Value of Atopy Patch Test (APT) in the Diagnosis of Food Allergy

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LIST OF ABBREVIATIONS

Abbrev.	Meaning
AE	Atopic eczema
AEDS	Atopic eczema dermatitis syndrome
Ag	Antigen
APT	Atopy patch test
CD	Celiac disease
CMP	Cow's milk protein
DBPCFCS	double-blind,placebo-controlled food challenges
DC	Dendritic cells
EE	Eosinophilic esophagitis
EGIDs	Primary eosinophilic gastrointestinal disorders
FA	food allergy
FAHF	food allergy herbal formulas
FDEIA	Food-dependent exercise-induced anaphylaxis
FPIES	Food protein-induced enterocolitis syndrome.
GALT	Gut associated lymphoid tissue
IFN- g	Interferon- gamma
IgA	Immunoglobulin A
IgE	Immunoglobulin E
IgG	Immunoglobulin G

IL	Interleukin
LP	Lamina propria
MALT	Mucosal associated lymphoid tissue
OAS	Oral allergy syndrome
OFC	oral food challenge
PP	Peyer's patches
TNF	Tumor necrosis factor
TH	T helper cell
MHC	Major histocompatibility complex .
TGF	Transforming growth factor.
TLR	Toll-like receptor.
UC	Ulcerative colitis.
UV	Ulta violet light.
RASTs	Radio allergosorbent tst.
SPT	Skin prick test
SLIT	sublingual immunotherapy.
OIT	Oral immunotherapy
pDNA	plasmid DNA.
TLR	Toll-like receptor

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Introduction

Food allergy (FA) is an adverse immune response to food allergens. It can be classified into IgE mediated, non-IgE mediated. The IgE mediated reactions are acute, frequently have rapid onset and characterized by: anaphylaxis, urticaria, angioedema and asthma or respiratory symptoms **(Sampson, 2004)**.

Non-IgE reactions, which are poorly defined both clinically and scientifically, are believed to be T-cell mediated. Some reactions involve a mixture of both IgE and non-IgE responses and are classified as mixed IgE and non IgE allergic reactions **(Lee et al., 2008).**

Non-IgE-mediated food sensitivities are becoming increasingly recognized. This group is represented by a spectrum of clinical diseases attributed to adverse immune responses to food, for which IgE antibodies to the causal food cannot be demonstrated, at least not by routine test. The onset of these reactions is slower than immediate IgE-mediated reactions, ranging from a few hours to more than a week after the ingestion of the causative agent **(Jesak et al., 2008).**

Non-IgE mediated reactions are generally characterised by: atopic eczema, asthma and chronic pulmonary disease, enteropathy and eosinophilic oesophagitis.

Diagnosing of FA is very challenging and not as easy as it seems at first sight. As in other diseases, the allergy diagnosis is established in several steps, with detailed analysis of personal and family history, and a careful physical examination to start with. Diet diaries are used as an adjunct to history over a specified time period and may help to reveal unknown sources of food allergens **(Gerez et al., 2010**).

Skin -food-prick test (SPT) with native foods or with commercially extracts is widely used in screening patients with suspected IgE-mediated FA. While negative SPT, according to some authors, nearly exclude IgE-mediated allergy, positive tests do not prove relevant allergy. In few studies specific IgE to food allergens showed good correlation with provocation test results. Specific elimination diets should be initiated before oral exposition test, which remains "the gold standard" in the diagnosis of FA **(Sicherer and Teuber, 2004)**.

A simple, inexpensive, and reliable test for food allergy has been sought by food allergists for decades. Recently, the atopy patch test "APT" (atopic patch test, skin patch test, allergen patch test) has been introduced into clinical use and is increasingly used as a standard diagnostic procedure for characterizing patients with aeroallergen- and food-triggered disorders. The test procedure of APT is very similar to the classic patch test; it differs in the nature of allergens used **(Keskin et al., 2005).**

Atopy patch tests (APTs) seem to be important for diagnosis of cellular, delayed immune reactions. This is shown in studies conducted on infants with cow's milk allergy, in which APTs demonstrated an improved utility for determining delayed responses to oral food challenges compared to SPTs, which were better correlated with immediate symptoms **(Spergel and Brown-Whitehorn, 2005).**

ATP is done with the epicutaneous application of intact protein allergens in a diagnostic patch test setting to evaluate cell-mediated responses to various sensitizers. It is considered a

potentially-valuable additional arm in the diagnostic workup of food allergy in infants and children **(Canani et al., 2007).**

Aim of the work

The aim of the present work is to investigate the possible significance of APT with common food allergens in the diagnosis of non IgE mediated food allergy.

