

Title: The beneficial effects of probiotics in peritoneal dialysis patients.

I-Kuan Wang^{1,2}, Ya-Fei Yang², I-Wen Ting², Chung-Chih Lin², Yao-Lung Liu², Che-Yi Chou², Jiung-Hsiun Liu², Shih-Yi Lin², Hung-Chih Lin³, and Chiu-Ching Huang²

¹Graduate institute of clinical medical science, College of medicine, China medical University, ²Division of nephrology, China medical university hospital, ³Department of pediatrics, China medical university hospital.

Background

Inflammatory markers such as interleukin 6 (IL-6) and tumor necrosis factor- α (TNF- α) are elevated in dialysis patients and can predict cardiovascular events and all-cause mortality. Endotoxin is an important source and another marker of inflammation in patients with chronic kidney disease. The aim of this study was to evaluate the impact of oral probiotics on serum levels of cytokines and endotoxemia in peritoneal dialysis (PD) patients.

Materials and methods

From March 2011 to June 2012, a randomized, double-blind, placebo-controlled trial was conducted in PD patients at China Medical University Hospital. After obtaining informed consent, the intervention group received probiotics containing 10^9 colony-forming units (CFU) *B. bifidum* A218, 10^9 CFU *B. catenulatum* A302, 10^9 CFU *B. longum* A101, and 10^9 CFU *L. plantarum* A87 daily for six months, while the placebo group received similar capsules containing maltodextrin for the same duration. Levels of serum TNF- α , INF- γ , IL-5, IL-6, IL-10, IL-17, and endotoxin were measured before and six months after intervention.

Results

Thirty-nine patients completed the study (21 in the probiotics group and 18 in the placebo group). In patients receiving probiotics, levels of serum TNF- α , IL-5, IL-6, and endotoxin significantly decreased after six months of treatment, while levels of serum IL-10 significantly increased. In contrast, there were no significant changes in levels of serum cytokines and endotoxin in the placebo group after six months.

Conclusions

Probiotics could significantly reduce the serum levels of endotoxin, pro-inflammatory cytokines (TNF- α and IL-6), IL-5, and increase the serum levels of anti-inflammatory cytokine (IL-10) in PD patients.

Table 1. Baseline demographic and laboratory characteristics

	Probiotics (n = 21)	Placebo (n = 18)	p value
Age (year)	47.9 \pm 12.4	51.7 \pm 10.7	0.313
Sex (male/female)	10/11	8/10	0.999
Automatic peritoneal dialysis	7 (33.3%)	3 (16.7%)	0.299
Diabetes	4 (19.1%)	4 (22.2%)	0.999
Hypertension	19 (90.5%)	13 (72.2%)	0.216
Coronary artery disease	3 (14.3%)	5 (27.8%)	0.432
Chronic hepatitis B	1 (4.8%)	2 (11.1%)	0.586
Chronic hepatitis C	0 (0%)	1 (4.2%)	0.461
Dialysis duration (month) (range)	39.5 \pm 32.9 (2-124)	48.8 \pm 29.4 (2-96)	0.361
BMI (kg/m ²)	22.9 \pm 4.1	24.3 \pm 3.3	0.038
Statin use	7 (33.3%)	4 (22.2%)	0.497
ACEI/ARB use	14 (66.7%)	8 (44.4%)	0.206
Icodextrin use	5 (23.8%)	5 (27.8%)	0.999
Smoking	4 (19.1%)	0 (0%)	0.110
Hemoglobin (g/dL)	10.6 \pm 1.7	9.8 \pm 1.6	0.104
Albumin (g/dL)	3.8 \pm 0.3	3.7 \pm 0.3	0.539
nPNA	1.1 \pm 0.2	1.0 \pm 0.2	0.222
Kt/V (total)	2.1 \pm 0.3	2.1 \pm 0.3	0.966
Kt/V (renal)	0.4 \pm 0.4	0.3 \pm 0.4	0.597
TNF- α (pg/ml)	1.94 (0.76 to 3.28)	1.61 (0.95 to 2.78)	0.735
INF- γ (pg/ml)	7.67 (4.33 to 11.66)	8.5 (3.67 to 39.65)	0.508
IL-5 (pg/ml)	15.02 (10.94 to 21.05)	12.39 (9.88 to 21.33)	0.622
IL-6 (pg/ml)	2.93 (1.21 to 6.75)	1.07 (0.33 to 2.7)	0.083
IL-10 (pg/ml)	13.15 (10.22 to 19.31)	15.55 (13.99 to 19.5)	0.422
IL-17 (pg/ml)	2.7 (1.66 to 4.01)	2.81 (1.48 to 4.01)	0.866
Endotoxin (EU/ml)	1.61 (0.52 to 2.59)	0.35 (0.28 to 0.82)	0.007

