Antihypertensive Effect of Calcium Loading on Salt-induced Hypertension: the Role of its Suppressive Effect of Stress Reactivity.

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Although oral calcium (Ca) loading decreases blood pressure (BP) in hypertension, its precise mechanism is unknown. However, the effect of Ca may be intimately related to pressor action of sodium (Na) because Ca loading reduced BP especially in salt-induced hypertension. Enhanced sympathetic nervous system is suggested to contribute to BP rise with salt loading so we hypothesize that Ca loading decreased BP in salt hypertension by suppressing the sympathetic nerve activity. To clarify this concept, we examined the effect of Ca loading on BP, plasma catecholamine (CA) concentration, and stress reactivity in salt-sensitive hypertensive model rats.

First, we examined the effect of Ca loading on BP and plasma CA in angiotensin II (ANGII)-Na rats. ANGII was administered at 125ng/min by osmotic minipump implanted intraperitoneally for 12 days in 7 week-old Sprague-Dawley rats. In sham rats, saline was administered by the similar way. These rats were fed on normal (0.26%) and high (3.15%) Na-containing diet. Also, Ca content in the diets was modified as normal (1.17%) and high (4.07%) Ca. After 12 days of treatment, catheter was inserted into femoral artery to measure mean BP. BP was measured under conscious and unstimulated condition. BP was increased in ANGII group compared with sham group (108±2 vs. 134±4 mmHg, $p<0.05$). Concomitant administration of high Na diet accelerated ANGII-induced hypertension (161±4 mmHg, $p<0.05$), suggesting that ANGII-Na rats is salt-sensitive hypertensive model. In contrast, high Ca diet decreased BP in ANGII-Na rats (126±4 mmHg, $p<0.05$) but not in ANGII rats (119±4 mmHg), indicating that the antihypertensive effect of Ca loading is specific for salt hypertension. Plasma CA was increased in ANGII+Na group compare with sham group (176±15 vs. 276±30 pg/ml, $p<0.05$) but Ca loading normalized the increased plasma CA in ANGII+Na rats (182±13 pg/ml, $p<0.05$). Thus, the sympathetic nervous system may play a role in the depressor effect of Ca loading.

In the second experiment, we investigated the effect of Ca loading on BP and stress reactivity in salt-loaded young (6 week-old) spontaneously hypertensive rats (SHR). Young SHR were fed on normal and high Na diet for 4 weeks. Ca loading was done in these groups of rats. Salt loading increased BP in young SHR (156±5 vs. 189±6 mmHg, $p<0.05$). Ca loading decreased BP in salt-loaded SHR (165±6 mmHg, $p<0.05$) but not in non-salt-loaded SHR (153±5 mmHg). Stress reactivity was evaluated by BP response to electrical footshock (1 and 2.5 mA). The BP response was enhanced in salt-loaded SHR (1 mA: +3±2 vs. +8±2 mmHg; 2.5 mA: +7±4 vs. +27±6 mmHg, $p<0.05$, respectively). Ca loading normalized the enhanced response (1 mA: -4±2 mmHg; 2.5 mA: +10±4 mmHg, $p<0.05$, respectively). In conclusion, the antihypertensive effect of Ca loading, which is specific for salt-induced hypertension, may be intimately relate to its sympathoinhibitory effect and/or its suppressive action on stress reactivity.