



Alimentary Tract

Intestinal permeability in patients with adverse reactions to food

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Abstract

Background. An abnormal intestinal permeability could contribute to establish an altered sensitivity to food-allergen.

Aim. To evaluate the intestinal permeability in subjects with adverse reactions to food on allergen-free diet.

Subjects. Twenty-one patients with food allergy and 20 with food hypersensitivity on allergen-free diet were enrolled and divided in four groups according to the seriousness of their referred clinical symptoms when they were on a free diet.

Methods. Intestinal permeability was evaluated by Lactulose/Mannitol ratio urinary detection determined by anion-exchange chromatography.

Results. Statistically significant different Lactulose/Mannitol ratio was evidenced in subjects with food allergy ($p=0.003$) or hypersensitivity ($p=0.0008$) compared to control patients. The correlation between Lactulose/Mannitol ratio and the seriousness of clinical symptoms, by using Spearman test, was statistically significant for food allergy ($p=0.0195$) and hypersensitivity ($p=0.005$) patients.

Conclusions. The present data demonstrate that impaired intestinal permeability, measured in our conditions, is present in all subjects with adverse reactions to food. In addition, for the first time, we report a statistically significant association between the severity of referred clinical symptoms and the increasing of Intestinal Permeability Index. These data reveal that intestinal permeability is not strictly dependent on IgE-mediated processes but could better be related to other mechanisms involved in early food sensitisation, as breast-feeding, or microbial environment that influence the development of oral tolerance in early infancy.

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1. Introduction

Intestinal permeability (I.P.) is the mucosal capacity to allow the passage of molecules from the intestinal lumen to the blood stream. Recent laboratory techniques enable to evaluate the I.P. through urinary detection of sugars probes, administered in couples that passively cross the intestinal epithelium. Recent studies suggest the use of Lactulose (La) and Mannitol (Ma) as probes; indeed these sugars cross the mucosal epithelium, are recovered in the urine and the ratio

of their clearance is used as I.P. assessment [1,2]. Recently, it has demonstrated that the use of a highly dedicated chromatographic device permits to measure appropriately the presence of La and Ma in the urine, providing a good methodology to explore the I.P. in normal and pathological conditions [3]. Thanking to the availability of these technologies, many studies have been performed to determine the I.P. in diseases that involve the gastrointestinal tract, in which the gut integrity is altered, such as Crohn's disease [4,5] and coeliac disease [6,7]. In addition, our previous data on newborns [8] and researches on animal models [9–11] have demonstrated that, during the first months of life, when the intestinal mucosa is still immature, there is an incomplete gut integrity that

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allows the passage of large molecules to blood. Such passage of macromolecules in this phase of life could impair the early mechanisms involved in the physiological establishment of the oral tolerance, predisposing to food sensitisation.

Adverse reactions to food are divided into IgE-mediated (food allergy, FA) and non-IgE-mediated (food hypersensitivity, FH) reactions. FA is correlated to the production of food specific IgE antibodies. These antibodies, binding to high affinity FcεRI receptors on mast cells and basophiles, cause histamine release and correlated allergic symptoms. Also in FH, which in some cases clinically mimic the IgE-dependent syndromes, the histamine release occurs, even though it is not dependent on IgE binding to specific receptors on mast cells [12].

In literature, many works on I.P. in FA patients are available. In a paper, focusing on I.P. evaluation in subjects with IgE-mediated reactions [13], the authors have shown an increased I.P., compared to healthy controls, when the patients were on allergen-free diet, that augments more after food allergens ingestion. In the same patients the contemporary administration of sodium chromoglycate prevented such increase. On the contrary, very few and disaccording data in FH patients can be found [14–16].

The lack of defined data on the I.P. in patients with FH and the absence, to our knowledge, of studies that compare the seriousness of clinical symptoms referred by the patients on a free diet with the I.P. levels, prompted us to perform the present study.

2. Patients and methods

2.1. Subjects

In this study we included 41 patients with adverse food reaction. Pregnant women and patients with gastrointestinal, immunologic, metabolic and/or neoplastic diseases were excluded from the protocol. As controls, 41 healthy volunteers, matched for age and gender, selected from the medical

staff (10 men and 31 women, mean age 29, range 21–50), with no symptoms or signs of gastrointestinal disease for at least two weeks, were included. They had no FA, cardiovascular and respiratory insufficiencies, liver cirrhosis, signs of malnutrition or rheumatic disease. None of the enrolled subjects had undergone recent gastrointestinal surgery, smoked more than two cigarettes per day, drunk more than 20 g/day of alcohol, and were not receiving corticosteroids from at least two months and antihistamines from at least two weeks, at the enrolment in this study. All the participants provided their written informed consent.

The study protocol was approved by the Ethical Committee of the Policlinico Hospital, University of Bari, Italy. When the analyses were carried out, all patients were on an allergen free diet since six months. Moreover, the medical history of adverse reactions, the correlation with the consumption of a specific food, the quantity of food ingested, and the gap between ingestion and symptoms' onset were examined.

As stated by the European Academy of Allergology and Clinical Immunology position paper on FA, the diagnosis of FA should be confirmed by positive skin prick tests (SPT) [17], radioallergosorbent tests (RAST) [18] and double-blind placebo-controlled food challenges (DBPCFCs) [19–21]. According to the revised nomenclature for allergy, FH is defined as a reaction with appearance of symptoms at a dose tolerated by normal subjects, without an IgE-mediated mechanism and, consequently, with negative SPT and RAST [22], positive to DBPCFCs.

On the basis of these diagnostic tools, we divided all patients into two classes: 21 patients with FA and 20 patients with FH.

All patients with FA exhibited SPT positive reaction and for 10 subjects (48%), the diagnosis was further confirmed by RAST positivity. Concerning patients with FH, with negative SPT and RAST, the DBPCFCs confirmed the diagnosis on a clinical basis for at least one of the suspected food. In the control group, SPT and RAST resulted negative.

Table 1 shows the number of patients reacting to specific foods at DBPCFCs for each group. Hazelnut, Peanuts, Celery

Table 1
Reactivity of patients (FA and FH) to specific foods determined by DBPCFCs as reported in Section 2

	Patients with FA <i>n</i> = 21		Patients with FH <i>n</i> = 20	
	Patients reacting to the specific food	Percentage	Patients reacting to the specific food	Percentage
Hazelnut	15	71.4	2	10
Peanuts	13	62	1	5
Celery	9	42.8	2	10
Soy	8	38	0	0
Codfish	7	33.3	2	10
Fruit (banana, peach)	7	33.3	8	40
Flour	6	28.6	2	10
Rice	6	28.6	0	0
Maize	5	23.8	0	0
Tomato	3	14.3	4	20
Milk	1	4.8	5	25
Egg white	1	4.8	0	0

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