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State of the art

Kiwifruit allergy across Europe

L'allergie au kiwi en Europe

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Abstract

Kiwifruit has a high nutritive and health value. Commercial plantings of kiwifruit started a few decades ago and in the last 30 years, it has become a widely consumed fruit. Nowadays, it is one of the most common causes of food allergy. Symptoms vary between mild symptoms in the oral cavity to severe anaphylactic reactions. To date, 13 kiwifruit allergens have been identified and are termed as Act d 1 through Act d 13. The use of kiwifruit components improves the diagnostic performance compared to skin prick-test and immunoCAP with kiwifruit extract. Kiwifruit allergen sensitization patterns differ across Europe with patients from Iceland, mainly sensitized to Act d 1 (actinidin), those from western/central and eastern Europe mainly sensitized to the birch pollen-related Act d 8, and patients from southern Europe mainly sensitized to Act d 9 (profilin) and Act d 10 (nsLTP). Act d 1 and having kiwifruit allergy in Iceland are independent risk factors for a severe kiwifruit allergy. Some kiwifruit cultivars (the common gold kiwifruit Hort16A and the more recently introduced green kiwifruit Summer 3373) may be less allergenic than the common green kiwifruit Hayward and may be a safe alternative for (part of) kiwifruit allergic patients.

Keywords: EuroPrevall; Component-resolved diagnosis; Diagnosis; Food allergy; Kiwi

Résumé

Le kiwi est un fruit à haute valeur nutritionnelle. Les plantations de kiwi datent de quelques dizaines d'année et depuis 30 ans il est devenu un fruit très largement consommé. Malheureusement c'est aussi un des fruits les plus en cause en allergie alimentaire. Les symptômes sont variés depuis des syndromes oraux de faible intensité jusqu'à des réactions anaphylactiques sévères. À ce jour, 13 allergènes ont été identifiés, leur dénomination internationale allant de Act d 1 à Act d 13. L'utilisation des allergènes moléculaires est plus performante pour le diagnostic que les prick-tests et que les immunoCAP avec l'extrait entier de kiwi. La sensibilisation au kiwi n'est pas homogène à travers l'Europe et les patients islandais réagissent essentiellement à Act d 1 (actinidine), ceux de l'Europe de l'ouest, de l'Europe centrale et de l'est sont principalement sensibilisés à Act d 8 relié à l'allergène majeur du pollen de bouleau, alors que les patients du sud de l'Europe sont réactifs à Act d 9 (profiline) ou à Act d 10 (LTP). En Islande, la sensibilisation à Act d 1 et le fait d'être allergique au kiwi sont des facteurs de risque indépendants de présenter des manifestations cliniques sévères. Certains cultivars du kiwi (le commun kiwi doré Hort 16 a et plus récemment le kiwi vert Summer 3373) pourraient être moins allergéniques que le classique kiwi vert Hayward et pourraient être une alternative pour certains patients allergiques à ce fruit.

Mots clés : EuroPrevall ; Allergène moléculaire ; Diagnostic ; Allergie alimentaire ; Kiwi

1. Introduction

Kiwifruit is considered a fruit with high nutritional value because of the vitamin C content and antioxidant capacity. Allergy to kiwifruit was first described in 1981 [1]. Several studies have shown an increase in kiwifruit allergy in the past

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Table 1
Kiwifruit allergens.

Allergen	Protein family/biochemical designation
Act d 1	Actinidin
Act d 2	Thaumatin-like protein
Act d 3	Glycoprotein of unknown function
Act d 4	Phytocystatin
Act d 5	Kiwellin
Act d 6	Pectin methylesterase inhibitor
Act d 7	Pectin methylesterase
Act d 8	Pathogenesis-related protein 10 family
Act d 9	Profilin
Act d 10	Non-specific lipid-transfer protein
Act d 11	Major latex protein
Act d 12	11S globulin
Act d 13	2S albumin

few decades [2–4] and nowadays, it is one of the most common causes of food allergy. In a Finnish study investigating the prevalence of food allergy, kiwifruit was reported to be the most frequent cause of adverse reactions (38.4%) [5]. In French schoolchildren, it was after egg and milk, the most common allergy reported [6]. In a large European population-based study, sensitization to kiwifruit was in the top 6 of most common food sensitizations in Europe [7].

