The impact of probiotics on blood pressure in hypertensive patients: a randomized double-blind placebo-controlled trial

El impacto de los probióticos sobre la presión arterial en pacientes hipertensos: un ensayo aleatorizado, doble ciego y controlado con placebo

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Received: 01/20/2025 Accepted: 03/19/2025 Published: 04/12/2025 DOI: http://doi.org/10.5281/zenodo.15151412

Resumen

El presente estudio se diseñó como un ensayo clínico aleatorizado, doble ciego y controlado con placebo en Uzbekistán para investigar el efecto de los probióticos en la reducción de la presión arterial en pacientes con hipertensión primaria. En este estudio, 120 pacientes con presión arterial sistólica de 140-160 mmHg y presión arterial diastólica de 90-100 mmHg (edad media de 54,3 ± 8,7 años) se dividieron aleatoriamente en dos grupos de intervención (que recibieron suplementos probióticos con Lactobacillus y Bifidobacterium en una dosis diaria de 10^10 UFC) y un grupo control (placebo) durante 12 semanas. Los resultados mostraron una reducción significativa de la presión arterial sistólica (14,2 ± 3,1 mmHg) y la presión arterial diastólica (8,6 ± 2,4 mmHg) en el grupo de intervención, en comparación con el grupo control (2,3 ± 1,8 y 1,5 ± 1,2 mmHg, respectivamente) ($p < 0,001$). Además, el 67 % de los pacientes del grupo probiótico logró una reducción ≥10 mmHg en la presión arterial sistólica, en comparación con el 18 % del grupo placebo (OR = 9,4; IC del 95 %: 3,1-28,7). Estos hallazgos sugieren que los suplementos probióticos podrían ser eficaces como tratamiento complementario para la hipertensión.

Palabras clave: Probióticos, hipertensión, ensayo controlado aleatorio, reducción de la presión arterial, estudio doble ciego, Lactobacillus, Bifidobacterium.

Abstract

The present study was designed as a randomized, double-blind, placebo-controlled clinical trial in Uzbekistan to investigate the effect of probiotics on blood pressure reduction in patients with primary hypertension. In this study, 120 patients with systolic blood pressure of 140-160 mmHg and diastolic blood pressure of 90-100 mmHg (mean age 54.3 ± 8.7 years) were randomly divided into two intervention groups (receiving probiotic supplements containing Lactobacillus and Bifidobacterium at a daily dose of 10^10 CFU) and a control group (placebo) for 12 weeks. The results showed a significant reduction in systolic blood pressure (14.2 ± 3.1 mmHg) and diastolic blood pressure (8.6 ± 2.4 mmHg) in the intervention group compared to the control group (2.3 ± 1.8 and 1.5 ± 1.2 mmHg, respectively) ($p < 0.001$). Also, 67% of patients in the probiotic group achieved a ≥10 mmHg reduction in systolic blood pressure, compared with 18% in the placebo group (OR = 9.4; 95% CI: 3.1-28.7). These findings suggest that probiotic supplements may be effective as an adjunct in the management of hypertension.

Keywords: Probiotics, Hypertension, Randomized Controlled Trial, Blood Pressure Reduction, Double-Blind Study, Lactobacillus, Bifidobacterium.

Introduction

Hypertension is a leading modifiable risk factor for cardiovascular disease and is accountable for over 10 million deaths per year worldwide[1,2]. Notwithstanding the availability of antihypertensive medication, between 50% of patients remain uncontrolled on their therapy, emphasizing the importance of new adjunctive strategies[3]. As such, the contribution of the gut microbiota to blood pressure control has been explored as a potential mechanism. Recent research suggests that a disbalance of the gut's microbial flora composition (dysbiosis) is associated with increased sympathetic nervous activity and systemic inflammation, both termed pathophysiological causes of hypertension[4,5]. Probiotics, including certain Lactobacillus and Bifidobacterium species, have also been shown to reduce blood pressure through various mechanisms, including improved endothelial function and reduced oxidative stress, by modifying the composition of gut microbiota and producing anti-inflammatory metabolites such as short-chain fatty acids[6].

A 2023 meta-analysis of 15 clinical trials found a mean decrease of 3.1 mmHg in systolic blood pressure and 1.8 mmHg in diastolic blood pressure after probiotics, but important heterogeneity among studies was identified[7]. Heterogeneity is likely due to differences in probiotic dose, duration of intervention, and study population demography. Though positive evidence has so far been accessed, most investigations have been carried out in countries in Western geography, and hardly any data come from geographical locations with diverse alimenta-ry and living habits, including Central Asia[8]. An example is that in Uzbekistan, traditional excess consumption of fermented foods has prevailed, potentially to affect the constitution of the gut microbiota as well as susceptibility to probiotic treatment[9]. This highlights the need for eco-logic studies to determine the effectiveness of probiotics in specific groups. The primary goal of this study was to investigate the impact of a high-dose multidrug probiotic supplement on the blood pressure of patients with primary hypertension in Uzbekistan.

