

Study of the effect of probiotics on the therapeutic effect obtained in the reduction of allergic symptoms in patients diagnosed with atopic dermatitis

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ABSTRACT

Introduction: Atopic dermatitis (AD) is a chronic inflammatory skin disease posing a significant burden on healthcare resources and patients' quality of life. It is a complex disease with a wide spectrum of clinical presentations and combinations of symptoms. Atopic dermatitis affects up to 20% of children and up to 3% of adults. Recent data show that its prevalence is still increasing, especially in low-income countries. This study aimed to check whether the use of probiotic therapy affects the reduction of allergic symptoms in patients diagnosed with AD.

Material and methods: Questionnaires of 70 respondents diagnosed with AD who took a probiotic for at least 5 days were analysed. To conduct the study, an anonymous, original survey was used in the form of a form created on Google Drive consisting of 19 questions with the possibility of answering both single and multiple choice and with the possibility of providing your own answer.

Results: The most beneficial strains affecting the reduction of allergic symptoms are bacteria of the genus *Lactobacillus*. The average duration of use of probiotic therapy to reduce allergic symptoms is from 2 weeks to 3 months.

Conclusions: The study showed that the implementation of probiotic therapy shortens the duration of therapy for AD and reduces allergic symptoms such as redness, itching of the skin and allergic rhinitis co-occurring in patients with AD.

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Keywords: atopic dermatitis, probiotics, *Lactobacillus*, *Bifidobacterium*

INTRODUCTION

Atopic dermatitis (AD) is a chronic disease and the number of potential treatment options is growing, however, they are typically associated with immunosuppressive or immunomodulating effects, and do not guarantee a permanent cure [1]. Atopy is defined as the heritable tendency to produce immunoglobulin E antibodies in response to small amounts of common environmental proteins such as pollen, house dust mites and food allergens [2].

Probiotics are live microorganisms that, when consumed in a certain amount, exert beneficial effects on the body by improving the balance of the intestinal ecosystem [3]. The microorganisms with a positive effect on the general

condition of the skin include especially lactic acid bacteria of the genus *Lactobacillus* and *Bifidobacterium* [4]. It has been shown that the use of probiotic preparations reduces inflammation due to the reduction of INF- γ , IL-4 and Th17 cytokines in splenic CD4+ T lymphocytes and increases the expression of IL-10 and cytokines associated with regulatory T cells in mesenteric lymph nodes [5]. Probiotics have an inhibitory effect on the maturation of dendritic cells, thus blocking the differentiation of naive T cells into Th2 lymphocytes, which contributes to the reduction of inflammation in the skin [5]. This study aimed to evaluate whether the use of probiotic therapy affects the reduction of allergic symptoms in patients diagnosed with AD.

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MATERIAL AND METHODS

To conduct the study, an anonymous, original survey was used in the shape of a form created on Google Drive consisting of 19 questions with the possibility of answering both single and multiple choice and with the possibility of providing your own answer. Respondents had the opportunity to select different versions of the answers.

The responses of 70 respondents diagnosed with AD who took a probiotic for a minimum of 5 days were analysed. Survey data was collected from January 18, 2022, to June 15, 2022. The author's survey was posted on social networking sites regarding the treatment of AD. The study was approved by the Ethical Committee of the Nicolaus Copernicus University in Toruń at the Ludwik Rydygier Collegium Medicum in Bydgoszcz No. 5/2022.

The criteria for inclusion of the respondents in the study were to answer all the questions asked in the author's questionnaire consisting of 19 questions, including 8 single-choice questions and 11 multiple-choice questions, including 10 questions with the possibility of giving their own answers. The criteria for inclusion in the study were the need to be at least 18 years old, a diagnosis of AD, and the need to take a given strain of probiotics for a minimum of 5 days. At the beginning, the questionnaire was completed by 76 correspondents, 6 of whom were excluded from the survey due to the failure to complete all the questionnaire questions: failure to provide symptoms of the disease, failure to provide the exact location of the atopic lesions, failure to provide information about other allergic symptoms such as rhinitis, redness or itching of the skin, failure to provide the location of allergic lesions, failure to provide pharmacological agents taken on a daily basis in the treatment of AD, failure to provide the exact type of probiotic strain in the treatment of AD, failure to specify the period of use of probiotic therapy to reduce allergic symptoms, failure to provide the exact time during which allergic symptoms have been reduced since the use of a given probiotic strain, failure to provide an answer regarding satisfaction with the implementation of probiotic therapy for the treatment of AD, failure to provide the source of information of the respondent regarding the possibility of including probiotic therapy in the treatment of AD.