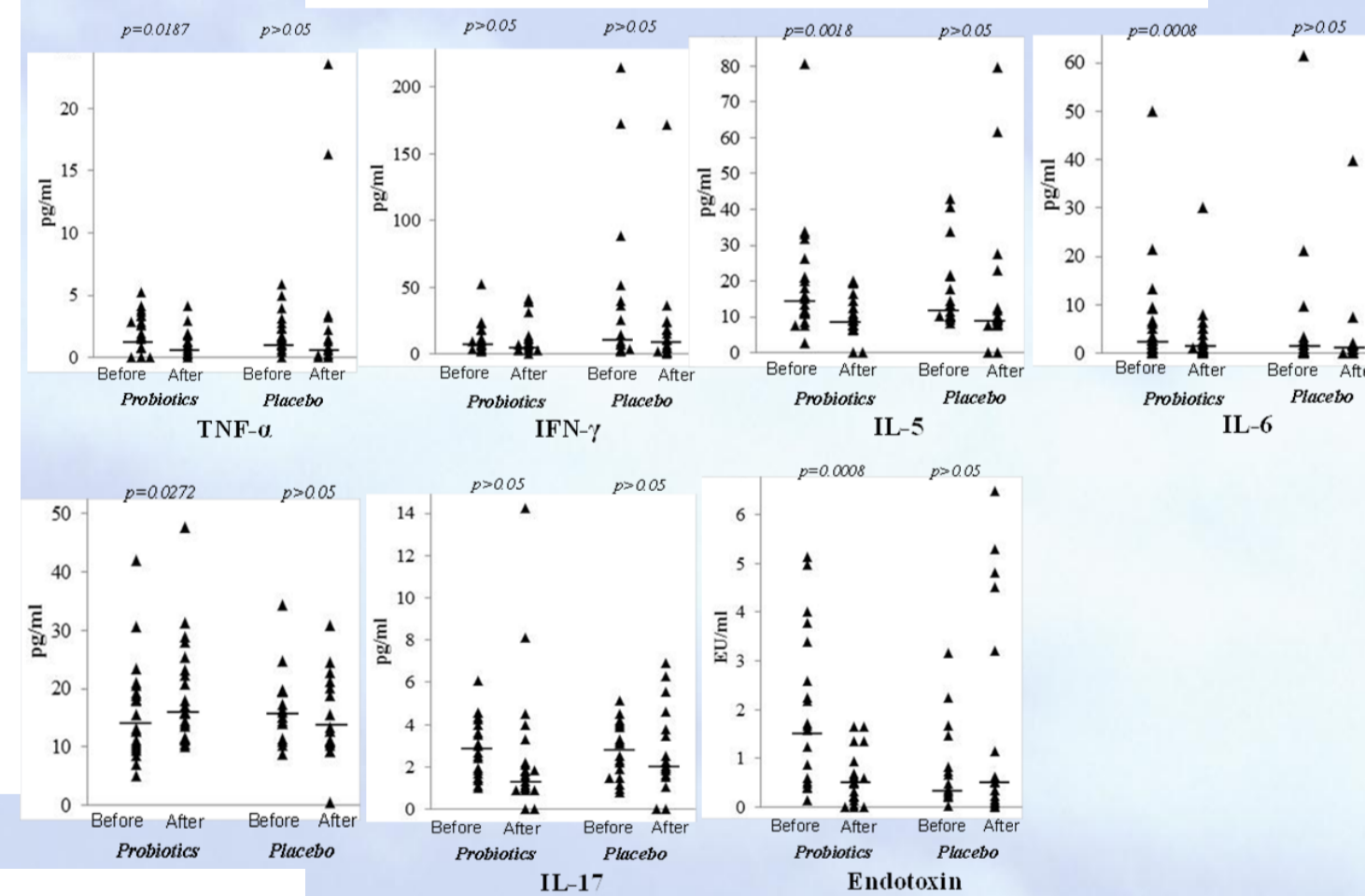
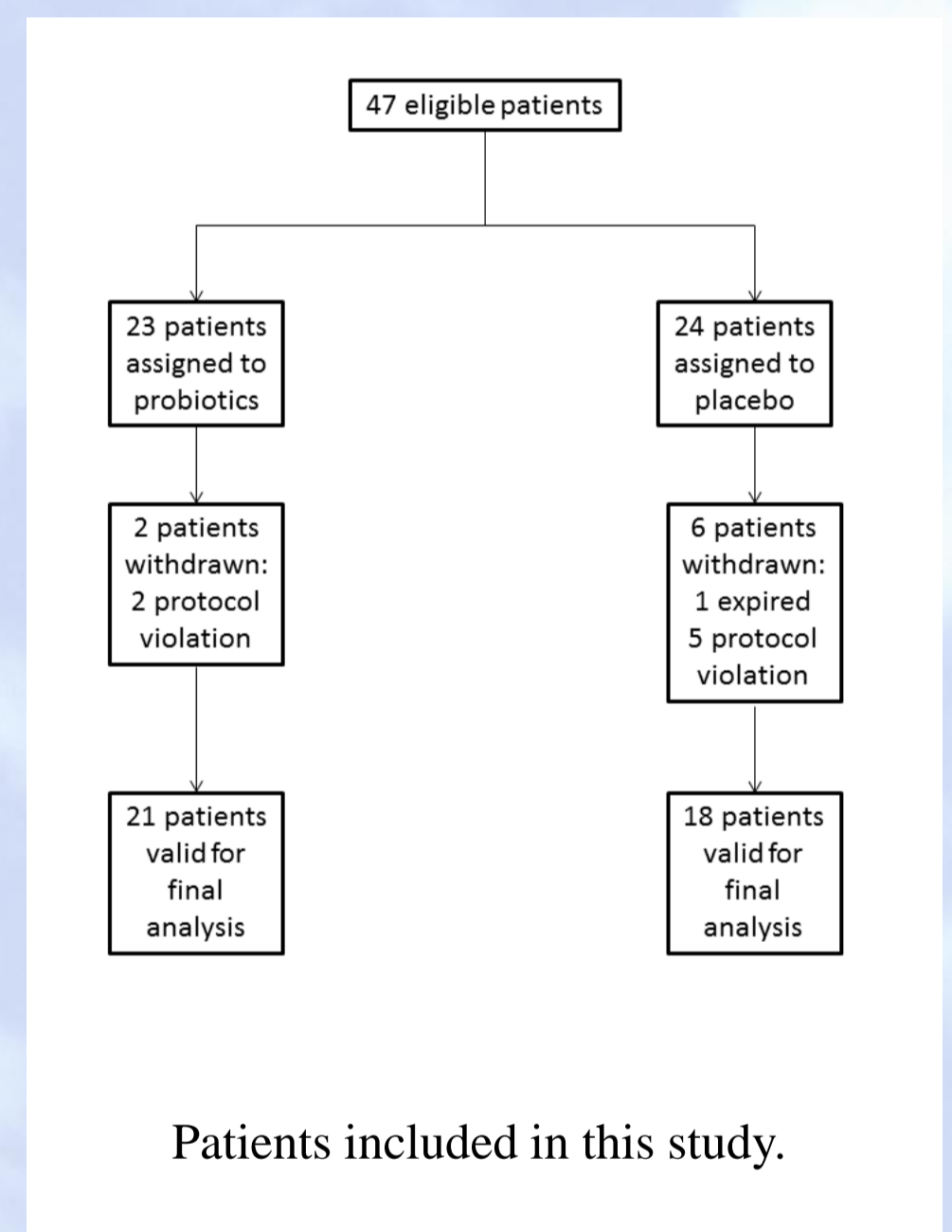
Values are mean \pm SD or median and interquartile range in parentheses.

