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Sodium balance, circadian BP rhythm, heart rate variability, and intrarenal renin–angiotensin aldosterone and dopaminergic systems in acute phase of ARB therapy

Abstract

We have revealed that even in humans, activated intrarenal renin–angiotensin–aldosterone system (RAAS) enhances tubular sodium reabsorption to facilitate salt sensitivity and nondipper rhythm of blood pressure (BP), and that angiotensin receptor blocker (ARB) could increase daytime urinary sodium excretion rate (UNaV) to produce lower sodium balance and restore nondipper rhythm. However, the sympathetic nervous system and intrarenal dopaminergic system can also contribute to renal sodium handling. A total of 20 patients with chronic kidney disease (61 ± 15 years) underwent 24-h ambulatory BP monitoring before and during two-day treatment with ARB, azilsartan. Urinary angiotensinogen excretion rate (UAGTV, pg/gCre) was measured as intrarenal RAAS; urinary dopamine excretion rate (UDAV, pg/gCre) as intrarenal dopaminergic system; heart rate variabilities (HRV, calculated from 24-h Holter-ECG) of non-Gaussianity index λ 25s as sympathetic nerve activity; and power of high-frequency (HF) component or deceleration capacity (DC) as parasympathetic nerve activity. At baseline, glomerular filtration rate correlated inversely with UAGTV ($r = -0.47$, $P = 0.04$) and positively with UDAV ($r = 0.58$, $P = 0.009$). HF was a determinant of night/day BP ratio ($\beta = -0.50$, $F = 5.8$), rather than DC or λ 25s. During the acute phase of ARB treatment, a lower steady sodium balance was not achieved. Increase in daytime UNaV preceded restoration of BP rhythm, accompanied by decreased UAGTV ($r = -0.88$, $P = 0.05$) and increased UDAV ($r = 0.87$, $P = 0.05$), but with no changes in HRVs. Diminished sodium excretion can cause nondipper BP rhythm. This was attributable to intrarenal RAAS and dopaminergic system and impaired parasympathetic nerve activity. During the acute phase of ARB treatment, cooperative effects of ARB and intrarenal dopaminergic system exert natriuresis to restore circadian BP rhythm.