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Metabolomic signatures associated with blood pressure in healthy Australians: a cross-sectional study

H. Supple[2,1], C. Collins[2,1], E. Clarke[2,1] and J. Stanford[2,1]

[1]*Food and Nutrition Research Program, Hunter Medical Research Institute, New Lambton Heights, New South Wales, Australia*

[2]*The University of Newcastle, Callaghan, New South Wales, Australia*

Identifying reliable blood pressure biomarkers is essential for understanding how dietary interventions might supported a reduction in hypertension. Metabolomics, which involves the analysis of small molecules in biological samples[(1)], offers a valuable tool for uncovering metabolic biomarkers linked to both dietary patterns and blood pressure, providing insights for more effective dietary strategies to manage or prevent hypertension. The aim was to evaluate associations between plasma and urinary metabolite concentrations with blood pressure measures (systolic blood pressure [SBP] and diastolic blood pressure [DBP]) in healthy Australian adults. This cross-sectional secondary analysis used baseline data from a randomised, cross-over feeding trial[(2)]. Plasma and urinary metabolomic data were generated using Ultra-high Performance Liquid Chromatography-Tandem Mass Spectrometry (UHPLC-MS/MS) through Metabolon Inc.'s (Morrisville, USA) Global Discovery Panel. Blood pressure was assessed in clinic using the Uscom BP+ supra-systolic oscillometric central blood pressure device, with the cuff positioned on the upper arm at the strongest pulse signal location. Participants sat relaxed and comfortably for 5 minutes before their measurements were taken. They remained seated with legs uncrossed, feet flat on the floor, and were instructed to maintain even breathing throughout the tests. Blood pressure was measured with three consecutive readings taken from the supported left arm, with a 1-minute rest between each reading. The first reading was discarded, and the average of the remaining two was used as the final measurement. Metabolite concentrations were log-transformed. Associations among blood pressure measures and urinary or plasma metabolites were evaluated using linear regression models, adjusting for age and sex. A total of 34 healthy Australian adults (mean age 38.4 ± 18.1 years, 53% females) baseline data was included. After adjusting for multiple comparisons using the Benjamini-Hochberg procedure with a significance threshold of $q < 0.2$, a negative association between two urinary metabolites (gamma-glutamyl histidine and gamma-glutamyl phenylalanine) and DBP was identified. In addition, 32 plasma metabolites were associated with SBP with 18 showing a negative association, including 1,2-dilinoleoyl-GPC (18:2/18:2) and 1-linoleoyl-GPC (18:2), and 14 showing a positive association (beta-hydroxyisovalerate, 3-Hydroxyisobutyrate). Potential mechanisms based on existing research that might explain these associations include the role of gamma-glutamyl peptides in lowering DBP by reducing oxidative stress and improving endothelial function[(3)]. In contrast, 3-hydroxybutyrate may elevate blood pressure due to metabolic disturbances linked to impaired branched-chain amino acid catabolism[(4)]. Furthermore, 1,2-Dilinoleoyl-GPC and 1-linoleoyl-GPC, both contain linoleic acid, which could contribute to lowering systolic blood pressure (SBP) by mitigating vascular inflammation[(5)]. Although some of these metabolites have been implicated in blood pressure regulation in prior research, others revealed new associations. These findings suggest potential candidate nutritional biomarkers for blood pressure, but further research is needed to confirm their reproducibility, and causal role in blood pressure regulation.

References

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