Kidney Int. 2016 Aug;90(2):325-333.

Higher diet-dependent renal acid load associates with higher glucocorticoid secretion and potentially bioactive free glucocorticoids in healthy children.

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Metabolic acidosis induces elevated glucocorticoid (GC) levels. However, the influence of less strong daily acid loads on GCs is largely unexplored. To investigate this, we studied whether higher acid loads in children, fully within the normal range of habitual diets, associate with endogenous GCs. In a specific quasi-experimental design, we examined 200 6- to 10-year-old healthy participants of the Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study equally divided to either high or low 24-hour renal net acid excretion. Major urinary GC metabolites were analyzed by gas chromatography-mass spectrometry to assess daily adrenal GC secretion and metabolites of tissue cortisol catabolism (6β-hydroxycortisol and 20α-dihydrocortisol). Liquid chromatography-mass spectrometry was used to quantify urinary free cortisol and cortisone. After confounder adjustment, significant positive associations were unmasked for urinary potential renal acid load and net acid excretion with adrenal GC secretion, free cortisone, free cortisone plus cortisol, 6β-hydroxycortisol, and 20α-dihydrocortisol. An inverse association emerged for an enzymatic marker (5β-reductase) of irreversible GC inactivation. Our data suggest that existing moderate elevations in diet-dependent acid loads suffice to raise GCs and affect cortisol metabolism. Thus, potential detrimental effects of high acid loading appear to be mediated, in part, by increased GC activity via increased GC secretion and/or reduced GC inactivation. Higher cortisone levels, directly available for intracrine activation to cortisol may play a special role.