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MICROBIAL DYSBIOSIS AND HYPERTENSIVE DISEASE: EXPLORING THE CONNECTIONS BETWEEN THE MICROBIOME AND CARDIOVASCULAR HEALTH

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Abstract: INTRODUCTION: Microbial dysbiosis, characterized by imbalances in the composition and function of the human microbiota, has emerged as a critical factor influencing various systemic diseases, particularly those related to cardiovascular health. The human microbiota, a diverse ecosystem of microorganisms residing throughout the body, actively contributes to crucial physiological processes, including nutrient metabolism, immune system modulation, and protection against pathogens. Dysbiosis, often implicated in conditions such as obesity, metabolic disorders, and autoimmune diseases, disrupts this delicate equilibrium. **OBJETIVE:** To analyze and describe the main aspects microbial dysbiosis in hypertensive disease of the last 10 years. **METHODS**: This review has included studies available in MEDLINE–PubMed (National Library of Medicine, National Institutes of Health) databases. The descriptor used was "dysbiosis" AND "blood pressure". The use of the above descriptor helped to identify studies related to the use of dysbiosis and its effects. **RESULTS:** At the end of the selection process, 5 articles involving 479 subjects were included. The age range of subjects was 56 years. **DISCUSSION:** Firmicutes and Bacteroidetes, major microbial phyla, play essential roles in metabolic homeostasis, with their balance serving as a potential biomarker for metabolic health. Specific microbial genera, such as Akkermansia and Faecalibacterium, have been associated with health benefits, emphasizing the potential for targeted interventions. Recent research has unveiled a significant connection between the intestinal microbiota and blood pressure regulation, with microbial-derived short-chain fatty acids and modulation of the renin-angiotensin-aldosterone system influencing hypertension. This comprehensive review explores the intricate interplay between

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microbial dysbiosis and hypertensive disease over the past decade, shedding light on the potential effects both beneficial and harmful of dysbiosis on human arterial pressure. The focused question addresses the impact of dysbiosis on blood pressure, and the selected studies employing human interventional designs offer valuable insights into the complex relationship between the microbiome and hypertensive conditions. **CONCLUSION:** Various studies elucidate the complex relationship between gut microbiota and physiological changes, shedding light on connections to metabolic outcomes. Lee et al. found significant weight reductions linked to changes in gut bacteria. Gomez et al. noted associations between microbiota, blood pressure, and butyrate production in obese pregnant women. Xue et al. highlighted dietary fiber's role in improving blood pressure. Su et al.'s research proposed controlling glucose and blood pressure through diet and microbiota transplantation, while Jing et al. identified sex-specific microbiota associations in hypertension, suggesting potential interventions for metabolic conditions.

Keywords: Microbial Dysbiosis; Hypertensive Disease; Metabolic Homeostasis.

INTRODUCTION

The human microbiota, a complex and dynamic ecosystem of microorganisms residing in various niches throughout the body, plays a pivotal role in maintaining host health and homeostasis[1]. This microbial community encompasses a vast array of bacteria, viruses, fungi, and archaea, predominantly residing in the gastrointestinal tract[2]. The significance of the microbiota is underscored by its involvement in essential physiological processes, including nutrient metabolism, immune system modulation, and protection against pathogenic invaders[1]. Commensal bacteria contribute to the breakdown of complex dietary components, facilitating the absorption of nutrients and energy production[3]. Furthermore, these microorganisms actively shape the development and function of the host immune system, influencing both local and systemic immune responses[1]. Perturbations in the microbiota composition, known as dysbiosis, have been implicated in various health conditions, including inflammatory bowel diseases, metabolic disorders, and autoimmune diseases. Understanding the intricate interactions within the microbiota-host axis is crucial for unraveling the complexities of human health and disease[1,3].

The human microbiota, comprising diverse microbial communities, plays a critical role in maintaining host health and influencing systemic diseases[4]. One of the most studied microbial phyla in relation to systemic diseases is Firmicutes[4]. An increased abundance of Firmicutes has been associated with conditions such as obesity and metabolic syndrome[5]. This phylum includes bacteria involved in energy metabolism and nutrient absorption, and alterations in its composition have been linked to metabolic dysregulation[5]. On the other hand, Bacteroidetes, another major phylum in the human microbiota, has been found to be reduced in individuals with obesity and metabolic disorders[4,5]. The balance between Firmicutes and Bacteroidetes, known as the F/B ratio, is considered a potential biomarker for metabolic health[4]. Understanding the dynamics of these phyla in the context of systemic diseases provides valuable insights into the intricate relationship between the microbiota and metabolic homeostasis[4,5].

In addition to Firmicutes and Bacteroidetes, certain bacterial genera within the microbiota have been implicated in systemic diseases[5]. One such genus is Akkermansia, a mucin-degrading bacterium associated with a healthy gut mucosal layer[5].

