

Effect of Probiotics on Blood Pressure: A Systematic Review and Meta-Analysis of Randomized, Controlled Trials

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Effect of Probiotics on Blood Pressure

A Systematic Review and Meta-Analysis of Randomized, Controlled Trials

Saman Khalesi, Jing Sun, Nicholas Buys, Rohan Jayasinghe

Abstract—Previous human clinical trials have shown that probiotic consumption may improve blood pressure (BP) control. The aim of the present systematic review was to clarify the effects of probiotics on BP using a meta-analysis of randomized, controlled trials. PubMed, Scopus, Cochrane Library (Central), Physiotherapy Evidence Database, and Clinicaltrial.gov databases were searched until January 2014 to identify eligible articles. Meta-analysis using a random-effects model was chosen to analyze the impact of combined trials. Nine trials were included. Probiotic consumption significantly changed systolic BP by -3.56 mm Hg (95% confidence interval, -6.46 to -0.66) and diastolic BP by -2.38 mm Hg (95% confidence interval, -2.38 to -0.93) compared with control groups. A greater reduction was found with multiple as compared with single species of probiotics, for both systolic and diastolic BP. Subgroup analysis of trials with baseline BP $\geq 130/85$ mm Hg compared with $<130/85$ mm Hg found a more significant improvement in diastolic BP. Duration of intervention <8 weeks did not result in a significant reduction in systolic or diastolic BP. Furthermore, subgroup analysis of trials with daily dose of probiotics $<10^{11}$ colony-forming units did not result in a significant meta-analysis effect. The present meta-analysis suggests that consuming probiotics may improve BP by a modest degree, with a potentially greater effect when baseline BP is elevated, multiple species of probiotics are consumed, the duration of intervention is ≥ 8 weeks, or daily consumption dose is $\geq 10^{11}$ colony-forming units. (*Hypertension*. 2014;64:00-00.) • [Online Data Supplement](#)

Key Words: blood pressure ■ hypertension ■ meta-analysis ■ probiotics ■ review

Blood pressure (BP) has been strongly and positively associated with the risk of chronic diseases, including ischemic heart disease, heart failure, stroke, and kidney disease.^{1,2} BP can be controlled through diet and lifestyle modification to prevent hypertension (systolic BP [SBP] ≥ 140 mm Hg or diastolic BP [DBP] ≥ 90 mm Hg) or related complications.³ Evidence suggests that low-fat diets rich in fruits and vegetables and low in sodium can lower BP.⁴⁻⁶ Previous studies have also found that dietary constituents and supplements such as omega-3 fatty acids,⁷ garlic,⁸ and green tea^{9,10} can improve BP control.

In recent years, the health benefits of probiotics have attracted increased attention. Probiotics are defined as live microorganisms that may have health benefits for the host if consumed in adequate amounts.¹¹ Probiotics are well studied for their health benefits in improving immune system function¹² and preventing diarrhea.^{13,14} It has also been demonstrated that probiotics and their products can improve BP through mechanisms including improving total cholesterol and low-density lipoprotein cholesterol levels,¹⁵⁻¹⁷ reducing blood glucose level and insulin resistance,^{18,19} and regulating the renin-angiotensin system.^{20,21}

A recent systematic review and meta-analysis of 14 randomized, controlled trials showed that consumption of fermented

milk containing inhibitory peptides (with or without probiotics) can significantly reduce SBP and DBP.²² However, the effects of probiotics (live bacteria) and their species or dose were not systematically investigated. Some previous studies on probiotics have reported that consumption of probiotic yogurt for 8 weeks can significantly improve BP,^{23,24} whereas another study showed no benefit.²⁵ Because of inconclusive reports on the effect of probiotics on BP and lack of information on effective intervention characteristics, the current systematic review and meta-analysis of randomized, controlled trials has been conducted. The findings from this meta-analysis may provide further information on the effective probiotic species, duration or dose of consumption required to confer health, and BP benefits.

