REVIEW ARTICLE

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Diet therapy and pharmacotherapy in the prevention and prophylaxis of food allergies and intolerance

Dietoterapia i farmakoterapia w profilaktyce alergii i nietolerancji pokarmowej

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Abstract

Introduction and Objective. The global problem of allergies, including food allergies, affects every age group. For many years, the treatment of allergies has been limited to therapy consisting in administration of drugs suppressing the activity of the immune system. The aim of this review is to compile information about food allergies and food intolerance, assess the importance of diet therapy and pharmacotherapy in the treatment of these conditions, and discuss the role of the intestinal microbiome in the prevention of food allergies.

Review Methods. A review of available literature was conducted using electronic databases (PubMed and Google Scholar) and appropriate key words. Publications from the last eight years constituted 80%.

Brief description of the state of knowledge. Observations carried out in recent years indicate a constantly increasing problem of food allergy in both children and adults. Some of the most common food disorders are gluten, lactose, and histamine intolerance. The development of food allergies is complex and multifaceted. A key role in their development is played by genetic and environmental factors. Allergens of plant and animal origin can trigger food allergies. The role of the bacterial intestinal microbiome and proper nutrition in organism response to contact with a potential allergen is increasingly being highlighted.

Summary. The current medical knowledge does not provide quick therapies for food allergies. Improvement of the quality of life of patients with food allergy or intolerance is primarily achieved by introduction of an elimination diet,and pharmacological treatment aimed at enhancement of the efficacy of therapies.

Key words

food allergy, pharmacotherapy, allergens, microbiome, diet therapy, food intolerance

Streszczenie

Wprowadzenie i cel pracy. We współczesnym świecie problem alergii, w tym alergii pokarmowej, ma charakter globalny i dotyka osób z każdej grupy wiekowej. Przez wiele lat sposób leczenia alergii ograniczał się do terapii polegającej na przyjmowaniu leków zmniejszających aktywność układu immunologicznego. Celem niniejszej pracy jest przedstawienie informacji na temat alergii pokarmowej i nietolerancji pokarmowej, określenie znaczenia dietoterapii i farmakoterapii w ich leczeniu, a także omówienie roli mikrobiomu jelitowego w profilaktyce alergii pokarmowej.

Metody przeglądu. Przegląd dostępnej literatury przeprowadzony został z wykorzystaniem elektronicznych baz danych (PubMed i Google Scholar) i odpowiednich słów kluczowych. Publikacje z ostatnich ośmiu lat stanowią 80% użytej w przeglądzie literatury.

Opis stanu wiedzy. Obserwacje przeprowadzone w ostatnich latach wskazują na stale rosnący problem alergii pokarmowej zarówno u dzieci, jak i u osób dorosłych. Najczęściej występującymi zaburzeniami pokarmowymi są m.in. nietolerancja glutenu, laktozy oraz histaminy. Powstawanie alergii pokarmowej ma charakter złożony i wieloaspektowy. Kluczowe znaczenie w rozwoju alergii pokarmowej mają czynniki genetyczne i środowiskowe. Przyczyną alergii pokarmowej są alergeny pochodzenia roślinnego i zwierzęcego. Coraz częściej zwraca się uwagę na rolę prawidłowego żywienia i mikrobiomu bakteryjnego zasiedlającego jelita w reakcji organizmu na kontakt z potencjalnym alergenem.

Podsumowanie. Obecna wiedza medyczna nie pozwala na szybką terapię alergii pokarmowej. Poprawa jakości życia chorego z alergią lub nietolerancją pokarmową wiąże się przede wszystkim z wprowadzeniem diety eliminacyjnej i leczenia farmakologicznego, mającego na celu zwiększenie skuteczności terapii.

Słowa kluczowe

alergia pokarmowa, farmakoterapia, alergeny, mikrobiom, dietoterapia, nietolerancja pokarmowa

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INTRODUCTION AND OBJECTIVE

In the 21st century, allergies are a global problem which affect every age group, regardless of gender. As shown by the latest data from the Central Statistical Office in Poland, in 2019, allergic diseases were reported by approximately 7.5–10% of respondents. In the respondent group, females were almost twice as likely to be affected by allergies [1].

