Gut microbiota-derived Hydrogen Sulfide is reduced in Spontaneously Hypertensive Rats

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Introduction: Gut bacteria play a significant role in host homeostasis, and gut dysbiosis has been associated with many conditions including hypertension (HTN). In circulation, endogenously produced hydrogen sulfide (H_2S) is an important freely-diffusing molecule that plays a role in modulation of neural, cardiovascular and immune systems. In view of this, reduced circulating levels of H_2S have been shown in animal and human HTN. However, research to date has mainly focused on the H_2S endogenously produced by the host, while scarce evidence suggests that gut bacteria may also contribute to the overall levels of H_2S in host circulation. However, the role of gut bacteria-derived H_2S in HTN has not been determined.

Objective: To investigate whether spontaneously hypertensive rat (SHR), an established model of HTN, has a disruption in the gut bacteria-derived H_2S production.

Material and Methods: Bacterial DNA from fecal samples of adult male normotensive Wistar–Kyoto (WKY) and SHR was isolated for 16s bacterial genomic sequencing. WKY and SHR fecal and plasma samples were analyzed for H_2S levels using modified methylene blue assay. Blood pressures were determined in all rats at several time points using tail cuff to confirm established HTN in the SHR. Data were expressed as mean±SEM. $P<0.05$ was considered statistically significant.

Results: We observed a significant reduction in the abundance of two H_2S-producing gut bacteria in the SHR compared to WKY (*Enterobacteriaceae*: 1.423e-005±1.056e-005 vs. 0.0002329±7.853e-005, n=6, $P<0.05$; *Clostridiaceae*: 0.01134±0.00431 vs. 0.06408±0.01416, n=6, $P<0.01$). This decrease in the H_2S-producing gut bacteria also

reflected in a significant reduction in fecal H_2S levels (SHR: 0±0.01703 AU vs. WKY: 0.094±0.03385 AU, n=5; P<0.05) and lower plasma H_2S levels (SHR: 0.3265±0.07817 AU vs. WKY: 0.6850±0.1790 AU, n=2) in the SHR compared to the WKY.

Conclusions: These results suggest that diminished gut bacterial production of H_2S may contribute to the reduced H_2S observed in host circulation in established HTN.

Keywords: Hydrogen sulfide; Hypertension; Gut

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