Methods

Literature Search

The online databases PubMed (MEDLINE), Scopus, Cochrane Library (Central), Physiotherapy Evidence Database, and Clinicaltrial.gov were searched until January 2014 for relevant studies. The following terms were used to search for relevant publications: probiotic*, lactobacill*, bifidobacter*, saccharomyces*, enterococcus*, streptococcus* in combination with blood pressure. In searching the literature and presenting the results, the guidelines

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provided in the *Preferred Reporting Items for Systematic Reviews and Meta-Analysis: The PRISMA Statement* were followed.²⁶ The methodology of this systematic review is registered at the International Prospective Register for Systematic Review with the registration number CRD42014007088.

Study Eligibility and Selection

Studies were included if they met the following inclusion criteria: (1) were human randomized, controlled trials, (2) included adults ≥ 18 years of age with or without hypertension, (3) used probiotic products with live bacteria, and (4) had accessible full articles in English. Studies were excluded if the total number of bacteria in the probiotic product used was not reported. Publications were discarded if they did not meet the review's initial objectives, were duplicate publications, reported an inappropriate population type, did not report defined BP as an outcome variable, used an alternative study design, or were not in English.

Two researchers conducted an initial screening of studies based on the titles. The next phase involved a review of abstracts and an examination of the full text in terms of the eligibility criteria. The final eligibility of the articles was determined through agreement between the 2 reviewers, with any disagreement resolved in consultation with a third reviewer. A summary of the review is presented in the PRISMA flow chart (Figure 1). Included articles were reviewed to assess their publication bias and extract relevant data (refer to the online-only Data Supplement for an expanded description).

Data Synthesis and Analysis

Meta-analysis of data was performed using RevMan software (Cochrane Review Manager, version 5.2). The effect of probiotic use on BP was defined as the weight mean difference of BP changes between the intervention groups and control groups. Statistical analysis was performed in accordance with the *Cochrane Handbook for Statistical Review of Interventions*.^{27,28} The DerSimonian and Laird random effect²⁹ was chosen, because variation between studies' populations and high heterogeneity in BP analysis was observed. A P value < 0.05 was considered statistically significant. Sensitivity and

subgroup analysis was also performed (refer to the online-only Data Supplement for an expanded description).

Results

Characteristics of Included Studies

Nine trials, with 543 participants in total, were included in the final meta-analysis and systematic review. The included studies were all parallel randomized, controlled trials, with 7 studies reporting a double-blind design,^{23,30–34} 1 reporting a single-blind design,³⁵ and 1 not reporting the blinding process.²⁴ Four studies reported that participants did not know the difference between intervention and control.^{23,30,32,33} Six studies reported the similarity in intervention and placebo products,^{24,25,31–34} and 4 studies reported blinding of treatment allocation and measurements.^{23,24,30,34} All included articles had a Rosendal score $> 50\%$, with the smallest score of 53% for the study by Kawase et al³⁵ and the highest score of 85% for the study by Jones et al³¹ (Table S1 in the online-only Data Supplement). The funnel plot of studies also showed slight asymmetry, which can be interpreted as publication bias (data not shown).

