

Synbiotic Supplementation May Relieve Anterior Uveitis, an Ocular Manifestation in Behcet's Syndrome

A **Gholamreza Askari**
ABE **Amir Reza Moravejolahkami**

Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, I.R. Iran

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G





Corresponding Author: Amir Reza Moravejolahkami, e-mail: a.moravej@mail.mui.ac.ir
Conflict of interest: None declared

Patient: Female, 49
Final Diagnosis: Behcet's syndrome (with anterior uveitis)
Symptoms: Ocular problems: redness • tearing • severe pain • photophobia • blurred vision
Medication: Synbiotic supplementation
Clinical Procedure: —
Specialty: Nutrition and Dietetics

Objective: Rare disease
Background: To relieve the signs and symptoms of anterior uveitis (AU), an ocular manifestation of Behcet's syndrome, we prescribed a synbiotic supplementation (probiotics and prebiotics) for a 49-year-old woman.
Case Report: Seven strains of bacteria – *Lactobacillus casei*, *Lactobacillus rhamnosus*, *Streptococcus thermophilus*, *Bifidobacterium breve*, *Lactobacillus acidophilus*, *Bifidobacterium longum*, and *Lactobacillus bulgaricus*, each 10⁸ colony-forming units (CFU) – and fructo-oligosaccharide (FOS; 100 mg) were given as a capsule 2 times per day. After 7-month treatment, AU was improved and serum inflammatory markers – C-reactive protein (CRP), high-sensitivity CRP (hs-CRP), and estimated sedimentation rate (ESR) – were suppressed. Now, if a mild AU attack occurs, the problem is resolved by treatment with 1 gtt (from the Latin “guttae”, meaning drops) eye drop (prednisolone 1%) for 1 week.
Conclusions: Synbiotic supplementation may contribute to treating AU, which is one of the most disastrous manifestations of BS, by controlling the proinflammatory processes.

MeSH Keywords: Behcet Syndrome • Prebiotics • Probiotics • Synbiotics • Uveitis, Anterior

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/912023>

 1008  1  —  11



Background

Behcet's syndrome (BS) is a chronic, multi-systemic disorder characterized by oral and genital ulcers, as well as other manifestations in other organs, mainly in the skin and the eyes [1]. The prevalence of this disease is wide-ranging from East to West, and countries on the "Silk Road" have the highest prevalence rates. Ocular manifestations include anterior uveitis (AU), posterior uveitis (PU), retinal vasculitis (RV), and, partially, conjunctivitis and cataracts. Uveitis appears as the first manifestation in 8.6% of patients living in Iran, and, in rare situations, the time between the first and the second manifestation can be several years [2].

An inflammation of the uveal duct, called uveitis, is one of the most important manifestations of Behcet's syndrome, and is responsible for 15–10% of the most severe vision problems in Western countries [3].

The microbial environment of the digestive system is an active component of the immune system, protects health from birth and throughout life [4,5]. A case-control study by Consolandi et al. found a particular state of dysbiotic gut microbiota, as well as a decrease in the number of bacteria producing butyrate, in patients with Behcet's syndrome [6].

Here, we report a BS patient with frequent uveitis attacks who was received synbiotic supplementation. The positive effects on this patient are a key point of our discussion.

Case Report

A 49-year-old woman presented to our rheumatology outpatient clinic with a special referral from an ophthalmologist (August 2, 2017; unilateral AU diagnosis without retinitis or iritis; symptoms: redness, tearing, severe pain, photophobia, blurred vision) on August 16, 2017. An expert rheumatologist had believed that in this rare case, the first clinical manifestation of Behcet's syndrome (BS) was AU, and other manifestations would probably show up in the future. According to the revised International Criteria for Behcet's Disease (rICBD) [7], skin manifestations, neurological manifestations, and vascular manifestations each get 1 point. Genital aphthous (GA), oral aphthosis (OA) and ocular lesions each get 2 points. With 3 points or more, the patient is classified as having BS. In this case, ocular manifestation and pathergy test were positive, so the score of rICBD [7] was 3. In addition, HLA B5 (human leukocyte antigen) was positive, HLA B27 and B51 were negative, and ESR (estimated sedimentation rate), CRP (C-reactive protein), hs-CRP (high-sensitivity CRP), and R. F. (rheumatoid Factor) were high or close to high; therefore, the BS diagnosis became more definitive.

Treatment with Azathioprine 50 mg BID (from the Latin "bis in die", twice a day) and Prednisolone 5 mg QD (from the Latin "quaque die", once a day) was started; however, after 1 month, an eye attack recurred. Injection of methyl prednisolone 40 mg/mL Stat was the only way to suppress the attacks. At the last visit by the rheumatologist on September 21, 2017, the above drugs were repeated and colchicine 1 mg was added. Due to concerns about the recurrence of breast cancer, the drugs were tapered off slowly. The patient was referred to a dietitian on October 23, 2017.

We decided to start synbiotic therapy. The administered capsules contained 7 strains of live bacteria as a probiotic (*Lactobacillus casei*, *Lactobacillus rhamnosus*, *Streptococcus thermophilus*, *Bifidobacterium breve*, *Lactobacillus acidophilus*, *Bifidobacterium longum*, and *Lactobacillus bulgaricus*) with a dose of 10^8 colony-forming units (CFU) and concentrated fructo-oligosaccharide (FOS) 100 mg as a prebiotic, which were taken BID.

