



## Current nutritional approaches in the treatment of autism spectrum disorder

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### ABSTRACT

Autism Spectrum Disorder (ASD) is a neurocognitive disorder that occurs in children 2-3 years of age with the etiology not fully understood. Its prevalence has increased in recent years.. Experts report that there are many factors such as physiological, psychological, genetic and environmental factors as the cause of autism. However, it has not been proven whether these factors cause autism or not. Individuals with autism exhibit many negative behaviors toward the environment and their families. Some of these behaviors are repetitive behaviors, excessive attention or indifference to certain items or people, inability to focus, playing with or being unresponsive to peers, and hyperactivity. With the increase in the number of individuals with autism, many methods are being tried to treat it. One of these methods is the field of nutrition. Gluten-free and casein-free diets, Feingold diet, elimination diet, special carbohydrate diet, ketogenic diet, and Candida diet are among the treatment methods. The purpose of these diets is to investigate the effect of some food groups on autism. Since

some foods are eliminated in dietary approaches, some micro- and macronutrients are restricted; side effects may occur as a result of dietary restrictions. In order to detect early symptoms that may occur due to diets, the application of diets should be carried out by a multidisciplinary team consisting of a doctor and a dietitian. In addition to diets, there are micronutrients added to the nutrition plan which are vitamins and minerals, fatty acids and probiotics. Treating physiological disorders in Autism Spectrum Disorder is one of the primary goals. This study is aimed to teach the nutritional approaches used for the treatment of autism and the effects of micro- and macronutrients on autism.

**Keywords:** Autism spectrum disorder, gut, gluten-free and casein-free diet, nutritional therapies, *Candida albicans*

### INTRODUCTION

With the development of science in recent years, the number of children diagnosed with ASD has been increasing (1). Autism Spectrum Disorder was identified by Leo Kanner in the 1940s (2). Autism is a lifelong neurodevelopmental disorder that occurs with the interaction of many genes that are not in contact with each other. This disorder usually occurs in early childhood (2 -3 years of age). According to studies, the incidence of ASD in boys is 4-5 times higher than in girls. While the prevalence of autism was less than 10 per 10,000 children in previous studies, it was reported as 110 per 10,000 children in current studies (3,4). Individuals with autism exhibit limiting, repetitive movements, and behaviors

in many behaviors and activities (5,6). Examples of situations such as inability to communicate with peers, difficulty in learning, indifference to some of the people and things around, obsession with certain objects, and not making eye contact can be given as examples (1,7). Studies have shown that these problems improve with nutrition (8). There are some diet plans that are implemented to improve the negative behavior disorders and health of the person with autism. These are the elimination diet, Feingold diet, Candida diet, gluten-free and casein-free diet, special carbohydrate diet, and ketogenic diets. Apart from diets, in addition to nutritional therapy, vitamin and mineral, probiotic and fatty acid supplements are also given (4,8).

### **1. Gluten-Free-Casein-Free (GFCF) Diet**

In a gluten-free and casein-free diet, all foods made from grains such as barley, rye, oats, boza, bulgur, semolina, and wheat containing gluten the diet, and dairy products such as milk, yogurt, cheese, kefir, buttermilk, and cream, that is, foods containing casein from the diet. it is a nutrition plan (9,10). A series of peptides are formed as a result of the breakdown of gluten and casein. These peptides easily cross the blood-brain barrier and interact with the opioid receptor to affect the brain (11). Opioids are chemical compounds that cross the blood-brain barrier with opioid receptors, particularly affecting the cognitive functions of the central nervous system (12). While the absorption of nutrients is ensured, the peptides in the structure of the proteins are broken, but the opioid peptide formation as a result of not breaking due to some reasons is called the opioid excess theory (9,13). As a result of this situation, it is thought that permeability in the intestines of individuals with autism, especially in the children's group, increases and it causes disruption in many cognitive biological activities of individuals with autism (8). Increased intestinal permeability allows excess opioids to pass into the bloodstream and central nervous system. Diets devoid of gluten and casein cause a decrease in opioid peptides, reducing the permeability of the intestines in the gastrointestinal tract and reducing the