For many years, the treatment of allergies has been limited mainly to pharmacological therapies consisting in administration of drugs suppressing the activity of the immune system. Research has been focused mainly on anaphylactic reactions, development of allergy symptoms, and application of biological drugs in therapeutic treatment [2]. The role of prevention, appropriate nutrition and a proper bacterial intestinal microbiome in the organism response to contact with a potential allergen is currently important [3, 4]. Therefore, the aim of this study is to compile information about food allergies and food intolerance, assess the importance of diet therapy and pharmacotherapy in the treatment of these conditions, and highlight the role of the intestinal microbiome in the prevention of the development of allergic inflammation.

Review methodology. The review and analysis of available literature reports was carried out using PubMed and Google Scholar electronic databases. The following key words were used to find relevant articles: 'food allergy', 'food intolerance', 'food allergy diagnostics', 'allergy and intestinal microbiome', 'diet therapy of food allergy', 'methods for food allergy treatment', 'immunotherapy in food allergy'. Reports published in Polish and English were included in the review. Publications from the last eight years constituted 80%.

STATE OF KNOWLEDGE

In medicine, there are several criteria for division of allergies, one of which takes into account the route of allergen entry into the organism. Hence, contact allergy – skin contact with the allergen, inhalant allergy – inhalation of air with suspended pollen grains and fungal spores, and food allergy – through consumption of allergens with food, are distinguished [5].

An abnormal response of the organism to consumed food is called intolerance. It is divided into immunological intolerance, i.e. food allergy, and non-immunological intolerance, called food intolerance. The main difference between food allergy and food intolerance is related to the time of appearance of the first symptoms of the disease. An IgE-mediated immunological reaction is an immediate reaction in which clinical symptoms of food allergy occur relatively soon after consumption of food. In the case of an Ig-E-independent immune reaction, food allergy symptoms may appear later, a few hours to a few days after exposure to the allergen. Similarly, symptoms of food intolerance may appear even several days after the organism comes into contact with the allergen [6].

In recent years, there has been much interest in the role of the digestive system in proper immune response induction. The intestinal mucosa plays an indisputable role in the development of an allergic reaction due to its large absorption surface colonized by bacteria. It is estimated that there are over 1,000 bacterial species constituting the natural intestinal microbiome, but there are also reports of bacteria whose presence may exert an adverse effect on organism function [7]. The gastrointestinal tract is the site of contact with foreign proteins. Each year, the intestinal mucosa comes into contact with approximately 30 kilograms of food proteins [8]. Allergenic proteins present in food reach the stomach and intestines and undergo degradation by digestive enzymes. Proteins that do not undergo proper decomposition, e.g. due to intake of proton pump inhibitors, can penetrate the epithelial barrier in the small intestine [9]. Through phagocytosis and transcytosis induced by M lymphocytes, antigens are taken up from the intestinal lumen into the lymphoid tissue. Next, they are distributed throughout the body. Allergens in blood are captured by antigen-presenting cells (APOs), including dendritic cells, which present them to T lymphocytes, which stimulate B lymphocytes to produce antigen-specific immunoglobulins (IgE). IgE immunoglobulins bind to mast cells, causing their degranulation, release of numerous mediators, and the induction of an allergic reaction [10].

Recent scientific research has also reported non-genetic factors in the development of allergies. The increasing percentage of allergy sufferers has generated greater interest in the microbiome-mucosa-intestine system, which is an important interface between the immune system and the external environment. The mucosa of the digestive system is lined with columnar epithelium, which comprises immune cells which form clusters and are the first line of recognition and combating pathogens [7]. The activation of the immune response in allergic diseases results from an imbalance between helper lymphocytes producing cytokines, pro-allergic compounds, and Th lymphocytes producing cytokines involved in the inflammatory process. Th2 lymphocytes are sometimes produced more abundantly than Th1 cells, which results in the production of a large number of IgE antibodies and, consequently, the development of allergic reactions. Disturbed balance between Th1 and Th2 lymphocytes results in an excessive immune reaction of the body. Regulatory T cells (Treg) also play a key role in the pathogenesis of food allergy by regulating the immune response to food allergens by inhibiting Th1 and Th2 activity. Reduced tolerance to some food allergens may be related to impaired function of T cell (Treg) [3].

