Gastrointestinal Allergy or Intolerance to Multiple Foods in Severe Chronic Diarrhea in Early Infancy

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When total parenteral nutrition was first used in the therapy of infants with intractable diarrhea as defined by Avery et al. (1), it was clearly demonstrated that many of these patients had gastrointestinal allergy or intolerance to food components (2–6). In fact, after weeks or months of total parenteral alimentation, some of these infants were able to be orally fed if one or more foods were excluded from the diet.

In recent years, we have had fewer cases requiring total parenteral nutrition than previously. Various factors have contributed to the improved prognosis of severe chronic diarrhea in early infancy. In our experience, the most important of these are the following: (a) precocious use of sufficient quantities of food, excluding the offending foods, in the few cases of chronic diarrhea in which this is necessary (7–9) (It is important to stress that these elimination diets must be administered only in the few cases of chronic diarrhea in which they are really necessary. In such cases, the diet must be used in quantities sufficient to avoid malnutrition, which is an important cause of the persistence of diarrhea.), (b) the more frequent use of rectal and colonic endoscopy for the diagnosis of colitis when intestinal allergy or infection is suspected (10–16), and (c) administration of drugs such as antibiotics, cholestyramine, or sodium chromoglycate in the very few cases in which they are necessary (17–32).

We have summarized the experiences accumulated by our group in Naples over the last 6 years of caring for young infants with severe chronic diarrhea. Attention is focused on the importance that GI allergy or intolerance to multiple food components has in the pathogenesis of this syndrome.

DIAGNOSIS OF GASTROINTESTINAL ALLERGY OR INTOLERANCE OF MULTIPLE FOODS

Over the last 6 years, 32 young infants suffering from allergy or intolerance to multiple foods were seen in our department. All were cow's milk protein
intolerant. Nineteen were also intolerant to soy-based formula, three to casein hydrolysate formula, and 11 to soy-based formula and casein hydrolysate formula.

The diagnosis of cow's milk protein intolerance was based on three criteria: (a) symptoms (such as acute diarrhea with vomiting and shock, chronic diarrhea with malabsorption syndrome, or colitis) with onset during the first 3 months of life on a diet containing cow's milk protein, (b) disappearance of the symptoms on a soy or protein hydrolysate formula, and (c) after six weeks of successful dietary treatment, return of the symptoms within a few hours or days of the readministration of cow's milk protein, in most cases associated with occult blood and leukocytes in feces and colitis by endoscopy and histology (33). In 12 of the 13 cases, clinical symptoms (diarrhea, vomiting, and shock) reappeared from 1 to 96 hr after the challenge. Clinical response to the challenge was the most reliable test for the diagnosis. A more accurate diagnosis may be made by simple laboratory tests, particularly demonstration of occult blood in feces, which was present in 12 of the 13 cases, and the reappearance of fecal leukocytes in nine of our 13 cases. Endoscopic and histologically demonstrable colitis, which was present in all six cases examined, is a useful adjunctive test for diagnosis. Other tests proposed for diagnosing cow's milk protein intolerance were less frequently positive; neutrophil count increase (34) was found in only six of the 13 cases, lactose in the feces in only four, decrease in xylose blood levels after a test dose (35) in three, and histologically proven damage of jejunal mucosa in four (36,37).

The diagnosis of soy milk intolerance in young infants allergic to cow's milk protein was based on three criteria as well: (a) the reappearance of gastrointestinal symptoms such as diarrhea, vomiting, and blood and mucus in the feces at the mean age of 62 days (ranging between 27 and 96 days)—in most cases, the symptoms appeared some days after the introduction of soy milk in the diet; in only a few cases did the symptoms appear immediately (mean 14.6 days; range 0–45 days); (b) disappearance of the symptoms on a protein hydrolysate formula; and (c) reappearance of the clinical symptoms in the few cases (only three) challenged with soy milk.

The diagnosis of intolerance to casein hydrolysate formula (Nutramigen®) in young infants allergic to cow's milk protein was based on similar symptoms (diarrhea, vomiting, mucus and blood in feces) appearing at the mean age of 67 days (range 45–105 days) in most cases immediately or a few days after the introduction of Nutramigen® into the diet (mean value 4.6 days; range 0–23 days). The symptoms disappeared on a rice–chicken formula. No case was challenged with Nutramigen®, as it would have been ethically unacceptable to do many challenges in these severely malnourished infants.

Three illustrative cases are presented below:

Case 1. C.F. (Fig. 1) was born with a body weight of 3.6 kg and was fed cow's milk from birth. Diarrhea began on the 38th day of life, when body weight was 4.4 kg. From the 45th to the 55th day, he was fed Nutramigen®, and diarrhea persisted with mucus and blood in the stool. On Isomil®, diarrhea disappeared
and then returned after 7 days. At the age of 2 months, 20 days, the infant was admitted to our department with a body weight of only 4.7 kg, almost the same as 40 days before. He was at the 10th percentile for age with a weight/height ratio also at the 10th percentile. No bacterial pathogens or parasites were present in the feces. On a chicken–rice diet (see below), the stools became normal. The infant gained weight at a rate of 15 g/day in the hospital and then 50 g/day at home. The weight/height ratio rose to a value between the 25th and 50th percentile. In this case (and in the following cases), a cow’s milk challenge confirmed the diagnosis of cow’s milk protein intolerance.

