Food intolerance And Related Disease

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ÖZET

Gıda tahammülsüzlüğünün teşhisi ve allerjik gıdanın belirlenmesi genellikle güçtür. Bu durumun tesbiti için kesin sonuçlar verebilen inceleme yöntemi ve testlerde henüz geliştirilememiştir. Gıdanın alınmasından hemen sonra ki saatlerde ortaya çıkan allerji IgE yükselmesi ile beraberdir ve bu durum R A S T veya cilt testi ile gösterilebilir. Eğer reaksiyon gıdanın alınmasından 24-48 saat sonra gelişmiş ise allerjik gıdanın tanınması oldukça zordur.

Son zamanlarda uygulanan ve gıda seçimi esasına dayanan yöntemlerle (exclusion diet) belirlenen allerjik gıdanın hasta diyetinden çıkarılması semptomların önemli ölçüde kaybolmasına yardımcı olmaktadır. IBS ve Crohn hastalığında da gıda allerjisinin etiyolojik rol oynadığı düşünülmekte ve gıda seçimi yöntemiyle yardımcı olunmaya çılışılmaktadır. Şimdilik elde edilen neticeler ümit verici olup, daha geniş çalışmaların yapılmasına ihtiyaç vardır.

FOOD INTOLERANCE AND RELATED DISEASE

The role of food intolerance in producing disease is one of the most contentious topics in gastroenterology. Many doctors dispute the cocept that foodstuffs may be the cause of acute or chronic ill health, whilst others claim that a wide variety of disorders are susceptible to dietary control. Those conditions in which food intolerance is most likely to be involved are shown in Table 1. The problem is further complicated by a lack of appropriate diagnostic tests, indicating our ignorance of the mechanisms by which foods may cause adverse effects (1).

The term "food intolerance" should be used to describe all abnormal reactions to foodstuffs whilst "food allergy" should be reserved for those reations in which the immune system is involved. Ideally the role of food intolerance in producing the patients symptoms should be confirmed by double blind challenge tests.

Symptoms of food intolerance may be immediate i.e. occurring in less than an hour, or delayed for hours or days (Table 1.). In immediate reactions the offending food is often obvious and, unless a severe reaction such as angioedema occurs, the sufferer may not seek his doctor's advice. Many of these immediate reactions are due to IgE mediated hypersensitivitiy or to pseudo-allergy (see page 5.). Where the reaction is delayed and the offending food is one that is eaten often the resultant symptoms may be near-continuous and the association between the two may not be obvious. It was, for instance, many years before the association between gluten and coeliac disease was made. Some of these delayed reactions may be due to immune mechanisms, whilst others are not (e.g. lactose intolerance). In many cases the mechanisms are unkonwn.

DISORDERS RELATED TO FOOD INTOLERANCE

Coeliac Disease

In coeliac disease small bowel mucosal damage (villous atrophy) occurs when the wheat protein, gluten is eaten. However, the mechanism by which gluten induced damage occurs is not known. There is much evidence to suggest that an immune response to gluten is involved (2,3). Increased numbers of lymphocytes are found at all levels of the epithelium, and antibodies to gluten are found in patients with coeliac disease. IgA antibodies to gluten have been found disease specific and the test could detect 94% of children and 80% of adults at presentation (4).

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Table 1

Diseases Related to Food Intolerance

A. IMMEDIATE REACTIONS

Acute urticaria

Anglo oedema (swelling of tongue and upper respiratory mucosa)

Abdominal pain, diarrhoea, nausea, vomiting

B. DELAYED REACTIONS

Gastrointestinal Conditio its	Other Conditions
Coeliac disease	Asthma
Crohn's disease	Atopic eczema
Irritable bowel syndrome	Chronic urticaria
Cows milk protein enteropathy	Dermatitis herpetiformis
	Food induced migraine
	Overactivity in children

Abdominal pain, diarrhoea, nausea, vomiting

Intestinal permeability is abnormal in coeliac disease with an increase in absorption of large molecules such as xylose, dissacharides (5) and 51Cr ethylene diamineteteraeetate-EDTA (6). It has been postulated that altered permeability many facilitate the entry of gluten or a fraction thereof into the lamina propria where it causes a cascade of immunological events (7). However, it is most likely that the increased intestinal permeability is a secondary effect rather than the primary defect.

Dermatitis herpetiformis, a bullous skin disease, may be associated with coeliac disease and usually responds to a gluten free diet.

