Effect of Probiotics on Serum Cytokines in Irritable Bowel Syndrome with Gulf War Illness

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Background

- The symptoms of Gulf War (GW) illness include chronic widespread pain, cognitive difficulties, unexplained fatigue, memory and concentration problems, as well gastrointestinal (GI) symptoms including irritable bowel syndrome (IBS).
- IBS occurs in up to 30% of Gulf War (GW) Veterans
- There is inconsistent evidence that low-grade chronic gastrointestinal (GI) inflammation may play a part in the pathogenesis of IBS and GWI.

Aim

- The aim of this study was to examine the blood cytokine profiles of Veterans with IBS and GW illness before and after treatment with probiotics. (De Simone Formulation; formally known as VSL#3 and Visbiome).
- A multiplexed immunoassay was used to assess the serum concentration of 13 cytokines/ inflammatory markers: interferon (IFN)-γ; interleukins (ILs)-1β, 2, 4, 5, 6, 8, 10, 12, 13, and 17; tumor necrosis factor (TNF-α) and IL-2 receptor.
- This is secondary analysis of our previously published study on the Effect of probiotics on IBS with Gulf War illness

Methodology

- GW Veterans who served in Operation Desert Storm between August 1990 and March 1991 were enrolled in this study.
- The study population consisted of GW Veterans who had IBS and two or more of the non-intestinal symptoms (e.g., fatigue, joint pains, insomnia, general stiffness, and headache) of GW illness.
- In a randomized double-blind placebo controlled trial, we enrolled Veterans with IBS and two or more symptoms of GWI.
- Rome III criteria were used to define IBS and its subtypes.
- Veterans were randomized to receive probiotic (De Simone Formulation; formally known as VSL#3) or an identical placebo.
- Blood was collected at enrollment and after 8-week treatment with probiotics.
- The cytokine levels were compared to reference intervals established on 120 healthy controls.

Statistical Methods:

We compared the baseline to post-treatment changes between the placebo and probiotic groups using a two-sample Wilcoxon-Mann-Whitney test.

We describe the changes with the median and interquartile range (IQR), where IQR is the 25-th and 75-th percentiles.

Results

Table. Cytokine values of patients with IBS and GW illness*
*The cytokine values in IBS are no different from normal controls.

measure	statistic	total sample baseline [n=39]	normal reference range, pg/mL
IL-13	out of range, n (%)	9 (23)	≤2.3
	mean±SD	2.5±6.4	
	median (IQR)	0 (0 , 2.0)	
IL-17	out of range, n (%)	3 (8)	≤1.4
	mean±SD	0.6±2.3	
	median (IQR)	0 (0 , 0.5)	
IL-4	out of range, n (%)	2 (5)	≤2.2
	mean±SD	0.2±0.6	
	median (IQR)	0 (0 , 0.3)	
IL-2R	out of range, n (%)	2 (5)	175.3 – 858.2
	mean±SD	485.4±214.4	
	median (IQR)	426.2 (303.5 , 621.3)	
IL-6	out of range, n (%)	2 (5)	≤2.0
	mean±SD	0.6±0.7	
	median (IQR)	0.3 (0.2 , 0.7)	
TNFα	out of range, n (%)	1 (3)	≤7.2
	mean±SD	1.1±1.8	
	median (IQR)	0.4 (0 , 0.7)	
IL-12	out of range, n (%)	0 (0)	≤1.9
	mean±SD	0.1±0.3	
	median (IQR)	0 (0 , 0)	
IL-2	out of range, n (%)	0 (0)	≤2.1
	mean±SD	0.1±0.2	
	median (IQR)	0 (0 , 0)	
IL-10	out of range, n (%)	1 (3)	≤2.8
	mean±SD	1.0±0.5	
	median (IQR)	1.0 (0.7 , 1.3)	
IL-5	out of range, n (%)	1 (3)	≤2.1
	mean±SD	0.1±0.4	
	median (IQR)	0 (0, 0.04)	
IL-1β	out of range, n (%)	1 (3)	≤6.7
	mean±SD	0.8±2.6	
	median (IQR)	0 (0, 0)	
IFNγ	out of range, n (%)	0 (0)	≤4.2
	mean±SD	0.1±0.4	
	median (IQR)	0 (0, 0)	
IL-8	out of range, n (%)	0 (0)	≤3.0
	mean±SD	0.03±0.1	
	median (IQR)	0 (0, 0)	

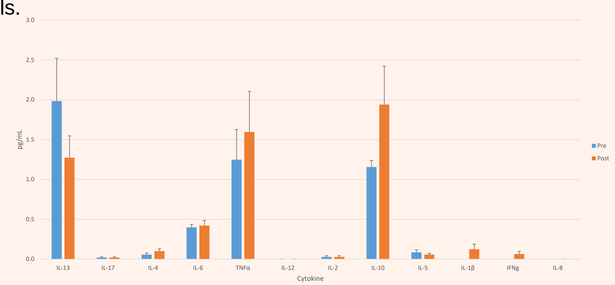

Figure: Comparison of Pre and Post treatment with probiotics cytokines (mean±SE)

- Data was analyzed from 42 Veterans who provided baseline and 11 Veterans who provided both pre and post treatment blood samples for cytokine analysis.
- The serum pro- and anti-inflammatory cytokines levels were no different between IBS with GWI and healthy controls. (Table)
- There was no change in pro- or anti-inflammatory cytokines after treatment with probiotics (Figure).

Conclusion

- The level of pro- and anti-inflammatory cytokines were no different in Veterans with IBS and GWI compared with healthy controls.
- The levels of cytokines are not altered after treatment with probiotics.

Clinical Implications:

- The role of cytokines in the pathophysiology, and as a biomarker of treatment of IBS and GWI is likely complex and remains unknown.

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