Lifelong TMAO Exposure Exerts Hypotensive Effects in Aged Spontaneously Hypertensive Rats

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Abstract

Purpose / Objectives: Trimethylamine N-oxide (TMAO), a bacterial metabolite linked to cardiovascular risk, has a contentious role as either harmful or protective. The long-term effects of TMAO on circulatory homeostasis remain unclear. We hypothesized that chronic TMAO supplementation modulates hypertension-related complications by influencing the tissue renin-angiotensin system (RAS).

Materials / Methods: Ten-week-old male spontaneously hypertensive rats (SHRs) were divided into two groups and provided either water or water supplemented with TMAO for 80 weeks. Circulatory system parameters including hemodynamics, echocardiography, pathomorphology, tissue RAS expression (RT-qPCR), and biomarkers were evaluated.

Results: TMAO-treated rats had significantly lower blood pressure and NT-proBNP levels, along with a smaller left atrium and numerically increased diuresis and natriuresis. No pathological circulatory effects were observed, and age-related histopathological changes were comparable between groups. TMAO supplementation upregulated RAS components, including angiotensinogen and AT1/AT2 receptors, in the heart, kidneys, and colon. However, it also increased blood and urinary levels of trimethylamine (TMA), a toxic TMAO precursor.

Conclusions: Lifelong TMAO exposure appears beneficial for hypertensive circulation, potentially via enhanced natriuresis and RAS compensation. However, the concurrent rise in TMA levels necessitates further investigation into its potential toxicity.