Reduced levels of Akkermansia have been observed in individuals with obesity and metabolic disorders, and its supplementation has shown potential benefits in ameliorating metabolic dysregulation[6]. Another genus, Faecalibacterium, known for its anti-inflammatory properties, has been found to be decreased in conditions such as inflammatory bowel disease and metabolic disorders[6]. The role of these specific microbial genera in influencing systemic diseases highlights the potential for targeted interventions to modulate the microbiota and promote host health[5,6].

The intricate interplay between the intestinal microbiota and blood pressure regulation has emerged as a significant area of interest in recent research[7]. Studies have demonstrated that the composition and diversity of the gut microbiota can influence blood pressure through various mechanisms[2,6]. One such mechanism involves the production of short-chain fatty acids (SCFAs) by specific gut bacteria. SCFAs, such as butyrate, propionate, and acetate, are byproducts of microbial fermentation of dietary fibers[7]. These SCFAs have been shown to exert anti-inflammatory effects, enhance endothelial function, and contribute to blood pressure homeostasis[8]. Moreover, the gut microbiota plays a crucial role in modulating the renin-angiotensin-aldosterone system (RAAS), a key regulator of blood pressure. Dysregulation of the RAAS, influenced by the gut microbiota, can contribute to hypertension. Understanding the molecular and metabolic interactions between the gut microbiota and blood pressure regulation provides novel insights into potential therapeutic strategies for managing hypertension[7,8].

OBJECTIVE

To analyze and describe the main aspects microbial dysbiosis in hypertensive disease of the last 10 years.

METHODS

FOCUSED QUESTION

This review was performed to answer the focused question*: Can dysbiosis exert beneficial or harm effects on human arterial pressure?*

LANGUAGE

Only studies in English were selected.

DATABASES

This review has included studies available in MEDLINE–PubMed (National Library of Medicine, National Institutes of Health) databases. The descriptor used was "dysbiosis" AND "blood pressure". The use of the above descriptor helped to identify studies related to the use of dysbiosis and its effects.

STUDY SELECTION

Abstracts, conferences, letters to editors and other sources were consulted but not included. Furthermore, other relevant studies about dysbiosis and human heath were included to help in the Introduction and Discussion sections.

This study included studies that reported the effects of the green coffee in human health. The inclusion criteria applied in this review were only human interventional studies.

The exclusion criteria for this search were reviews, studies not in English, editorials, case reports, and poster presentations. We also excluded studies with animal models.

DATA EXTRACTION

we selected articles published in the last 10 years.

RESULTS

At the end of the selection process, 5

articles involving 479 subjects were included. The age range of subjects was 56 years.

Reference	**Population / Intervention/ Comparison**	Outcomes
Studies on microbial dysbiosis and hypertensive disease		
Lee et al., 2014	A randomized, double-blind, placebo-controlled study was conducted with 50, in which patients with higher BMI and waist circumference were enrolled and randomly assigned to receive Bofutsushosan with either probiotics or placebo capsules for a period of eight weeks.	Correlations between gm and change in body composition indicate that probiotics may influence energy metabolism in obesity. Correlation between endotoxin level and weight reduction indicates that probiotics may play an important role in prevention of endotoxin production, which can lead to gut microbiota dysbiosis associated with obesity.
Gomez et al., 2016	involved 205 women at 16 weeks gestation from the SPRING study, utilizing 16S ribosomal RNA sequencing to determine the gut microbiota composition	Overall, the findings suggest that, at 16 weeks gestation, the gut microbiota's abundance of butyrate-producing bacteria and butyrate production are significantly and negatively associated with BP and plasminogen activator inhibitor-1 levels in overweight and obese pregnant women
Xue et al., 2021	Fifty participants who met the inclusion criteria were randomly divided into the DF group (n = 25) and control group (n = 25). All the participants received education on regular dietary guidance for HTN. In addition to dietary guidance, one bag of oat bran (30 g/d) supplement (containing DF 8.9 g) was delivered to the DF group	Increased DF supplement improved BP, reduced the amount of antihypertensive drugs, and modulated the GM.
Su et a., 2022	90-day controlled open-label trial to evaluate the health improvement ability of a specially designed diet, and the diet combined with FMT	FMT changed the gut microbiota more quickly than diet. Beneficial bacterium, such as Bifidobacterium, increased along the study and was negatively correlated with blood glucose, BP, blood lipid and BMI. SRB, Bilophila and Desulfovibrio, decreased significantly after treatment, showed a positive correlation with blood glucose indices. Thus, the specially designed diet is beneficial to improve blood glucose control in diabetic patients, it also showed the potential to reverse dyslipidemia and dysarteriotony.
Jing et al., 2023	A total of 87 HTN subjects and 45 controls were recruited with demographic and clinical characteristics documented. Fecal samples were collected for 16S rRNA gene sequencing and metagenomic sequencing.	fecal GM characteristics in HTN females and males in a northwestern Chinese population, further supporting the notion that GM dysbiosis may participate in the pathogenesis of HTN, and the role of sex differences should be considered.