Statistical analysis

The differences between the two nominal variables were analysed using the chi-square test. In statistical analyses, the significance level $p < 0.05$ was assumed. Analysis was performed using IBM SPSS Statistics version 24.

RESULTS

The study included 70 patients. Among the respondents were 64 (91%) women and 6 (9%) men. The 49% (n = 34) of respondents were between the ages of 21 and 30,

Table 1. Characteristics of the study population

Criteria	Number of respondents	Percentage of respondents
Sex		
Woman	64	91%
Man	6	9%
Age		
From 21 to 30 years	34	49%
From 18 to 20 years	12	17%
From 31 to 40 years	20	29%
From 41 to 50 years	2	3%
From 51 to 60 years	2	3%
Domicile		
Village	13	19%
Cities of all sizes	57	81%
Education		
Average	23	33%
Higher	41	59%
AD diagnosis time		
For at least one year	54	77%
A year ago	10	15%
Half a year ago	1	1%
A month ago	3	4%
A week ago	1	1%
A few days ago	1	1%

AD — atopic dermatitis

17% (n = 12) of respondents were aged 18 to 20 and 29% (n = 20) were aged 31 to 40, 3% (n = 2) were aged 41 to 50 years, and 3% (n = 2) were 51 to 60 years. 19% (n = 13) of respondents lived in the countryside 81% (n = 57) lived in cities of different sizes. 33% (n = 23) of respondents had secondary education and 59% (n = 41) had higher education. The 77 per cent of subjects (n = 54) surveyed had been diagnosed with AD for at least one year. The remaining subjects were diagnosed a year ago (15%; n = 10), half a year ago (1%; n = 1), a month ago (4%; n = 3), a week ago (1%; n = 1), a few days ago (1%; n = 1) (Tab. 1).

The most common symptoms of the disease were dry skin (86%; n = 60), skin irritation (83%; n = 58), itching (83%; n = 58), the appearance of red spots (76%; n = 53) and itchy eruptions (64%; n = 45). Less frequently, the disease was manifested by the appearance of lichen-like papules (24%; n = 17) and eruptions (17%; n = 12).

Atopic lesions were most often located on the dorsal surface of the hands, feet (54%; n = 38), face, lip, and neck (40%; n = 28), and on the skin of the eyelids (39%; n = 27). They were less common in the upper chest (31%; n = 22) or shoulder girdle (29%; n = 20).

Table 2. Clinical characteristics of the study population

Criteria	Number of respondents	Percentage of respondents
Symptoms		
Dry skin	60	86%
Skin irritation	58	83%
Itching	58	83%
The appearance of red spots	53	76%
Itchy eruptions	45	64%
Lichen-like papules	17	24%
Eruptions	12	17%
Localization of atopic lesions		
On the dorsal surface of the hands, feet	38	54%
Face, lip, neck	28	40%
On the skin of the eyelids	27	39%
In the upper chest	22	31%
Shoulder girdle	20	29%
Allergic symptoms		
Rhinitis, redness or itching of the skin	59	84%
Dry skin	51	73%
Itching	48	69%
Irritated skin	45	64%
Red spot	41	59%
Itchy eruptions	31	44%
Excoriations	12	17%
Red papules	10	14%
Localization of allergic lesions		
On the hands and feet	37	53%
In the face area	36	51%
In the upper torso area	24	34%
In the elbow and axillary bends	23	33%
Around the shoulder girdle	16	23%
Around the lower torso	14	20%
AD substrate		
Non-allergic dermatitis		
Woman	7	10.9%
Man	4	66.7%
Allergic dermatitis		
Woman	57	89.1%
Man	2	33.3%
Use of probiotic therapy in the past to alleviate AD symptoms	39	56%

AD — atopic dermatitis

The majority of respondents claimed that they had allergic symptoms such as rhinitis, redness or itching of the

skin (84%; n = 59). The most common allergic symptoms are dry skin (73%; n = 51), itching (69%; n = 48), irritated skin (64%; n = 45), red spots (59%; n = 41) and itchy eruptions (44%; n = 31). Less frequent were excoriations (17%; n = 12) and red papules (14%; n = 10).