The characteristics of included studies are presented in Table 1. All studies reported changes in SBP and DBP, except for the study by Kawase et al,³⁵ which only reported changes in SBP ($n=543$ for SBP analysis; $n=522$ for DBP analysis). Of the 9 studies, 3 included healthy participants,^{30,32,33,35} 2 included patients with hypercholesterolemia,³¹ 1 included patients with hypertension,²⁴ 1 included overweight and obese subjects,²³ and 1 included patients with metabolic syndrome.³⁴ One study reported a significant reduction of body mass index (BMI) after consuming probiotics,³⁴ and another reported a significant increase in BMI.²³ The remainder of the studies did not report significant changes in BMI. Changes in body weight was not significant in 6 studies.^{23–25,31,32,35} However, it reduced significantly in the intervention group in 1 study³⁰ and in both intervention and control groups in another study.³⁴ Nutrition intake was measured in 3 studies,^{23,32,33} which showed no significant changes in intervention or control group. Three studies only reported that participants were advised to maintain their diet^{25,30,31}; however, no measurement of intake was conducted. Four studies used yogurt as the source of probiotic bacteria,^{23,30,31,33} 2 studies used fermented and sour milk,^{24,35} 1 study used encapsulated probiotic supplements,³¹ 1 study used probiotic rose-hip drinks,³² and another study used probiotic cheese.³⁴ The probiotic species and dose used varied between studies. Four studies used a single species of probiotics,^{31,32,34} whereas the others used a combination of 2^{23,24,33,35} or 3 strains.³⁰ The total daily dose of probiotic consumption varied from 10^9 colony-forming units (CFU)³³ to 10^{12} CFU.³⁴ The duration of the studies varied from 3 weeks³⁴ to 9 weeks.³¹ All studies reported good compliance with no side effects of consuming probiotics, except 2 studies that reported mild stomach gas and flatulence.^{24,33}

Main Outcomes

BP changes were reported in all studies. Similar changes across participants of each group were reported in 5 studies.^{23,32–35} Five studies also mentioned similar changes of BP

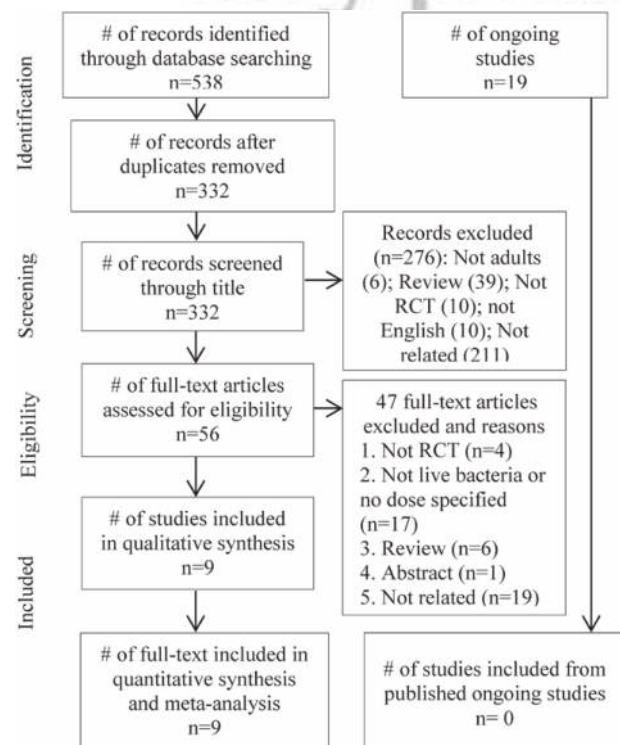


Figure 1. Study flow diagram. RCT indicates randomized, controlled trial.