Symptoms vary between mild oral symptoms to severe anaphylactic reactions [8–11]. Cross-reactivity with birch pollen and latex has been described, but monosensitization also occurs [11–17]. Current diagnostics of kiwifruit allergy, using skin prick-test and serum sIgE measurement, have a low sensitivity [2,11]. Together, this makes kiwifruit allergy an interesting field to further explore.

2. Diagnostic performance of kiwifruit allergens

According to the current records of the international union of immunological Societies Allergen Nomenclature Subcommittee (http://www.allergen.org) 13 kiwifruit allergens have been identified and are termed as Act d 1 through Act d 13 (Table 1). The most important allergens will be highlighted here. Act d 1 (actinidin, a cysteine protease) is a major allergen, is associated with severe kiwifruit allergy and is frequently recognized by kiwi-monosensitized patients and therefore has been proposed as a marker for genuine sensitization to kiwifruit [18,19]. Act d 8 is a member of the pathogenesis-related class 10 protein (PR-10) family. Primary sensitization to Act d 8 occurs predominantly via the major birch pollen allergen Bet v 1. Act d 9 (profilin) is also involved in pollen-related kiwifruit allergy [18,19]. Act d 10 is a non-specific lipid transfer protein (nsLTP). Recently, two novel allergens have been discovered in the seeds of kiwifruit that are involved in in vitro IgE cross-reactivity with peanut and tree nuts: Act d 12 (11S globulin) and Act d 13 (2S albumin) [20,21].

In the EuroPrevall study, a large multi-center European study investigating several aspects of food allergy, kiwifruit allergy across Europe has been investigated [22]. It showed that using a panel of kiwifruit allergens (Act d 1, act d 2, Act d 5, Act d 8, Act d 9 and Act d 10) in ImmunoCAP, the diagnostic sensitivity increased to 65% compared to 20% for skin prick-test and 46% for ImmunoCAP with kiwifruit extract. Another European study also showed an increase in diagnostic sensitivity from 17% for ImmunoCAP with commercial extract to 77% using a panel of kiwifruit allergens [18]. Using a component-based allergen microarray in a large group of patients across Europe showed a diagnostic sensitivity of 66%, a specificity of 56% and positive predictive value of 73% [19].

The recently discovered Act d 12 and Act d 13, which are found in the seeds of kiwifruit, were recognized by 85% of kiwifruit allergic patients [20]. The inclusion of Act d 12 and Act d 13 in component-resolved diagnosis of kiwifruit allergy might contribute to a further increase in diagnostic sensitivity.

3. Geographical differences in kiwifruit allergy across Europe

The EuroPrevall study showed that patients from Iceland were more likely to have a severe kiwifruit allergy and more often recognized Act d 1 (actinidin) compared to other European regions [22]. Concomitant birch pollen allergy was most frequently seen in western, central and eastern Europe and accordingly patients from these regions were mainly sensitized to the birch pollen-associated Act d 8. Concomitant grass pollen allergy was frequently seen in patients from southern Europe and they were predominantly sensitized to Act d 9 (profilin). Also sensitization to Act d 10 (nsLTP) was frequently seen in patients from southern Europe [22].

4. Predictors of a severe kiwifruit allergy

Multivariate analysis with logistic regression was performed in the EuroPrevall study to assess the effect of various factors (sex, age of onset of kiwifruit allergy, concomitant allergies, geographic region and sensitization to kiwifruit components) on the clinical severity of kiwifruit allergy [22]. This showed that two factors were independently and significantly associated with a severe kiwifruit allergy: sensitization to Act d 1 (odds ratio [OR] 5.69; 95% CI 2.63–12.29) and living in Iceland (OR 4.07; 95% CI 1.62–10.24). Other studies confirmed the association of Act d 1 with severe symptoms [18,23]. The stability of Act d 1 regarding thermal processing and gastro-intestinal digestion might explain the association with severe symptoms [24]. It is unknown why patients from Iceland have more severe kiwifruit allergy. It could be that patients from Iceland recognize an allergen which was not present in the allergen panel and kiwifruit extract used, for example the recently discovered Act d 12 (11S globulin) and Act d 13 (2S albumin).

5. Allergenicity of different kiwifruit cultivars

Kiwifruit belongs to the genus *Actinidia*, which contains about 60 species, and each species has different cultivars. Until a few years ago, kiwifruit production was mostly based on the green kiwifruit species *Actinidia deliciosa* cultivar (cv) Hayward. In 1999, a closely related species, *Actinidia chinensis* (cv