A properly balanced diet has a considerable impact on the condition and function of the intestinal mucosa and its lining cells. Vitamin A has been shown to increase the number of T and B cells producing IgA antibodies [11]. Research reports also suggest that the level of endothelial lymphocytes may be influenced by proper vitamin D saturation in the organism [12]. In turn, a BMI value of >30.0 is a pro-inflammatory factor that may aggravate inflammation in the intestinal mucosa [13]. Additionally, high-fat diets promote unfavourable changes in the intestinal microbiome. Changes in the intestinal bacterial flora may affect the production of T lymphocytes and inhibit the secretion of IgE immunoglobulins [14].

Food allergies and food intolerances. One of the most common food allergies is gluten encephalopathy, also known as celiac disease [15]. It is a disease of the small intestine with an immunological basis and genetic predisposition. A key aspect for celiac disease patients is cooperation with a dietician, who will review the patient's medical history and design a gluten-free diet plan. The rationale behind introduction of such a diet is the abnormal response of the patient's immune system to the mixture of gliadin and glutenin proteins contained in most cereal products [10]. Celiac disease reduces the quality of life dramatically. It is characterized by impaired gastrointestinal absorption, which leads to qualitative and quantitative malnutrition even with correct levels of micro- and macroelements in the diet [16]. Furthermore, disturbed digestion in the gastrointestinal tract causes bothersome symptoms in patients. In addition to typical symptoms of celiac disease, i.e. abdominal pain, diarrhea, or bloating, there is a group of non-specific symptoms, such as delayed development and behavioural changes [16].

The diet in celiac disease is primarily intended to eliminate gluten, i.e. the allergy factor, and to ensure coverage of the demand for essential micro- and macroelements. The necessity of modification of the diet with gluten-free cereals should be closely correlated with assessment of the condition of intestinal mucosa and intestinal villi. Cereal products are primarily modified in the diet. Wheat, barley, and oats should be replaced with gluten-free cereals, such as rice, millet, and sorghum or less popular cereals, e.g. quinoa or amaranth [10]. In specific cases of very high gluten sensitivity, it seems reasonable to use only products with a gluten-free certificate, in contrast to latent allergy where a small amount of gluten intake usually does not cause symptoms and does not change the morphology of intestinal villi. Oats should be introduced with great caution in the diet of celiac disease patients, as the cereal may be contaminated with gluten and contains avenin, which may trigger an immunological reaction in subjects with celiac disease [16] Wheat allergy is a distinct response of the body, being both an Ig-E dependent and Ig-E independent response. Wheat allergy is more common in children and can have an acute course, as this type of allergy is characterized by a high rate of anaphylaxis. In patients with food allergy symptoms, in whom celiac disease and wheat allergy have been ruled out, the form of intolerance may be non-celiac gluten sensitivity (NCGS). Currently, the pathophysiology of NCGS has not been fully explained and is a subject of great interest [16].

Another disorder associated with an abnormal response of the organism is intolerance of lactose, a sugar present in dairy products [10]. Milk and dairy products are the basic source of calcium in the human diet. Subjects with lactose intolerance are particularly susceptible to a deficiency of this element. Patients struggling with lactose intolerance most often follow a dairy-free diet. Dietary eliminations often have adverse consequences. Dairy-free diets pose a risk of calcium deficiency, which may lead to impaired bone formation, reduced bone mass, and osteoporosis development in old age. A solution for lactose intolerance patients is to consume lactose-free dairy products. In some cases, calcium-fortified plant products and plant products containing large amounts of calcium, e.g. beans, soy, kale, almonds, and poppy seeds are worth considering. Some fish, e.g. sprats, are also an important reservoir of Ca [17]. The process of composition of a lactose-free diet should take into account the lower bioaccessibility and bioavailability of calcium from food other than dairy products. In addition, phytic acid present in many legumes as well as large amounts of fibre and tannins, can reduce calcium absorption. Phytates, which form inseparable complexes with vitamins and minerals, can also prevent calcium absorption [18]. Therefore, a diet based on plant calcium sources should contain appropriately high concentrations of this element.