Table 1. Characteristics of Included Studies

Study	Design; Location	Probiotic Source (wk)	Participants, Age (No. of Intervention/ No. of Control)	Intervention Baseline Measures (Changes From Baseline)	Control Baseline Measures (Changes From Baseline)	Probiotic	Dose, CFU	Side Effects
Agerholm-Larsen et al ²³	DB, PC, P; Denmark	Yogurt (8)	OW, OB, 18–55 (16/14)	SBP: 131.9±6.9 (–6±2.3); DBP: 83±5.2 (–4±2.4)	SBP: 116.5±3.8 (–2.2±1.9); DBP: 76.4±2.9 (–1.5±1.3)	<i>Enterococcus faecium</i> plus <i>Streptococcus thermophilus</i>	4.7×10 ¹¹	No
Chang et al ³⁰	DB, PC, P; Korea	Yogurt (8)	Healthy, 20–60 (53/48)	SBP: 110.2±11.6 (–1.07±9.11); DBP: 70.7±9.2 (–0.32±8.41)	SBP: 110.9±11.5 (0.91±10.9); DBP: 71.6±12.8 (–0.43±10.0)	<i>S. thermophilus</i> plus <i>Lactobacillus acidophilus</i> plus <i>Bifidobacteria infantis</i>	4.8×10 ¹²	No
Hata et al ²⁴	PC, P; Japan	Sour milk (8)	HTN, 40–86 (17/13)	SBP: 158.5±11.1 (–14.1±3.1); DBP: 88.7±9.4 (–6.6±2.5)	SBP: 150.9±9.5 (–4.4±3.6); DBP: 87.6±9.1 (–2.2±1.9)	<i>Lactobacillus helveticus</i> plus <i>Saccharomyces cerevisiae</i>	7×10 ¹⁰	Yes
Jones et al ³¹	DB, PC, P; Czech Republic	Capsule (9)	HC, 20–75 (67/64)	SBP: 130.5±11.5 (0.18±11.8); DBP: 78.61±5.31 (–1.46±4.57)	SBP: 130.8±11.7 (–1.18±11.4); DBP: 78.05±6.78 (–0.16±5.16)	<i>Lactobacillus reuteri</i>	5.8×10 ⁹	No
Jones et al ³¹	DB, PC, P; Czech Republic	Yogurt (6)	HC, 18–74 (59/61)	SBP: 134.3±9.6 (–1.19±11.5); DBP: 78.88±6.50 (–0.98±7.06)	SBP: 134.5±10.1 (–3.07±12.3); DBP: 78.82±5.78 (–1.18±7.51)	<i>L. reuteri</i>	5.8×10 ⁹	No
Kawase et al ³⁵	SB, P; Japan	Milk (8)	Healthy men, 30–51 (10/10)	SBP: 124±6 (–7±5)	SBP: 124±6 (1±8)	<i>Lactobacillus casei</i> plus <i>S. thermophilus</i>	1.7×10 ¹¹	No
Naruszewicz et al ³²	DB, PC, P; Sweden	Drink (6)	Healthy smokers, 35–45 (18/18)	SBP: 134±20 (–13±16); DBP: 89±13 (–5±16)	SBP: 128±18 (–2±16); DBP: 89±17 (–4±15)	<i>Lactobacillus plantarum</i>	2×10 ¹⁰	No
Savard et al ³³	DB, PC, P; Canada	Yogurt (4)	Healthy men, 18–54 (20/18)	SBP: 104.6±9.3 (–2.5±10.3); DBP: 70.2±5.7 (–0.9±6.1)	SBP: 103.8±8.8 (–0.8±8.4); DBP: 69±8.1 (1.3±6.5)	<i>Bifidobacterium animalis lactis</i> plus <i>L. acidophilus</i>	10 ⁹	Yes
Sharafedinov et al ³⁴	DB, PC, P; Russia	Cheese (3)	Met.S, 30–60 (25/15)	SBP: 134±1.6 (–12.2±1.5); DBP: 82.4±1.2 (–8.0±0.9)	SBP: 131.4±1.8 (–11.4±1.9); DBP: 82.1±1.5 (–3.5±1.0)	<i>L. plantarum</i>	7.5×10 ¹²	No

CFU indicates colony-forming unit; DB, double blind; DBP, diastolic blood pressure; HC, hypercholesterolemia; HTN, hypertension; Met.S, metabolic syndrome; OB, obesity; OW, overweight; P, parallel; PC, placebo control; SB, single blind; and SBP, systolic blood pressure.