BMI, body mass index; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; nPNA, normalized protein nitrogen appearance.

Table 2. Changes in cytokines and endotoxin after six months of treatment

	Probiotics			Placebo		
	Basal	Final	P value	Basal	Final	P value
TNF- α (pg/ml)	1.94 (0.76 to 3.28)	0.74 (0.41 to 1.29)	0.019	1.61 (0.95 to 2.78)	0.74 (0.18 to 2.22)	0.611
INF- γ (pg/ml)	7.67 (4.33 to 11.66)	7 (4 to 12)	0.712	8.5 (3.67 to 39.65)	8.67 (2 to 18.66)	0.410
IL-5 (pg/ml)	15.02 (10.94 to 21.05)	9.19 (7.68 to 12.61)	0.002	12.39 (9.88 to 21.33)	9.6 (7.99 to 12.6)	0.369
IL-6 (pg/ml)	2.93 (1.21 to 6.75)	1.12 (0.75 to 3.93)	<0.001	1.07 (0.33 to 2.7)	0.95 (0.11 to 1.7)	0.154
IL-10 (pg/ml)	13.15 (10.22 to 19.31)	15.97 (13.47 to 23.17)	0.027	15.55 (13.99 to 19.5)	12.69 (10.25 to 20.02)	0.090
IL-17 (pg/ml)	2.7 (1.66 to 4.01)	1.61 (0.98 to 2.2)	0.085	2.81 (1.48 to 4.01)	2.13 (1.61 to 3.8)	0.932
Endotoxin (EU/ml)	1.61 (0.52 to 2.59)	0.51 (0.2 to 0.69)	<0.001	0.35 (0.28 to 0.82)	0.51 (0.16 to 3.2)	0.495

Values are medians and interquartile ranges are in parentheses.



The distribution of serum levels of cytokines and endotoxin in peritoneal dialysis patients before and after treatment.