In the first month of prescribing the synbiotic, 1 less intense eye attack occurred and was controlled with eye drops (prednisolone 1%≈1 gtt QID for 1 week) and atropine ophthalmic 1%≈3 times a day for 2 days. The second attack occurred with a longer interval – about 3 months later – which was corrected with a smaller dose of eye drop (prednisolone 1%≈1 gtt BID for 1 week). Seven months after the start of treatment with synbiotic (2 months after the last attack), no other attack occurred, except for mild pain at the top of the left eyelid, which was controlled by 1 gtt eye drop (prednisolone 1%) per week until recovery. In addition to suppressing systemic inflammation (Table 1), symptoms like redness, photophobia, tearing, and the sign of hypopyon were not observed after November 25, 2017.

Discussion

Here, we report the successful effects of 7-month synbiotic therapy prescribed for a 49-year-old woman with ocular manifestation of BS called AU. Administration of 7 strains of probiotic bacteria accompanied by FOS prebiotic improved physical symptoms, signs, and serum inflammatory markers.

BS is a rare disease with dangerous consequences such as blindness. Immunosuppressive agents are typically used as a first-line treatment, but the adverse effects of these drugs are problematic in some cases. The advantages of synbiotic supplementation have not been completely studied before, but here we attempt to explain this for the first time in humans. Horai et al., in an animal model of autoimmune uveitis, reported: "Retina-specific T cells receive an activation message from microbiota-derived antigen(s) in a state of dysbiosis, and this message leads to autoimmune uveitis" [8]. In another

Table 1. Biochemical evaluation during follow-up.

	ESR 1 h, mm	Neu count, 10 ⁹ /L	PLT, 1000/ μ L	CRP, mg/L	hs-CRP, mg/L	R.F, IU/ml	FBS, mg/dL
Aug 5, 2017	14	5.4	276	5.7	4.52	13.3	98
Dec 25, 2017	–	–	–	–	4.31	–	89
May 20, 2018	3	5.4	208	0.4	2.81	–	92

ESR – estimated sedimentation rate; Neu – neutrophil; PLT – platelets; CRP – C-reactive protein; hs-CRP – high-sensitivity CRP; R.F – rheumatoid factor; FBS – fasting blood glucose; ‘–’ – lack of data due to the patient's agitation and inability to take blood in the lab, so it was not possible to conduct these tests ethically.

animal interventional study with 5 bacterial strains (*L. casei*, *L. acidophilus*, *L. reuteri*, *B. bifidum*, and *S. thermophiles*; 10⁹ CFU for 3 weeks), Kim et al. indicated that administration of probiotics can modify the clinical manifestations of autoimmune uveitis. Increasing the percentage of Treg cells in the intervention group was significant [9]. This is the closest study to ours until now.

The results of the present study conflict with some previous reports. Shimizu et al. observed the relative abundance of genera *Bifidobacterium*, *Eggerthella* and *Lactobacillus* species in BD patients compared to normal adults, and considered this condition as a dysbiosis [10], and rapid onset of rheumatoid arthritis

in germ-free mice, induced by oral intake of *Lactobacillus bifidus*, was reported by Abdollahi-Roodsaz et al. [11].

Conclusions

Synbiotic therapy, possibly by suppressing systemic inflammation, may relieve signs and symptoms of AU and create a new complementary therapy for BS.

This study has not been published or submitted elsewhere. The authors received no financial support for the research and/or authorship of this article. The authors declare that they have no conflict of interest regarding the publication of this article.

References:

- Addimanda O, Pazzola G, Pipitone N, Salvarani C: Epidemiology of Behçet syndrome. In: Emmi L (ed.), Behçet's syndrome: From pathogenesis to treatment. 1st ed. Florence, Italy, Springer Science & Business Media, 2014; 17–24
- Davatchi F, Chams-Davatchi C, Shams H et al: Behçet's disease: Epidemiology, clinical manifestations, and diagnosis. *Expert Rev Clin Immunol*, 2017; 13(1): 57–65
- Miserocchi E, Fogliato G, Modorati G, Bandello F: Review on the worldwide epidemiology of uveitis. *Eur J Ophthalmol*, 2013; 23(5): 705–17
- Candela M, Biagi E, Turrioni S et al: Dynamic efficiency of the human intestinal microbiota. *Crit Rev Microbiol*, 2015; 41(2): 165–71
- Centanni M, Turrioni S, Consolandi C et al: The enterocyte-associated intestinal microbiota of breast-fed infants and adults responds differently to a TNF-alpha-mediated pro-inflammatory stimulus. *PLoS One*, 2013; 8(11): e81762
- Consolandi C, Turrioni S, Emmi G et al: Behçet's syndrome patients exhibit specific microbiome signature. *Autoimmun Rev*, 2015; 14(4): 269–76
- Davatchi F, Abdollahi BS, Chams-Davatchi C et al: Validation of the revised International Criteria for Behçet's Disease (ICBD) in Iran. *Clin Rheumatol*, 2015; 34(2): 315–20
- Horai R, Zarate-Blades CR, Dillenburg-Pilla P et al: Microbiota-dependent activation of an autoreactive T cell receptor provokes autoimmunity in an immunologically privileged site. *Immunity*, 2015; 43(2): 343–53
- Kim J, Choi SH, Kim YJ et al: Clinical effect of IRT-5 probiotics on immune modulation of autoimmunity or alloimmunity in the eye. *Nutrients*, 2017; 9(11): pii: E1166
- Shimizu J, Kubota T, Takada E et al: Bifidobacteria abundance-featured gut microbiota compositional change in patients with Behçet's disease. *PLoS One*, 2016; 11(4): e0153746
- Abdollahi-Roodsaz S, Joosten LA, Koenders MI et al: Stimulation of TLR2 and TLR4 differentially skews the balance of T cells in a mouse model of arthritis. *J Clin Invest*, 2008; 118(1): 205–16