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Faecal excretion of alpha-1-antitrypsin in acute diarrhoea

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SUMMARY High levels of faecal α -1-antitrypsin were found in children suffering from acute rotavirus diarrhoea and in children with diarrhoea in whom no microbial pathogen could be established. The results suggest that transient protein-losing enteropathy is common in acute childhood diarrhoea and may influence the outcome of the disease.

Gastrointestinal protein loss is a common phenomenon that has been demonstrated in association with more than 70 disorders affecting the gastrointestinal tract.¹ There is a lack of information about protein loss during diarrhoea because methods have been cumbersome.¹

Crossley and Elliott,² and later Bernier *et al.*,³ have shown that measurement of faecal α -1-antitrypsin (α -1-AT) is a simple and reliable index of excessive loss of plasma proteins into the gastrointestinal tract. Recently Thomas *et al.*⁴ demonstrated its value in screening for various gastrointestinal mucosal disorders in children.

Diarrhoeal diseases are a leading cause of child death in developing countries, and the existence of a vicious circle of malnutrition and gastroenteritis is well known.⁵ Since rotavirus is a major pathogen of childhood diarrhoea in both temperate and tropical climates, it would be helpful to know if gastrointestinal protein loss occurs in acute rotavirus diarrhoea. We have now studied α -1-AT content of stools from children in hospital because of diarrhoea.

Materials and methods

During a 1-year prospective study of the aetiology of

childhood diarrhoea⁶ stool samples were randomly collected in the acute and convalescent stage of the disease for α -1-AT measurements. The faecal samples were freshly frozen at -20°C .

The patients were divided according to the aetiology of the diarrhoea into two study groups: rotavirus-associated diarrhoea with no evidence of other simultaneous enteropathogen (91 patients) and non-specific diarrhoea with no demonstrable microbial aetiology (60 patients). In the latter group no rotavirus, adenovirus, *Salmonella* sp., *Shigella* sp., *Yersinia* sp., *Campylobacter* sp., diarrhoeal *Escherichia coli* or *Giardia* sp. could be demonstrated. For comparison the α -1-AT content of stools was measured again in the same patients about 4 weeks after diarrhoea (60 patients, the control group).

Faecal α -1-AT determinations were made according to Crossley and Elliott,² using commercially available immunodiffusion plates (M-Partigen, Behringwerke, Marburg, W. Germany).

Results

Mean faecal α -1-AT concentration ($\pm$ SE) in the rotavirus patients was 2.74 ± 0.34 mg/g dry weight (range 0-16.88). There was no statistically significant difference when compared with the non-specific diarrhoea group (3.34 ± 0.62) (range 0-28.13). Both groups of patients with diarrhoea differed significantly ($P < 0.001$) from the control group (0.44 ± 0.06) (range 0-2.80) (Fig. 1).

Faecal α -1-AT concentration was over 1.39 mg/g dry weight (mean of controls $+2$ SD) in 56%, 57%, and 3% of the children in the respective groups.

Fig. 1 Faecal α -1-antitrypsin concentration (mean $\pm$ SE) in children suffering from acute rotavirus ($n=91$) and nonspecific ($n=60$) diarrhoea and in the same children at the convalescent stage one month later (controls, $n=60$).

Fig. 2 Faecal α -1-antitrypsin concentration in serial stool specimens from 5 children with rotavirus diarrhoea (closed circles) and from 5 children with nonspecific diarrhoea (open circles).

Fig. 2 shows the faecal output of α -1-AT during the acute and convalescent stage of the diarrhoea in some children from whom serial stool specimens were available. Transiently high levels of α -1-AT were seen in both study groups.

Discussion

Abnormal random faecal α -1-AT concentrations have been found to reflect excessive serum protein loss from the gut.²⁻⁴ The test is non-invasive, non-isotopic, and is easily carried out; therefore it is suitable for children. In a recent study by Thomas *et al.*⁴ high levels of faecal α -1-AT were found in children with coeliac disease, allergic gastroenteropathy, lymphangiectasia, nonspecific colitis, acute gastrointestinal bleeding, and active chronic inflammatory bowel disease but not from healthy children. These disorders have all previously been found to cause protein-losing enteropathy by ⁵¹Cr-labelled albumin excretion tests. It seems obvious that if faecal output of this protease inhibitor exceeds normal, increased permeability of plasma proteins to the gut lumen must occur because food does not contain α -1-AT.

In the present study protein-losing enteropathy was screened in about 150 children suffering from acute diarrhoea. We measured α -1-AT from random stool specimens and freeze-dried the samples to eliminate the influence of faecal water on the results.

The findings were clear. Transiently high levels of faecal α -1-AT were found in many children suffering from acute rotavirus diarrhoea and also in those in whom no diarrhoeal pathogen could be established. Therefore, unlike some previous observations,⁴ leakage of plasma proteins into the gut lumen appears a common phenomenon and one which may lead to hypoproteinaemia.² This was not observed in our series of infants with good nutritional status. The underlying lesion leading to protein leakage during intestinal infection may vary, since similar quantities of α -1-AT were found in rotavirus diarrhoea and in 'nonspecific' diarrhoea. In evaluating this finding one might recall that protein loss has also been shown to occur in measles enteritis.⁷

In conclusion, transiently high faecal α -1-AT concentration is often found in acute childhood diarrhoea, suggesting the presence of protein-losing enteropathy. Excessive gastrointestinal protein loss may pass unnoticed in well-nourished children but may be an important trigger to the development of malnutrition in already undernourished children. These results also support the view that food intake should continue whenever possible during a diarrhoeal episode.⁸

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Haemoglobin levels and blood requirement in thalassaemia

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SUMMARY The relationship between blood requirement and the mean level of maintained haemoglobin was examined in 392 patients with homozygous β -thalassaemia. Pre- and post-transfusional haemoglobin levels and the amounts of blood transfused were measured during a 1-year period. No significant differences were noted in the blood requirements of patients (splenectomised or not) irrespective of the haemoglobin level. It may be supposed that if the mean haemoglobin level is high the haematopoietic activity is inhibited, and hence the bone marrow mass and total blood volume are reduced. High haemoglobin levels may thus be obtained with no increase in blood intake.

An understanding of the relationship between the amount of blood transfused and the mean haemoglobin (Hb) level maintained in patients with homozygous β -thalassaemia is important when assessing the risks and benefits of transfusion; it is important, too, in the clinical management of the patient. Data are scanty and conflicting. Modell¹ reported a linear correlation between these two measurements, but Propper *et al.*² found that the Hb level could be raised without increasing the amount of blood transfused, except during the initial few

months. It was decided therefore to examine this question on a larger scale, using patients collected from three centres.

Material and methods

A total of 392 subjects aged between 2 and 23 years (166 from Turin, 158 from Ferrara, and 68 from Milan) were studied for 2 years. One hundred and eighty-four of them had been splenectomised. Any patient with hypersplenism or signs of isoimmunisation, or any patient who underwent splenectomy during the period of observation was excluded. Patients were transfused as outpatients every 25-30 days with one or two blood units. The amount that Hb levels increased by transfusion was 3.5-4 g/dl. The mean Hb level maintained was calculated as the average of the pre- and post-transfusional values during one year.¹ The blood consumption was determined as the amount of blood (ml of concentrated red cells with haematocrit (75-85%)) transfused during the same period, divided by the body weight in June.

The Hb levels were classified into groups so that the mean blood consumption could be statistically analysed by means of Student's *t* test; the paired-data *t* test was used to compare the requirement in each year of any patient in whom the Hb level increased.