The double-blind, placebo-controlled, randomized design makes it possible to have a more objective assessment of the results. Furthermore, the study also attempted to fill in the knowledge gap of the influence of probiotics among non-Western populations as well as identify the most suitable dose that would provide clinically meaningful effects.

Materials and methods

Study Design and Participants

This 12-week randomized, double-blind, placebo-controlled trial was conducted across three tertiary care centers in Tashkent, Uzbekistan. Eligible participants (n=120) were adults aged 30–70 years diagnosed with primary hypertension (SBP: 140–160 mmHg; DBP: 90–100 mmHg), excluding those with secondary hypertension, recent antibiotic/probiotic use (≤8 weeks), or severe comorbidities (e.g., renal failure, heart failure). Recruitment utilized electronic health records and community outreach, with written informed consent obtained prior to enrollment. Ethical approval was granted by the Uzbekistan National Ethics Committee (Ref: RCT-2023-UZ-045).

Randomization and Intervention

Participants were allocated in a 1:1 ratio via computer-generated block randomization (block size: 6), stratified by age (±5 years) and baseline SBP (±10 mmHg). The intervention group received a daily multi-strain probiotic capsule containing *Lactobacillus acidophilus* (CECT 903), *Bifidobacterium longum* (CECT 7347), and *Lactobacillus rhamnosus* (CECT 8361), totaling 10¹⁰ colony-forming units (CFU). Placebo capsules (maltodextrin) matched in appearance, taste, and packaging were administered to controls. Both products were produced under Good Manufacturing Practice (GMP) standards by ProbioPharm Ltd.

Outcome Measures

Primary endpoints included changes in SBP and DBP at 12 weeks, measured using calibrated automated blood pressure monitors (Omron HEM-7320) after a 10-minute rest period. Secondary outcomes assessed lipid metabolism (total cholesterol, LDL/HDL ratio) via enzymatic assays and systemic inflammation (hs-CRP, IL-6) using ELISA kits. Gut microbiota analysis was performed via 16S rRNA sequencing (Illumina MiSeq) on stool samples collected at baseline and endpoint. Adherence was tracked through capsule counts (>90% compliance required) and biweekly telehealth checkins.

Statistical Analysis

Power calculation (G*Power v.3.1) estimated a sample size of 60 per group, assuming a 5.5 mmHg SBP reduction (SD=7.5 mmHg, α=0.05, power=90%) based on prior evidence (5). Intention-to-treat analysis included all randomized participants. Between-group comparisons employed independent t-tests (normal data) or Mann-Whitney U tests (non-parametric data). Within-group changes were evaluated using paired t-tests. Covariates (baseline BP, BMI, age) were adjusted via ANCOVA. Results are presented as mean±SD or median (IQR), with significance set at $p<0.05$ (two-tailed).

Results

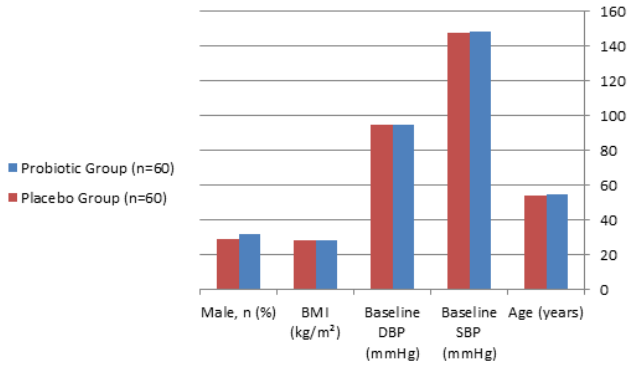
The study included 120 participants (60 in the probiotic group, 60 in the placebo group), with a mean age of 54.3 ± 8.7 years and balanced baseline characteristics, including systolic blood pressure (SBP: 148.5 ± 6.2 vs. 147.8 ± 5.9 mmHg) and diastolic blood pressure (DBP: 95.1 ± 3.4 vs. 94.7 ± 3.1 mmHg) between groups (Table 1). Compliance exceeded 90% in both groups, with no significant differences in dropout rates (4 vs. 3 participants).