Allergic lesions were most often located on the hands and feet (53%; n = 37) and in the face area (51%; n = 36). Less often in the upper torso area (34%; n = 24), in the elbow and axillary bends (33%; n = 23), around the shoulder girdle (23%; n = 16), around the lower torso (20%; n = 14).

It is important to note the difference in the cause of AD. Non-allergic dermatitis (IgE-independent) was present in 10.9% (n = 7) of women and 66.7% (n = 4) of men. The occurrence of IgE-mediated AD with the presence of a large number of IgE antibodies and the IgE-antibody reaction caused by a given allergen manifested by allergic changes such as allergic rhinitis, redness or allergic itching of the skin was experienced by: 89.1% (n = 57) of women, including 33.3% (n = 2) of men (Tab. 2).

More than half of the respondents have used probiotic therapy in the past to relieve the symptoms of AD (56%; n = 39). Most often, the reduction of disease symptoms was observed during therapy with the following strains: *Lactobacillus* (59%; n = 41), less often with *Bifidobacterium* (28%; n = 20), *Streptococcus* (21%; n = 15), *Enterococcus* (18%; n = 13), *Saccharomyces* (18%; n = 13). No improvement during the implementation of probiotic therapy was reported by 31% (n = 22) of respondents (Fig. 1).

Most often, a reduction in allergic manifestations was observed during probiotic therapy with strains: *Lactobacillus* (54%; n = 38), less often with *Bifidobacterium* strains (23%; n = 16), *Streptococcus* (13%; n = 9), *Enterococcus* (10%; n = 7), *Saccharomyces* (10%; n = 7). Reduction of allergic symptoms was not experienced by 31%, n = 22 of respondents (Fig. 2).

All respondents who were diagnosed with AD for less than a year and used probiotic therapy showed a reduction in the severity of allergic symptoms. Among subjects suffering from the disease for more than a year, this was smaller and amounted to 59% (n = 41). This difference was statistically significant (p = 0.014). According to the subjects, the time of probiotic therapy necessary to notice a reduction in the severity of allergic symptoms ranged from 2 weeks (28%; n = 20) to 3 months (31%; n = 22), less often a few days (5%; n = 3) or a year (Fig. 3).

The 62% (n = 43) of respondents using it were satisfied with the probiotic therapy used in the treatment of AD. All respondents who had been diagnosed with AD less than one year were satisfied with probiotic therapy (100%; n = 70), the percentage of such subjects was lower among patients with a longer period of disease (48%; n = 34). This difference was statistically significant (p = 0.004).

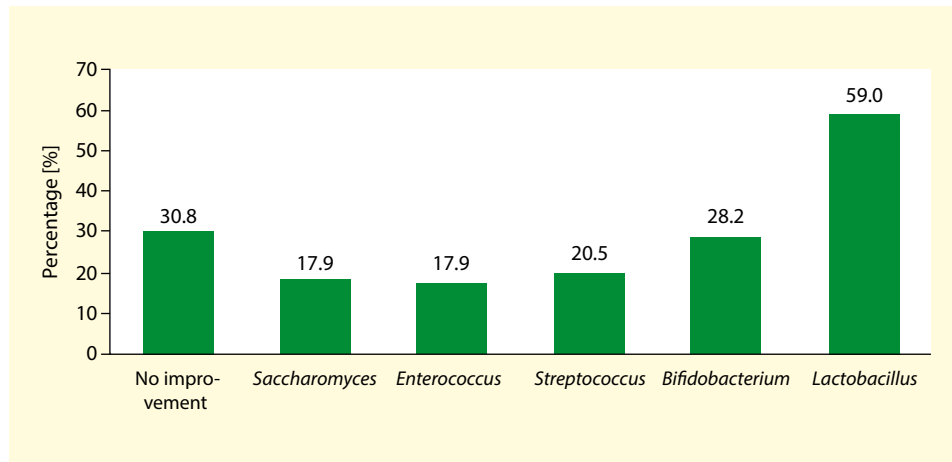


Figure 1. Types of probiotic strains that reduce the symptoms of atopic dermatitis

