

## Elevated cholinergic activity in irritable bowel syndrome: A potential biomarker?

K. Hod<sup>1,2</sup>, A.D. Sperber<sup>3</sup>, N. Maharshak<sup>4</sup>, R. Yishay<sup>4</sup>, N. Waiskopf<sup>5</sup>, Y. Friedler<sup>5</sup>, I. Shapira<sup>6</sup>, D. Zeltser<sup>6</sup>, O. Rogowski<sup>6</sup>, H. Soreq<sup>5</sup>, S. Berliner<sup>6</sup>, S. Shenhar-Tsarfaty<sup>6</sup>, R. Dekel<sup>4</sup>

<sup>1</sup>*Department of Epidemiology and Preventive Medicine, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Israel*

<sup>2</sup>*Research Division, Epidemiology Service, Assuta Medical Centers, Israel*

<sup>3</sup>*Faculty of Health Sciences, Ben-Gurion University of the Negev, Israel*

<sup>4</sup>*Department of Gastroenterology and Liver Diseases, Tel-Aviv Sourasky Medical Center, Israel*

<sup>5</sup>*Department of Biological Chemistry, The Life Sciences Institute and the Edmond and Lily Safra Center of Brain Science, The Hebrew University of Jerusalem, Israel*

<sup>6</sup>*Internal Medicine 'C', 'D' and 'E', Tel Aviv Sourasky Medical Center, Israel*

Background and aims: Micro-inflammation is an element in the pathogenesis of irritable bowel syndrome (IBS). The parasympathetic nervous system, via Acetylcholine (ACh) and the ACh hydrolytic enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), exerts anti-inflammatory effects. Increased serum cholinesterase activity (Cholinergic Status, CS) is associated with decreased inflammatory inhibition (pro-inflammation). We assessed associations between CS, IBS and the putative anti-inflammatory effect of probiotics. Methods: We compared cholinergic parameters between women with diarrhea-predominant IBS (IBS-D) and healthy female volunteers (HV) who participated in a randomized, double blind, placebo-controlled trial of IBS-D treated with a probiotic or placebo for 8 weeks. Cholinergic parameters were evaluated at baseline, 4 and 8 weeks. Results: One hundred women with IBS-D and 116 HV participated. CS and AChE activity were significantly higher in the IBS-D than the HV group (1754 [1526 -1962] vs. 1049 [968 -1159] mmol/min\*ml, respectively for CS, P0.001). Both tests discriminated accurately between IBS-D and HV (sensitivity, specificity, positive and negative predictive values of 96.0%, for AChE). The probiotic group showed reduced cholinergic parameters at weeks 4 and 8 compared to baseline. Conclusions: CS and AChE activities were elevated in women with IBS-D treated with probiotics, compared to HV. CS may be a useful biomarker for IBS-D and may offer a new perspective on the mechanism of action of probiotics. Thus, further studies into the potential role of CS as a biomarker for IBS and its relation to the mechanism of action of probiotics on IBS-D are justified.