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PROBIOTICS IN TREATMENT OF ATOPIC DERMATITIS – TRUE OR MYTH WHAT IS THE EFFECTIVENESS OF PROBIOTICS IN REDUCING ECZEMA SYMPTOMS AND IMPROVING QUALITY OF LIFE IN CHILDREN WITH ECZEMA?

PROBIOTICI U LEČENJU ATOPIJSKOG DERMATITISA – ISTINA ILI MIT KOJA JE EFIKASNOST PROBIOTIKA U SMANJENJU SIMPTOMA EKCEMA I POBOLJŠANJU KVALITETA ŽIVOTA DECE OBOLELE OD EKCEMA?

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Summary Atopic dermatitis (AD) is the most common chronic inflammatory skin disorder affecting up to 20% of children. AD is usually the first step of the atopic march, with a sequential progression to respiratory allergic diseases (asthma and allergic rhinitis). The aim of this prospective real life study was to follow up the efficacy of mixture of $3x10^9$ CFU (colony forming unites) of 3 probiotic strains Lactobacillus Casei BL 2401, Lactobacillus Salivarius BL 2201, Bifidobacterium Breve BL 3406 in combination with 7mg Zinc in Hypro-ri form for better resorption and 1200 IJ Vitamin D3 (Imunolak Kids D3 Zn) in the group of children with atopic dermatitis. Tretament period was3 months. Children with mild to moderate AD who have received Imunolak Kids D3 Zn were followed up for the next 6 months after cessation of the probiotic supplementation for AD and respiratory tract diseases (including both upper and lower respiratory tract infection and exacerbation of asthma and/or allergic rhinitis in children with those comorbidities). Our observation showed that 6 months after cessation of the treatment AD was under control, while although during the study we noticed less respiratory tract diseases, 3 months of probiotic usage didn't have prolonged effects.

Keywords: atopic dermatitis, children, probiotics, prevention

Sažetak Atopijski dermatitis (AD) je najčešći hronični inflamatorni poremećaj kože, pogađa čak 20% dece. AD je obično prvi korak atopijskog marša, sa uzastopnom progresijom ka respiratornim alergijskim bolestima (astma i alergijski rinitis). Cilj ove prospektivne studije bio je da se prati efikasnost mešavine $3x10^9$ CFU od 3 probiotička soja Lactobacillus Casei BL 2401, Lactobacillus Salivarius BL 2201, Bifidobacterium Breve BL 3406 u kombinaciji sa 7mh cinka u Hipro-ri formi resor za bolju resorpciju i sa 1200 IJ Vitamin D3 (Imunolak Kids D3 Zn), u grupi dece sa atopijskim dermatitisom. Tretman je trajao 3 meseca. Deca sa blagim do umerenim AD koja su primala Imunolak Kids D3 Zn praćena su narednih 6 meseci nakon prestanka uzimanja probiotika zbog AD i bolesti respiratornog trakta. Naše zapažanje je pokazalo da je 6 meseci nakon prestanka upotrebe probiotika, AD simptomi su bili pod kontrolom, dok su respiratorne tegobe bile ređe tokom 3 meseca upotrebe probiotika, ali ne i nakon završene terapije.

Ključne reči: atopijski dermatitis, deca, probiotici, prevencija

INTRODUCTION

Atopic dermatitis (AD) is the most common chronic inflammatory skin disorder affecting up to 20% of children, and 3-8% of adults. AD has a complex pathophysiology, which comprise a strong genetic component as well as highly dynamic immunological response (immunological march) and a broad clinical phenotype that reflects all of this.