Case 2. L.S. (Fig. 2) was born with a body weight of 4.9 kg and was fed cow’s milk from birth. Since birth, there was vomiting, one episode of shock-like symptoms after bottle feeding, and, from the 15th day, diarrhea, which became more severe at the age of 42 days. At the age of 48 days in the hospital, soy-based formula was initiated. After only 1 day on this diet, severe diarrhea ensued, and blood was present in the stool. No bacterial pathogens or parasites were present in the feces. At 50 days of age, Nutramigen® was given, and again there was diarrhea and vomiting. After 4 days, at the age of 54 days, the body weight was decreasing, and the ratio of weight/height was at the 5th percentile; a chicken–rice diet was given. There was a rapid normalization of the stool, and discharge home after 10 days on the same diet with a mean increase of body weight of 40 g/day.
Case 3. C.A. (Fig. 3) was born with a body weight of 3.5 kg. He was fed with cow's milk formula from birth. Vomiting began a few days after birth, and after 15 days of diarrhea, a decrease in body weight was noted. Soy-based formula was started at the age of 25 days. Normalization of the stools and an increase in body weight were noted. At the age of 37 days, vomiting and diarrhea resumed. On hospitalization at the age of 45 days, body weight was 3.3 kg, and weight/height ratio was below the 5th percentile.

The infant was begun on Nutramigen®. After only 2 days, diarrhea with blood in the stool and shock-like symptoms were noted. No bacterial pathogens or parasites were present in the feces. At the age of 47 days, a chicken–rice diet was started. Normalization of feces and disappearance of the other symptoms were reported. The patient was discharged home after 10 days with a mean increase in body weight of 20 g/day.

RICE-CHICKEN DIET

For 12 years, we have been using a chicken–rice diet to treat severe chronic diarrhea in early infancy supposedly caused by gastrointestinal allergy or intolerance to multiple food components. In infants who are not able to tolerate soy-based formula or protein hydrolysate formula, we use this diet even at the
end of the first month of life. It contains 26 g of precooked rice meal, 5 g of lyophilized chicken meat, and 10 ml of olive oil or 5 ml of olive oil and 5 ml of medium-chain triglycerides in 200 ml of water. It is supplemented with calcium, potassium chloride, minerals, and vitamins. Nestlé® precooked rice, which is supplemented with calcium, constitutes half the total quantity of rice meal. One hundred milliliters contains 97 kcal, 2.4 g protein (10% of the total caloric intake), 4.8 g fat (42% of the total caloric intake), and 11.6 g carbohydrate (48% of the total caloric intake). In very young infants, the contents of one-half capsule of Pancrex V® is added to the bottle a few minutes before feeding. The quantity is increased up to 200 ml/kg body weight in 4 days providing the Kerry test for reducing substances on the stool is negative. All products used in this diet are commercially available, and the diet can be prepared at home.

The chicken-rice diet, which provides the calories, proteins, minerals, and vitamins necessary for the young malnourished infant, has been successful in treating 18 infants with severe diarrhea that began during the first month of life. All of these patients had cow’s milk protein intolerance, and, in addition, three had intolerance to casein hydrolysate formula, eight had soy intolerance, and seven soy and casein hydrolysate intolerance. In six of these patients, cholestyramine (1 g q.i.d.) was also given for a few days.

In all of the patients, the body weight increase during hospitalization ranged from 20 to 60 g/day (mean value 31 g/day), and they were discharged home after a mean period of 14 days (ranging from 6 to 30 days). The mean age at
the beginning of the diet was 82 days, ranging between 30 and 116 days. Nine of these patients were followed as outpatients. On discharge from the hospital, the body weight was 68% of the 50th percentile, ranging between 51% and 79% at the mean age of 95 days (range 71-135 days). After a mean period of 68 days (ranging between 60 and 90 days), the body weight was increased to a mean value of 84% of the 50th percentile, ranging between 74% and 91%.

During this relatively short time, the laboratory data that had indicated malnutrition (anemia, sideropenia, and hypoproteinemia) normalized. The oldest patient treated with this diet, not included in this series, is now 12 years of age and is in good health. Good results with a similar diet were reported in England by John Harries and colleagues (38,39).

During the same period of 6 years, the chicken-rice diet was unsuccessful in treating nine young infants with a clinical picture of intractable diarrhea of early infancy. The final diagnoses in these nine patients were one case of previously undiagnosed Salmonella infection, one case of multiple food allergy who was able to tolerate the chicken-rice diet after 6 weeks of total parenteral nutrition, three cases of gastrointestinal allergy or intolerance of rice, two cases of immunodeficiency syndromes, and two cases of familial intractable diarrhea of unknown origin beginning at birth. One of the two latter children was born from first-degree cousins, and a sibling of the other died at the age of 4 months with diarrhea. These two cases probably belong to the group of patients who die of intractable diarrhea (6,38,40) as a consequence of some unknown error of intestinal electrolyte absorption or secretion.

