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Personalized Algorithm for Conducting Oral Food Challenge Tests with Milk in Children of the First Year of Life

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Abstracts

Cow's milk protein allergy is a topical issue in pediatrics. The diagnostic algorithm for cow's milk protein allergy includes thorough history taking, examination, physical development assessment, determination of specific cow's milk IgE, and oral food challenge tests.

The study aimed to develop a step-by-step algorithm for conducting oral food challenge tests with milk in young children, taking into account individual indications and risks.

Materials and methods. The task is to diagnose the cow's milk protein allergy in children in the first year of life. It is solved by allergy history taking, examination, assessment of physical development, detection of specific cow's milk IgE and based on the obtained results, oral food challenge test is performed: in age category before reaching one year when the specific IgE is more than 0.7 kU/L, testing is performed in the intensive care unit, if the specific IgE is less than 0.7 kU/L – in a specialized inpatient department.

Patients. The algorithm for diagnosing cow's milk protein allergy in 96 children under 12 months of age was tested in the City Children's Clinical Hospital.

During the oral food challenge test, the dose is increased logarithmically until the desired amount of product is reached, depending on the predicted risk of the reaction. Children at medium risk (specific IgE less than 0.7 kU/L) are tested in a

specialized inpatient department by “five steps”, and at high risk (specific IgE greater than 0.7 kU/L) – in the intensive care unit by “eight steps”.
Results. Among 96 children who underwent an oral food challenge test with milk, cow's milk protein allergy was diagnosed in 42 (43.75%). After the oral food challenge test, patients were given further recommendations, of which 27 (64.29%) were transferred to a formula with total protein hydrolysis, and 15 (35.71%) began to take oral tolerance induction (regular administration of acidified milk formula from lower doses to larger).
Conclusions: The developed algorithm for conducting oral food challenge tests with milk in children of the first year of life gives a possibility to personally select the examination technique taking into account the indications and risks. Appropriate preparation for the oral food challenge test enables to correctly conduct it, interpret the results, and develop a therapeutic approach.

Keywords: cow’s milk allergy, food allergy, oral food challenge test.

Introduction

Food allergy is a topical issue in pediatrics. The major food allergen in young children is cow's milk. According to statistics, 0.5% to 3% of children are allergic to cow's milk protein before the age of one [7].

The diagnostic algorithm for cow's milk protein allergy includes thorough history taking, examination, assessment of physical development, detection of specific cow's milk IgE, and oral food challenge tests (OFC), which are the golden standard for diagnosing food allergies. OFC is a set of diagnostic tests, the purpose of which is to achieve a safe diet expansion or to justify the avoidance of a particular allergen. The main value of OFC is that the test provides an opportunity to get the answer to the question in each case: “tolerance” or “allergy” [9].

The study aimed to develop a step-by-step algorithm for conducting oral food challenge tests with milk in young children taking into account individual indications and risks.

Materials and methods

The task is to diagnose the cow's milk protein allergy in children in the first year of life. It is solved by allergy history taking, examination, assessment of physical development, detection of specific cow's milk IgE and based on the obtained results, oral food challenge test is performed: in age category before reaching one year when the specific IgE is more than 0.7 kU/L, testing is performed in the intensive care unit, if the specific IgE is less than 0.7 kU/L – in a specialized inpatient department.

Patients. The algorithm for diagnosing allergy to cow's milk proteins in 96 children under 12 months of age was tested in the City Children's Clinical Hospital.
Indications to prescribe oral food challenge tests are different, including confirmation of tolerance, confirmation of allergies, monitoring of food allergy therapy.

I. Confirmation of tolerance:
- the presence of tolerance to a particular food;
- assessment of perception of different forms of products (whole milk and kefir);
- fear of the patient and his/her parents to try a new product at home, although allergy tests show tolerance;
- risk of cross-reactivity;
- a very strict diet, in which many foods are not included in the diet due to the symptoms of the disease and the difficulty of predicting the causative allergen;
- determination of the tolerance threshold to the allergen;
- the subjectivity of numerous dietary restrictions.
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II. Allergy confirmation:
- suspicion of a certain allergen and the test results are negative (skin testing, the level of specific IgE in the blood);
- suspicion of a specific allergen in the case of ambiguous and contradictory symptoms after its consumption.
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III. Monitoring of food allergy therapy:
- evaluation of the effectiveness of oral tolerance induction [4, 9].

OFC is performed by allergists in a medical facility with an intensive care unit after the patient has signed informed consent.
In recent years, various methods of challenge tests have been described. The diagnostic value of an open challenge test is limited, as the psychological influence of the patient and the doctor on the course of the challenge is possible. In particular, a negative result of an open challenge test eliminates hypersensitivity and therefore has a high diagnostic value. Instead, a positive result may be questionable and is an indication for a double (or single) placebo-controlled study [5].

A single-blinded placebo-controlled trial is performed so that the patient does not know the test product. The conditions of the double-blind placebo-controlled trial (classic challenge trial) are as follows: neither the patient nor the person conducting the study knows the test product. It should be done when the test result is needed to form recommendations in a clinical trial. This applies to children with food allergies, atopic dermatitis, chronic urticaria, bronchial asthma, etc. [8].

An oral food challenge test is usually the identification of oral allergic syndrome. Often the result will indicate a cross-allergic reaction in people with IgE-dependent allergy to grass and tree pollen. The product is taken into the oral cavity, chewed thoroughly, and held for a few minutes or held under the tongue [2].