An example of an abnormal reaction of the organism to lactose consumption is hypolactasia, which affects three-quarters of the population, most often adults. It is associated with impairment of the gene responsible for the production of lactase, i.e. a lactose-decomposing enzyme. Lactase is active in the brush border of the small intestine epithelium, and its activity gradually declines with age. In both lactose intolerance and hypolactasia, the symptoms and degree of lactose tolerance depend on coexisting disorders. As shown by research results, there is a dose of lactose which does not produce unpleasant symptoms. If the dose exceeds a value that triggers symptoms, gastrointestinal problems, such as abdominal pain, stomach gurgling, or diarrhea, may occur [19]. The threshold level for the development of symptoms depends on many factors, e.g. the qualitative and quantitative composition of the intestinal microbiome, the source of lactose, and such comorbidities as IBS (*Irritable Bowel Syndrome*), SIBO (*Small Intestinal Bacterial Overgrowth*), and SIFO (*Small Intestinal Fungal Overgrowth*). As reported in the literature, patients with hypolactasia respond better to fermented foods, e.g. kefir or buttermilk. Similarly, hard cheeses (Parmesan) are a better choice for these patients than cottage cheese [20].

The food intolerances described above are classified as metabolic intolerances. In the group of intolerances, reactions with a pharmacological basis can also be distinguished, e.g. caffeine intolerance [10]. Coffee is a popular stimulant and a common source of caffeine. The final composition of phytochemicals contained in coffee depends on the roasting method. Various proteins, sugars, chlorogenic acid, organic acids, and caffeine are active compounds exerting an impact on human health. These ingredients represent the so-called nutraceuticals, present in small amounts in food and exert a positive effect on human health [21].

Current literature indicates a strong correlation between regular consumption of coffee and the caffeine it contains and the reduced risk of cardiovascular diseases. Moderate consumption of coffee lowers the risk of heart failure, prevents arrhythmia, and stimulates the secretion of GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide 1), i.e. two key compounds secreted after food intake to reduce intestinal glucose uptake [22]. Coffee allergy very often affects plantation workers who have direct contact with allergens contained in unroasted beans. The first identified allergen in coffee is *Cof a 1*. A detailed description of the coffee allergen could elucidate the mechanism of caffeine allergy. Currently, caffeine-intolerant subjects have to consume decaffeinated coffee [23].

Nutritional treatment is also applied to patients with histamine intolerance. Histamine is a biogenic amine present in the human organism. It is also found in many food products. Highly processed products, such as cold cuts, canned products, cheeses, and pickled vegetables and fruits are a rich source of histamine [10, 24]. The content of histamine depends on many factors, e.g. the presence of vitamins, fermentable carbohydrates, product pH, and temperature [25]. The content of histamine in products is also associated with the presence of bacteria, particularly in fermented food and improperly stored products [26]. The diagnostics of histamine intolerance is difficult. Its specific symptoms are related to the digestive system, while non-specific symptoms are observed in other organs. The classic symptoms of histamine intolerance include facial erythema and skin rash all over the body. The DAO (diamine oxidase) enzyme is involved in the mechanism of histamine intolerance, and its defect results in incorrect histamine degradation [24]. The threshold dose of histamine that can cause symptoms of intolerance is in the range of 5–10 mg. The amount of the enzyme produced is influenced by genetic factors, intestinal microbiomes, and some medications [10]. Subjects struggling with histamine intolerance should try an elimination diet. Limitation of histamine-rich products for several weeks followed by exposure to high-histamine products helps to confirm or rule out intolerance. A low-histamine diet contributes to reduction of the plasma histamine level and elimination of intolerance symptoms. Diet therapy consists in exclusion of fermented products (e.g. sourdough bread), pickled products (cucumbers, cabbage), and other foods (tofu, soy sauce). After the elimination phase, the patient should undergo a long-term phase. It is therefore important to identify foods to which the patient's organism reacts with increased sensitivity. Efficacy in reducing of food allergy symptoms in patients with histamine intolerance was observed when exogenous DAO was supplemented. DAO enzyme supplementation reduces the symptoms of histamine intolerance and enhances the effect of a low-histamine diet [27].

Gluten, lactose, and histamine intolerance are examples of the most common digestive disorders. However, allergy can be triggered by any food ingredient of both animal and plant origin.

Food allergies and cross-reactions. An inherent element in the diet therapy of food allergies is the phenomenon of cross-allergy. This relatively new concept is currently a major challenge for dietetics and medicine. In the phenomenon of cross-allergy, two allergens of different origin have a similar molecular structure; the organism cannot recognize the difference between these allergens and secretes antibodies after contact with both. Then, allergic symptoms also appear as a result of the body's contact with an allergen similar to the one that originally caused the allergy [28]. IgE antibodies produced against one allergen recognize and bind to an allergen with a similar structure but from a different source. Then, one type of antibody reacts not with one specific allergen, but with two or more.

