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Probiotics in the Treatment and Prevention of Atopic Dermatitis

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Atopic dermatitis (AD) is the most common chronic inflammatory skin disease in infancy, which has increased steadily in the industrialized countries over the last 3 decades. Clinically the disease is characterized by dry skin, intractable pruritus and current relapses or chronic course which is associated with reduced quality of life for patients and their families. The therapy is mainly symptomatic and includes moisturizing the skin and topical anti-inflammatory treatment such as corticosteroids and calcineurin inhibitors. Additionally patients have to avoid irritants and allergens.

The main cause of AD is still not clearly understood. Apparently, it is the result of a complex interaction between genetic and environmental factors leading to disturbed epidermal differentiation, impaired epidermal barrier function and dysbalance of the immune system. The latter is characterized by a disruption of the Th1/Th2 cytokine balance towards an activation of Th2 cells, which is followed by induction of IgE and the activation and recruitment of eosinophils. It has been suggested that the absence of the exposure to microbes in the early childhood predisposes an infant to develop atopic diseases (hygiene hypothesis) [1]. Furthermore, patients with AD have significantly increased colonization by superantigen-secreting *Staphylococcus aureus*, which is associated with immunosuppressive activity of regulatory T cells [2].

The environmental factors which may influence atopic diseases also include probiotics such as lactobacilli or bifidobacteria. They are defined as specific microbial cultures which confer health benefits by prophylactic or therapeutic effects. These effects include the stabilization of the intestinal barrier, stimulation of intestinal IgA production, and modulation of specific and nonspecific immune responses to environmental factors like allergens [3–6].

In the end probiotic bacteria lead to a reduction in Th2 cytokines and increased production of IL-10 and TGF-β by regulatory T cells [5, 6–9]. However, there are conflicting results, as recently reported by authors from Denmark [10]. They showed that certain probiotic strains can modify antigen-presenting cells to cause reduced activity of regulatory T cells. So far the results regarding the immunomodulatory effects of probiotics appear variable, which may be due to using different probiotic strains and different methods of stimulating cytokine production.

Based on these findings probiotics have been considered to improve and prevent AD. The Finnish group headed by Isolauri (1997) was the first to show significant reduction in SCORAD (Scoring Atopic Dermatitis) in the probiotic group compared to a placebo group [11]. Four years later the same study group reported a positive effect

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Table 1. Probiotics in the prevention of AD (randomized controlled studies)

First author, year	Patients	Probiotic	Duration of application	Age at follow-up years	Effect of probiotics
Kalliomäki [12–14] 2001, 2003, 2007	132	*Lactobacillus rhamnosus* GG	Prenatal 4 weeks, postnatal 6 months	2 4 7	Significantly reduced rate of AD in the verum group
Abrahamsson [18] 2007	188	*Lactobacillus reuteri*	Prenatal 2 weeks, postnatal 1 year	1	Significantly reduced rate of AD in the verum group (only IgE-associated AD)
Kukkonen [19] 2007	925	Mix of various probiotics + prebiotics	Prenatal 2–4 weeks, postnatal 6 months	2	Significantly reduced rate of AD in the verum group
Taylor [20] 2007	178	*Lactobacillus acidophilus*	Only postnatal (6 months)	1	No difference between verum and placebo
Wickens [21] 2008	474	*Lactobacillus rhamnosus* or *Bifidobacterium animalis* subsp. lactis	Prenatal 4 weeks, postnatal 2 years	2	Significantly reduced rate of AD in the verum group (only for *L. rhamnosus*)
Kopp [22] 2008	94	*Lactobacillus rhamnosus* GG	Prenatal 4–6 weeks, postnatal 6 months	2	No difference between verum and placebo
Kim [23] 2009	112	Mix of probiotics	Prenatal 4–6 weeks, postnatal 6 months	1	Significantly reduced rate of AD in the verum group
Niers [24] 2009	102	Mix of probiotics	Prenatal 4–6 weeks, postnatal 12 months	2	Significantly reduced rate of AD in the verum group
Soh [25] 2009	253	*Lactobacillus rhamnosus* + *Bifidobacterium longum*	Only postnatal (6 months)	1	No difference between verum and placebo

in the prevention of AD. The results showed a 50% reduction in the incidence of AD in the probiotic group compared to a placebo group at a 2-year follow-up [12]. In their follow-up study prevention of AD by probiotics extended beyond infancy [13, 14].

