Global Prebiotic Association Young Researcher Awards - Entry #345

Name

Hamdi Jama

Your Title

Dr

Your Affiliation

Monash University

Email

hamdi.jama@monash.edu

Phone

+61422034722

Please indicate which category you're applying for:

GPA Young Researcher Award for Applied Research (115 points possible)

Please upload your paper as a PDF

s44161-022-00197-4.pdf

Please provide a link to your published paper (if open access) or abstract:

https://www.nature.com/articles/s44161-022-00197-4

Please provide a summary of your research(limit 250 words)

High blood pressure (BP) is a modifiable risk factor for death globally, contributing to approximately half of all cases of heart attacks and stroke. More than 1 billion people globally live with high BP, and nearly two-thirds of people struggle with uncontrolled high BP, even with medication, underscoring the urgency for effective interventions.

For decades, epidemiological and clinical studies have supported the notion that diets rich in fibre lower BP; however, the underlying mechanisms remained unclear, impeding novel treatments for this silent disease. More recently, perturbations in the gut microbiome emerged as a contributing factor to the development of high BP and thus provided crucial insights for novel therapeutic targets. Emergent preclinical evidence showed that the gut microbiome plays a vital role in breaking down dietary fibre and releasing short-chain fatty acids (SCFAs), potent

BP-lowering agents.

Clinical evidence supporting the manipulation of the gut microbiome for the treatment of hypertension is nonexistent. Thus, to address this gap, we conducted a phase II trial using a novel prebiotic fibre supplement modified to release high levels of SCFA in a randomised, placebo-controlled, double-blind cross-over clinical ’

Please provide a summary of methods (limit 250 words)

We conducted a phase II randomised placebo-controlled double-blind crossover trial approved by the Monash University Human Research Ethics Committee and registered with the Australian New Zealand Clinical Trials Registry (ACTRN12619000916145).

Twenty treatment-naïve subjects with high BP were recruited between 2019 and 2021 through various avenues, including print and digital media. Office BP measurements were used to enrol subjects, and gold standard 24-hour BP (Mobil-O-Graph device) monitoring was used to confirm high BP. Once enrolled, participants were instructed to consume 40 grams of the prebiotic high amylose maize starch modified to release SCFAs or an equivalent amount of regular/corn flour as a placebo control, and the intervention period lasted three weeks, followed by a 3-week washout period between arms.

Each participant documented a 3-day dietary intake, which was analysed using Foodworks Software. Our primary endpoint was a change in 24-hour systolic BP. Secondary endpoints included SCFA levels and changes in the gut microbiome. We assessed 24-hour BP changes, measured plasma SCFA using liquid chromatography, sequenced the 16S gene V4-V5 region in stool samples, and analysed compositional changes using MicrobiomeAnalyst.

Please provide a summary of your results (limit 250 words)

Subjects were, on average, 55.8±11.2 (mean±SD) years old, had a body mass index (BMI) of 25.7±2.5km2/m, and 30% were female. The mean 24-hour SBP baseline was 136±6mmHg. Our results demonstrated a clinically relevant reduction in 24-hour systolic BP irrespective of age, sex, and BMI. Our study achieved a mean reduction of –6.1±9.9mmHg (P= 0.027) within the HAMSAB treatment group, equivalent to taking one BP-lowering medication, compared to the placebo arm. This decrease was observed as early as two weeks into the three-week intervention. Day and night systolic BP were reduced by –6.5±12.3mmHg (P=0.01) and –5.7±9.8mmHg (P=0.02), respectively, and 24-h central BP by –7.2±14.7 mmHg (P=0.005). There was no change in stroke volume, cardiac output or heart rate; however, HAMSAB reduced total vascular resistance(P=0.045). Compared to the placebo, the HAMSAB intervention elevated plasma acetate and butyrate levels by 7.8-fold (p=0.016), an amount that would not be achieved through a regular diet. HAMSAB shifted the faecal microbial ecosystem (P=0.037) and increased the prevalence of the acetate and butyrate-producing microbes such as Parabacteroides distasonis and Ruminococcus gauvreauii (q-value<0.05).

Please provide a statement about what, in your opinion, makes this paper outstanding and why it fits into the grant category you selected. (limit 250 words)

Our study marks a pivotal milestone in advancing the understanding of gut microbiota-mediated BP regulation, presenting prebiotic fibre as a promising dietary intervention for treating high BP. Importantly, it demonstrates how readily diet can manipulate the beneficial substances microbiota produce. This sets the stage for exploring targeted interventions based on the gut microbiome, paving the way for innovative therapies in the management of high BP. Our study's innovative approach, using a modified prebiotic intervention, showcases a clear

commitment to translating basic scientific knowledge into practical solutions to explore novel and effective interventions to treat high BP, which continues to kill millions globally.
The trial design, a randomised, placebo-controlled, double-blind method, represents a rigorous and robust approach, ensuring the reliability and validity of the results. We successfully overcame practical challenges associated with delivering SCFA to patients by using a supplement formulated to release high levels of SCFA. This was a critical aspect of translating our preclinical findings and represented a significant hurdle for clinical applications. Moreover, we used highly palatable foods developed in collaboration with a dietitian and a research chef, highlighting our comprehensive strategy for ensuring patient compliance (93% in both arms).
The clinical impact of our research extends beyond traditional high BP management, including the potential applications in stroke and heart failure patients, both of which currently have poor outcomes and lack effective therapies. This broadens the scope of applied relevance and underscores the transformative potential of fibre-based interventions for noncommunicable diseases globally.

By typing your full name below and completing this application, you verify that you are the first author of this research and that this paper is original research.

Hamdi Jama

Global Prebiotic Association