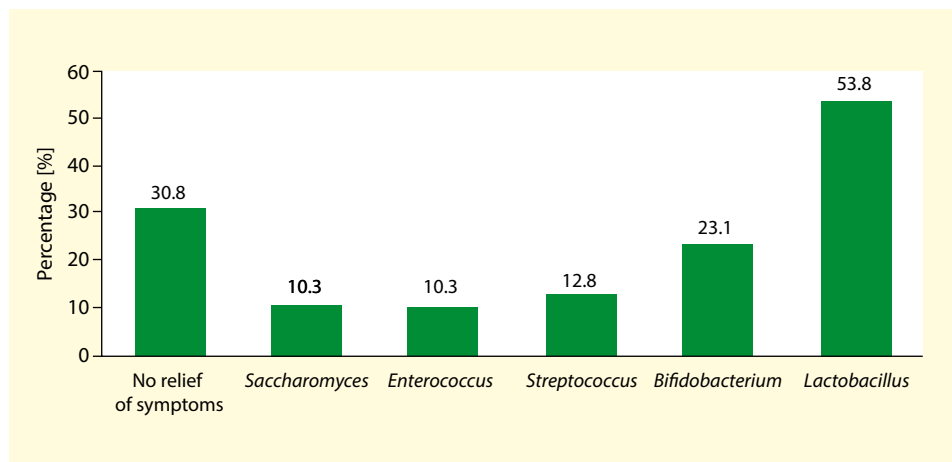


Figure 2. Types of probiotic strains that reduce the severity of allergic symptoms

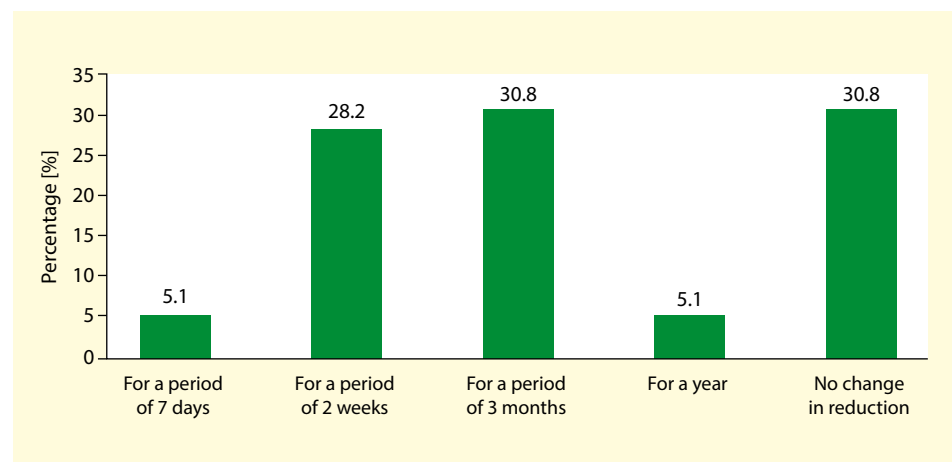


Figure 3. The duration of probiotic therapy to reduce the severity of allergic symptoms