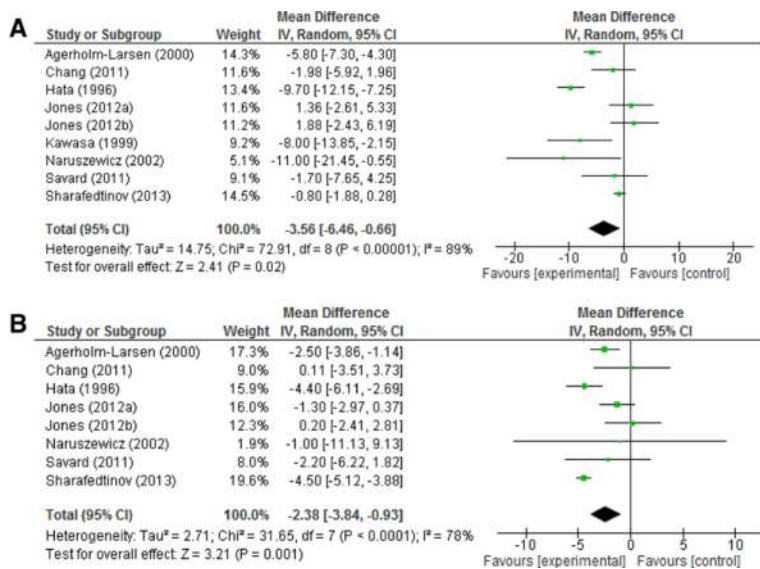


Figure 2. The effect of probiotics on (A) systolic blood pressure and (B) diastolic blood pressure. CI indicates confidence interval.

over time,^{23–25,31,34} but no follow-up data were reported in any study. Of the 9 studies included, 8 reported a reduction in SBP after consuming probiotics with a mean reduction ranging from 1.07 mmHg³⁰ to 14.10 mmHg.²⁴ Five studies reported a clinically significant reduction of SBP of >5 mmHg after probiotic consumption.^{23,24,32,34,35} The meta-analysis of 9 studies showed a significant reduction of SBP by 3.56 mmHg (95% confidence interval, -6.46 to -0.66; $P < 0.01$) compared with control groups. The forest plot of the effect is presented in Figure 2. A high level of statistical heterogeneity was observed for the meta-analysis of SBP ($I^2 = 89\%$; $P < 0.05$).

Eight of 9 studies presented changes in DBP, with all reporting a reduction of DBP after consuming probiotics. However, only in 2 studies did the reduction in DBP reach

a statistically significant level.^{24,34} The lowest reduction in DBP was 0.9 mmHg,³³ and the greatest reduction was 8 mmHg.³⁴ The meta-analysis result showed a significant change of -2.38 mmHg (95% confidence interval, -3.84 to -0.93; $P < 0.01$) in mean difference of DBP compared with control groups (Figure 2), with high heterogeneity ($I^2 = 78\%$; $P < 0.05$).

Sensitivity, Subgroup, and Dose-Dependency Analysis

Limiting analysis to double-blind trials showed a significant reduction in DBP, but a nonsignificant reduction in SBP. Sensitivity analysis of individual studies showed that the overall meta-analysis of SBP changes was influenced by 3 studies.^{23,24,35} Excluding these studies resulted in nonsignificant meta-analysis

Table 2. Results of Sensitivity and Subgroup Analysis of Included Randomized, Controlled Trials in Meta-Analysis of Probiotics and BP

