

## **Effect of probiotic and prebiotic on psychological outcomes in patients with major depressive disorder: A randomized clinical trial**

Kurosh Djafarian<sup>1</sup>, Asma Kazemi<sup>1</sup>, Ahmad Ali Noorbala<sup>2</sup>

<sup>1</sup>*Department of clinical nutrition, School of Nutritional Sciences and Dietetic, Tehran University of Medical Sciences, Tehran, Iran;* <sup>2</sup>*Psychosomatic Medicine Research Center, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran;*

**Background:** Major depressive disorders have been associated with potential psychological outcomes, but there are few data on the effects of probiotics and prebiotics on these outcomes.

**Objective:** The aim of this double blind, placebo-control trial, was to investigate the effect of prebiotic and probiotic on serum inflammatory cytokines (TNF- $\alpha$ , IL-1 $\beta$ , IL-6 and IL-10), Beck Depression Inventory (BDI) score, serum kynurenine/tryptophan ratio and tryptophan/BCAAs ratio, BMI, and urinary cortisol in patients with major depressive disorder (MDD).

**Design:** One hundred and ten depressed patients were randomized to receive the probiotic (*Lactobacillus helveticus* and *Bifidobacterium longum*), prebiotic (galactooligosaccharide) or placebo for 8 weeks. BDI score was determined by means of a self-compiled questionnaire. Serum tryptophan and BCAAs were measured by HPLC, kynurenine and leptin by ELISA kits and urinary cortisol via chemiluminescence.

**Results:** A total of 81 subjects completed the trial (28 in the probiotic group, 27 in the prebiotic group, and 26 in the placebo group). Patients in probiotic group resulted in a significant decrease in BDI score ( $17.39\pm 9.1$ ) compared to the placebo ( $18.18\pm 15.55$ ) and prebiotic ( $19.72\pm 14.14$ ).

Inter-group comparison indicated no significant differences among the groups in terms of serum kynurenine/tryptophan ratio and tryptophan/BCAAs ratio. However, the kynurenine/tryptophan ratio decreased in the probiotic compared to the placebo group (0.036) and the tryptophan/BCAAs ratio decreased in the prebiotic compared to the placebo group (0.031). Moreover, the tryptophan/iso-leucine ratio increased significantly in the probiotic ( $p=0.018$ ) and prebiotic (0.025) group when compared to the placebo. No significant difference in both BMI and weight was seen among the groups.

**Conclusion:** This study confirmed that probiotic supplements for 8 weeks among MDD patients resulted in an improvement in BDI score whereas prebiotic administration had no significant effect on BDI score. Probiotic decreased serum kynurenine/tryptophan ratio while prebiotic decreased serum tryptophan/BCAAs ratio. Supplementations had no significant effects in modulating inflammatory marker levels and urinary cortisol in MDD patients.

Key words: probiotic, prebiotic, major depressive disorders.