

Letter to the Editor

Probiotics in spondyloarthropathy associated with ulcerative colitis: a pilot study

Dear Editor,

ulcerative colitis (UC) is an inflammatory bowel disease associated with a variety of extra-intestinal manifestations (EIMs) that may produce greater morbidity than the underlying intestinal disease and may even be the initial presenting symptoms. An arthritis affecting the spine and/or peripheral joints has been considered the most common EIM of UC. It is characterized by the absence of serum rheumatoid factor, the peripheral and axial form occurring in about 10-23% and about 10-15%, respectively¹⁻³. Articular and musculoskeletal manifestations in UC patients are included in the spondyloarthropathies (SpAs) that are a group of seronegative autoimmune related disorders with common characteristics including: ankylosing spondylitis, reactive arthritis, psoriatic arthritis, inflammatory bowel disease, some forms of juvenile arthritis and acute anterior uveitis⁴.

Evidence coming from many studies in genetically susceptible animal models of colitis suggests the crucial role of enteric flora in activating the immune system against bacterial antigens and contemporary against colonic mucosa on the basis of an antigenic cross-reactivity ("antigen mimicry"). The sharing of these colonic antigens by joints, associated with a genetic susceptibility, would lead to an immune attack against these sites^{5,6}. Several studies in animal models of experimental arthritis have demonstrated the beneficial effects of probiotics, in particular *Lactobacillus species*, on articular inflammation⁷⁻¹⁰. Preliminary results suggest that a probiotic mixture (VSL#3) may be an alternative treatment for arthralgia in patients with inflammatory bowel disease¹¹. Nevertheless, a recent internet-based randomized controlled trial in patients with SpA has showed no statistical or clinical significant improvement with the use of probiotics¹².

We performed an open-label, non-controlled study to determine if an association of probiotics, *Lactobacillus Acidophilus* (LA) and *Lactobacillus Salivarius* (LS), could improve SpA in patients with quiescent UC. Eighteen patients (10:8=F:M, mean age 49 years) with quiescent UC and active SpA received an open label association of LA and LS, two billions bacteria daily in two divided doses for four weeks. The clinical parameters evaluated included Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), assessing disease activity, Bath Ankylosing Spondylitis Functional Index (BASFI), assessing patient's functional limitations and visual analogue scale (VAS), assessing subjective pain perception. Laboratory parameters evaluated included C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). CRP was measured by a highly sensitive turbidimetric method (normal value <5 mg/L). ESR was assessed using a quantitative capillary photometry-based technology. At baseline and at the end of the study mean \pm standard deviation (SD) values were calculated. Data were analyzed using Student's t-test ($p < 0.05$ was considered significant). At baseline UC was quiescent according to UC Disease Activity Index (UCDAI), activity of SpA was documented by BASDAI score ≥ 4 .

At the end of the study a significant reduction of BASDAI score (5.8 ± 1.5 vs 4 ± 1.8 , $p < 0.05$) and VAS score (58.1 ± 16.8 vs 41.5 ± 14.3 , $p < 0.05$) was seen. No significant reduction of BASFI score (33.6 ± 10 vs 28.6 ± 6.3 , $p = 0.08$), CRP (25.2 ± 11 vs 19.8 ± 6.4 , $p = 0.08$) and ESR (28 ± 11.6 vs 22.5 ± 7.1 , $p = 0.1$) was evidenced (Table I). During the study no one of the patients had a relapse of UC or relevant adverse effects.

Table I. Mean \pm Standard Deviation (SD) Values at baseline and at the end of the study. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; VAS, visual analogue scale; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NS, not significant.

	Baseline	End	<i>p</i>
BASDAI Score	5.8 \pm 1.5	4 \pm 1.8	< 0.05
BASFI Score	33.6 \pm 10	28.6 \pm 6.3	NS
VAS Score	58.1 \pm 16.8	41.5 \pm 14.3	< 0.05
CRP (mg/L)	25.2 \pm 11	19.8 \pm 6.4	NS
ESR (mm/hr)	28 \pm 11.6	22.5 \pm 7.1	NS

These preliminary data suggest that the association of LA and LS determines a significant reduction in SpA activity and in patient's perception of pain. Moreover, these bacteria don't induce relapse of intestinal disease as non-steroidal anti-inflammatory drugs (NSAIDs) can do¹³. We believe that these probiotics may give a contribute in the management of SpA in patients with UC. However, controlled randomized clinical trials are necessary to confirm these results.

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