number of opioid peptides that cross the blood and blood-brain barrier (14,15). As a result of the gluten-free and casein-free diet, positive results were obtained such as contributing to the intellectual development of children, increasing the ability to focus, playing with peers and decreasing mobility, which was prevented by the symptoms of autism (4). It has also been reported as a result of studies that this diet improves the gastrointestinal system of individuals with autism (16). In a study conducted by Gahalichi et al. in 80 children, it was observed that a gluten-free diet improved gastrointestinal problems (17). In another study, they divided children with autism into 2 separate groups. One group followed a gluten- and casein-free diet and the other group followed a standard diet for 2 years. As a result of the study, it was observed that the deterioration of the gastrointestinal systems of children in the gluten-free and casein-free groups improved significantly (18).

Due to the restriction of foods in gluten-free and casein-free diets, the disadvantages of the diet are low in minerals such as vitamin D, calcium, phosphorus, sodium and total energy intake. It has been reported that fiber ratios are high because these individuals consume the most vegetables and legumes. At the same time, gluten-free products contain more sugar and sodium. The effect of gluten-free and casein-free diets on autism in individuals with autism is a controversial treatment method (19,20-23).

### **2. Feingold Diet**

Doctor Benjamin F. Feingold and his friends reported that low molecular weight dyestuffs in foods cause behavioral disorders in children in the 1960s. Based on the information they gathered from a large number of cases, these reports showed that additives and similar chemicals cause hyperactivity and negative effects on the central nervous system in some children. These conditions were observed in some natural salicylates in the analysis (21). The aim of the Feingold diet is a dietary approach based on the elimination of dietary food additives, salicylates, salicylate-containing products, artificial coloring sweeteners, corn syrup, aspartame, and other

preservatives from the diet (16,22). In the Feingold diet, foods containing phenols and salicylates such as tomatoes, peppers, peanuts, almonds, peaches, apricots, cocoa, grapes, honey, milk, almonds, strawberries, tomatoes, and oranges are eliminated from the diet (3,23). Most of the studies on the effect of the Feingold diet on autism have not been specific to the disease yet. In these studies, it was observed that children who followed the diet had fewer hyper-kinetic symptoms than before (8,19).

### 3. Special carbohydrate diet

The purpose of a special carbohydrate diet is to prevent intestinal damage caused by leaky gut syndrome and to control the growth of pathogenic bacteria in the intestinal microbiota. This is to regulate the internal hemostasis of the body by eliminating the types of carbohydrates that pathogenic bacteria feed on. While the portion of complex carbohydrates is restricted in the diet, simple carbohydrates are completely prohibited. (9, 10). In this diet, grain products such as wheat, oats, rice, processed meats, canned vegetables and fruits, dried legumes, some spices and high-starch tuber vegetables such as potatoes are limited. Meat, chicken, fish, fresh vegetables, and fruits are consumed (10,19,24). Specifically, only monosaccharides are allowed in the diet, while many disaccharides and polysaccharides are restricted (25). In a study, a special carbohydrate diet applied to a 4-year-old individual with autism and fragile X syndrome showed a decrease in symptoms in the gastrointestinal tract and improvements in the child's behavior. Although the special carbohydrate diet is a widely used nutritional therapy, there is insufficient evidence for the effectiveness of this diet in individuals with autism (9,25).

