Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

Revue française d'allergologie 55 (2015) 444–447

State of the art

The influence of gastric digestion on the development of food allergy

Influence de la digestion gastrique sur le développement de l'allergie alimentaire

E. Untersmayr

Department of pathophysiology and allergy research, center of pathophysiology, infectiology and immunology, medical university of Vienna, Waehringer Guertel 18–20, 1090 Vienna, Austria

Received 18 August 2015; accepted 17 September 2015
Available online 27 October 2015

Abstract

Food allergy represents an increasing health concern worldwide. To identify mechanisms and risk factors associated with the development of food allergy, major research efforts are ongoing. For a long time, only food allergens that are resistant to gastric enzymes were believed to have sensitizing capacity via the oral route. However, in recent years several studies reported that even important food allergens can be readily degraded by digestive enzymes. Interestingly, a number of in vitro experiments have confirmed that by elevating gastric pH levels, the resulting reduction of physiological gastric digestion was associated with protein resistance. Additionally, pharmacological gastric acid suppression was found to be a risk factor for the induction of food allergy. In contrast, protein modifications resulting in increased susceptibility to digestive enzymes were reported to decrease the sensitizing capacity of these proteins via the oral route. The data reviewed here highlight the important gate-keeping function of physiological gastric digestion in food allergy.

Keywords: Food allergy; Gastric digestion; Sensitization; Protein allergenicity

Résumé

L'augmentation de la prévalence de l'allergie alimentaire est un problème mondial de santé publique. La reconnaissance des mécanismes physiopathologiques et des facteurs de risque suscite de nombreux travaux de recherche fondamentale ou appliquée. Depuis de nombreuses années on a estimé que les seuls allergènes alimentaires capables d'induire une sensibilisation par voie orale étaient résistants aux enzymes gastriques. Cependant, plusieurs travaux récents ont démontré que même des allergènes alimentaires majeurs pouvaient subir une dégradation préalable par les enzymes digestives. De nombreuses études expérimentales in vitro ont confirmé que la réduction de la digestion gastrique physiologique par augmentation du pH gastrique était associée à la résistance des structures protéiques. De plus, la suppression pharmacologique de l'acidité gastrique est un facteur de risque pour l'induction d'une allergie alimentaire. À l'opposé, les modifications protéiques secondaires à l'augmentation des capacités des enzymes digestives sont associées à une diminution du pouvoir sensibilisant par voie orale. Cette revue se propose de mettre en avant le rôle des importantes fonctions barrières de la digestion gastrique physiologique dans l'allergie alimentaire.

Mots clés : Allergie alimentaire ; Sensibilisation ; Digestion gastrique ; Allergénicité

1. Introduction

From a psychological point of view food intake should be associated with pleasure and well-being. However, an increasing number of patients especially in the Western population experience unpleasant, in some cases even life-threatening reactions upon ingestion of specific dietary compounds. Over the past decades food allergy, i.e. the immunological reaction against harmless dietary protein compounds [1], has steadily increased. To date it is generally accepted that more than 2% and less than 10% of the general population are affected by this disease

E-mail address: eva.untersmayr@meduniwien.ac.at

http://dx.doi.org/10.1016/j.reval.2015.09.004
1877-0320/

[1] corresponding to approximately 220–250 million patients worldwide. Additionally, several studies demonstrate that the number of food allergic patients has considerably increased over the past decades [2]. Furthermore, a substantial economic burden comprising of health care as well as personal expenses has been identified directly related to the diagnosis of food allergy. While in the US the overall cost associated with childhood food allergy was defined to be as high as 25 billion $ per year, a large European study reported a doubling of patients' based health care costs associated with food allergy irrespective of the different countries included in the study [3,4]. Thus, it is not surprising that this disease has also gained awareness of regulatory authorities with the aim to enhance the safety of allergic consumers. In the European Union, an adopted regulation has become affective in December 2014 requiring labeling of the 14 main food allergens not only on manufactured, pre-packed food products, but also food directly sold e.g. in restaurants [5].

To enhance patients' safety and to develop prevention and treatment strategies it is essential to identify mechanisms and risk factors for the development of food adverse reactions.

