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Diet of the 21st-century person — food intolerances and elimination diets

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Review article

Abstract

In a dynamically changing world and environment, the human diet is subject to numerous changes, as well as the quality of selected products. More and more often, patients who report gastrointestinal complaints after eating certain foods come to doctors. This situation often ends with the introduction of an elimination diet, which conducted without the supervision of a specialist, can have various negative effects. The work aims to present the latest results of research on the diet of modern man, published in international journals, available in the PubMed database and the Google Schoolar.

The review discusses the most common food intolerances, their mechanisms and treatment options with particular emphasis on therapy with elimination diets and their potential health consequences. The discussed health problems are related to environmental changes and at the same time, significantly reduce the quality of life of people struggling with them.

Keywords

- food hypersensitivity
- diet
- lactose
- gluten
- histamine

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Introduction

According to the WHO, a healthy diet protects against malnutrition and numerous diseases. A proper diet should be balanced and varied, providing all the necessary nutrients. Elimination diets used in the treatment of food intolerances, consisting in the strict exclusion of a specific ingredient, are often associated with high costs, consumption of more processed food (as in the case of gluten-free products with an extended shelf life), social and psychological barriers or, as a consequence of long-term use, may result in nutritional deficiencies. The analysis of the most common food intolerances allows to explain many gastrointestinal symptoms in patients who have not been diagnosed on the basis of laboratory, imaging and histopathological tests.

It is estimated that about 30% of the population report bothersome symptoms after eating certain foods.[1] It is currently one of the most common reasons for patients to visit a doctor in order to find the cause of often recurring and often affecting the daily functioning of ailments. Although these symptoms can be subjective and difficult to assess by a doctor, analyzing the problem and proposing a causal solution or dietary treatment can improve the quality of life of these people. It is worth noting that allergic causes affect only about 10% of children and 1%–2% of adults with gastrointestinal complaints.[2]

Intestinal microflora undoubtedly has a key influence on food intolerances and the overall functioning of the digestive tract. Its composition and proportions between individual strains of bacteria are closely related to the diet used and the living environment, which, as we know, is constantly changing, not without affecting human health.

The aim of the study is to present the latest articles on the most common food intolerances, which are one of the reasons for patients with symptoms of functional gastrointestinal disorders to report to doctors, in order to collect and summarize the current state of knowledge. The work also emphasizes the need for differential diagnosis between food intolerances and allergies. Articles were searched in Pubmed and Google Schoolar using terms such as: food intolerance, lactose intolerance, histamine intolerance, non-celiac gluten sensitivity, elimination diets, FODMAPs, food allergy.

There are two types of adverse food reactions that differ in the mechanisms causing them, which entails differences in the diagnostic and therapeutic process. Food intolerance, unlike food allergies, is a non-immune reaction of the body to a specific food. It may result from a real deficiency of an enzyme that decomposes a given nutrient – as is most often the case with lactose intolerance or apparent deficiency – in the case of eating too much of the substrate for this enzyme at one time. Additives currently present in highly processed food, such as monosodium glutamate or sulphites, may also play an important role in the occurrence of symptoms.[3]

There is also a hypothesis of a connection between unpleasant gastrointestinal sensations and the proven development of specific body reactions through classical (Pavlovian) conditioning.[4] That means a potential aversion to a particular food due to the association of unpleasant gastric complaints with the consumption of a particular food product in the past.

Food intolerance may also result from the consumption of products containing pharmacologically active or toxic ingredients, e.g. caffeine or alcohol.[5]

A relationship was also observed between the type of diet, taking antibiotics or undergoing surgery (e.g. caesarean section) and the change in the intestinal microflora, which in turn may lead to the appearance of food intolerances.[6]

In order to comprehensively discuss the problems of intolerance as the cause of gastrointestinal ailments, food allergy should also be mentioned. It is crucial to correctly diagnose, distinguish and then treat an adverse reaction after eating food. What is more, epidemiologists now note a global increase in food allergies, also – which was previously rare – among elderly. This may be due to a variety of factors, including environmental and cultural reasons. This is also explained by the emergence of new dietary patterns.[7]

A food allergy is an abnormal immune response of the body to food. They are most common among children and often get worse with age. Allergies whose symptoms persist with similar severity throughout life include peanut allergies.[8] At a younger age, the most common allergens are eggs, cow's milk, nuts, wheat or soy. It is also more common among adults to show symptoms after eating fish and shellfish.

