Is there a link between the gut microbiome and arterial hypertension?

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Abstract

The human microbiota consists of a variety of bacterial species which populate the mucosal surfaces and contribute a great deal to the education of our immune system. In terms of metabolism, the microbiota plays an important role by decomposing nutrients that we consume in our food and degrading environmental toxicants and environmental chemicals and drugs. Changing the state of eubiosis to dysbiosis represents an area of extreme interest nowadays, as researchers try to understand the pathophysiology behind it fully. Blood pressure can be influenced by changes in ratios of gut microbiota categories, short-chain fatty acids, specific kidney and blood vessel receptors, gut metabolites trimethylamine (TMA), and trimethylamine N-oxide (TMAO). This minireview aims to reveal some of the major aspects that support the hypothesis that gut microbiota contributes to the regulation of blood pressure. The purpose of all research is to discover the possibility of future personalized microbiome targeted therapy in order to lower the prevalence and incidence of some of the most common afflictions of our time, especially arterial hypertension.

Keywords: microbiota, microbiome, blood pressure, hypertension, TMAO, short chain fatty acids, Olfr 78.

Introduction

The microbiota represents a multitude of bacterial species which can be found on mucosal surfaces. Its widest category, the gut microbiota, is believed to be in correlation with a considerable variety of afflictions and susceptibility to diseases. The microbiome, which is now considered our hidden organ, received excessive attention in recent years. There are between 3 and 10 microorganisms for every human cell; therefore, humans are nowadays considered holobionts [1].

However, the attention over the microbiota is focused mainly on the gut because of its digestive functions and connections to the brain. It is a continuous...
Is gut dysbiosis a cause of hypertension?

The relationship between BP and microbiome has been intensely investigated so far. Growing evidence suggests that changes in the ratio of the microbiota Firmicutes/Bacteroidetes categories could be considered an indicator for some health imbalances [11, 12].

Massive gut colonization with Firmicutes and Bacteroidetes species proved to be in correlation with high blood pressure. The use of antibiotics, besides expected adverse effects (shrinking gut microbiota), can also cause BP variations, which can be influenced by the microorganisms’ genotype. Compounds of bacterial fermentation can lead to BP adjustments through variations of energy consumption, ion transport at renal and gastrointestinal levels, and consequently salt sensitivity. Furthermore, antibiotic administration can modify blood pressure by changing the gut microbiota [13].

A cohort study of 48 hypertensive and 32 normotensive Brazilian individuals showed that hypertensive patients also had dysbiosis (intestinal microbiota with reduced biodiversity). The Firmicutes/Bacteroidetes (F/B) ratio in the category of hypertensive patients was found to be higher than the normotensive group, through a lowering proportion of Bacteroidetes. The F/B ratio was also used as an indicator of obesogenic microbiota, its raised values being linked to high fat and low fiber Western diet and inflammatory status of the patient [14]. Thus, oxidative stress-sensitive butyrate-producing commensal bacteria could develop into a novel target of therapy. This way, the preservation of immunity generated by microbiota can be preserved, and several serious local and systemic disruptions can be avoided. It should be mentioned that Roseburia, one of the main butyrate-producing bacteria that seem to be underrepresented in patients suffering from hypertension, also produces conjugated linoleic acid. This acid was proven to possess anti-inflammatory properties and also possible blood pressure lowering effects [14, 19–22].

Microbiota is influenced by a variety of factors ranging from diet, physical activity to genetics and epigenetics. SCFAs produced by the gut microbiota include the favorable SCFAs (acetate, butyrate and propionate) and non-favorable (lactate). SCFAs act on surface cell receptors, such as G protein-coupled receptors (GPR) 43 and 41, olfactory receptor-78 (Olfr-78), exerting relaxing effects on resistance arteries [23], thus regulating blood pressure [24]. Olfr-78 can be found in kidneys and vascular resistance beds, including also renal afferent arteriole. These are receptors for SCFAs, in particular propionate and acetate. Propionate can modify BP in a manner dependent on the presence/absence of either Olfr-78 or GPR 41. Also, propionate can influence renin release through mechanisms dependent on Olfr-78. The identification of Olfr-78 as an SCFA receptor, along with its localization, led to the possibility that Olfr-78 may be triggered by gut microbiota-derived SCFAs, with the purpose to control BP [25–28].

Important contributions in hypertension have gut metabolites trimethylamine (TMA) and trimeth-
**The search for solutions**

Gut microbiota dysbiosis was proved to be associated with high blood pressure. Low levels of acetate and butyrate-producing microorganisms were correlated with a diminished gut microbial abundance and variety. Nevertheless, a solution was developed. Treatment with oral minocycline (an anti-inflammatory antibiotic) revealed promising results. Besides rebuilding gut microbiota and decreasing the *Firmicutes/Bacteroidetes* ratio, minocycline led to lower BP values [55, 56], lower levels of glycated hemoglobin (HbA1C) and weight loss [57, 58].

A handful of clinical trials aimed to assess the effect of probiotics use on BP modulation. A meta-analysis of nine randomized control trials displayed a considerable lowering of both systolic and diastolic blood pressure levels for patients who received 109 to 1012 colony-forming units (CFU) of probiotics daily for 3 to 9 weeks. The adjustment of BP was higher in those patients with higher BP before the treatment, who underwent probiotic supplementation for more than 8 weeks, with daily doses of more than 1011 CFU [59].

An unfit gut microbiota configuration and activity at young ages can affect the function of the immune system and general health. Probiotics can be seen as a method of prevention for chronic immune-mediated conditions. Epigenetic mechanisms...
generated by probiotics through SCFA formation could be the solution for unraveling the vast beneficial effects of probiotics on general health [60].

Conclusion

The effects of the gut microbiome on blood pressure embody the results of various factors, ranging from individual genetic susceptibility and epigenetics to lifestyle and medication. Much evidence remains to be gathered and much research to be done. However, one thing is for sure: the faster the discovery of most of the intrinsic and extrinsic influences of the gut microbiome over blood pressure values, the better one can use targeted therapy in order to provide the best patient care there can possibly be.

Conflict of interest

The author confirms that there are no conflicts of interest.

References