The problem of cross-allergy was first highlighted in the last century, when allergic reaction symptoms were detected in patients with plant pollen allergy after consumption of fruit. Scientists attempted to explain this phenomenon and concluded that the similar structure of allergens triggers cross-allergy, i.e. an allergic reaction caused by contact of the organism with unrelated allergens. This type of allergy may occur even without exposure to a given allergen [29]. Most frequently, these reactions are initiated by pollen grain and food allergens. They are described in the scientific literature as pollen-food syndromes [30].

Previous studies indicate the potential occurrence of cross-allergy at structural similarity between two allergens of at least 70%. The work of the International Union of Immunological Societies (IUIS) has resulted in identification of the structure of approximately 880 allergenic proteins, which contributes to more effective diagnostics of cross-allergy [31]. The analyses of allergens have revealed their structure and this knowledge helps to discriminate allergens with a similar structure that can be involved in such cross-reactions as latex-fruit syndrome, pork-cat syndrome, bird-egg syndrome, and the common oral allergy syndrome [32].

Oral allergy syndrome (OAS), also known as Amlot-Lessof syndrome, is characterized by the development of allergic symptoms in the oral cavity, e.g. redness and itching of the mucous membrane. Less typical symptoms, such as gastrointestinal disorders, may sometimes occur [33]. OAS is associated with the consumption of allergens from fruit or vegetables by pollinosis sufferers. An example is the cross-reaction induced in a patient with allergy to birch pollen allergens by consumption of certain types of fruit, e.g. apples, cherries, or peaches. Clinical symptoms may appear quite rapidly, which is associated with low tolerance of the allergens to saliva and gastric juice enzymes [34]. Nutritional treatment of OAS is not simple, as not all allergens are deactivated by heat treatment. An elimination diet and pharmacotherapy under strict medical supervision are advisable in this syndrome.

Diagnostics of food allergy. The severity of allergy symptoms and the subjective assessment of the quality of a patient's life depend on the type of allergy. The diagnostics of food allergy can be complex, as it is often difficult to identify a food ingredient that causes an allergic reaction. The diagnosis is most frequently based on skin tests, immunological tests, and a reliable food diary, which should be part of the first-line diagnostics [35, 36]. Analysis of the food diary by a dietician or allergist should be combined with observation of the patient. Only a combination of symptoms with anatomical and functional disorders of organs, assessment of the condition of the nasal and oral mucosa, and an otoscopic examination can ensure a full diagnosis [37].

Currently, the gold standard in the diagnosis of food allergy is the double-blind, placebo-controlled challenge (DBPCFC), which involves the patient taking increasing doses of a potentially allergenic substance or a placebo [35]. A contraindication to performing a provocation test is life-threatening anaphylaxis. Evaluation of allergen-specific IgE (sIgE) concentration in blood using various *in vitro* tests is another type of test helpful in diagnosing food allergy. Due to their widespread availability, and low invasiveness, they are one of the basic screening tests used in the diagnostics of food allergies. Elevated slgE values indicate sensitization, but do not always indicate allergic disease [35]. In turn, the skin prick test (SPT) is performed using standardized reagents containing target allergens [35, 38]. Importantly, the patient should be properly prepared for the test by discontinuation of intake of biological medications that may potentially falsify the test result.

Intestinal microbiome in allergy and food intolerance diet therapy. The basic principle of diet therapies for allergies and food intolerance is the introduction of an elimination diet, from which the causative factor of the allergic reaction should be excluded. The objective of the elimination diet is to reduce the over-reactivity of the immune system, identify allergens that trigger immune reactions, and regenerate the gastrointestinal mucosa [10]. In recent years, the human microbiome has attracted great interest from many fields of science and medicine, as many diseases in the human organism originate from the intestines. The human intestinal microbiota changes dynamically and depends on diet, medications, and environmental factors. This microbial ecosystem comprises various representatives of bacteria and fungi [39]. Given the multitude of its functions and processes in which it participates, some authors consider the intestinal microbiome to be a separate system [40].

The intestinal microbiome is represented by approximately 1,200 microbial species. This composition is variable, depending on internal and external factors, e.g. the use of antibiotics, abdominal surgery, secretion of digestive enzymes, intestinal passage, diet, and stress. Human intestines are primarily colonized by the bacterial genera *Bifidobacterium*, *Bacteroides*, and *Eubacterium*. The jejunum is dominated by the genus *Streptococcus*, while *Clostridium* bacteria are most frequently present in the distal ileum. The biodiversity of the microbiome also depends on age. The microbiota in infants differs significantly from that in adults. The first period of life is characterized by very large changes in the microbiome. The process of colonization of the organism by bacteria depends on many factors, e.g. infant's nutrition, quality of mother's milk, and type of childbirth [41].