Gastrointestinal Allergy or Intolerance of Rice

More relevant to our topic are the three cases of GI allergy or intolerance of rice. Two cases are summarized below:

Case 4. S.S. was formula fed from birth. Diarrhea began during the third month of life while the patient was on a diet containing cow's milk. At the age of 5 months, on rice and a casein peptide formula, there was normalization of the stools. The casein peptide formula was replaced by Isomil®, and this was followed a few days later by diarrhea with mucus in the stools and a decrease in body weight. On rice and chicken, the stools normalized, and body weight increased. A challenge with cow's milk confirmed the diagnosis of cow's milk protein intolerance. The patient was hospitalized at the age of 5½ months; body weight was 5.4 kg (5th percentile). On a chicken-rice diet, there was a gradual deterioration of the stools and a decrease of the body weight. After 20 days, vomiting, severe diarrhea with reducing substances in the stools, and stools containing mucus and leukocytes as well as blood occurred. The endoscopic and histologic examination revealed colitis. The body weight was decreased to 5.2 kg. The patient was treated with a casein hydrolysate formula (Nutramigen®) and a diet containing wheat. There was a rapid normalization of the stools, and body weight increased to 7.7 kg (10-25%).
At the age of 9 months, a rice challenge was performed. On the second day, vomiting and diarrhea with blood, mucus, leukocytes, and reducing substances in the stools recurred. The endoscopic and the histologic examination of rectal biopsies revealed an erosive colitis. On elimination of rice from the diet, there was disappearance and normalization of all symptoms.

Case 5. F.A. had diarrhea and vomiting with slow increase in body weight from birth, first on cow's milk, and then on soy formula. We saw the patient for the first time at the age of 6 months; body weight was 5.3 kg, and weight/height ratio was below the 5th percentile. The diarrhea resolved on a diet of rice, wheat, and meat without cow's milk or soy proteins. We saw the patient again at the age of 10 months. The body weight was 7.6 kg (<5%), and the weight/height ratio was between 10 and 20%. Thereafter, diarrhea resumed with mucus, leukocytes, and guaiac-positive stools.

Rice was then eliminated from the diet. The diarrhea disappeared, and there was a rapid body weight increase to the 5th percentile (8.85 kg) with a weight/height ratio of 25% at age 13 months following the change in diet. At this age, a challenge with rice was followed 1 day later by vomiting and diarrhea with bloody stools containing mucus and leukocytes. No pathogens or parasites were detected in the feces. The endoscopy before the challenge with rice revealed a normal rectal mucosa, which was also histologically normal. After the challenge, endoscopy and histological examination of rectal biopsies revealed a severe colitis.

SUMMARY: DIETARY TREATMENT OF INFANTS WITH SEVERE CHRONIC DIARRHEA BEGINNING DURING THE FIRST TWO MONTHS OF LIFE AND SUSPECTED FOOD INTOLERANCE

When an infant has diarrhea with reducing substances in the fecal water as revealed by the Kerry test, lactose malabsorption can be suspected, and a lactose poor milk such as Galactomin® or AL 110 should be used (Fig. 4). If diarrhea persists, we suspect cow's milk protein intolerance, which is an important cause of secondary lactose malabsorption. This diagnosis is made at the first examination if the diarrhea is accompanied by symptoms of shock, vomiting, and/or signs of noninfectious colitis such as blood or leukocytes, especially eosinophils, in the feces without fecal pathogens or parasites.

These patients are then given a soy formula diet. If the diarrhea disappears, the diagnosis of cow's milk protein intolerance is confirmed, as mentioned previously, by a challenge with cow's milk or cow's milk protein 6 weeks later. In some of these patients, the diarrhea disappears but returns after a few hours or days of the soy formula. In these cases, we may suspect soy milk intolerance. A protein hydrolysate formula is initiated such as Nutramigen®, Pregestimil®, or Alfare®. If diarrhea persists or reappears, particularly if accompanied by symptoms of shock and blood and leukocytes in feces, we suspect that the patient is also allergic to cow's milk protein peptides. In such cases, we use a chicken-
Diarrhea with reducing substances in the feces on cow’s milk-containing diet
(Lactose malabsorption?)

Diarrhea with symptoms of shock, vomiting, and blood and leukocytes in feces
Lactose-poor milk
(Galactomin®, AL110)

Diarrhea persists
(Cow’s milk protein intolerance?)

Soy protein formula
Diarrhea
(Soy milk intolerance?)

Casein hydrolysate formula (Nutramigen®)
Diarrhea
(Allergic to casein peptides?)

Chicken–rice diet
Diarrhea disappears
(Multiple food intolerance)

FIG. 4. In the absence of pathogens in the feces.

rice diet prepared as described above. If the patient is also allergic to cow’s milk protein peptides, the diarrhea disappears, and the patient begins to gain weight.

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