Unlike food intolerances, allergies can be life-threatening in the event of acute anaphylactic reactions, when it is necessary to administer epinephrine intramuscularly as soon as possible.[9] Symptoms may appear immediately after ingestion of food or may be related to the late phase response, when the first symptoms do not appear until several hours later.[10]

Lactose intolerance

Lactose intolerance is one of the most widespread food intolerances in today's society. It is estimated that it affects up to 65% of people.[11] It results from a decrease or

loss of activity of lactase – an intestinal enzyme present in the brush border of the epithelium of the small intestine – responsible for the hydrolysis of lactose disaccharide into its two components: glucose and galactose. It shows the greatest activity in the jejunum.

This situation may be caused by primary genetic lactase deficiency as well as secondary by infections or other disease states leading to damage to the integrity of the small intestine mucosa.[12] Lactose intolerance often coexists with irritable bowel syndrome, bacterial overgrowth of the small intestine or celiac disease.[13]

People with impaired lactase activity report symptoms such as accelerated intestinal peristalsis, diarrhoea, bloating, and nausea.[14] They result from the increase in the osmolality of the intestinal contents and the fermentation of unsettled lactose. Less commonly associated with lactose intolerance may be constipation.[15]

Lactose intolerance should be distinguished from cow's milk allergy, which is one of the most common childhood allergies.[16] It affects an average of 2%–3% of children, although this number may change due to the simultaneous occurrence of overdiagnosis and underdiagnosis.[17]

It is extremely important to properly differentiate between these two diseases, because allergy – although in milder cases it may also manifest itself as gastrointestinal ailments – in more severe forms may lead to a life-threatening anaphylactic reaction. Appropriate diagnosis should be based on skin prick tests, measurement of IgE specific for cow's milk, as well as a detailed medical history including questions about other allergic diseases and their presence in the patient's family.[18]

A non-invasive test useful in diagnosing lactose intolerance is the hydrogen breath test. It consists in measuring the concentration of hydrogen in the exhaled air after administration of lactose. Methane may be an additional investigated parameter, however, it has not yet entered into routine practice and is still a subject of discussion.[19]

Treatment usually begins with limiting lactose-containing dairy products, which often leads to the needless exclusion of all dairy products from the diet. Therefore, it is worth considering the potential consequences of such decisions: the calcium contained in dairy products is necessary to maintain bone mass due to the reconstruction of this tissue that lasts throughout human life. For this reason, the complete abandonment of dairy products may result in an increased risk of osteoporosis.[20] The best option is to determine the tolerated dose of lactose for a given person – it is estimated that on average it is about 12 g per serving.[21]

What is more, if intolerance does not result from congenital lactase deficiency, the amount of this disaccharide added to technological processes in the production of foods or medicines should not cause adverse symptoms.

Currently, the offer of lactose-free food products available in almost every store is developing dynamically. An alternative to the elimination diet is the use of tablets containing lactase, choosing products with reduced lactose content, ripening cheeses, fermented products.[20] Interestingly, the latter – products of lactic fermentation – are quite well tolerated, despite the fact that the lactose content in them is comparable to its content in unprocessed milk. This tolerance is due to the lactase activity of the bacteria found in these dairy products. By choosing, for example, yoghurts with the following bacteria: *S. thermophilus* and *L. bulgaricus*, you can achieve a similar reduction in symptoms as in the case of lactase supplementation.[22]

Histamine intolerance (HIT)

Histamine intolerance is a hypersensitivity caused by impaired breakdown of histamine in the intestine by reducing the activity of diamine oxidase (DAO). This results in an increase in the concentration of histamine in the plasma, which in turn leads to the appearance of specific symptoms.[23]

It is important to distinguish HIT from histamine poisoning, also known as Scombroid syndrome, which occurs after eating fish of the Scombroidae family: tuna, mackerel, bonito.[24] The risk of poisoning increases significantly if the fish is stored in inappropriate conditions – for example, when stored for too long or at too high a temperature. In the case of this syndrome, symptoms appear from a few minutes after eating food to 2–3 hours.