Sensitivity and Subgroup Analysis	Weight Mean Difference (95% Confidence Interval)	
	SBP, mm Hg	DBP, mm Hg
Sensitivity analysis		
Studies with double-blind trials	-1.91 (-4.66, 0.83); $\rho = 0.17$; $n = 7$	-1.95 (-3.67, -0.22); $\rho < 0.05$; $n = 7$
Baseline BMI ≥ 30 kg/m ²	-3.27 (-8.17, 1.63); $\rho = 0.19$; $n = 2$	-3.60 (-5.55, -1.64); $\rho < 0.05$; $n = 2$
Subgroup analysis		
Intervention duration ≥ 8 wk	-4.90 (-8.41, -1.40); $\rho < 0.05$; $n = 4$	-2.35 (-3.94, -0.75); $\rho < 0.05$; $n = 3$
Intervention duration < 8 wk	-0.93 (-3.71, 1.86); $\rho = 0.51$; $n = 5$	-2.26 (-5.36, -3.88); $\rho = 0.15$; $n = 5$
Source of probiotics: dairy products	-3.79 (-6.97, -0.61); $\rho < 0.05$; $n = 7$	-2.65 (-4.21, -1.09); $\rho < 0.05$; $n = 6$
Source of probiotics: other	-3.84 (-15.79, 8.12); $\rho = 0.53$; $n = 2$	-1.29 (-2.94, 0.36); $\rho = 0.12$; $n = 2$
Single species of probiotics	-0.28 (-2.95, 2.39); $\rho = 0.84$; $n = 4$	-1.99 (-4.79, 0.81); $\rho = 0.16$; $n = 4$
More than 1 species of probiotics	-5.79 (-8.66, -2.93); $\rho < 0.05$; $n = 5$	-2.72 (-4.35, -1.08); $\rho < 0.05$; $n = 4$
Daily dose of probiotics $\geq 10^{11}$ CFU	-3.78 (-7.30, -0.25); $\rho < 0.05$; $n = 4$	-2.86 (-4.96, -0.76); $\rho < 0.05$; $n = 3$
Daily dose of probiotics $< 10^{11}$ CFU	-3.42 (-9.49, 2.65); $\rho = 0.27$; $n = 5$	-1.99 (-3.99, 0.02); $\rho = 0.05$; $n = 5$
Baseline BP of participants $\geq 130/85$ mm Hg	-3.49 (-7.18, 0.20); $\rho = 0.06$; $n = 6$	-2.68 (-4.25, -1.10); $\rho < 0.05$; $n = 6$
Baseline BP of participants $< 130/85$ mm Hg	-3.59 (-7.34, 0.16); $\rho = 0.06$; $n = 3$	-0.93 (-3.62, 1.77); $\rho = 0.50$; $n = 2$
All trials (meta-analysis result)	-3.56 (-6.46, -0.66); $\rho < 0.05$; $n = 9$	-2.38 (-3.84, 0.93); $\rho < 0.05$; $n = 9$

BP indicates blood pressure; BMI, body mass index; CFU, colony-forming unit; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

results for SBP. Sensitivity analysis of individual studies did not affect the overall significance of changes in DBP. Limiting analysis to studies with a baseline BMI ≥ 30 kg/m² showed a significant reduction in DBP compared with control groups; however, the effect on SBP was not significant (Table 2).

Using fermented dairy products as the source of probiotics resulted in significant reductions in both SBP and DBP; similar results were not found for other sources of probiotics (Table 2). Meta-analysis of trials with multiple species of probiotics found a significant reduction in both SBP and DBP (-5.79 and -2.72 mmHg, respectively). Those trials using a single species of probiotics as the treatment did not show a meaningful reduction compared with control groups. Duration of intervention ≥ 8 weeks resulted in a significant reduction in both SBP and DBP. However, limiting the analysis to those interventions with duration of intervention < 8 weeks did not produce the same results. Subgroup analysis of studies with a baseline BP $\geq 130/85$ mmHg showed a significant improvement in DBP, with no significant reduction in SBP. Subgroup analysis of trials with a baseline BP $< 130/85$ mmHg did not find meaningful improvements in SBP or DBP (Table 2).

The rearranged forest plots of the relationship between dose of probiotics and the effect on BP are presented in Figure S1. The rearranged plots did not show any meaningful relationship between the daily dose of probiotics consumed and reduction in SBP or DBP. However, a subgroup analysis of those studies with a daily dose of probiotic consumption $\geq 10^{11}$ CFU showed a significant reduction in both SBP and DBP. No significant reduction was found for those studies with a daily dose of probiotics of $< 10^{11}$ CFU (Table 2).