Subjects and Methods

Our study will include **60** patients suffering from food allergy as proved by history, elimination and challenge test. They will be recruited from the allergy outpatient clinics at Ain Shams University Hospitals,in addition to **20** Healthy volunteers as control group .

- All subjects are matching age and sex.

- **Exclusion criteria**
  1. Patients with pure aero allergens allergy.
  2. Patients with other major medical disease.
  3. Patients with recent or current infections.

- **All subjects are subjected to the following;**
  1. History and clinical examination.
  2. Routine investigations.
  3. Elimination diet.
  4. Food challenge test.
  5. Skin prick test.
  6. Total serum IgE.
  7. Atopy patch test.

Introduction

Despite the knowledge of the existence of food adverse reactions in the ancient world documented in Greek and Roman literature, it was not until the beginning of the 19th century when clinicians started to define these reactions and to investigate their underlying mechanisms. In 1902, Portier and Richet discovered and described anaphylaxis in animal experiments. Their report prompted multiple clinical descriptions of food allergic reactions in the following years due to the analogy between reactions observed in animals and patients. (**Untersmayr and Jensen-Jarolim,2006)**

The diagnosis of food allergy (FA) is still based primarily on a detailed medical history and comprehensive physical examination. Clinical or laboratory tests only serve as an add-on tool to confirm the diagnosis. The standard techniques include skin prick testing and in-vitro testing for specific immune globulin E (IgE)-antibodies, and oral food challenges. Oral food challenges continue to be the gold standard in the diagnostic workup**. (Gerez et al.,2010).**

Adverse food reactions were in a first line divided into toxic or nontoxic responses. Reactions due to toxic components occurring naturally in the foodstuff or being present as contaminating agents are developed in anyone given the dose of the toxin is high enough. Nontoxic reactions depend on the individual susceptibility and are based on IgE- or non- IgE-mediated immune mechanisms (allergy or hypersensitivity) or non-immune mechanisms (intolerance). **(Sampson,1999).**

Definitions of Food allergy:

A food allergy is defined as an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.

A food is defined as any substance (whether processed, semi-processed, or raw)that is intended for human consumption, and includes drinks, chewing gum, food additives, and dietary supplements. Substances used only as drugs, tobacco products, and cosmetics (such as lip-care products) that may be ingested are not included.

Food allergens: are defined as those specific components of food or ingredients within food (typically proteins, but sometimes also chemical haptens) that are recognized by allergen-specific immune cells and elicit specific immunologic reactions, resulting in characteristic symptoms. Some allergens (most often from fruits and vegetables) cause allergic reactions primarily if eaten when raw. However, most food allergens can still cause reactions even after they have been cooked or have undergone digestion in the stomach and intestines. A phenomenon called cross-reactivity may occur when an antibody reacts not only with the original allergen, but also with a similar allergen. In food allergy , cross-reactivity occurs when a food allergen shares structural or sequence similarity with a different food allergen or aeroallergen, which may then trigger an adverse reaction similar to that triggered by the original food allergen. Cross-reactivity is common, for example, among different shellfish and different tree nuts.

Food oils such as soy, corn, peanut, and sesame range from very low allergenicity (if virtually all of the food protein is removed in processing) to very high allergenicity (if little of the food protein is removed in processing).**(NIAID,2010)**

Epidemiology of food allergy:

Around 11–26 million of the european population are estimated to suffer from food allergy. Although there are surveys on the natural history and prevalence trends for symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood, we do not have a study assessing the prevalence of food allergy and its time trends. **(*Fiocchi et al.,2010*).**

Approximately 20% of the population alters their diet for a perceived adverse reaction to food, but the application of double-blind placebo-controlled oral food challenge, considered as gold standard for diagnosis of food allergy, shows that questionnaire-based studies overestimate the prevalence of food allergies and food intolerance (**Mansueto et al.,2006**).

The problem is complicated by the fact that perceived food allergy (ie, the self-reported feeling that a particular food negatively influences health status) is not actual food allergy. Allergy prevalence is much greater in the public's belief than it has ever been reported by double-blind studies. Back in the 1980s, the perceived incidence of allergy to food or food additives in mothers with young children was reported between 17 and 27.5%. Thirty percent of women reported that they or some member of their family were allergic to some food product. In the after decade, a British study using a food allergy questionnaire reported a 19.9% incidence of food allergy.

From the mid-1990s onwards, self reports began to be compared with challenge-confirmed diagnoses; reported incidence data of between 12.4 and 25% could be confirmed by oral food challenge in only 1.5 to 3.5% of cases, illustrating how reports of adverse reactions overestimate true food allergy. This was further confirmed when prevalence figures of