In affected patients the development of food allergy is associated with the lack of induction or the loss of oral tolerance towards dietary compounds [6]. Together with immunological events such as immune exclusion and cellular interactions associated with regulatory mechanisms, also physical properties of the intestinal epithelium, an intact mucosal barrier consisting of tight epithelial cells as well as mucus and bacterial layers are of paramount importance for the development and maintenance of oral tolerance [7]. Also specific characteristics of dietary proteins acting as allergens i.e. small size, solubility, and stability to food processing and food digestion during the transit trough the gastrointestinal tract contribute to food allergy induction [8]. Especially stability to digestive enzymes and food processing is well accepted to represent an important characteristic of allergenic food compounds and are considered in test procedures defining the allergenicity of novel dietary proteins, which enter the food market [9].

2. Assessment of protein digestibility in vitro

In laboratory settings, food protein digestibility is evaluated simulating the physiological degradation along the gastrointestinal tract upon protein ingestion. After a rapid passage through the esophagus food proteins enter the gastric lumen together with all other food components in a macerated chyme. Here, substances are exposed to low gastric pH resulting in protein denaturation. Additionally, major gastric proteases, pepsins, being secreted into the gastric lumen by chief cells of the gastric glands get activated by intraluminal acidity. These enzymes have their optimal activity at pH levels below 3.2 and cleave protein amino acid (AA) chains preferentially at phenylalanine, tyrosine, and leucine residues [10]. After initiating protein cleavage in the stomach, resulting peptide fragments are peristaltically transported into the duodenum where low pH levels of the chyme trigger secretin secretion [11]. This hormone stimulates a subsequent release of pancreatic proteases and peptides into the intestinal lumen, and peptide fragments are further degraded to short AA chains or single AAs serving as nutrition of the human body [11]. However, they are too small to interact with the human immune system [10]. Based on this knowledge sequential exposure of specific proteins to gastric and/or intestinal proteases in simulated gastric fluid (SGF) and simulated intestinal fluid (SIF) experiments is performed to assess digestibility of food proteins [12]. Results generated in these assays have led to the assumption that only digestion-stabile, so-called class I food proteins to harbor the capacity to induce food allergy via the oral route [8]. However, there is growing evidence that a number of major allergen, which are responsible for severe allergic reactions, are degraded in SGF experiments (Fig. 1) and, thus, may not be able to trigger allergic sensitization via the oral route [10]. We have demonstrated that physiological gastric digestion extensively reduces IgE binding and histamine releasing capacity of cod fish allergens [13]. Taking into consideration these data, it remains questionable whether in vitro digestion assays might at all provide reliable results regarding protein allergenicity as important food allergens would not prove digestion stability in these assays [14].

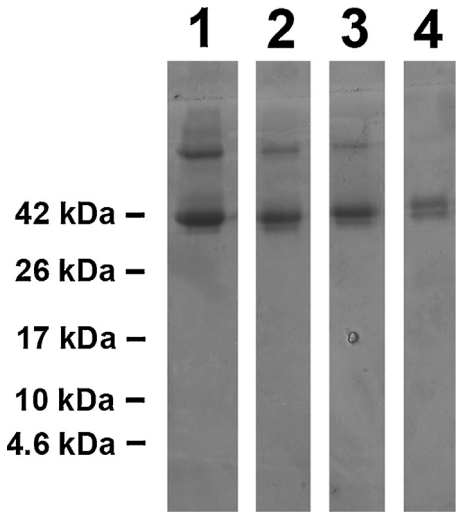

Fig. 1. Digestion of OVA proteins by SGF experiments. The major hens' egg allergen OVA (undigested, lane 1) was incubated with SGF made of NaCl and pepsin containing drug Enzynorm f® (Nordmark, Germany) at pH 1.5 for 1 min (lane 2), 30 min (lane 3) and 2 hours (lane 4). Proteins were separated by SDS-PAGE.

3. Hindered gastric digestion and induction of food allergy

When gastric digestion was impaired due to hypoacidity in SGF assays, digestion-labile food proteins remained stable for the average gastric transit time of 2 hours [13,15]. As reviewed previously [10], there are numerous situations which may be associated with elevated pH levels in the gastric lumen: the first two years of live, atrophic gastritis, and intake of gastric acid suppression drugs. Of interest, several experimental studies in mouse models repeatedly revealed a direct link between gastric acid suppression by all different forms of available pharmacological acid reducing medication (Sucralfate, H2 receptor blockers, proton pump inhibitors, antacids and base powder)