### 4. Candida Body Ecology Diet (BED)

*Candida albicans* is a yeast species found in the oral flora of healthy individuals which is one of the most common strains of yeasts, having both adhesion and pathogenicity, and is naturally found in the oral mucosa of individuals (26). It was reported that this yeast is 2 times more common in autistic individuals in early childhood compared to adults. This yeast

releases harmful toxins such as ammonia that cause many negative behaviors in autism. It causes less absorption of carbohydrates and minerals, which are essential for the body (9). The primary purpose of the Candida diet is to provide hemostasis of the microbiota in the body and to eliminate *Candida albicans*. The Candida diet is a diet approach based on preserving the flora in the intestine with a high pH, low sugar and starch content, and probiotics. It has been reported that the increase of *Candida albicans* causes individuals with autism to have focusing problems, increase in hyper-kinetic activities, gastrointestinal problems, excessive interest or reaction to some objects and people, inadequacy in language skills, and asociality of the person (8). Candida also allows the consumption of cereals such as quinoa and buckwheat. Rice, corn, and soy are prohibited in consumption, which is allowed by a gluten-free and casein-free diet. With this diet, the body protects its natural flora and the number of pathogenic bacteria in the intestinal flora decreases (15).

### 5. Ketogenic Diet

Epilepsy affects approximately 12% of individuals with autism in early childhood and 26% of young individuals. As a result of epilepsy, cognitive activities such as old age, difficulty in speaking, retardation in growth and development and inability to focus occur. The treatment applied in the ketogenic diet varies according to the age and symptoms of the individual. Although studies on the ketogenic diet and autism are insufficient, it is reported that this diet is a promising treatment method for improving the symptoms of individuals with autism (12). In studies conducted with individuals with autism, it has been reported that a ketogenic diet may be beneficial for the treatment of autism, but it is difficult for individuals to comply with the diet (27). The use of ketone bodies as an energy source has been shown in studies to help correct metabolic disorders and symptoms in autism, and reduce symptoms such as mental retardation, inability to focus, and hyperactivity (27,10).

In a study, 18 individuals with autism applied a ketogenic diet, but only 10 individuals reported

improvement in behavioral and cognitive symptoms. Due to the small number of studies and the small sample size, it could not be concluded that the ketogenic diet is a definitive treatment for autism (23,25).

Since the ketogenic diet does not contain enough protein and carbohydrates, it negatively affects growth and development due to the inability to take amino acids and micronutrients, which are essential for the body. At the same time, it causes serious weight loss in people who follow the diet. In order to prevent any complications that may occur as a result of this diet, it is recommended to be done under the supervision of a doctor and dietitian (4,28).

### **Micronutrient supplements**

The deficiencies of various vitamins and minerals, which are not caused by a single factor, can cause autism (9). Other causes of vitamin and mineral deficiency are gastrointestinal system problems, chronic diarrhea or constipation, and dietary restrictions (13,15,25). Iron, zinc, selenium, calcium, iodine, magnesium, and chromium are the most deficient minerals. Vitamin A, thiamine, niacin, pantoic acid, biotin, pyridoxine, vitamin C, folate, and vitamin D are the most deficient vitamins (9,11,29).

Vitamin D is an important neurodevelopmental vitamin in individuals with autism spectrum disorders. Vitamin D has been suggested to be used as a hopeful treatment in autism as well as in many diseases for recent years (9,29). In a study, it was predicted that vitamin D levels in individuals with autism are low, and as a result, the reason for negative behaviors in children may be due to low levels of vitamin D.

Studies have reported that vitamin C positively affects social behaviors in individuals with autism (9). They reported that it causes an increase in oxidative stress due to the decrease in the levels of antioxidant vitamins such as vitamin E and vitamin C in children with autism (14). In a study, it was reported that vitamin A supplementation had a positive effect on autism symptoms (25). In a study, the addition of vitamin A to the diet showed an increase in the number of Bacteroidetes in

individuals with autism, but the relationship between vitamin A and microbiota has not been fully elucidated (14). As a result of pyridoxine deficiency, disruptions occur in the functioning of the central nervous system in individuals with autism (10). In a study, B<sub>12</sub> supplementation caused an increase in cysteine and glutathione concentrations, and as a result of these increases, positive results were observed in autistic behaviors (25). It has been reported that multivitamin supplements given in addition to individuals with autism have a positive effect on growth, development and hyperactivity, speech disorders and anger control resulting from autism (11). In the study, there is no relationship between autism and zinc levels, but it is important for the treatment of autism because zinc regulates gene expressions and reduces the toxic effect of heavy metals that cause behavioral disorders in autism (25). Micronutrient deficiencies such as selenium and carnitine have been reported (9).

