



## Original article

Possible prevention of food allergies in children with short bowel syndrome: A retrospective pediatric study<sup>☆</sup>M.I. Spagnuolo<sup>\*</sup>, F. Chiatto, I. Liguoro, M.A. Caiazzo, S. Orlando, C. Langella, A. Guarino

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## SUMMARY

**Background and aims:** Short bowel syndrome is the major cause of intestinal failure. Patients often require parenteral nutrition for a variable period of time to survive, but there is no consensus on the optimal feeding formula during the weaning from parenteral nutrition. Aim of this study was to retrospectively analyze the development of food allergy in children with short bowel syndrome weaned with a hydrolyzed or an amino acid-based formula.

**Methods:** Clinical data were recorded for each patient. We also collected results of allergy tests of patients who had allergic reactions.

**Results:** Forty-seven children with intestinal failure (26 males; mean age of  $4.53 \pm 3.85$  years), followed-up at the Department of Pediatrics since 2000, were retrospectively evaluated. Thirty-eight of 47 children (80%) had residual bowel < 100 cm requiring a mean duration of  $17.36 \pm 6.7$  months of parenteral nutrition. In this group 22/38 children were weaned from parenteral nutrition with amino acid-based formula and 16 with hydrolyzed formula. Adverse events were reported in 16/38 children and 10 of these, all weaned with hydrolyzed formula, received diagnosis of cow's milk allergy. None of the 22 children weaned with amino acid-based formula developed allergic reactions.

**Conclusions:** Children weaned with hydrolyzed formula have an increased risk of developing cow's milk allergy in comparison to those weaned with amino acid-based formula and its use may have a role in the prevention of food allergies. The reduced length intestinal residual (<100 cm) is a risk factor for the development of allergic reactions.

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## 1. Introduction

Intestinal Failure (IF) can be defined as the ending result of any disease that implies chronic dependence on Parenteral Nutrition (PN) providing at least 75% of total calories for not less than 4 weeks, or at least 50% of total calories for not less than 3 months in order to maintain adequate growth, hydration, or micronutrient balance [1,2]. The main etiology of IF in children is represented by Short Bowel Syndrome (SBS) resulting from surgical resection of the small bowel [3].

**Abbreviations:** SBS, short bowel syndrome; IF, intestinal failure; PN, parenteral nutrition; EN, enteral nutrition; HF, hydrolyzed formula; AF, amino acid-based formula; CMA, cow's milk allergy.

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The most desirable aim in the management of these patients is to promote weaning from PN to the oral feeding by the slow transition firstly to Enteral Nutrition (EN) and finally to a free diet, according to the functional capacity of the gastrointestinal tract [4]. However, several years may be required to reach this goal. In fact, the tolerance to enteral feeding is conditioned by the primary disease, the extent of bowel resection, the presence (or absence) of the ileocecal valve, the remaining functional length and it is related to individual factors [2,5].

Although there are different methods to improve bowel adaptation, such as growth hormone therapy, epidermal growth factor, and bowel lengthening procedures, EN is universally considered the best way [1,6–10]. It should be initiated as soon as possible, even immediately after bowel resection and in parallel with PN to promote intestinal adaptation [11–13].

The European Society of Parenteral and Enteral Nutrition (ESPEN) guidelines provide evidence-based recommendations for the indication, application and type of formula of EN, oral nutritional supplements or tube feeding, but there is still no consensus

on the optimal feeding formula to wean patients with IF [11]. The current options are represented by standard (not hydrolyzed), semi-elemental (hydrolyzed) and an amino acid-based formulas. The ideal formula should provide adequate calories and nutrients and should not determine osmotic diarrhea, allergies, poor increase in height-weight [14,15]. Even if the most common practice in referral centres is mainly based on individual experience, hydrolyzed formulas, including semi- or complete elemental diet, are recommended, if breast milk is not available [14,16–18].

Furthermore, weaning should be guided by the need for prevention of food allergies. As reported by several authors [19–22], food sensitization, in particular Cow's Milk Allergy (CMA), has been commonly observed in infants with SBS and it could be due to the loss of the important role of bowel in digestion of antigens, absorption, and defense [23].

Aims of this study were to retrospectively analyze the development of food allergies in a population of children with IF weaned from PN with a hydrolyzed formula (HF) or with an amino acid-based formula (AF), and to evaluate several risk factors for food sensitization in order to establish possible prevention strategies.