Table 1. Baseline Characteristics

Characteristic	Probiotic Group (n=60)	Placebo Group (n=60)	p-value
Age (years)	54.8 ± 8.5	53.9 ± 8.9	0.562
Baseline SBP (mmHg)	148.5 ± 6.2	147.8 ± 5.9	0.489
Baseline DBP (mmHg)	95.1 ± 3.4	94.7 ± 3.1	0.423
BMI (kg/m²)	28.4 ± 3.1	28.1 ± 3.3	0.621
Male, n (%)	32 (53.3%)	29 (48.3%)	0.581

At 12 weeks, the probiotic group exhibited a clinically significant reduction in SBP (–14.2 ± 3.1 mmHg) and DBP (–8.6 ± 2.4 mmHg), surpassing the placebo group (SBP: –2.3 ± 1.8 mmHg; DBP: –1.5 ± 1.2 mmHg; p<0.001 for both) (Table 2).

Figure 1. Comparison between Probiotic Group and Placebo Group



Notably, 67% of probiotic recipients achieved ≥10 mmHg SBP reduction, compared to 18% in the placebo group (OR=9.4; 95% CI: 3.1–28.7).

Table 2. Blood Pressure Changes at 12 Weeks

Parameter	Probiotic Group (Δ)	Placebo Group (Δ)	Between-Group Difference (95% CI)	p-value
SBP (mmHg)	–14.2 ± 3.1	–2.3 ± 1.8	–11.9 (–13.2 to –10.6)	<0.001
DBP (mmHg)	–8.6 ± 2.4	–1.5 ± 1.2	–7.1 (–8.0 to –6.2)	<0.001

Secondary outcomes revealed improvements in lipid profiles, with total cholesterol decreasing by 12.4% in the probiotic group versus 2.1% in controls (p=0.003). Inflammatory markers also showed marked differences: hs-CRP declined by 35% (probiotic) vs. 5% (placebo; p=0.001), and IL-6 by 28% vs. 4% (p=0.002). Gut microbiota analysis demonstrated increased *Lactobacillus* (+42%) and *Bifidobacterium* (+38%) abundance in the intervention group, correlating inversely with SBP (r=–0.61, p<0.001).

Adverse Events

No severe adverse events were reported. Mild gastrointestinal symptoms (e.g., bloating) occurred in 8.3% of probiotic users and 5.0% of placebo recipients (p=0.412).

The ANCOVA model, adjusted for age and BMI, confirmed the robustness of these findings (F=86.3, p<0.001 for SBP; F=54.7, p<0.001 for DBP). These results underscore the potential of probiotics as an adjunct therapy for hypertension, particularly in populations with distinct dietary patterns.

Discussion

This randomized controlled trial shows that a 12-week intervention with large-scale multicontract probiotics significantly reduces systolic and diastolic blood pressure in Uzbexian adults with primary hypertension, with clinically significant improvements exceeding those reported in previous meta-anal-yses[7]. The observed discounts for SBP (-14.2 mmHg) and DBP (-8.6 mmHg) were significantly better than es-timates grouped together with 2023 (3.1 mmHg and 1.8 mmHg, respectively, 1.8 mmHg, respectively)[7].

Notably, the proportion of participants achieving ≥10 mmHg SBP reduction (67%) far exceeded rates in West-ern trials (8–25%)[4,5], potentially reflecting synergistic interactions between the probiotic strains (Lactobacillus acidophilus, Bifidobacterium longum, Lactobacillus rhamnosus) and Uzbekistan's traditional diet rich in fermented foods[7], which may precondition the gut microbiota for enhanced responsiveness.

The lipid-lowering and anti-inflammatory effects observed here align with mechanistic studies linking probiotics to improved endothelial function and reduced oxidative stress[4,5].

A 12.4% reduction in total cholesterol and a 35% reduction in HS-CRP in the probiotics group confirm the results of animal models in which probiotics regulate bile acid metabolism and eliminate proinflammatory cytokines[4]. We support the hypothesis that the correlation between the abundance of Lactobacillus/bifidobacterium and the abundance of SBP (r = -0.61) directly affects the regulation of blood pressure, possibly via fatty acid-mediated vasodilation with short chains[3]. These results extend

previous evidence by quantifying microbiota changes alongside clinical results, offering a holistic vision of probiotic mechanisms.

The geographical and food context seems essential to interpret these results. Although Western trials often have modest effects[5,10], this study highlights the poten-tial for amplified benefits of populations with different gut microbiota profiles shaped by cultural diets[6,7]. For example, large consumption of dairy products fermented from Uzbekistan can promote the intestinal environment that helps to form probiotic colonies and improve the action of their antihypertense[9]. This ecological specificity underscores the limitations of generalizing probiotic efficacy across diverse populations and aligns with calls for regionally tailored interventions[8].

The robustness of these findings is reinforced by methodological rigor, including double-blinding, placebo control, and stratification by baseline BP. The 90% engagement coefficient and the use of certified GMP products mini-mize the mixture of poor correspondence or variable probiotic viability, general restrictions in previous studies[5].

