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Glucocorticoid activity and metabolism with NaCl-induced low-grade metabolic acidosis and oral alkalization: results of two randomized controlled trials.

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Low-grade metabolic acidosis (LGMA), as induced by high dietary acid load or sodium chloride (NaCl) intake, has been shown to increase bone and protein catabolism. Underlying mechanisms are not fully understood, but from clinical metabolic acidosis interactions of acid-base balance with glucocorticoid (GC) metabolism are known. We aimed to investigate GC activity/metabolism under alkaline supplementation and NaCl-induced LGMA. Eight young, healthy, normal-weight men participated in two crossover designed interventional studies. In Study A, two 10-day high NaCl diet (32 g/d) periods were conducted, one supplemented with 90 mmol KHCO3/day. In Study B, participants received a high and a low NaCl diet (31 vs. 3 g/day), each for 14 days. During low NaCl, the diet was moderately acidified by replacement of a bicarbonate-rich mineral water (consumed during high NaCl) with a non-alkalizing drinking water. In repeatedly collected 24-h urine samples, potentially bioactive-free GCs (urinary-free cortisol + free cortisone) were analyzed, as well as tetrahydrocortisol (THF), 5α-THF, and tetrahydrocortisone (THE). With supplementation of 90 mmol KHCO3, the marker of total adrenal GC secretion (THF + 5α-THF + THE) dropped ($p = 0.047$) and potentially bioactive-free GCs were reduced ($p = 0.003$). In Study B, however, GC secretion and potentially bioactive-free GCs did not exhibit the expected fall with NaCl-reduction as net acid excretion was raised by 30 mEq/d. Diet-induced acidification/alkalization affects GC activity and metabolism, which in case of long-term ingestion of habitually acidifying western diets may constitute an independent risk factor for bone degradation and cardiometabolic diseases.