Blood Pressure (BP); Body Mass Index (BMI); Dietary Fiber (DF); Fat Matter Transplantantion (FMT); Gut Microbiota (GM); Hypertension (HNT); Reverse Ribonucleic Acid (Rrna); Sulfate-Reducing Bacteria (SRB).

TABLE 1.

DISCUSSION

Lee et al.'s study demonstrated significant reductions in weight and waist circumference in both study groups, with no discernible differences in body composition and metabolic markers. Correlation analysis revealed positive associations between changes in body composition, endotoxin levels, and the population of gut Lactobacillus plantarum, as well as positive correlations between Gram-negative bacterial population and changes in body composition and total cholesterol levels. Conversely, the gut Bifidobacterium breve population showed a negative correlation with endotoxin levels. These findings highlight the intricate interplay between gut microbiota and physiological changes, shedding light on potential connections between microbial populations and metabolic outcomes.

In the investigation by Gomez et al., the study involving overweight and obese pregnant women revealed intriguing associations between gut microbiota composition and blood pressure. Elevated blood pressure in obese individuals was linked to a decrease in butyrate production capacity and an increase in plasminogen activator inhibitor-1 concentrations. The inverse correlation between systolic blood pressure and the abundance of the butyrate-producing genus Odoribacter suggests a potential role for microbiota in blood pressure regulation. These findings emphasize the importance of understanding the gut microbiota's influence on metabolic health during pregnancy, with implications for developing strategies to maintain normal blood pressure in overweight and obese pregnant women through enhancing butyrate-producing capacity.

Xue et al. conclude that supplementing diets with sufficient dietary fiber is a valuable strategy for effectively improving blood pressure in individuals with hypertension or pre-hypertension. Their findings underscore the importance of considering dietary factors, specifically dietary fiber intake, in the development of clinical nutritional therapy for hypertensive patients.

Su et al.'s study suggests that both diet and diet plus fecal microbiota transplantation hold promise in controlling blood glucose and blood pressure levels. The shifts observed in the intestinal microbial community, particularly the increase in beneficial bacteria like Bifidobacterium and decrease in sulfate-reducing bacteria, Bilophila, and Desulfovibrio after treatments, underscore the potential role of the gut microbiota in metabolic health. These findings provide insights into the dynamic interactions between dietary interventions, fecal microbiota transplantation, and the gut microbiota in influencing metabolic outcomes.

Jing et al.'s study on hypertension in Northwestern China highlights the diverse gut microbiota composition between males and females with hypertension. The enrichment of specific microbial taxa in hypertensive females suggests potential sex-specific associations. The functional analysis further identified effective classifiers associated with hypertension in females, indicating potential pathways linking gut microbiota to blood pressure regulation. These findings contribute to understanding the intricate relationships between gut microbiota, sex differences, and hypertension in the studied population.

CONCLUSION

In conclusion, these diverse studies collectively illuminate the intricate interplay between gut microbiota and various physiological changes, offering valuable insights into potential connections between microbial populations and metabolic outcomes. Lee et al.'s investigation demonstrated significant reductions in weight and waist circumference, correlating positively with changes in body composition, endotoxin levels, and the population of gut Lactobacillus plantarum. Gomez et al.'s study on overweight and obese pregnant women highlighted intriguing associations between gut microbiota composition, blood pressure regulation, and the decrease in butyrate production capacity. Xue et al. emphasized the role of dietary fiber supplementation in effectively improving blood pressure in individuals with hypertension or pre-hypertension. Su et al.'s research suggested promising outcomes in controlling blood glucose and blood pressure levels through both diet and fecal microbiota transplantation, showcasing dynamic interactions within the gut microbiota. Additionally, Jing et al.'s exploration of hypertension in Northwestern China revealed sex-specific associations within the gut microbiota composition, providing valuable insights into potential pathways linking microbiota to blood pressure regulation. Together, these findings underscore the importance of understanding and harnessing the influence of gut microbiota in shaping metabolic health and offer potential strategies for clinical interventions in conditions such as obesity, pregnancy-related metabolic changes, hypertension, and dietary management.

REFERENCES

1. Sender, R., Fuchs, S., & Milo, R. (2016). Revised Estimates for the Number of Human and Bacteria Cells in the Body. PLOS Biology, 14(8), e1002533. https://doi.org/10.1371/journal.pbio.1002533

2. Belkaid, Y., & Hand, T. W. (2014). Role of the Microbiota in Immunity and Inflammation. Cell, 157(1), 121–141. https://doi.org/10.1016/j.cell.2014.03.011

3. Kamada, N., Seo, S.-U., Chen, G. Y., & Núñez, G. (2013). Role of the gut microbiota in immunity and inflammatory disease. Nature Reviews Immunology, 13(5), 321–335. https://doi.org/10.1038/nri3430.