The main complaints are: headache, redness of the skin and conjunctiva, abdominal pain, diarrhoea, nausea and vomiting. In more severe poisoning, cardiac arrhythmias, breathing difficulties and hypotension may occur. The symptoms result from the accidental ingestion of a large dose of histamine, which is formed from the transformation of histidine contained in fish under the influence of enzymes found in bacteria present in this food, including *Escherichia*, *Acinetobacter* and *Clostridium*. Treatment consists of administration of antihistamines.

It has been noted that histamine intolerance affects women more often however, this disproportion has not yet been sufficiently explained.[24] It is possible that diamine oxidase activity is reduced during the follicular

phase of the menstrual cycle.[25] The symptoms of HIT can be both gastrointestinal and extra-intestinal. The most frequently reported symptom is bloating. People struggling with this problem also report: diarrhoea, abdominal pain worsening after a meal, constipation or a feeling of fullness, and often also burning mouth, weakness, anxiety, hoarseness, itching, redness of the skin or runny nose.[26] Symptoms usually appear after eating foods rich in histamine and other biogenic amines.[27] These include: alcohols such as beer, wine or champagne, dried meats, long-ripening cheeses, pickled vegetables, chocolate, spinach, citrus fruits, bananas, legumes, seafood or tomatoes.[28]

What is more, histamine is also produced and degraded by the human body, in which the intestinal microbiome plays a key role.[2] At the same time, alcohol increases the toxic effects of histamine by competing with it for aldehyde dehydrogenase, an enzyme necessary to metabolize both substances.[28,29] This information explains the exacerbation of symptoms when alcohol is consumed.

There is no single, reliable diagnostic method, and the situation is complicated by the multitude of possible symptoms. In this disorder, it is also crucial to exclude other diseases, including other food intolerances. The diagnosis may be closer to the use of a diet for a certain period of time, excluding products rich in histamine, while observing the symptoms and analyzing the correlation between the type of food intake and the severity of the symptoms. Such observation should last 4–8 weeks.[2] There are genetic analyzes available on the market to detect DAO deficiency however, this deficiency may also result from other causes – pathological or pharmacological – which cannot be diagnosed using these tests.[23] An alternative may be the determination of DAO activity in plasma by measuring the amount of degraded histamine in a blood sample.[30]

The basis of treatment to reduce the occurrence of symptoms is a low-histamine diet.[28] There are also situations when patients, despite choosing products with low histamine content, still report ailments. This may be due to the presence of other biogenic amines, which are competitive substrates for diamine oxidase. Drawing inspiration from the method of treating lactose intolerance by supplementing the lactase enzyme, an option of diamine oxidase supplementation appeared. The possibility of taking the exogenous DAO enzyme may improve the quality of life by, on the one hand, reducing the severity of ailments and, on the other hand, reducing the need to decide on restrictive diets.[31,32]

Food additives

Nowadays, ubiquitous processed food is added to food products with numerous additional ingredients to change the physical, sensory or biological properties of a given food.[33] We distinguish here, among others: dyes, thickeners, stabilizers, sweeteners, emulsifiers, pH regulators or texturizers – nowadays present in virtually every available food product.

Like all adverse reactions of the body after food, those caused by food additives can have both immune and non-immune mechanisms. It is important to note that not everyone will be hypersensitive to food additives or will react to only some of them, which allows us to conclude that there is no need to rigorously exclude all food additives. An example is monosodium glutamate, which naturally occurs, for example, in sardines or Parmesan cheese in a much larger amount than when it is used as an additive to food products.[34]

There are studies focusing on the impact of a wide variety of food chemicals on the gut microbiota, which plays a key role in digestion. Long-term exposure of the digestive system microflora to food additives may consequently lead to a change in the composition and proportions of these microorganisms.[35]

Nowadays, awareness of the impact of intestinal microbiota on the functioning of the human body is rapidly increasing. Research is also underway on the possibility of improving the quality of microbiota through treatment with probiotics to increase tolerance, e.g. lactose.[36]

