The article presents the main results of prospective multicenter study of effectiveness of using amino acid formula (AAF) in diet therapy for the infants with severe atopic dermatitis (AD) and allergy to cow's milk protein (CMP).

**The aim of the study:** To increase effectiveness of therapy for infants with AD and CMP food allergy by rationalization of the elimination diet.

**Objectives of the study**
1. Evaluate tolerance and nutritional quality of AAF in infants.
2. Evaluate the effectiveness of AAF in the treatment of severe AD in infants with food allergy to CMP.
3. Study the effectiveness of AAF in the treatment of gastrointestinal manifestations of food allergy to CMP in infants.
4. Define the role AAF in the treatment of infants with AD and food allergy to CMP in the national guidelines.

**Material and methods**

The prospective multicenter study enrolled 30 bottle-fed infants with severe AD (EASI score > 18) aged 29 days to 11 months. 22 infants completed the study. The study was conducted in 5 centers of Ukraine: Kyiv, Lviv, Kharkiv, Zaporizhzhya, and Simferopol.

During 4 weeks of the study the all infants were fed with a special AAF “Nutrilon Amino”, which included 100% free amino acids (UK manufacturer).

Evaluation of clinical effectiveness of AD and allergy to CMP diet therapy with amino acid formula was carried out on the 7th, 14th and 28th day after reaching the full daily volume of the formula. Provocative test was performed on the 28th day with extensively hydrolyzed whey protein formula followed with evaluation of immediate and late reactions.

Six medical examinations were performed during the study period. The examinations included evaluation of main growth parameters, scores of atopic dermatitis severity (EASI and SCORAD scores), the effectiveness of diet with a 10-point scale (according to parents’ and doctor’s conclusions separately). The degree of manifestation of AD skin symptoms were assessed in the area of maximum skin lesion. Topical treatment of severe dermatitis was performed with topical corticosteroids class I-III activity according to clinical indications and age restrictions, as well as with moisturizers.

**Key study findings.**

The all infants involved into the study were full term with normal weight and body length measurements (3458.64 ± 464.064 g and 52.14 ± 2.38 cm accordingly). Apgar scores in all infants were more than 7 points; 86% of them were attached to mother's breast during the first hour of life. Children were breastfed, on average, for 3-12 days. The first signs of AD appeared in average age of 4.5 weeks. In most cases, the disease characterized by recurrent course and ineffectiveness of diet and other treatment measures. Prior to inclusion into the study 5 (22%) of infants were on elimination diet with an extensively hydrolyzed infant formula, 10 (45%) – on a partially hydrolyzed infant formula, and 7 (33%) were fed with a standard formula. Age of infants at study enrollment and administration of AAF was 5.5 ± 2.3 months. The average initial EASI score representing severity of AD was 34.49 ± 13.59 points. Impairment of multiple organs and systems was typical for infants with severe AD (EASI score > 18): in 68% of cases cutaneous symptoms were associated with the gastrointestinal signs like changes in stool frequency (constipation, diarrhea), appearance of pathological admixtures in feces (mucus, blood), vomiting and so on.

Administration of AAF generally was well tolerated by patients, however, it caused vomiting in one infant (5%), diarrhea – in 5 (23%), constipation – in 8 (36%), appearance of mucous in stool – in 4 children (18%). At the same time, after administration of AAF improvement in weight and length gain was seen almost in all children. The average monthly weight and body length gain were respectively 500 g and 1.0 cm. Within a week after administration of full daily volume of AAF significant reduction of EASI (from 32.16 ± 12.6 points to 14.98 ± 9.92 points; p = 0.000001) and SCORAD (from 71.23 ± 11.43 points to 47.086
± 16.76 points, \( p < 0.000001 \) scores were observed. By the 28th day of treatment the corresponding scores decreased to 1.46 ± 1.31 points and 14.18 ± 6.17 points accordingly. In addition to skin lesions, 6 (27 %) infants initially had symptoms of diarrhea without fever, 5 (23 %) – vomiting, 7 (32 %) – constipation, and 8 (36 %) – infantile colic. In average the infants had 2 stools per day. 9 infants (41 %) had at least one of these disorders, 3 infants (14 %) – 2 or 3 disorders. Seven patients (32 %) had gastrointestinal disorders.

After 28 days of treatment with AAF the only one infant (5 %) kept on recurrent vomiting (not more than 2 times last week) and three others (14 %) still had signs of constipation. 18 patients (82 %) had no gastrointestinal disorders. According to the results of correlation analysis initial severity of AD determined at the time of full daily volume administration of AAF according to EASI and SCORAD scores was not associated with expression and severity of gastrointestinal symptoms.

The overall effectiveness of the diet was assessed separately by parents and doctors with a simple 10-point scale. The both groups of respondents almost equally emphasized a clear positive trend of cutaneous and gastrointestinal symptoms. After completion the diet period three infants (14 %) had immediate or delayed response to provocative test with extensively hydrolyzed whey protein formula within 72 h of its administration that required resuming of administration of AAF.

**Conclusions**

The obtained results allow optimizing approaches to the complex treatment of AD in terms of growing ineffectiveness of traditionally available diet therapy with extensively hydrolyzed whey protein formulas.

Infants with severe AD (EASI score > 18) had multiple impairments of organs’ and systems’ functions: in 68 % of cases skin symptoms were associated with gastrointestinal disorders like change in stool frequency (constipation, diarrhea), appearance of pathological admixtures in feces (mucus, blood), vomiting, and others. With administration of AAF significant decrease in severity of skin (98 %) and gastro-intestinal manifestations of food allergy (82 %) were seen. AAF was well tolerated by children with severe AD and, if needed, it might be used as a therapeutic formula for an exclusive feeding of infants with severe allergies to CMP. Duration of the diet therapy should not be less than 4 weeks. High effectiveness of this formula in infants with AD was proved by parents and doctors.