An important stage of the OFC is the preparation of the studied products. Before the test, care must be taken to prepare the product. There are various possibilities for presenting the studied products. It is necessary to mask the organoleptic properties of the product. In this context, a favorable medium is a formula with a high degree of casein hydrolysis. The bitter taste and specific taste of the mixture will not allow the product to show notes of taste and smell. Another way to present a challenging product with the use of gelatin capsules is possible. However, in this case, there is a limitation – it is impossible to assess the response of the oral cavity and respiratory tract, the limited amount of product, and the impossibility of use in young children [5].

In clinical practice, however, preference is given to conducting open OFC. They provide an opportunity for the allergist to answer several key questions about the place of the tested product in the child's diet (elimination, tolerance, induction of oral tolerance) [4].

When planning an OFC, it is important to know the patient's drug load and recommendations on the need to discontinue medications to exclude their possible impact on the interpretation of oral food challenge tests. Table 1 lists the drugs that may affect the outcome of oral food challenge tests [3].

Table 1. The list of drugs and recommendations for excluding their possible impact on the interpretation of oral food challenge tests

Medication	**Last dose before tests**	**Medication**	**Last dose before tests**
Oral antihistamines	from 3 to 10 days	Inhaled sodium nedocromil	28 hours
Cetirizine	5 – 7 days	Sodium nedocromil (eye drops)	12 hours
Systemic steroids	from 3 days up to 2 weeks	Ipratropium bromide	4 – 12 hours
Loratadine	7 days	Oral/intranasal alpha-adrenergic drugs	12 hours
Nasal antihistamines	12 hours	Antileukotrienes	24 hours

The protocol of oral food challenge tests

The OFC plan is written in advance. However, you can never predict how it will develop. The results are most difficult to interpret when the symptoms are mild, subjective, or atypical. In particular, mild symptoms can be induced by emotional factors or become an onset of severe reactions such as anaphylaxis [1]. Therefore, the OFC can be conducted only by an experienced team of medical staff. In case of mild symptoms it is necessary to switch the patient's attention (turn on the tablet, read a book, play with toys), show interest in communicating with the patient, ask about leisure in kindergarten, school, hobbies, clubs, music, etc. At the same time, the doctor should not lose vigilance in assessing the child's condition, behavior, and symptoms. The number of doses and the interval between them are determined individually [6].

Patients are usually selected for testing before the oral food challenge test. Medical history, evaluation of serum specific IgE for milk, or skin test results are taken into account. If necessary, molecular testing can be performed (accurate determination of the concentration of a certain type of cow's milk protein) [10].

During OFC, the dose is increased logarithmically to achieve the desired amount of product, depending on the predicted risk of reaction. A personalized approach is that children at medium risk (specific IgE less than 0.7 kU/L) are tested in a specialized hospital by "five steps": 6, 12, 25, 50, 100; and with high risk (specific IgE more than 0.7 kU/L) – in the intensive care unit by "eight steps": labial test, 1, 3, 6, 12, 50, 25, 100 [5, 9].

Keep in mind that the time interval for testing can range from 10 to 60 minutes, on average 15-30 minutes. A short time can complicate the interpretation of the results and compromise the development of the reaction [3].

Table 2. The protocol of open oral food challenge test to confirm allergy to cow's milk protein in patients at medium risk according to the "Five Steps" scheme

Step	Product volume, ml	Amount of protein, g	Disturbances of the child's condition during the test
100 ml of milk - 3.3 g of milk protein			
1	5 ml	0.165	-
2	15 ml	0.495	-
3	30 ml	0.99	-
4	50 ml	1.65	-
5	100 ml	3.3	
The total volume of milk is 200.0 ml.		**The total amount of milk protein is 6.6 g**	

Table 3. The protocol of open oral food challenge test to confirm allergy to cow's milk protein in patients at medium risk according to the "Eight steps" scheme

Step	Product volume, ml	Amount of protein, g	Disturbances of the child's condition during the test
100 ml of milk - 3.3 g of milk protein			
1	Traces	-	-
2	1 ml	0.033	-
3	3 ml	0.099	-
4	6 ml	0.198	-
5	10 ml	0.33	-
6	40 ml	1.32	-
7	60 ml	1.98	-
8	80 ml	2.64	-
The total volume of milk is 200.0 ml.		**The total amount of milk protein is 6.6 g**	

Among 96 children who underwent an oral food challenge test with milk, allergy to cow's milk protein was diagnosed in 42 (43.75%).

91 (94.79%) children were tested in a specialized hospital (allergology department), and 5 (5.21%) – in the intensive care unit.

None of the children tested in the hospital had severe reactions. There were mainly acceptable skin symptoms (itching, rash) or gastrointestinal ones (abdominal pain). Three children had combined symptoms.

Among children tested in the intensive care unit, three patients (60%) had symptoms of moderate severity: prolonged sneezing and rhinorrhea, development of bronchospasm, and generalized urticaria.

After the oral food challenge test, patients were given further recommendations, of which 27 (64.29%) were transferred to a formula with complete protein hydrolysis, and 15 (35.71%) began to take oral tolerance induction (regular administration of acidified milk formula from lower doses to larger).

Conclusions

1. The developed algorithm for conducting oral food challenge tests with milk in children of the first year of life allows you to personally select the method of examination, taking into account the indications and risks.
2. Appropriate preparation for the oral food challenge test allows you to properly conduct it, interpret the results, and develop a therapeutic approach.

3. The proposed diagnostic measures and their sequence enable to make the correct diagnosis while spending as little time as possible for patients who are diagnosed with “Food hypersensitivity. Cow's milk protein allergy”.

Conflict of interest. The authors do not report any financial or personal connections with other persons or organizations that might negatively affect the content of this publication and/or claim authorship rights thereto.

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