Discussion

This review systematically analyzed randomized, controlled trials to clarify the effects of probiotic consumption on BP control. Overall, the results showed that consuming probiotics could significantly reduce SBP by 3.56 mmHg and DBP by 2.38 mmHg. The reduction in BP reported by the current meta-analysis was similar to that reported in a recent meta-analysis of salt reduction of < 2 g per day³⁶ and resistance training.³⁷ The reduction reported by the current meta-analysis is modest; however, even a small reduction of BP may have important public health benefits and cardiovascular consequences.³⁸ The findings from the Heart Outcome Prevention Evaluation study showed that a modest reduction of SBP by 3.3 mmHg and DBP by 1.4 mmHg was associated with a 22% reduction in relative risk of cardiovascular mortality, myocardial infarction, or stroke.³⁹

Administration of probiotic type and product varied between the trials included in this meta-analysis. The majority of trials (7) used fermented dairy products. Subgroup analysis of studies using dairy products showed a significant reduction of BP. Microorganism-fermented dairy products may contain angiotensin-converting enzyme inhibitors,^{40,41} which can act on the renin-angiotensin system and inhibit the production of angiotensin II and reduce BP.^{20,42} However, the inadequate number of trials using other sources of probiotics (capsules and rose-hip drink) limits the conclusions that can be drawn regarding the best source of probiotic consumption for maximum effect on BP.

The number of probiotic species used in the trials also varied. Subgroup analysis of studies using > 1 species of probiotics (5 trials) found a significant reduction with greater magnitude in both SBP and DBP compared with studies using a single species of probiotics ($-5.79/-2.72$ vs $-0.28/-1.99$ mmHg). Similar findings were reported in a meta-analysis by Ritchie and Romanuk,⁴³ where a greater impact of multiple species of probiotics on risk ratio of gastrointestinal disease was observed. Although these findings may provide important information for future interventions using probiotics, caution is required because the effect may be due to the low number of randomized, controlled trials included in the subgroup analysis (5 trials for multiple species and 4 trials for single species). These findings may also be explained by the variation in the characteristics and effect of different species and strains of probiotics on metabolism.^{44,45} Unfortunately, the lack of trials on specific species and strains of probiotics made it not practical to analyze the effect of different probiotic species or strains on BP control. Further research is required to clarify these findings.

There seems to be no trend between the daily dose of probiotics consumed and changes in SBP or DBP. However, findings from the subgroup analysis indicate that the reduction in BP may be greater when the daily dose of probiotics consumed is $\geq 10^{11}$ CFU. These findings may be because of the bias of the low number of trials in each subgroup. Further trials with different doses are required to confirm these findings.

Another important finding of this meta-analysis was the variation in the effect of probiotics on BP based on baseline BP level. The mean baseline SBP in the majority of the studies (6 trials) was > 130 mmHg; only 1 study reported a mean baseline SBP of > 140 mmHg.²⁴ Subgroup analysis of those studies with a baseline BP $\geq 130/85$ mmHg showed a meaningful reduction in DBP, but no significant reduction in SBP. There also seemed to be a trend between consumption of probiotics and SBP among trials including participants with elevated BP. Four of the 6 trials included in the baseline BP $\geq 130/85$ mmHg subgroup reported a significant reduction in SBP. Although results on SBP were not significant, the reduction reported by the subgroup analysis was close to the overall meta-analysis result. The nonsignificant meta-analysis result could be because of the low number of studies included in the subgroup analysis. Moreover, only 1 of the trials²⁴ included hypertensive patients. This study reported a significant change of -14.1 ± 3.1 mmHg in SBP after the intervention. Meta-analysis of the studies with a baseline BP $< 130/85$ mmHg did not show a significant reduction in SBP or DBP. This finding suggests that probiotics may have an important effect in the management and control of elevated BP.