Current studies have evidenced a close relationship between nutrition and the quantitative and qualitative status of the intestinal microbiota [42]. Great importance is ascribed to fibre present in cereal products, fruits, vegetables, seeds, nuts, and seeds [43]. Present knowledge indicates that a diet rich in soluble and insoluble fibre fractions can increase the biodiversity of the microbiome. In turn, a diet rich in processed foods and poor in fibre significantly reduces microbial biodiversity. Additionally, inulin and oligofructose preparations introduced into the diet, may selectively increase the abundance of individual strains [43].

The relationship between the microbiome and allergy was first reported in the 1980s, when it was observed that children from large families were less likely to suffer from allergic rhinitis and atopic dermatitis. This suggestion was called the hygiene hypothesis. It was based on the assumption that these children were exposed to a greater number of pathogenic factors and their organisms managed potential allergens more effectively. An increased risk of allergy development is often associated with microbiota disorders in early childhood. This risk is also greater in residents in urban areas using the so-called Western diet [44].

The intestinal microbiome participates in the development of food allergy. Qualitative and quantitative changes in the intestinal mucosal microbiota may increase the risk of allergy development. As reported by Huang et al. (2017), bacteria from the genus *Enterobacteria* have an adverse effect on the gastrointestinal microenvironment. Similar changes were also observed in the case of *Bacteroides*. In turn, *Clostridium* and *Lactobacillus* exert a beneficial effect on the organism by protection against allergens. Microbiome disorders caused by allergies to specific allergens have also been reported. Changes in the microbiome have been observed in, e.g. peanut allergy sufferers, while oral supplementation with *Lactobacillus rhamnosus* GG had a beneficial effect and mitigated nut allergy [45].

Pharmacotherapy of food allergy. Elimination diets used to prevent food allergies and intolerances are associated with great concerns and anxiety, especially in the group of the youngest patients. Parents often eliminate an allergen-containing product without replacement with other food with similar nutritional value [46]. Hence, the elimination diet does not always bring expected results. A common therapeutic method for management of food allergy is the controlled administration of appropriate amounts of the allergenic protein to patients as part of the so-called oral immunotherapy (OIT). This method effectively increases the threshold of organism reactivity to contact with a strongly allergenic factor and is currently one of the best-studied immunotherapies for food allergy, especially in allergic reactions to peanuts, milk, and eggs [47]. The largest number of studies is focused on OIT in food allergy to peanuts. Randomized studies are currently underway in a group of 1–10-year-old peanut allergy sufferers. They are focused on comparison of different treatment methods: low-dose and high-dose OIT in combination with a probiotic (*Lactobacillus rhamnosus*) taken daily for 18 months (NCT06297083, phase II). Similarly, Polish research teams have been involved in the assessment of the safety and effectiveness of OIT in sesame, cashew, and peanut allergies (Tab. 1). Other alternative therapies to OIT include subcutaneous immunotherapy (SCIT), sublingual immunotherapy (SLIT), and epidermal immunotherapy (EPIT) [48, 49]. The application of SCIT and SLIT in food allergy treatment is ambiguous and poorly described in the literature. Currently, there are only two registered trials of SLIT therapy, one of which additionally assesses peanut tolerance in patients aged 4–65 years (NCT05440643, phase I). The EPIT therapy is characterized by a lower number of systemic reactions than OIT; hence, it can be used with high efficacy for desensitization of patients with IgE-dependent allergies [49]. The aim of current EPIT studies is to evaluate the effectiveness of DBV712 administered at a dose of 250 μg in the desensitization of 4–7-year-old children with peanut allergy during a 12-month treatment period (NCT05741476, phase III).

There are currently 139 registered active clinical trials focused on food allergy and the treatment of the disease conducted by teams from around the world in the categories: Not yet recruiting (15), Recruiting (95), and Active, not recruiting (29) (as of 5 August 2024) [50] (Tab. 1). Noteworthy is the study proposed by an Australian research team to assess the potential contribution of vitamin D supplementation (at a dose of 400 IU/day) in the first year of life of infants to reduce the risk of food allergy and other allergic diseases in children aged 12 months to 6 years (NCT02112734, phase IV). The validity of the study seems to be crucial, as there are no recommendations for prophylactic vitamin D supplementation in infants in this region.