## 2. Materials and methods

A retrospective analysis was carried out in a group of children with IF on PN, followed-up at our Reference Center for Pediatrics Artificial Nutrition since 2000. All patients' clinical, nutritional and surgery data were collected. In details, we recorded for each child: anthropometrics, underlying disease, residual intestinal length, presence of ileocecal valve, presence of jejunum/ileo-stomy. In addition, we analyzed the immune system of our patients, in order to include only those with normal levels of total IgA, G and M.

Once children were able to tolerate feeding through enteral route, they were weaned from PN either with HF or AF. This retrospective study is based on data of patients previously enrolled for testing the efficacy and safety of an amino acid-based formula milk [24]. During the follow-up period we observed no allergic reaction, therefore we compared these results to those registered with the use of HF. Adverse reactions were documented during 4 weeks of nutritional rehabilitation and clinical and serologic data were collected in a Chart Registered Form. All patients were weaned according to the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guidelines [25].

We introduced the following foods: cow's milk, wheat flour, chicken, tomato, egg white, egg yolk, fish, peanuts, soy. The timing of food introduction is not defined by these guidelines, but potentially allergic foods, such as egg and fish are usually delayed. The diagnosis of CMA was based on:

- disappearing of symptoms after attempting to eliminate cow's milk proteins
- recurrence of identical symptoms after a single re-exposure (after 4–6 months from the beginning of the allergic reactions)
- the exclusion of lactose intolerance and most common gastrointestinal infections.

All these criteria were universally accepted according to the ESPGHAN Working Group for Diagnostic criteria for Food Allergy and the European Academy of Allergy and Clinical Immunology Subcommittee on adverse reactions to food [26–28].

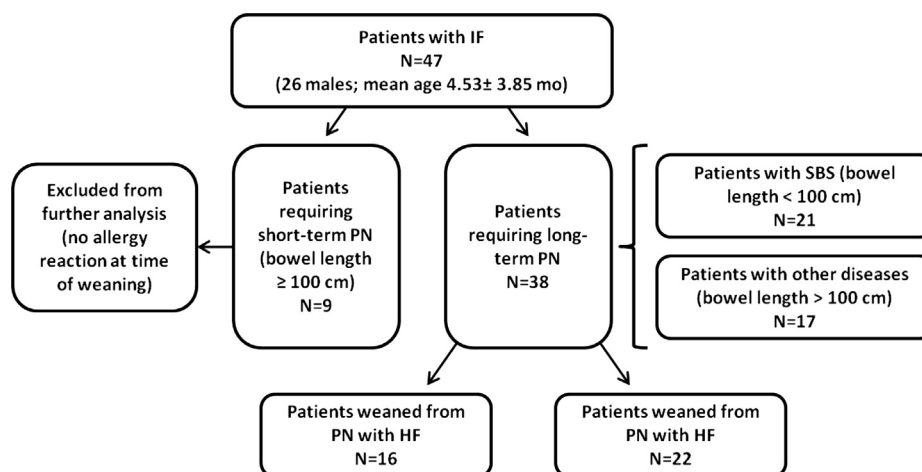
Sensitization to cow's milk and to other major antigens was detected in all symptomatic patients by Skin Prick Tests (SPT), total and specific IgE levels (Method radioallergosorbent test, RAST) and Atopy Patch Test (APT). The most common food allergens tested were:  $\alpha$ -lactalbumin, beta-lactoglobulin, casein, cow's milk, egg white, egg yolk, wheat flour, chicken, tomato, stockfish, peanuts, soy, exposure to dogs, wall pellitory, parietaria. A specific IgE value  $>0.35$  kU/l was considered an indicator of sensitivity. A patient was considered sensitive having positive SPT, APT and IgE-RAST.

### 2.1. Statistical analysis

Data tests were expressed as number/percent or as mean  $\pm$  SD. Comparison of continuous data between groups was carried out using the *T*-test. For each variable, *P* (two-sided)  $<0.05$  was considered significant. Data were analyzed with the GraphPad Prism 6 and GraphPad Instat.

## 3. Results

Forty-seven children with IF (26 males; mean age  $4.53 \pm 3.85$  years) were retrospectively evaluated. Even if the etiologies of IF in the study group were heterogeneous, all patients had severe intestinal impairment, mainly due to SBS, and required PN for a long



IF = Intestinal Failure; SBS= short bowel syndrome; PN= Parenteral Nutrition; HF= Hydrolyzed formula; AF= Amino acid-based formula; mo=months.

Fig. 1. Study design: flow-chart of the participants.

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