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Clinical effectiveness of amino acid formula in infants with severe atopic dermatitis and cow's-milk protein allergy

Skuteczność kliniczna mieszanki aminokwasów u niemowląt z ciężkim atopowym zapaleniem skóry i alergią na białko mleka krowiego

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ABSTRACT

Introduction: The incidences of food allergies and related allergic diseases have been increasing in the recent years. **Objective:** The aim of this study is to evaluate clinical effectiveness of dietary intervention with amino acid-based formula (AAF) containing 100% free amino acids in the management of severe CMP allergy and atopic dermatitis (AD). **Material and methods:** Thirty infants aged from 29 days to 11 months with severe AD (Eczema Area and Severity Index [EASI] score >18) and confirmed CMP allergy were enrolled into the study. Twenty two patients have completed the study. The evaluation AAF's clinical effectiveness was carried out on the 7th, 14th and 28th day after reaching the full daily feeding volume. **Results:** In infants with severe AD (EASI score >18) the involvement of several organs and systems into the pathological process was typical: *i.e.* in 68% of the cases the skin symptoms were combined with the impaired function of the gastrointestinal tract and changes in the frequency of bowel movement (constipation, diarrhea), appearance of pathological admixtures in feces (mucus, blood), vomiting, etc. Feeding with AAF was associated with reliable reduction of severity not only of isolated skin (98%) but of combined skin and gastrointestinal manifestations of food allergy (82% of the cases). The formula was well tolerated by infants with severe AD and may be used for exclusive feeding of babies with severe CMP allergy. **Conclusions:** The

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described positive treatment effects were obtained with the diet duration of 4 weeks, the optimal period for the elemental diet administration needs further investigation.

Introduction

The incidences of food allergies and related allergic diseases have been increasing in the recent years. This is especially noticeable in developed countries in families with high socioeconomic status [1]. Clinical symptoms of allergic reactions which are mainly related to the peculiarities of nutrition could already be observed in infancy [2].

Food allergy in infants and toddlers is mainly represented by immunological response to one or more cow's milk proteins (CMP) [3]. Its exact prevalence in infants is unknown, approximately ranging from 2 to 6% [4–6]. Clinical manifestations of CMP allergy decrease or disappear at the end of the first year in almost half of the affected children, and in nearly 80% of the cases within the first 3 years of life [7, 8].

According to Emilia-Romagna working group on Allergology and the Working Group on Children's Gastroenterology (EWGPAG), CMP allergy occurs in 2–6% of children with the greatest prevalence during the first year of life [6]. Australian scientists reported that CMP allergy is manifested in 2% of young children [4]. According to recent studies in Japan, the prevalence of allergy to CMP is 0.2% in newborns and 0.35% in preterm babies with birth weight less than 1000 g [9]. Most of the authors estimate the prevalence of CMP allergy in infants and toddlers at the level of 5–8%, in adults – 1–2% [10–12]. According to American authors, among the 28% of young children with the likely clinical manifestations of food allergy, controlled oral food challenge confirmed the diagnosis of CMP allergy only in 8% of the cases [13].

Epidemiological data on the incidence of CMP allergy, confirmed with controlled oral food challenge, are mainly based on the following five studies:

1. In Denmark, 1749 children of the first year of life – 2.2% [14].
2. In Finland, 6209 babies aged less than 15 months – 1.9% [15].
3. In Norway, 193 preterm babies and 416 term infants under the age of 6 months – 4.9% [16].
4. In the UK, 969 infants – 2.16% [17].
5. In the Netherlands, 1158 infants – 2.24% [18].

Epidemiological data on the incidence of CMP allergy in Ukraine require clarifications and additional studies.

According to the pooled data, CMP allergy is clinically manifested by skin symptoms in 5–90% of the cases, gastrointestinal symptoms – in 60%, respiratory symptoms – in 19–30% and anaphylaxis – in 0.8–9% of the cases [19]. Clinical symptoms of CMP allergy vary from mild to moderate and severe.

Analysis of etiological spectrum of food allergies in infants and toddlers indicates that CMP belongs to one of three major allergens, but in all the countries where researches were carried out, CMP was the second leading cause of food allergy after egg allergens [19]. Peanut allergens (the United States, Switzerland), wheat (Germany, Japan), fish (Spain) or sesame (Israel) placed third among the major allergens.

However, despite the fact that CMP allergy is not the most common type of food allergy, it represents a significant problem because we cannot simply eliminate milk from the infant's diet like we do it with any other cause-significant allergen in the case of food allergy of another origin or in the early treatment of any other allergic disease.

Infancy is characterized by the highest rates of physical and psychomotor development. Such intensive plastic processes require an appropriate supply of energy, food ingredients, biologically active substances, the need for which is the greatest (per kg of body weight) compared to all other periods of child development. The said intensive development occurs on the background of functional immaturity of the main enzymatic systems of the gastrointestinal tract and under the conditions of evolutionary formed exclusively lactotrophic nutrition. Elimination of milk from infant's diet is not an issue, but another question is what should be fed to the baby? Only milk or dairy products contain all the necessary nutrients, and only milk is a proper physiological product for baby's first months of life.

On the other hand, if we do not eliminate a cause-significant allergen, sensitization will increase with the likely formation of severe forms of allergic diseases. CMP is the first food allergen to which all bottle-fed infants and many breastfed infants are exposed. So called 'atopic march' begins from CMP allergy with gradual extension of the sensitization range and change of the target organ: AD, bronchial asthma, allergic rhinitis. Not only the infant's physical growth and anatomical–physiological properties of all organs and systems, but a whole scenario of atopic march development throughout life depend on physician's competency in the management of a patient demonstrating the first clinical signs of sensitization to CMP with the possibility of its modification and improvement of the prognosis.

For several decades scientists have worked on the problem of CMP allergy during infancy. The evidence for this is not only hundreds of publications and creation of the new feeding products – that is, milk formulas with extensively hydrolyzed protein, but first of all in the development of International Guidelines devoted to CMP allergy. There are no such separate guidelines for any other allergen. On the other hand, CMP allergy guidelines cover the specific allergy issue, not a particular disease, which indicates exceptional global importance of the problem. The key guidelines created on the basis of evidence-based medicine and reflecting the achievements in solving the said problem are as follows: 'Diagnostic Approach and Management of Cow's-Milk Protein Allergy in Infants and Children: ESPGHAN GI Committee Practical Guidelines' (2012) [20], 'World Allergy Organization (WAO) Diagnosis and Rationale for