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Effects of Lactobacillus GG supplementation in type 2 diabetes: Are mucin genes expressions important?

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Abstract:
Background and aims: Recent studies indicate that dysbiosis of gut microbiota and low grade inflammation are important pathogenic determinants of type 2 diabetes (T2DM). Probiotics have been used in T2DM for the modification of intestinal microbiota and anti-inflammatory effects. This study was designed to determine the effects of *Lactobacillus GG* (LGG) on glycemic control, lipid profile, inflammation parameters and expression of certain genes linked to T2DM.
Materials and methods: This placebo-controlled clinical trial included 34 women with T2DM aged 30-60 years who were followed in Diabetes Outpatient Clinic, Istanbul Faculty of Medicine. Subjects were randomly assigned to take either probiotic ($1x10^{10}$ cfu LGG) or placebo for 8 weeks. Fasting blood samples were taken at baseline and post-treatment to measure glycemic and lipid profile, and biomarkers of inflammation. TLR2, TLR4, MUC2 and MUC3A genes expressions were investigated on stool samples at baseline and post-treatment. 3-day food records were taken at 4th and 8th weeks.
Results: There was no significant difference in daily energy intake between placebo and probiotic groups during the study; however daily fat intake, body weight, BMI, percent body fat and mass in the probiotic group were significantly decreased ($p<0.05$). Fasting blood glucose was significantly decreased in both groups ($p<0.05$), but there was no difference between the groups. HbA1c was insignificantly decreased in both groups. Fructosamine and insulin did not change in the probiotic group. Total and LDL-cholesterol levels reduced in both groups, but only total cholesterol was significant in the probiotic group ($p<0.05$). CRP and IL-6 did not change in both groups. In the probiotic group, expressions of MUC2 and MUC3A increased significantly ($p<0.05$), while the increase in TLR2 expression was not significant, and TLR4 expression levels did not change.
Conclusion: In our study, we investigated the effects of a single probiotic strain for 8 weeks in T2DM. However, there was no direct effect on the glycemic profile, LGG supplementation could be beneficial in T2DM due to inducing weight loss and increasing the expression of MUC2 and MUC3A (mucin) genes which are involved in maintaining the intestinal barrier. Before we generalize our results large, randomized-controlled prospective trials are needed to evaluate the effects of probiotics (especially LGG) in T2DM.

Table 1. Comparison of anthropometric and biochemical parameters of probiotic and placebo groups at baseline and post-treatment

Biochemical Parameters		Probiotic group (n=17) Ave ±SD; M (min-maks) *Baseline*	*Post-treatment*	Placebo group(n=17) Ave ±SD; M (min-maks) *Baseline*	*Post-treatment*	Probiotic group p value*	Placebo group p value*
Anthropometric measurements	**Weight (kg)**	87,75±14,07; 88,70 (62,60-110,50)	85,75±14,31; 85,10 (59,70-108,10)	80,99±14,70; 74,50 (60,80-113,10)	79,27±14,89; 73,50 (63,30-112,10)	***0.014***	0.121
	BMI (kg/m²)	35,51±7,33; 33,48 (25,08-48,20)	34,70±7,35; 32,50 (23,91-48,51)	33,65±6,17; 31,14 (24,68-44,01)	32,76±6,15; 31,44 (24,96-44,28)	***0.017***	0.140
Glycemic profile	**Fasting blood glucose (mg/dL)**	123,00±32,00; 113,00 (92,00-210,00)	115,82±26,07; 104,00 (87,00-188,00)	145,56±50,35; 134,50 (92,00-282,00)	128,68±44,39; 118,50 (88,00-268,00)	***0.049***	***0.028***
	Fructosamine (µmol/L)	2,92±0,52; 2,74 (2,38-3,95)	2,88±0,41; 2,81 (2,39-3,88)	3,33±0,96; 3,06 (2,55-6,08)	3,18±0,86; 2,89 (2,31-5,59)	0.900	***0.028***
	Insulin (µU/mL)	14,96±9,62; 11,88 (3,89-36,04)	13,46±8,60; 12,16 (2,91-37,39)	18,58±10,87; 18,10 (3,44-44,80)	15,19±10,26; 14,00 (3,20-47,73)	0.435	***0.026***
	HbA1c (%)	6,75±1,21; 6,40 (5,40-10,10)	6,60±1,00; 6,40 (5,30-9,30)	7,31±1,98; 6,55 (5,40-13,30)	7,10±1,69; 6,50 (5,50-12,10)	0.209	0.101
Lipid profile	**HDL (mg/dL)**	46,81±8,81; 45,00 (33,00-65,00)	44,87±6,07; 42,50 (35,00-56,00)	47,53±8,79; 46,00 (34,00-68,00)	45,62±9,46; 43,00 (35,00-71,00)	0.776	0.344
	LDL (mg/dL)	131,25±26,99; 130,50 (77,00-182,00)	122,81±28,62; 117,50 (59,00-169,00)	151,25±48,68; 150,00 (94,00-252,00)	126,06±31,05; 119,00 (80,00-193,00)	0.070	***0.011***
	Total cholesterol (mg/dL)	203,31±36,23; 203,50 (130,00-277,00)	188,25±39,85; 181,50 (109,00-251,00)	221,50±51,99; 221,00 (160,00-329,00)	194,62±35,04; 190,00 (150,00-268,00)	***0.052***	***0.004***
Inflammation parameters	**CRP (mg/L)**	6,44±7,11; 3,43 (0,25-24,33)	6,44±7,15; 3,43 (0,25-24,33)	6,28±3,94; 6,02 (1,33-12,85)	6,30±3,70; 5,54 (1,04-12,84)	0.326	0.889
	IL-6 (pg/mL)	7,85±4,67; 7,66 (0,58-18,56)	9,46±6,42; 7,66 (1,76-27,39)	13,53±9,85; 10,60 (4,71-42,11)	11,25±6,38; 10,60 (4,12-30,34)	0.334	0.422

**Statistically significant p values (p<0.05) are shown with italic and bold.*

Ave: Average, SD: Standard deviation, M: Median, Min-maks: Minimum-maksimum, BMI: Body mass index.

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