In conclusion, exposure to food additives is currently being attributed to possibly triggering a variety of hypersensitivity reactions, but a full causal relationship has not yet been demonstrated. More likely, an allergic basis is associated with the body's immune response to selected substances.[34]

Although many people see food additives as the culprit for more and more frequent hypersensitivity reactions or food intolerances, contrary to this opinion, their frequency is quite low – it occurs in about 1% of adults and 1%–2% of children.[37]

Non-celiac gluten sensitivity

Gluten is a mixture of proteins found in cereal grains such as wheat, spelt, barley and rye. Gluten-dependent diseases include: wheat allergy, celiac disease and non-celiac gluten sensitivity (NCGS). The latter disease entity is a type of food intolerance that brings together

symptoms associated with the consumption of gluten, which cannot be explained by the mechanism of an allergic or autoimmune response of the body.[38]

This disease consists in the appearance of repetitive intestinal and extraintestinal symptoms within a few hours after the consumption of gluten, which subsides completely after its exclusion from the diet.[39] It is estimated that about 10% of the population suffer from such ailments.[40]

The symptoms reported by patients often coincide with the symptoms of irritable bowel syndrome (IBS). These are: abdominal pain, flatulence, bowel movements and nausea. Headaches, joint and muscle pains, rashes, symptoms of general weakness, depression, anxiety and weight fluctuations are also reported.[41] Diagnosis and determination of the rank of the problem is disturbed by the huge popularity of gluten-free diets as well as the extremely dynamically developing market of gluten-free products in recent years. Interestingly, it is estimated that despite their significantly higher prices, people reaching for these products due to celiac disease constitute only a small percentage of consumers.[42]

It is problematic that the symptoms reported by patients with this disease entity cannot be confirmed during diagnostics using any known biomarkers. In addition, apart from a moderately elevated number of intraepithelial lymphocytes in the duodenal mucosa, no other abnormalities are found in the histopathological examination.[43]

The diagnosis should be made in two stages: the basis for considering the presence of this clinical entity and the first step in the diagnostic process is the exclusion of wheat allergy and celiac disease in a patient who is currently on a gluten-containing diet.[44]

This step may be difficult due to the often earlier and independent decision of the patient to exclude gluten. The next step is to start a gluten-free diet and continue it for about 4 weeks, followed by gluten challenge in a single-blind or double-blind trial, during which the patient must carefully observe his symptoms.[41]

Considering the gluten-free diet itself, one should consider whether and what risks it carries. It is known that a healthy and varied diet is extremely important in maintaining the composition of the intestinal microbiota. It has been proven that a gluten-free diet contributes to the reduction of beneficial intestinal bacteria, e.g. *Lactobacillus spp*. or *Bifidobacterium*, and the increase of potentially harmful, e.g. *Enterobacteriaceae*.[45]

A diet based on refined gluten-free flours often also contains a small amount of fiber necessary for the proper functioning of the digestive system. In addition, these products contain less vitamins E, B12, D and folic acid as well as potassium and magnesium, and they are more processed.[46] Therefore, the exclusion of gluten should be justified and the diet should be properly refined so that it does not lead to deficiencies. Last but not least, an important aspect of GF products is their high cost. One of the studies analyzing this topic states that it is 242% more expensive compared to a diet without exclusions.[47]

Intolerance of poorly absorbable, easily fermentable oligo-, di-, monosaccharides and polyols (FODMAPs)

It is one of the most common food intolerances that force you to seek help from doctors and dietitians, quite commonly co-occurring with irritable bowel syndrome. Also in this case, patients complain of numerous gastrointestinal symptoms such as: diarrhoea, bloating, gas, belching, nausea and abdominal pain. Easily fermentable carbohydrates include: fructose, lactose, fructans, xylitol, mannitol, maltitiol and sorbitol.[48] In a balanced diet without excluding nutrients, the FODMAP content ranges from 15 g to 30 g per day.[49] Fructose is naturally found in many foods. Moreover, humans have a limited ability to absorb it, so in some people it may be more limited, contributing to the symptoms listed above.