Crohn,s Disease

Crohn's disease is a chronic granulomatous inflammatory condition of the bowel of unkonwn cause. Its incidence, at present, is increasing (8,9). Evidence now suggests that food intolerance may be an important factor in provoking symptoms in the condition (1). Bowel rest and either total parenteral nutriton or an elemental diet (8) induce remission in active Crohn's disease. However, patients frequently relapse after returning to a normal diet (10). Recent studies have suggested that patients with active Crohn's disease have specific food intolerances and if these can be identified and the foods subsequently avoided remission can be maintained (8). This concept is discussed in a further article in this series.

Irritable Bowel Syndrome (IBS)

IBS is a very common condition associated with an abnormal bowel habit, abdominal pain, distention and excessive wind in the absence of any abnormality on haematological, histological or radiological investigation (11). Approximately a half of all new patient referrals to a gastroenterology clinic in the United Kingdom have this diagnosis made (12). There are probably several underlying conditions causing this symptom complex, but many patients, particularly those with diarrhoea, appear to have underlying food intolerances and if these can be identified and the food avoided they remain well (13). THis is discussed further in a later article.

Cow's Milk Protein Enteropathy

Cow's milk protein intolerance in infants may present as an acute syndrome with vomiting and diarrhoea after the introduction of cow's milk into the diet, or as chronic diarrhoea with failure to thrive (14). The clinical features may be indistinguishable from acute infective enteritis. It is diagnosed by jejunal biopsy which shows an eosinofhil infiltrate. Symptoms and mucosal changes rapidly recover when cow's milk is withdrawn, only to recur following chalenge with milk (15). Treatment involves substituting natural cow's milk feeds with commercially available cow's milk protein free formula feeds.

A cow's milk protein colitis has also been described (16). It is uncertain whether intolerance to milk or other foods is a cause of infantile colic.

Asthma

About 10% of asthmatics have food intolerance (17). Food antigens may be absorbed and reach the lungs or an allergic or pseudo-allergic reaction in the gut mucosa releases mediators or immune complexes into the circulation (18). When bronchospasm occurs rapidly the offending food may be obvious or may be identified by keeping a diary recording foods eaten and symptoms. In other patients bronchospasm may only occur slowly or after repeated exposure to the food. In such patients the diagnosis of food intolerance may be difficult but may be suspected if there are associated atopic symptoms (especially eczema), a family history of food allergy, positive food skin prick tests and a high serum IgE with specific food RASTs. If such patients have severe symptoms not readily controlled by medical treatment an exclusion diet (as described later) may be beneficial and peak flow measurements will helpassessthe response.

Urticaria and Eczema

Acute urticaria may be due to IgE mediated hypersensitivity to food allergens (19). The foods involved, most commonly nuts, fish, milk and eggs, are usually obvious from the history. Chronic urticaria is less often recognised as due to food intolerance although occasionally may be related to

Intolerance to food additives such as tartrazine or nitrites or naturally occuring salicylates.

Atopic eczema may be related to food allergy but it is particularly difficult to keep children on exclusion diets. Therefore dietary teratment should be reserved for children with severe atopic eczema resistant to medical treatment when an exclusion diet avoiding the most commonly implicated foods (dairy products, eggs and additives) can be tried (20).

Food Induced Migraine

Migraine is a common, multifactorial disease only related to food intolerances in a proportion of sufferers. Intolerance may be pharmacological following the ingestion of vasoactive amines such as tyrarnine in cheeses and phenylalanine in chocolate (21) or due to food allergy (22). Skin prick tests and RASTs do not often appear helpful although in those subjects with frequent migraine a trial of an exclusion diet as described for IBS may identify those with underlying food intolerances.

Hyperactivity in Children

The clinical picture is that of overactivity, impulsiveness, easy distractability and antisocial behaiour (23). One study reported that 70% of hyperactive children responded to a diet avoiding colourings, preservatives and salicylates (24), but subsequent controlled studies did not show such an effect (25).

MECHANISMS OF FOOD INTOLERANCE

Allergy

Immune system mediated reactions to foods occur and cause adverse effects. This is more likely in infancy and may be related to environmental factors. In adults, small amounts of food antigen normally enter the circulation (26), but adverse reactions are usually prevented by the incorporation of food antigen into IgA containing complexes (27).