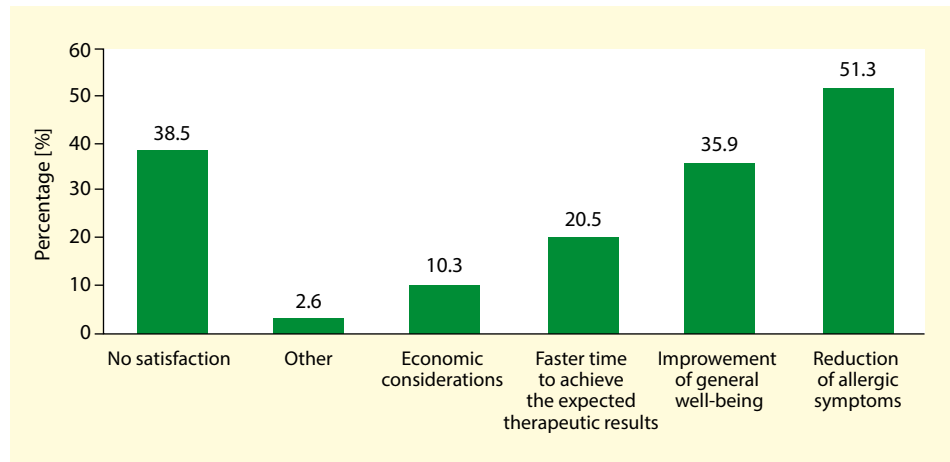


Figure 4. The time since the end of probiotic therapy from which allergic-type symptoms have decreased

The most common reason for satisfaction with the use of probiotic therapy in the treatment of AD was the reduction of allergic symptoms (51%; $n = 36$) and the overall improvement of well-being (36%; $n = 25$) (Fig. 4).

DISCUSSION

Atopic dermatitis is most often localized on the bent surfaces of the body, front and lateral neck, eyelids, forehead, face, wrists, back of feet and hands [6], which is confirmed by the majority of respondents. The latest research shows that the most effective pharmacological method in alleviating the local symptoms of atopy is emollients [7], which was also indicated by the majority of respondents in the survey (71%; $n = 50$). The reduction of itch sensitivity in patients with AD is attributed to the impairment of the epidermal barrier. The cause of this condition in individuals with AD is mutations in the filaggrin gene (FLG), which lead to decreased secretion of natural skin moisturizing factors [7]. Emollient therapy allows for the restoration of the damaged epidermal barrier, thereby reducing itching and skin dryness.

The implementation of probiotic therapy supports the treatment of atopy and contributes to the reduction of allergic symptoms. A significant portion of respondents (62%; $n = 43$) expressed satisfaction with the use of probiotic therapy in the treatment of AD, mainly due to the reduction of allergic symptoms (51%; $n = 36$), which were defined in the author's survey as dry skin, itching, irritated skin, red spots, itchy eruptions, excoriations, red papules. Probiotics, as living bacteria, can significantly contribute to the reduction of AD symptoms of various aetiologies. Several conducted studies, including meta-analyses, provide evidence supporting the use of probiotics as an effective method in supporting the treatment of allergic diseases [8]. Potential mechanisms explaining the health-promoting effects of

probiotic bacteria may involve restoring the normal gut microbiome through the modulation of the intestinal immune system and displacing potential pathogens through competitive exclusion.

A study conducted by Mastrandrea et al. [9] demonstrated that the administration of a mixture of *L. acidophilus*, *L. delbrueckii*, and *Streptococcus thermophilus* for 30 days in patients with clinical symptoms of asthma and/or conjunctivitis, rhinitis, urticaria, AD, food allergy, and irritable bowel syndrome resulted in a reduction in the number of circulating CD34+ haematopoietic precursor cells (HPCs). Based on this, it was inferred that an increase in circulating CD34+ HPCs is a factor in systemic allergic inflammation, suggesting that these cells may become a therapeutic target in the treatment of allergic diseases, including AD. Another analysis of flow cytometry subsets of peripheral blood lymphocytes in patients receiving probiotics showed that under the influence of probiotic therapy, the percentage of CD4+ and CD25+ lymphocytes decreased, while the percentage and absolute number of CD8+ lymphocytes increased, indicating the immunoregulatory effect of probiotics in AD patients. The authors suggest that the lymphoid tissue associated with the intestines, which remain in direct contact with probiotic bacteria, plays a role in the modulation of immunological response. The study showed a relationship between the reduction in CD4+ percentage and the reduction of typical clinical manifestations of AD [10].

