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Review

Probiotics in dermatologic practice

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ABSTRACT

Objective: Probiotics are live microorganisms that beneficially affect the host when administered in adequate amounts. They have an excellent safety profile. Probiotics have been used as immunomodulators in inflammatory skin conditions, such as atopic dermatitis. The aim of this study was to summarize the available evidence concerning the use of different strains of probiotics in dermatology practice.
Methods: We conducted a literature review of English and Spanish publications listed in standard databases (PubMed, Ovid, Google Scholar, Medline, and EBSCO), between 1994 and 2015 using the words "probiotics" and "dermatology." We found ~70 studies containing these criteria and selected 42 in which probiotics were used for dermatologic purposes.
Results: We found enough evidence to recommend the use of probiotics in specific conditions in dermatology practice, especially in children with atopic dermatitis.
Conclusions: Further well-designed, large population based trials are needed to validate the use of probiotics in dermatology practice, including innovative therapies to rebuild skin barrier defects, protection against microbial colonization, and restoration of immunologic balance.

Introduction

Probiotics are live microorganisms with beneficial effects on the host when administered in adequate amounts. They have an excellent safety profile [1]. Probiotics have been widely studied because of their effects on the gastrointestinal (GI) tract and digestive functions, but these live microbes have wider applicability as evidenced by the gut–brain–skin axis theory postulated 80 y ago [2]. Details regarding use of probiotics for dermatologic indications such as atopic dermatitis (AD), acne, and sexually transmitted infections are dispersed throughout medical literature. Overall, probiotics seem to be a promising and safe therapeutic modality, but evidence up to now is limited [3].

Prebiotics have been defined as "non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or the activity of one or a more bacterial species already resident in the colon, and thus attempt to improve host health." A synbiotic is defined as "a product that contains both prebiotic(s) and probiotic(s)" [4].

The most widely used bacteria as probiotics are the *Lactobacilli* and *Bifidobacteria*, but products incorporating other organisms as gram-positive cocci, bacilli, yeasts, and *Escherichia coli* have been applied [5]. Probiotic preparations are widely available to consumers as powders, tablets, drinks, and fermented dairy products.

Probiotics and prebiotics offer a novel concept to modulate digestive functions. Probiotics have been shown to improve calcium bioavailability, reduce risk for development of colon cancer, ameliorate mucosal inflammation in numerous GI disorders; other beneficial effects include hypoinsulinemia and control of triacylglycerol levels [6–8]. These effects occur by selectively stimulating the growth of beneficial bacteria in the colon. Probiotics can be used as a preventive measure for many diseases; however, their mechanism of action remains unclear [9,10]. The rapid increase in the medical use of probiotics and prebiotics in recent years has confirmed their excellent safety profile. As immunomodulators, they have been used in inflammatory skin conditions, such as AD [11].

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Potential application of probiotics in prevention of atopic dermatitis in the pre- and postnatal periods

AD is a chronically relapsing skin disease that occurs most commonly during early infancy and childhood. It is frequently associated with abnormalities in skin barrier function, allergen sensitization, and recurrent skin infections [12]. There are many applications on the role of nutrition in AD. Some examples are dietary restriction and supplementation, interventions with vitamin and mineral supplementation, as well as probiotics and essential fatty acids, from the prenatal period through infancy and adulthood [13].

The pathogenesis and treatment of AD, including prevention, skin care, environmental modifications, nutrition, education, and anti-inflammatory medications, have been studied. One study demonstrated the potential utility of prenatal probiotics in prevention of AD, as well as the interplay of food allergies and eczema [14].

A recently published meta-analysis aimed to find evidence regarding the effect of probiotics in children with AD. The study found 21 articles that met the inclusion criteria. The best evidence relies with the use of probiotics in mothers and infants in preventing the development and reducing severity of AD [15]. Specifically, *L. rhamnosus GG (LGG)* was shown to be effective in long-term prevention of AD. Prebiotics administered simultaneously with black currant seed oil was effective in reducing the development of AD [16].

One study reviewed the literature on the effect of controlled use of prebiotics, probiotics, or both to help prevent the development or reduce the severity of AD in children <3 y. Eight of the 13 (61.5%) studies reported a significant effect on the prevention of AD. They found that specific probiotic strains prevented AD among infants. There was a long-term reduction in the incidence of AD, with a reduction in severity. The study concluded that additional interventional studies are imperative before firm recommendations can be made [16].