... ty occurs when antigen binds
: ci the surface of mast cells and
. c . . . ..,ge amounts of stored, pharma-
cvbstances including histamine,
iglandins (28). Type I reactions
minutes of exposure often
the patient to recognise the
. i reactions are most likely to
uals.

Pseudo-allergy

Pseudo-allergy reactions occur when mast cells or basophills are activated and release mediators without specific antibody antigen binding. This may be provoked by naturally occuring chemicals such as lectins in legumes (29). The results will be similar to IgE mediated hypersensifivety although EAST and skin prick tests will be negative.

Experience in the management of patients with gastrointestinal food intolerance suggests that the majority are not food allergic. The incidence of atopic symptoms in our patients with IBS and Crohn's disease is no greater than in the general population (13). Patients with food related diarrhoea have normal serum IgE concentrations, eosinophil counts, immune complexes, and plasma histamine concentrations; their blood basophils respond normally to incubation with food antigens (30, 31).

Enzyme Deficiencies

Genetic and acquired enzyme deficiencies can give rise to different examples of food intolerance, Alactasia is the classic example of food intolerance due to an enzyme deficiency. Lactose in. milk products is not digested and enters the colon where it is fermented by bacteria to produce short chain fatty acids, CO_2, H_2. methane and cause an osmotic diarrhoea. In patients, apparently with IBS, in whom an exclusion diet identifies intolerance to dairy products a lactose tolerance test can be performed to identify those with lactose intolerance (31). We have performed hydrogen breath tests after giving 50 gin of lactose in 9 patients who presented with symptoms compatible with IBS and which were provoked by dairy products, and 4 of them were shown to be lactase deficient (82).

Platelet phenosulphotransferase which Inactivates monoamines such as tyrosine is reduced in patients with dietary migraine (33).

DIETARY MANAGEMENTS

No test will reliably identify those patients with food intolerance or indicate which, if any, foods are involved. The diagnosis of food intolerance and identification of the foods concerned can only be made by showing that sympotms resolve when the food(s) is avoided and are provoked by subsequent challenge. Food challenging should be performed on two or three occasions and, unless there are objective changes such as jejunal biopsy changes in coeliac disease, should be repeated double-blind.

The patient's history or, if they are atopic and thought to have an IgE mediated food allergy, RAST and skin prick tests may suggest which foods should be avoided. Otherwise the diet chosen is based on experience. In eczema a diet avoiding the most commonly implicated foods (dairy products, eggs and additives) is used. In other conditions, such as IBS a much wider range of foods may provoke symptoms

and in addition cereals and some fruits and vegetables are avoided. This diet, which has also been used for migraine, is discussed in a later article. If sympotms improve whilst a range of foods are being avoided these foods are then reintroduced and tested one by one so that those provoking symptoms can be identified and those alone subsequently avoided. As in many conditions reactions do not occur immediately after eating a food (nor symptoms resolve immediately the food is avoided) it is important that the initial exclusion diet is continued for 2 weeks and then, if symptoms improve, each food is reintroduced and tested over two days.

If there multiple foods intolerances the final diet should be assessed by a dietition. She may be able to advise on alternative foods and also on mineral or vitamin supplements. Obviously if there are multiple intolerances and the diet required is more demanding than the original symptoms it should be abandoned.

In some conditions such as eczema, asthma or Crohn's disease appropriate medical treatment is an alternative, and often simpler, form of treatment. However, medical teratment with sodiumcromoglycate or non-steroidal anti-inflammatory drugs is rarely effective in IBS.

In many conditions (apart from coeliac disease and lactose intolerance) food intolerances arc often transient and foods beign avoided should he retested every six months.

SUMMARY

The identification and diagnosis of food intolerance is potentially difficult. Unfortunately no objective investigation will Identify those patients who may have food Intolerance. Immediate reactions with symptoms within hours of eating a particular food are most readily shown to be due to food allergy and are often associated with the peresence of food-specific IgE as shown by RAST and skin prick tests. When reactions are delayed for 24 to 48 hours or more, underlying food intolerance is harder to recognise and much less often shown to be due to allergy. At present, diagnosis and management depends on dietaray manipulation,showing that symptoms improve on food avoidance and are produced by food challenge (preferably double blind). Further understanding of the mechanisms involved in food intolerance, in Crohn's disease and IBS may allow the development of simple tests to Identify the foods concerned and may help elucidate the causes of these conditions.

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