Regarding the type of probiotics, the most beneficial in AD therapy is the use of gram-positive, anaerobic lactic acid bacteria *Lactobacillus* and *Bifidobacterium* [11], which is also confirmed by the data obtained in the conducted study. Lactic acid bacteria, including *Lactobacillus* and *Bifidobacterium*, exhibit a multifaceted effect on the human body [11]. They contribute, among other things, to maintaining a healthy gut flora, regulating gut motility,

improving the absorption of certain nutrients, reducing toxic metabolites, and preventing gastrointestinal infections caused by *Salmonella typhimurium*, *Staphylococcus aureus*, *Escherichia coli*, *Clostridium perfringens*, and *Clostridium difficile* [11]. These findings are confirmed by studies conducted by Hoang et al. [12], which demonstrate that *Lactobacillus rhamnosus* significantly improved the quality of life in AD patients. These strains contributed to the alleviation of skin symptoms and irritations during the day and night in supplemented individuals [12].

The results of the study indicate that the most effective strains for reducing allergic symptoms are bacteria from the *Lactobacillus* genus. Majama and Isolauri [13] linked the improvement of clinical parameters in patients with AD receiving *Lactobacillus rhamnosus* preparation with a decrease in the concentration of tumour necrosis factor α (TNF- α) and α_1 -antitrypsin in the stool. In contrast, Rosenfeldt et al. [14] observed a decrease in the concentration of eosinophil cationic protein (ECP), and in subsequent years, researchers demonstrated an increase in the concentration of interleukin 10 in AD patients receiving *Lactobacillus GG* strain [15]. All these elements play a role in the comprehensive pathogenesis of AD, and the observed changes in their levels indicate the immunomodulatory effect of *Lactobacillus rhamnosus* on the body's inflammatory response. Studies on the regulation of the action of these cytokines and proteins may lead to the development of more effective methods of treatment and symptom alleviation in AD.

Most respondents reported that allergic symptoms were reduced most frequently within six months (18%; $n = 13$) and two months (21%; $n = 15$) after completing probiotic therapy. To observe changes in allergic symptom reduction, most surveyed individuals took probiotics for two weeks (28%; $n = 20$) or three months (31%; $n = 22$), less frequently for a few days (5%; $n = 3$) or one year. From available literature data, the time required for taking probiotics to reduce AD skin symptoms was about 56 days [16].

Clinical experience has shown that some patients with AD are resistant to conventional treatment methods such as emollients, corticosteroids, and other immunosuppressive drugs. The treatment of AD, depending on the severity of the disease according to the SCORing Atopic Dermatitis (SCORAD) scale, involves high-risk strategies for severe and serious adverse events. Therefore, it is necessary to seek alternative therapies, which is why researchers are interested in probiotics. Global literature provides numerous pieces of evidence for the effectiveness of probiotics in AD therapy in children [17–19], whereas data on the modulation of the immune system in adults with AD through probiotics use is limited. The effectiveness of probiotic therapy in adults with AD requires further research.

CONCLUSIONS

The study showed that all respondents who had been diagnosed with AD for less than a year and used probiotic therapy demonstrated a reduction in the severity of allergic symptoms. Among patients with the disease for more than a year, the reduction was smaller at 59%, which was statistically significant ($p = 0.014$). All respondents diagnosed with AD in less than a year were satisfied with probiotic therapy, while the percentage (48%) was lower among patients with longer disease duration. The difference was statistically significant ($p = 0.004$). The study also showed that *Lactobacillus* strains were more effective than *Bifidobacterium* strains in alleviating atopy symptoms. The study shows that the majority of the surveyed women had atopic changes caused by a concomitant allergic disease.

Article information and declarations

Acknowledgements

None.

Data availability statement

The study was based on an anonymous, proprietary questionnaire in the form of a Google Drive form consisting of 19 questions with the ability to make both single-choice and multiple-choice answers, and with the possibility of reply.

Ethics statement

Consent of the Bioethics Committee No. 5/2022 Nicolaus Copernicus University in Toruń at the Ludwik Rydygier Medical College in Bydgoszcz.

Author contributions

The largest contribution was made by the first author (50%). The contribution of the second and third authors in the creation of the review article was equal, accounting for 25% per author. The tasks performed by the authors included selecting the topic, conducting a literature review, performing an in-depth analysis of the subject, and writing the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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Supplementary material

None.

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