Hemodynamic abnormalities and tissue electrolyte accumulation during initiation of salt-induced hypertension in a rat model of primary aldosteronism

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Salt-dependent hypertension is a major cause of cardiovascular mortality. Primary aldosteronism is the most common form of secondary hypertension. Recent studies have shown that increased tissue Na^+ accumulation, without a parallel increase in blood volume, predisposes to hypertension. The aim of this study was to determine the time course of tissue electrolyte accumulation during the initiation of hypertension in response to increases in salt intake in unilaterally nephrectomized Sprague-Dawley rats given infusions of aldosterone or vehicle. In aldosterone-treated rats compared with vehicle-treated rats, switching from a low-salt diet to a high-salt diet was associated with reduced tissue concentrations of K^+ prior to increases in mean arterial pressure and systemic vascular resistance and decreases in heart rate and cardiac output that developed later during salt and aldosterone treatment. After initiation of hypertension, a secondary increase in tissue Na^+ and a parallel offset of the difference in tissue K^+ content, without water retention were observed in aldosterone-treated rats. Gene set enrichment analysis (GSEA) in skin prior to initiation of hypertension in aldosterone-treated rats compared to vehicle-treated controls revealed significant differential expression of genes from biological processes chloride ion homeostasis and hyperosmotic response, whereas after establishment of hypertension from biological processes muscle development and muscle contraction. In conclusion, the time course of events does not support the idea that aldosterone-driven salt-sensitive hypertension originates from an inability of the body to release sufficient amounts of Na^+. Gene expression analysis in the skin revealed a primary hyperosmotic response and a secondary vascular response. These results provide evidence for an important role of vasodysfunction theory and tissue electrolyte concentrations in the development of hypertension in a rat model of primary aldosteronism.