There has been an ongoing debate regarding gut microbiota and their mechanisms in disease control or prevention.^{46,47} The impact of probiotics on BP control and improvement may work through several different mechanisms. For example, probiotics may improve blood cholesterol.¹⁷ A recent meta-analysis on the effects of probiotics on blood lipids reported a significant 6.4 mg/dL reduction in total cholesterol, a 4.9 mg/dL reduction in low-density lipoprotein cholesterol level, and a 3.9 mg/dL reduction in triglycerides level.¹⁷ Probiotic fermented products may regulate the renin-angiotensin system through the production of angiotensin-converting enzyme

inhibitory peptides (Val-Pro-Pro and Ile-Pro-Pro).²⁰ A recent meta-analysis showed that probiotic-fermented milk produced a significant reduction of 3.1 mmHg in SBP and 1.1 mmHg in DBP compared with placebo groups. Other mechanisms such as an increase in the absorption of nutrients and phytoestrogens (which can act as vasodilatory factors) and a reduction in plasma glucose and the onset of inflammatory-induced diabetes mellitus may also explain the effect of probiotics on BP.^{19,42,48,49} A reduction in body weight can also reduce BP.⁵⁰ With the exception of 1 study,³⁴ no significant reduction of body weight was observed after consuming probiotics in this meta-analysis. In the study by Sharafedinov et al,³⁴ a significant reduction of BMI was observed in both the intervention and control groups, because participants consumed a low-calorie diet along with probiotic cheese or control cheese. Thus, the BMI reduction reported by this study may not be related to probiotic consumption. Sensitivity analysis also showed that excluding this study had no effect on the overall significance of the meta-analysis.

To date, few randomized, controlled trials have investigated the effect of probiotics on BP. This systematic review highlighted the need for future interventions to investigate the effect of probiotic consumption on BP and hypertension. However, the present study had some limitations. For instance, because of the limitation of resources, only studies published in English language were included in this systematic review. The bias of the included studies may have affected the results of the meta-analysis. For example, 2 studies did not use blinding,^{24,35} 3 studies did not report controlling or monitoring participants' pretrial diet or exercise,^{23,24,34} and all of the studies were lacking in justification of sample size or reporting either the method of blinding or the evaluation of the successfulness of blinding. Moreover, 2 studies had a short duration of 3 to 4 weeks of probiotic consumption.^{33,34} These short-duration studies may have affected the overall results of the meta-analysis, because the subgroup analysis of the studies with duration of intervention <8 weeks did not show a meaningful reduction of BP. More randomized, controlled studies with larger sample groups, longer durations, and adequate blinding of conditions trials are needed to confirm the effect of different probiotic species and products on BP and hypertension.

The results of this meta-analysis suggest that probiotic consumption with daily doses from 10^9 to 10^{12} CFU for a duration of 3 to 9 weeks may improve BP. The magnitude of improvement is greater among those with elevated BP, when daily dose of probiotic consumption is $\geq 10^{11}$ CFU and when intervention lasts ≥ 8 weeks. The study also suggests a greater effect from consuming multiple rather than single species of probiotics.

Perspectives

Improving BP may result in better hypertension and cardiovascular outcomes. The results of this study showed that consumption of probiotics may improve BP. These findings along with the results from the meta-analysis on the beneficial effect of probiotics on lipid profile¹⁷ suggest that probiotics may be used as a potential supplement for future interventions to prevent hypertension or improve BP control. Future studies investigating the effect of different products with different species and doses are recommended to clarify the findings

of this meta-analysis. The effect of probiotics on BP and the overall health of patients, especially hypertensive patients, as well as the mechanisms by which probiotics can affect BP and health need further investigation.

Disclosures

None.

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Novelty and Significance

What Is New?

- Evidence related to the effect of consuming probiotics, their effective dose, duration, and type on blood pressure is summarized in this study.

What Is Relevant?

- Probiotic consumption significantly improved blood pressure control.
- The prevalence and burden of high blood pressure and hypertension is still considerable worldwide. The results of this study may have important clinical and public health outcomes.

Summary

The results from this meta-analysis of 9 randomized, controlled trials showed that consuming probiotics may lead to a modest but significant reduction of both systolic and diastolic blood pressure. These results propose probiotics as potential supplement and dietary constituent to improve blood pressure and prevent or control hypertension.