Up to now there are only a few randomized controlled studies using probiotics for the prevention and treatment of AD [15–17], summarized in tables 1 and 2.

Two meta-analyses of trials studying the effects of probiotics on AD risk were recently carried out by Osborn and Sinn [35] as well as Lee et al. [36]. The emphasis of Osborn and Sinn [35] was the effect of probiotics in the prevention of food hypersensitivity and allergic diseases, while the meta-analysis of Lee et al. [36] focused on the prevention and treatment of AD. Lee et al. concluded that current evidence is more convincing for the efficacy of probiotics in the prevention than in the treatment of pediatric AD. Osborn and Sinn stated that there is insufficient evidence to recommend probiotics for the prevention of allergic disease and food hypersensitivity.

Both meta-analyses considered the research conducted by Rautava et al. [37] as well as Kalliomäki et al. [12, 13] as independent studies, even though both surveys originated from one and the same study.

Taken together there are conflicting results regarding the effects of probiotics in the treatment and prevention of AD. Probably, this is related to differences in study design (characterization of patients: number, age, severity of AD, sensitization to food and inhalative allergens, additional respiratory atopy), dosage of the probiotics, application of 1 probiotic strain or composition of different strains, duration of application, length of follow-up and time slot of administration. Therefore, at present probiotics cannot be generally recommended for the treatment and the prevention of AD. However, based on epidemiological, experimental and clinical results, it appears worthwhile to perform further randomized controlled

Table 2. Probiotics in the treatment of AD (randomized controlled trials)

First author year	Patients/age	Probiotic	Duration of application weeks	Effect of probiotics
Majamaa [11] 1997	27/2.5–15.7 months	*Lactobacillus rhamnosus* GG	4	Significant reduction in SCORAD in the verum group
Kirjavainen [26], 2003	35/5.5 months	*Lactobacillus rhamnosus* GG	7.5	Significant reduction in SCORAD in the verum group
Rosenfeldt [27] 2003	43/5.2 years	*Lactobacillus rhamnosus* + *Lactobacillus reuteri*	6	Significant reduction in SCORAD in the verum group (only IgE-associated AD)
Weston [28] 2005	53/10.9 months	*Lactobacillus fermentum*	8	Significant reduction in SCORAD in the verum group
Viljanen [29] 2005	230/6.4 months	*Lactobacillus rhamnosus* or mix of various probiotics	4	Significant reduction in SCORAD in the verum group (only IgE-associated AD)
Sistek [30] 2006	59/4.1 years	*Lactobacillus rhamnosus* + *Bifidobacterium lactis*	12	Significant reduction in SCORAD in the verum group (only food-sensitized patients)
Brouwer [31] 2006	50/5.2 months	*Lactobacillus rhamnosus* or *Lactobacillus rhamnosus* GG	12	No effect of probiotics
Passeron [32] 2006	39/5.9 years	Symbiotics or prebiotics (placebo)	12	Significant reduction in SCORAD in both groups
Fölster-Holst [33], 2006	47/18.8 months	*Lactobacillus rhamnosus* GG	8	No effect of *Lactobacillus rhamnosus* GG
Grüber [34] 2007	102/7.4 months	*Lactobacillus rhamnosus* GG	8	No effect of *Lactobacillus rhamnosus* GG

multicenter studies with standardized parameters in a representative number of patients. Regarding the heterogeneity of AD it is important to characterize the patients very accurately in order to define subgroups which could be susceptible to using probiotics as therapeutical and preventive measurements.

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R.F.-H. does not have any relationship to disclose.

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