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Probiotics Reduce Gut Microbial Translocation and Improve Adult Atopic Dermatitis

To the Editor:

We have carefully read the article by Iemoli et al¹ recently published in the *Journal of Clinical Gastroenterology*. We appreciate the efficacy of probiotics in the treatment of adult atopic dermatitis (AD) and take note that it could represent an adjuvant therapy for this disease. Indeed, in consideration of the fact that AD is a chronic disease leading to severe impairment of quality of life, any new effective therapy proposed is helpful for a better management of the disease.

However, we did find it somewhat surprising that no dermatologist participated in this study. We believe that some clinical and methodological aspects in this study should be clarified, which are as follows.

The SCORAD index is commonly used for the evaluation of the severity of AD, even though a proper clinical experience is required for a correct interpretation of the results; from the article, it is not clear which member of the group assessed the SCORAD and if the same investigator evaluated the SCORAD for all patients, as is the common practice in other studies.

Recently, a new severity score index for AD (the Patient Oriented SCORing Atopic Dermatitis, PO-

SCORAD)² has been validated and it seems more useful for the follow-up of AD than SCORAD. In fact, the SCORAD index represents an instantaneous image of this disease, but it is investigator-dependant.

Moreover, PO-SCORAD is easier to apply than SCORAD and it is done directly by the patient. This self-evaluation in the follow-up removes any clinical variability because of clinician observation.

In accordance with the inclusion criteria, patients were only allowed to use oral antihistamines or topical emollients. In addition, oral steroids and antibiotics or immunomodulators should be stopped, respectively, 1 month and 6 months before the start of the study. The authors did not clarify whether there was a possibility of using topical steroids during a flare, as rescue therapy, or whether it represented an exclusion criteria.

Therefore, the amount and the frequency of application of topical steroids can be considered a good marker for the evaluation of AD severity.

At baseline, patients enrolled in this double-blind study showed a very severe AD (SCORAD index value >45 in both groups). On the basis of these results, the patients in the placebo group were not given any treatment for 5 months.

In our experience and in the literature, in such cases, a withdrawal during the follow-up is frequently observed. Furthermore, at baseline, values of DLQI in the treated and in the placebo groups did not correspond to any impairment of quality of life, contrary to what can be expected in severe AD. Moreover, in patients with severe AD, itching is usually strong, disrupting both their social and working life, especially in the case of strenuous activities with heavy sweating.

AD manifestations in adults are confined to specific and localized areas of the body (hands, neck, and face). Often, there is also a concomitant allergic contact dermatitis that contributes to the severity of the AD.

In many of the patients involved in this study, AD was probably localized solely in these specific body sites. Therefore, in the cases examined, the high SCORAD index values were mainly because of the clinical severity of the involved areas, rather than to the extent of the body surface area. It would be interesting to get detailed information relative to the exact localization and extension of the lesions for each patient or for group of patients.

The authors declare that they have nothing to disclose.

What phenotype of adult AD (AD or AD associated with contact dermatitis, etc.) did show a significant improvement with probiotic therapy?

This could prove to be an important issue and might help the clinician to use probiotic treatment in AD in the proper way.

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In Response:

We really appreciated the interest shown by Raone et al¹ in our study on probiotics as adjuvant therapy in the treatment of atopic dermatitis (AD).² However, we are bewildered when the authors state that they were surprised by the fact that no dermatologists participated in the study.

Nowadays, AD is widely considered to be a multifactorial disorder and not only a disease simply limited to the skin; scientists involved in the field are convinced that only a multidisciplinary approach can give a real improvement to patients with AD.

The aim of the study was not only to evaluate SCORAD and DLQI but also, and above all, to study the immunological characteristics and any changes observed in the intestinal microflora of probiotic-treated and not treated patients.

From this point of view and to the best of our knowledge, no detailed data on the effects of the combination

of *Lactobacillus salivarius* and *Bifidobacterium breve* BR03 on T-regulatory cells, Th1 and Th2 cytokines, intestinal microflora, and intestinal colonization and fecal recovery of the administered probiotics are present.

A further strength of the study is that the probiotics combination is able to reduce intestinal permeability and decrease staphylococcal load in the feces. These last properties were considered by the referees and by many readers and experts as a crucial point for the management and outcome of the disease.

Concerning the questions of Raone and colleagues, here are our comments.

A senior allergist and clinical immunologist, as blinded investigators, led the enrollment. SCORAD index was calculated accordingly to the criteria of extension, intensity, and subjectivity provided by the score.

Design of our study was submitted to the Ethical Committee in 2009; at that time, only the study of Vourc'h-Jourdain et al³ evaluating only 15 children and 18 adults was available. These authors concluded that the study was the first step in validating the PO-SCORAD.

The paper mentioned by Raone and colleagues was published 2 years later, that is, in 2011.⁴ The same authors concluded that their study validated the use of PO-SCORAD to self-assess AD severity and demonstrated a good correlation with SCORAD. Therefore, we wonder why we have to use a method that correlates with an existing and worldwide accepted one such as SCORAD. Nonetheless, even assuming to apply it, given the paper by Stalder and colleagues was already available at the time we began the study, a comparison between PO-SCORAD and SCORAD would not have been among the purposes of the study.

Regarding the choice to avoid use of oral and topical steroids in the study, this choice was because of the willingness to reduce potential alteration of the immunological parameters induced by steroids.

Surprisingly, the DLQI in our study did not correlate with the severity of the disease. Similar observations have been reported in the literature.⁵

As described in the paper, 3 patients in the active treatment group and 2 in the placebo treatment had a diagnosis of DAC. This very small number of patients did not allow analyzing the response of different AD phenotypes to probiotic treatment.

In conclusion, we believe that AD is a disease, which needs to be better defined, where much scientific knowledge is necessary to better harmonize the various lights and shadows still present.

Only a strict cooperation between clinicians, immunologists, and microbiologists will be able to achieve consolidated results for patients health and scientific community as well.

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