The disease course can be associated with periods of symptomatology and relapses, and not so infrequent spontaneous remission is possible. AD is usually the first step of the atopic march, with a sequential progression of different allergic conditions (asthma and/or allergic rhinitis). The new treatments have notably modified the course of the disease and have immunological effects susceptible to introduce remission. It is the leading non-fatal health burden due to skin diseases, cause a substantial psychosocial burden on patients and their parents and/or caregivers. AD in infancy could be a risk factor for food allergy, asthma and allergic rhinitis development, but also it is more frequent seen in patients with other immune-mediated inflammatory diseases as well as in those with mental health disorders. The core stone of present prevention and treatment are focused on daily emollients usage to try to restore epidermal barrier function. The first line treatment are still topical steroids for acute flares, along with topical calcineurin inhibitors to maintain remission. Now days severe refractory cases could be treated with disease-modifying drugs (dupilumab). In perspective we need to improve our knowledge and understanding of the heterogeneity of the disease and its subtypes, the role of atopy and microbial dysbiosis and the comparative safety of therapies (1,2). Current data suggest that gut dysbiosis, especially if it happens early in life, contributes to the development of inflammatory conditions including allergies (atopic dermatitis, food allergies and finally respiratory allergies) (3-5). AD might occur at any age, but almost in half of the all cases begin within six months of life, with up to 80–90% developing their first symptoms by five years of age (6). It is well known that AD could be the

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main risk factor for further development of other allergic diseases such as food allergy, allergic rhinitis, and asthma later in life (the concept known as an atopic march). The natural course of the disease could be either relapsing-remitting or persistent, and even mild to moderate for of the disease could affect significantly the quality of life of the patients and/or their parents and/or caregivers (7-9). In the last couple of years there is a growing interest in identifying triggers factors as well as in finding the best approach for diagnosis and treatment of affected patients.

A majority of ongoing studies are focused on primary prevention of allergies mostly on nutrition and dietary factors that could be involved in AD pathogenesis. One thousand days concept best described the importance of pregnancy and the first two years of life in the development of allergies and other immune mediated diseases (10).

Since Kalliomäki et co authors have published one of the first studies on the efficacy of probiotics in primary prevention of atopic diseases, twenty years ago, there has been a growing interest in this field of research (11). The WAO guideline panel from 2015 suggests: a) using probiotics in pregnant women at high risk for having an allergic child; b) using probiotics in women who breastfeed infants at high risk of developing allergy; and c) using probiotics in infants at high risk of developing allergy (12).

METHODOLOGY

The aim of this real life was to follow up the long term efficacy of mixture of 3 x 10^9 CFU of 3 probiotic strains Lactobacillus Casei BL 2401, Lactobacillus Salivarius BL 2201, Bifidobacterium Breve BL 3406 in combination with 7mg Zinc in Hyprori form for better resorption and 1200 IJ Vitamin D3 (Imunolak Kids D3 Zn) in the group of children who have previously received those combination for 3 months as add on treatment for atopic dermatitis. 75 children with mild to moderate AD who have received Imunolak Kids D3 Zn were followed up for SCOARD and quality of life for the next 6 months after cessation of the probiotic supplementation.

RESULTS

The study showed persisting benefits 6 months after supplementation ceased, in terms of SCORAD and quality of life. During the probiotic usage we noticed less respiratory tract diseases (including both upper and lower respiratory tract infection and exacerbation of asthma and/or allergic rhinitis in children with those comorbidities), unfortunately without prolonged effects after cessation of the probiotics treatment.

DISCUSSION

Possible mechanisms of this sustained effect may relate to persistent changes in faecal flora and/or persistent immunological effects. The potential mechanisms of action of probiotics are not well understood, but are believed to be mediated by immunological effects initiated in the gastro- intestinal mucosa development and oral tolerance. If the beneficial effects of probiotics on AD are also associated with effects on developing immune responses, it is also possible that they could modify (or even prevent) allergic responses to aeroallergens and the expression of persistent airways disease.Our results are in accordance with the results from other studies implicated that certain probiotic strains as well as particular probiotic combination could be a useful therapeutic tool for treatment of children AD (13). It is also well known that the efficacy of probiotics is strain specific, with L. salivarius and L. acidophilus induce the largest clinical benefit. Although the results from the first study showed the decrease in AD severity and the improvement of quality of life in the probiotic group in comparison with the group of children who were only on standard treatment, it was not enough to reach conclusion about optimal duration and dose for probiotic treatment (14). This was the reason why we would like to show the possibility of long lasting effects of probiotic supplementation of children AD.

CONCLUSION

Our study showed long last effects of probiotic use on clinical symptoms of AD and quality of life in affected children. Children with AD are also at increased risk (up to 80%) of developing persistent respiratory tract disease (allergic rhinitis and asthma) and if we want also to prevent further development of atopic march and persisting effects on atopy overall we should continue supplementation with certain probiotic combination for a longer period (15).

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