microbiological tests.

In relation to clinical presentation, only 18 patients (all infected by rotavirus) presented exclusively acute diarrhoea, while vomiting was evidenced in 350/402 (87.0%) patients, fever in 309/402 (76.8%) patients and abdominal pain in 200 (49.7%). All patients with salmonella infection presented fever.

Most patients (374, 93.0%) presented diarrhoea exclusively between the first and fourth day of illness, while ten (all infected by rotavirus) persisted with diarrhoea after the fourth day. The greatest incidence of vomiting occurred on the second and third days of illness, but only 18 children (all infected by rotavirus) still presented that symptom on the fifth day.

Most patients (76.2%) had fever exclusively between the first and third days after admission, while only seven, infected by rotavirus, after the third day and three, positive for rotavirus, after the fourth day.

Anorexia was present in 215 (53.4%) patients and malaise in 118 (29.3%). Clinical signs of mild dehydration were observed in 13 children during the hospital stay (all infected by rotavirus), while no cases of metabolic acidosis, hypoglycaemia or hypovolaemic shock were documented.

All patients affected by Salmonella species infection were treated with ceftriaxone (50 mg/kg intravenously once a day), while only 5% of the patients affected by rotavirus infection were treated with ceftriaxone. Mean hospitalisation was 3.8 days (range 3-6 days).

Elevated serum levels of uric acid (mg/dl, mean value 8.7, range 6.1-10.5 with normal value 2-5 mg/dl) were evidenced in 13/302 (4.3%) of patients with rotavirus infection, while only one child out of 82 (1.2%) with acute diarrhoea, but negative for rotavirus infection, presented a minimal increase in serum uric acid level (5.5 mg/dl). In this patient the faecal sample was negative for salmonella, shigella and Yersinia enterocolitica.

No children presented familiarity for hyperuricaemia or another cause correlated with this disorder.

In all patients serum uric acid levels spontaneously returned to normal within five days (range 3-5 days). Renal ultrasound examination was normal for all patients with hyperuricaemia and no children had uric acid crystals in their urine.

5/13 (38.4%) patients with hyperuricaemia and infected by rotavirus presented clinical signs of mild hyponatraemic dehydration (range of serum sodium levels 131-134 mEq/L, normal value 138-150 mEq/L), with mild alterations of serum creatinine and urea levels.

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<th>Table 1 - Epidemiological and clinical results.</th>
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<td>Rotavirus</td>
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<td>Salmonella</td>
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(mean creatinine levels 1.9 mg/dl, range 1.5-2.4 mg/dl, normal value <1.2 mg/dl; mean urea levels 85 mg/dl, rage 67-93 mg/dl, range 10-50 mg/dl).

In all patients serum creatinine and urea levels spontaneously returned to normal within five days. The results are summarised in Table 1.

**DISCUSSION**

The results of the present study confirm previous data concerning the major epidemiological importance of rotavirus as the principal aetiological agent in hospitalised children affected by acute diarrhoea under 5 years of age. Indeed, among the 402 patients studied, most (310/402, 77.1%) were infected by rotavirus. Of the remaining 82 (22.9%) 40 proved infected by *Salmonella* spp. while in 42 no bacterial agent was evidenced by microbiological tests. Clinically, our data show that rotavirus infection causes more severe and prolonged intestinal infection than salmonella species.

Persistence of diarrhoea, vomiting and fever on the fourth day from onset was observed only in rotavirus-positive patients, while all patients infected by salmonella species presented a regression of all symptoms into the third day. Clinical signs of mild hyponatraemic dehydration were observed in 13 children during their hospital stay, all infected by rotavirus. This shows that rotavirus is potentially correlated with a debilitating enteric infection than salmonella species.

In all patients serum acid uric levels spontaneously returned to normal within five days, demonstrating that a degree of acute hyperuricaemia in infants and children can be tolerated without development of acute renal failure. As the main factor contributing to the hyperuricaemia is most probably ECF depletion, we suggest that drug therapy specifically aimed at lowering the serum uric acid level is unnecessary if adequate urine output is achieved.

In conclusion, our retrospective study confirmed the major epidemiological and clinical importance of rotavirus as the main aetiological agent in hospitalised children under five years of age affected by acute diarrhoea. We also showed a possible correlation between rotavirus infection and hyperuricaemia, probably connected with dehydration and reduction in ECF volume.

**Key words:** rotavirus, fever, diarrhoea, enteric infection.
To determine the aetiology of diarrhoea in children <5 years hospitalised for acute enteritis and to evidence the chief clinical aspects in correlation with different aetiologic agents, a total of 402 children with acute diarrhoea were examined between February 2003 and December 2006 in the Paediatric Department of Sondrio Hospital. Faecal samples were collected and processed by routine microbiological and biochemical tests. For all patients the clinical signs and symptoms on admission were evidenced. Most of the patients (310/402, 77.1%) were infected by rotavirus, while of the remaining 82 (22.9%) 40 were infected by salmonella species. In 42 patients, no bacterial agent was evidenced by microbiological tests. Clinical signs of mild dehydration were observed in 13 children during the hospital stay (all infected by rotavirus), while no case of metabolic acidosis, hypoglycaemia or hypovolaemic shock was documented. Elevated serum levels of uric acid were evidenced in 13/302 (4.3%) of patients with rotavirus infection, while only 1/82 (1.2%) rotavirus-negative children presented a minimal increase in serum uric acid level. Our retrospective study confirms the epidemiological and clinical importance of rotavirus as the main aetiologic agent in hospitalised children <5 years affected by acute diarrhoea. There also emerged a possible correlation between rotavirus infection and hyperuricaemia, probably connected with dehydration.

REFERENCES