4. Ley, R. E., Turnbaugh, P. J., Klein, S., & Gordon, J. I. (2006). Microbial ecology: Human gut microbes associated with obesity. Nature, 444(7122), 1022–1023. https://doi.org/10.1038/4441022a

5. Turnbaugh, P. J., Ley, R. E., Mahowald, M. A., Magrini, V., Mardis, E. R., & Gordon, J. I. (2006). An obesity-associated gut microbiome with increased capacity for energy harvest. Nature, 444(7122), 1027–1031. https://doi.org/10.1038/nature05414

6. Cani, P. D., & de Vos, W. M. (2017). Next-Generation Beneficial Microbes: The Case of Akkermansia muciniphila. Frontiers in Microbiology, 8, 1765. https://doi.org/10.3389/fmicb.2017.01765

7. Sokol, H., Pigneur, B., Watterlot, L., Lakhdari, O., Bermúdez-Humarán, L. G., Gratadoux, J.-J., Blugeon, S., Bridonneau, C., Furet, J.-P., Corthier, G., Grangette, C., Vasquez, N., Pochart, P., Trugnan, G., Thomas, G., Blottière, H. M., Doré, J., Marteau, P., & Seksik, P. (2008). Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. Proceedings of the National Academy of Sciences, 105(43), 16731–16736.

8. Marques, F. Z., Nelson, E., Chu, P.-Y., Horlock, D., Fiedler, A., Ziemann, M., Tan, J. K., Kuruppu, S., Rajapakse, N. W., El-Osta, A., Mackay, C. R., Kaye, D. M., & Burchill, L. (2017). High-Fiber Diet and Acetate Supplementation Change the Gut Microbiota and Prevent the Development of Hypertension and Heart Failure in Hypertensive Mice. Circulation, 135(10), 964–977. https://doi.org/10.1161/CIRCULATIONAHA.116.024545

9. Wilck, N., Matus, M. G., Kearney, S. M., Olesen, S. W., Forslund, K., Bartolomaeus, H., Haase, S., Mähler, A., Balogh, A., Markó, L., Vvedenskaya, O., Kleiner, F. H., Tsvetkov, D., Klug, L., Costea, P. I., Sunagawa, S., Maier, L., Rakova, N., Schatz, V., … Müller, D. N. (2017). Salt-responsive gut commensal modulates TH17 axis and disease. Nature, 551(7682), 585–589. https://doi.org/10.1038/nature24628

10. Lee SJ, Bose S, Seo JG, Chung WS, Lim CY, Kim H. The effects of co-administration of probiotics with herbal medicine on obesity, metabolic endotoxemia and dysbiosis: a randomized double-blind controlled clinical trial. Clin Nutr. 2014 Dec;33(6):973-81. doi: 10.1016/j.clnu.2013.12.006. Epub 2013 Dec 31. PMID: 24411490.

11. Gomez-Arango LF, Barrett HL, McIntyre HD, Callaway LK, Morrison M, Dekker Nitert M; SPRING Trial Group. Increased Systolic and Diastolic Blood Pressure Is Associated With Altered Gut Microbiota Composition and Butyrate Production in Early Pregnancy. Hypertension. 2016 Oct;68(4):974-81. doi: 10.1161/HYPERTENSIONAHA.116.07910. Epub 2016 Aug 15. PMID: 27528065.

12. Xue Y, Cui L, Qi J, Ojo O, Du X, Liu Y, Wang X. The effect of dietary fiber (oat bran) supplement on blood pressure in patients with essential hypertension: A randomized controlled trial. Nutr Metab Cardiovasc Dis. 2021 Jul 22;31(8):2458-2470. doi: 10.1016/j.numecd.2021.04.013. Epub 2021 Apr 28. PMID: 34090773.

13. Su L, Hong Z, Zhou T, Jian Y, Xu M, Zhang X, Zhu X, Wang J. Health improvements of type 2 diabetic patients through diet and diet plus fecal microbiota transplantation. Sci Rep. 2022 Jan 21;12(1):1152. doi: 10.1038/s41598-022-05127-9. PMID: 35064189; PMCID: PMC8782834.

14. Lv J, Wang J, Yu Y, Zhao M, Yang W, Liu J, Zhao Y, Yang Y, Wang G, Guo L, Zhao H. Alterations of gut microbiota are associated with blood pressure: a cross-sectional clinical trial in Northwestern China. J Transl Med. 2023 Jun 30;21(1):429. doi: 10.1186/s12967-023-04176-6. PMID: 37391847; PMCID: PMC10311887.