Probiotics seem to have a protective role in AD prevention if they are administered in the pre- and postnatal periods in both general and allergic risk populations, as shown by evidence proposed in a recently published [17]. In this meta-analysis, 1513 articles related to probiotics and AD were found; 26 studies satisfied the study criteria and only 16 were included in the final analysis. Probiotics conferred protection against the occurrence of AD (odds ratio [OR], 0.64; $P < 0.001$) in both subgroups of patients, one in the general population and the other, in a population at high risk for allergies. Prenatal administration followed by postnatal administration of probiotics was protective (OR, 0.61; $P < 0.001$), in contrast to only postnatal administration (OR, 0.95; $P < 0.82$). Both *Lactobacillus* alone and *Lactobacillus* with *Bifidobacterium* were protective against AD (OR, 0.70; $P = 0.004$ and OR, 0.62; $P < 0.001$, respectively). The study results concluded that probiotics seemed to have a protective role in AD prevention when they are administered in pre- and postnatally in both the general and the allergic risk population [17].

There are, however, conflicting views [18,19]. Another meta-analysis could not support probiotics as a viable treatment of established AD, and concluded that their use in preventing AD (rather than treatment) holds more promise [20].

Use of probiotics with SCORAD scores in children with AD

One study demonstrated that *LGG* (1×10^9 colony forming units [CFU]) supplementation reduced both the risk for and severity of AD. Three randomized controlled trials, two from the Finnish group and one from Denmark, conducted in infants with preexisting AD, showed a statistically significant reduction in the Scoring Atopic Dermatitis (SCORAD) score. SCORAD is a clinical tool used to assess the extent and severity of eczema. The criteria used are based on the following:

1. Extent criteria, which determine the approximate percentage of body surface covered by eczema, using the rule of 9s;
2. Intensity criteria, which score the features (erythema, edema/papulation, oozing/crusting, excoriation, xerosis, lichenification) on a scale of 0 to 3 (0 = *none*, 1 = *mild*, 2 = *moderate*, 3 = *severe*);
3. Subjective symptoms, which include cores for pruritus, insomnia, on a scale of 0 to 10. This tool is used before and after treatment to determine whether the treatment has been effective [21].

In one of these studies, the effect was confined to children who tested positive to at least one environmental allergen by the skin prick test and the Radio Allergo Sorbent Test. In this group, *LGG* supplementation also seemed to work prophylactically [22].

The effect of probiotics in children with AD was studied by administering a probiotic complex containing *B. bifidum, L. acidophilus, L. casei*, and *L. salivarius* (each with a dose of 2×10^9 CFU) for 8 wk. The placebo group received skim milk powder and dextrose. All of the parameters including serum cytokines, eosinophil cationic protein, SCORAD index, and total serum immunoglobulin (Ig) E were measured in both the probiotic group and the placebo group at the end of 8 wk. Study results concluded that probiotic intervention in pediatric AD patients effectively reduced the SCORAD index and serum cytokines interleukin (IL)-5, IL-6, interferon (IFN)-γ, and total serum IgE levels [23].

Results from another study reported that the appropriate use of prebiotics and optimal combinations of probiotics and prebiotics (synbiotics) could bring significantly better results as part of the treatment of AD in children age ≥2 y presenting AD and with a minimum SCORAD of 15. The children were given doses of (1.2×10^9 CFU) *L. rhamnosus* Lcr35 plus a prebiotic preparation or an exclusive identically appearing prebiotic preparation, three times daily for 3 mo. Forty-eight patients with a mean SCORAD score of 39.3 were studied before the treatment and a reduction in SCORAD score ≤24 after 3 mo ($P < 0.0001$) was documented. However, no statistical differences between the two treatment groups with regard to the SCORAD score were noted. Neither were there any statistical differences in the total use of ointment between patients receiving prebiotics or synbiotics. Both synbiotics and prebiotics used alone seemed to be able to significantly improve the manifestations of AD in children ages ≥2 y [24].

Use of probiotics with SCORAD scores in adults with AD

The effects of probiotics were studied using SCORAD scores and the Dermatology Life Quality Index (DLQI), a 10-question validated questionnaire that has been used in >40 different skin conditions to evaluate the effect of the disease and treatment in patient's lives [25]. In terms of improvement, the study showed cytokine production by peripheral blood mononuclear cells (PBMCs) and the ability to modify fecal microbial flora. No significant adverse events were recorded during the study. Patients treated with probiotics showed a statistical improvement of both clinical parameters (SCORAD, $P < 0.0001$ and DLQI, $P = 0.021$) at the end of treatment compared with the placebo