Vitamin and mineral supplements are recommended for individuals with autism, but there are not enough studies on the positive or negative effects of vitamin and mineral supplements (29). Individuals with autism do not need to take additional supplements if there is no deficiency of any vitamin or mineral in their blood results (30). Even if blood values are in the normal range, it is predicted that adding some vitamins to the diet will play an important role in the treatment of autism (13).

### **Fatty Acid Supplement**

Omega-3 supplementation is an alternative therapeutic nutritional support in individuals with autism and other diseases (9). It has been reported that the omega-6/omega-3 ratio is increased in individuals with autism (28). Omega-3 fatty acid supplementation reduces language development, hand-foot coordination problems, decrease in hyperactivity, decrease in violence and anger tantrums, aggression and self-harm in individuals with autism (25,31). However, there are not enough studies in the literature on the subject (14,15). In a study by Megoit et al. in the 2000s, as a result of their study with 30 autistic and 30 normal children, it was seen that the polyunsaturated fatty acid levels in individuals with autism were lower

than in normal children, and the children were given omega-3 and omega-6 supplements every day for 3 months. As a result of the study, an increase in polyunsaturated fatty acid levels in 20 individuals with autism and improvements in behaviors such as hyperactivity and inability to focus have been observed (15).

In another study, it was found that omega-3 supplementation improved social interaction, interest and behavior in autism, but had no effect on behaviors such as irritability and hyperactivity (9). Additionally, in a study on omega-3 fatty acids and autism, it was reported that there was an increase in the number of bacteria producing short-chain fatty acids such as in the microbiota, and improvements in the gastrointestinal systems of individuals with autism, in addition to the improvement of the microbiota (14).

### Probiotic supplement

One of the most controversial issues in the treatment of autism is the use of probiotics. Probiotics play a role in the immune system modulation by improving intestinal functions, in the composition of the microbiota, and by affecting three types of axes (intestine-brain, intestine-lung, intestine) (14). Probiotics have the effect of regulating gastrointestinal system disorders such as diarrhea and constipation caused by intestinal diseases caused by autism, synthesis of hormones and vitamins, excretion of drugs and toxins from the body, preventing attention problems, and regulating metabolic activities of the host such as energy metabolism (16,27). In a study on probiotics, it was reported that *Lactobacillus acidophilus* treatment resulted in improvement in the treatment of autism. In another study, it was reported that mercury, which has a toxic effect on autism, is removed from the body by probiotic bacteria (16). Some studies show that the use of probiotics has positive results in individuals with autism, while some studies say that the use of probiotics has no effect on autism. More studies on the subject are needed (10,14).

### CONCLUSION

Autism Spectrum Disorder is a disorder that is increasing in prevalence in our country and in

the world. However, the etiology of autism is not known precisely. One of the treatments developed for autism is nutrition. Due to the small sample size of the nutritional therapy studies conducted on autism and the small number of studies, it is not known exactly which of the nutritional therapy methods has a more positive effect on autism. In addition, due to dietary restrictions, individuals with autism cannot take the necessary vitamins, minerals, and macronutrients. Children cannot get calcium from dairy products on a gluten-free and casein-free diet. As a result of insufficient intake of calcium, growth and development also negatively affect intestinal health. It is necessary to increase the number of samples in all studies, to increase the number of studies, and to repeat the studies. In addition, all nutritional interventions should be done by a dietitian, doctor, and psychologist, since these treatment methods are not certain. More multidisciplinary studies are needed on the relationship between ASD and nutrition.

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