Absorption disorders through an overloaded or improperly functioning transporter – mainly GLUT-5 – lead to the formation of an osmotic force that increases the influx of water into the intestines, which then leads to the acceleration of peristaltic movements and the fermentation of intestinal content with the formation of, among others, hydrogen, methane or carbon dioxide and causing the symptoms listed above.[50] Intolerance of fructans, i.e. oligo- and polysaccharides, may result from a deficiency of enzymes responsible for their digestion, as in the case of lactose intolerance, which then, as in the case of fructose, leads to increased fermentation and the appearance of ailments.[48]

There is no reliable diagnostic method to confirm intolerance to all easily fermentable sugars. In the diagnosis of fructose intolerance, a breath test is used to measure the concentration of hydrogen and methane in the exhaled air after the previous administration of fructose. It is uncertain whether this test is sensitive enough to detect all fructose intolerance or only very severe fructose intolerance.[48]

A method of treatment that significantly increases the quality of life of patients is a diet low in fermentable

oligo-, di-, monosaccharides and polyols.[51] This diet has both therapeutic and, importantly, diagnostic significance.[49] It takes place in several phases: the first one lasts 2–8 weeks and consists in excluding all products containing large amounts of FODMAPs, after this time many people notice the disappearance of symptoms; the next stage is the gradual re-inclusion of excluded products in the diet – on average every 3 days – to assess which of them are well tolerated.[52] The third and final phase allows you to determine the tolerance threshold of a given product so as to optimize and personalize the diet in order to prevent the return of symptoms and reduce the risk of nutritional deficiencies.[53]

The most frequently excluded foods are: wheat products, in some cases all cereal products containing gluten, dairy products, legumes, onions, garlic, apples, pears, sweeteners such as xylitol or erythritol.

A diet excluding foods rich in FODMAPs has been used in the treatment of irritable bowel syndrome, which is currently one of the most common functional diseases of the gastrointestinal tract.[54] It is estimated that this disorder occurs in up to 20% of the population, and interestingly, it is diagnosed much more often in women.[48] Diagnosis of this disease is made according to the Rome Process Criteria. The diagnosis can be made if the patient reports recurrent abdominal pain at least one day a week regularly for 3 months. Other somatic disease entities that may have a similar clinical picture should also be excluded by performing endoscopic and radiological examinations as well as laboratory blood tests.

It should be emphasized that this is also an elimination diet and, if carried out incorrectly, it can lead to numerous deficiencies due to the large amount of food products, including fruits and vegetables, which should be excluded at least initially. Studies have noted a significant decrease in the intake of vitamin C, folic acid, riboflavin, calcium, magnesium and beta-carotene.[55] The risk of nutritional deficiencies can be reduced by working with an experienced dietitian. Long-term use of this diet also leads to a change in the composition of the intestinal microbiome through an increase in the number of *Bacteroides* strains and a decrease in *Bifidobacterium*.[56]

Conclusion

When reviewing the available literature on food intolerance and elimination diets, it can be concluded that this issue relates to the growing problem in society, including associated with the increasing amount of processed food in the diet, intestinal microflora disorders, eating habits changing with the development of civilization and the development of the food industry and the impact of the environment on the disruption of the functioning of the digestive tract. One can risk a statement that diseases associated with functional disorders of the digestive system are becoming new civilization diseases.

The increase in reported food intolerances indicates the need to develop objective diagnostic methods to confirm these disorders. It is also important because of the differential diagnosis with food allergies and because of the potentially possible anaphylactic reaction after eating an allergenic food in the absence or erroneous previous diagnosis.

It is also crucial to increase public awareness in this area as well and the development of accurate treatment regimens to significantly reduce the percentage of patients who decide to start an elimination diet on their own – these decisions are often inconvenient justified, on the one hand, lead to shortages of valuable nutrients, on the other hand, they can significantly prolong and hinder the correct diagnosis and making an accurate diagnosis.

The aspect of mental health in patients using elimination diets should also be emphasized, because the very fact of having gastrointestinal ailments affects the emotional state and restrictive diets can also disrupt the social functioning of patients. There may be fear associated with social exclusion, misunderstanding or loss of quality of life. For this reason, patients with food intolerances should be provided with appropriate care both in terms of somatic and mental health.

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