Considerable attention is paid to vitamin D in the modern world. It is possible that vitamin D deficiency may intensify food allergy in children. Another widely investigated issue is the application of biological preparations, i.e. Omalizumab, Dupilumab, and Ligelizumab, and the use of Abrocitinib as a JAK kinase inhibitor, which exhibits great effectiveness in atopic dermatitis (AD), in the treatment of food allergy (Tab. 1).

SUMMARY

Food allergy is a common disease worldwide, with the number of food allergy cases also constantly growing in Poland. This

Table 1. Examples of clinical trials of food allergy therapy (current status as of August 2024) [50]

Therapy/drug (dose)	Age group	Clinical Trials Phase	Clinical Trials Identifier	Locations
DRUG TREATMENT				
Abrocytynib (100mg, 200mg)	18 Years to 50 Years (Adult)	I	NCT05069831 (R)	United States
Ligelizumab (120mg, 240mg)	6 Years to 57 Years (Child and Adult)	III	NCT05678959 (R)	United States
Dupilumab	4 Years to 50 Years (Child and Adult with allergic to cow›s milk)	II	NCT04148352 (ANR)	United States
Omalizumab (injected every 2-4 weeks) Dupilumab (injected every 2 weeks)	4 Years to 55 Years (Child and Adult)	II	NCT03679676 (ANR)	United States
IGNX001 (in peanut-allergic)	15 Years to 55 Years (Child and Adult)	I	NCT06331728 (NYR)	Australia
Dupilumab (300mg)	6 Years to 25 Years (Child and Adult)	IV	NCT05247866 (ANR)	United States
DRUG TREATMENT + ORAL IMMUNOTHERAPY (OIT)				
Omalizumab (75mg, 150mg) Omalizumab + Multi-Allergen Oral Immunotherapy	1 Year to 55 Years (Child and Adult)	III	NCT03881696 (ANR)	United States
Vancomycin + VE416/with and before PNOIT (Low-Dose Peanut Oral Immunotherapy)	12 Years to 55 Years (Child and Adult)	I, II	NCT03936998 (R)	United States
Omalizumab (8mg, 16mg)/ Multi-food Oral Immunotherapy (1,500mg of food protein)	6 Years to 25 Years (Child and Adult)	II	NCT04045301 (R)	Canada
Adatapced + Peanut Oral Immunotherapy	14 Years to 50 Years (Child and Adult)	II	NCT04872218 (ANR)	Canada
ORAL IMMUNOTHERAPY (OIT)				
Sesame Oral Immunotherapy (300mg versus 1,200mg sesame protein)	4 Years to 17 Years (Child)	Not Applicable	NCT05158413 (R)	Poland
Sesame Oral Immunotherapy (300mg sesame protein)	3 Years to 17 Years (Child)	Not Applicable	NCT06261554 (R)	Poland
Oral Immunotherapy (Relevant allergy to 2-5 nuts)	6 Months to 15 Years (Child)	II	NCT03799328 (ANR)	Canada
Fish Oral Immunotherapy	2 Years to 10 Years (Child)	Not Applicable	NCT05590299 (ANR)	Hong Kong
Cashew Oral Immunotherapy	4 Years to 17 Years (Child)	Not Applicable	NCT06328504 (R)	Poland
Peanut Oral Immunotherapy	1 Year to 3 Years (Child)	Not Applicable	NCT04511494 (ANR)	Sweden
Peanut Oral Immunotherapy (150mg and 300mg of ground peanuts)	4 Years to 17 Years (Child)	Not Applicable	NCT04415593 (R)	Poland

Recruitment status: (R) - Recruiting, (NR) - Not yet recruiting, (ANR) - Active, not yet recruiting

condition affects an increasing number of patients in every age group; hence, this issue is still widely investigated and discussed. It is also increasingly being taken up by various fields of science. The complex and multifaceted mechanism of food allergies leaves many of their aspects ambiguous and not fully elucidated. A key element in food allergy diagnostics and therapy is an individual approach to the patient. It is important to know the safety profile as best as possible, as it may improve the quality of life of food allergy sufferers.

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