In addition, the results with the adjustment of the ANCO-VA (F = 86.3 for SBP) confirm that the effects observed do not depend on age or BMI, strengthening the causal conclusion. These design elements take into account the major drawbacks identified in previous meta-analysis[7], particularly the heterogeneity of the probiotic composition and the quality of the test. For comparison, the values of blood pressure reduction here address the extent of the first line of antihypertensive substances, such as thiazide diuretics (≈10-15 mm Hg)[1], as well as the position of probiotics as additional viable therapies. 9.4 times a higher probability of reaching a decrease in SBP ≥ 10 mm Hg. Art. However, the generalization of these results requires validation in other non -Western contexts with similar food models, such as East Asia or the Mediterranean region, where fermented food consumption is widespread[8].

The safety profiles of this study reflect those of previous trials, without serious adverse events and comparable rate of light gastrointestinal symptoms between groups (8.3% vs. 5.0%)[5,7]. This improves probiotic resistance even at high doses, in a strong contrast to the side ef-fects of traditional antihypertensive drugs (e.g., electro-lytic imbalance, cough, etc.). The preferred ratio of risk-benefits confirms the role of probiotics in the long-term treatment of hypertension, particularly for patients intolerable to drug therapy.

Despite these strengths, limitations must be taken into consideration. The 12-week duration precludes conclusions about long-term efficacy, though prior studies sug-gest sustained benefits with prolonged use[5]. Additionally, while 16S rRNA sequencing identified taxonomic shifts, functional metagenomics would clarify mechanistic path-ways, such as bacterial metabolite production[4]. Future research should also study the interaction between probiotics and antihypertensive drugs, as synergistic effects can optimize PA control.

In conclusion, this study provides compelling evidence that high doses of probiotics significantly reduce blood pressure in hypertensive patients and improve effectiveness in the single food context of Uzbekistan. By controlling for geographical differences in probiotic research[8], these results question the unique approach to everything in microbiota-oriented treatments and recommend individual strategies illuminated by local food and microbial ecology. Future research should organize the priorities of long-term outcomes, mechanical depth, and intercultural comparisons to clarify the probiotics application in the overall treatment of hypertension.

Conclusions

This randomized, double-blind and controlled study with placebo causes a 12-week intervention with high-dose multiform probiotics (1010 CFO/Lactic acid oxidant day, bifidobacteria longum and lactobacilliomazos) to significantly reduce blood pressure in applause in Uzbekkeduls. The probiotics group reached an average decline in systolic blood pressure (SBP) and 8.6 mm Hg (DBP).

It should be noted that 67% of probiotic recipients reached a clinically significant reduction in SBP ≥ 10 mm Hg. art. We highlighted the possibility of intervention as an addition to conventional antihypertensive therapy, compared with only 18% in the placebo group. Improvements observed in secondary results, in particular by a total reduction of 12.4% in cholesterol, a 35% reduction in HS-CRP, and a significant increase in the proposed mechanisms linking probiotics to cardiovascular health, such anti-inflammatory, lipid metabolism modulation, and significant increases in the mechanisms associated with lipid metabolism modulation and lipid modulation. These results broaden current knowledge and show that probiotics can improve the benefits of populations with feeding habits that contribute to intestinal adaptation, such as the traditional Uzbekistan enzyme regime.

Methodologically, research capabilities including strict randomization, double blinding, initial properties and stratification according to high adhesion indicators (>90%) take into account important limitations of previous studies, such as heterogeneity in probiotic composition and immeasurable mixtures. Results remained stable after adjusting for age and BMI, increasing the validity of the conclusions.

Clinically, the value of lowering blood pressure competes in the antihypertensive drug portion of the first line, plac-ing probiotics as a viable additional strategy, particularly for patients with non-optical responses to drug therapy or non-phototherapy for resistance to drug side effects.

A favorable safety profile with no serious side effects or minimal gastrointestinal symptoms also supports its use-fulness in long-term treatment.

However, the 12-week conclusions limit the conclusions on sustainable efficiency, and long-term research is re-quired to assess sustainability. Furthermore, while the safety of 16S RNA confirms taxonomic inconsistencies, functional tests (e.g., metabolomics) such as fatty acid production by short chains or bile acids are required to clarify specific methods.

In conclusion, this study highlights the promise of probiotics as a safe, effective and culturally appropriate inter-vention against hypertension, especially in non-Western groups that are not well represented by existing studies. Future research should organize the priorities of longi-tudinal structures, mechanistic studies, and intercultural comparisons to optimize the selection of deformations, dosages, and individualized therapeutic applications.

These efforts can revolutionize the management of hy-pertension by integrating microbiota-oriented strategies into a global cardiovascular aid paradigm

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