Adverse Effects of Sodium Chloride on Bone in the Aging Human Population Resulting from Habitual Consumption of Typical American Diets[1–3]

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Abstract

A typical American diet contains amounts of sodium chloride far above evolutionary norms and potassium far below those norms. It also contains larger amounts of foods that are metabolized to noncarbonic acids than to organic bases. At baseline, in a steady state, diets that contain substantial sodium chloride and diets that are net acid producing each independently induce and sustain increased acidity of body fluid. With increasing age, the kidney's ability to excrete daily net acid loads declines, invoking homeostatically increased utilization of base stores (bone, skeletal muscle) on a daily basis to mitigate the otherwise increasing baseline metabolic acidosis, which results in increased calciuria and net losses of body calcium. Those effects of net acid production and its attendant increased body fluid acidity may contribute to development of osteoporosis and renal stones, loss of muscle mass, and age-related renal insufficiency. The inverted ratio of potassium to sodium in the diet compared with preagricultural diets affects cardiovascular function adversely and contributes to hypertension and stroke. The diet can return to its evolutionary norms of net base production inducing low-grade metabolic alkalosis and a high potasium-to-sodium ratio by *1*) greatly reducing content of energy-dense nutrient-poor foods and potassium-poor acid-producing cereal grains, which would entail increasing consumption of potassium-rich net base-producing fruits and vegetables for maintenance of energy balance, and *2*) greatly reducing sodium chloride consumption. Increasingly, evidence supports the health benefits of reestablishing evolutionary norms of dietary net base loads and high potassium and low sodium chloride loads. We focus here on the American diet's potential effects on bone through its superphysiologic content of sodium chloride.   J. Nutr. 138: 419S–422S, 2008.

Introduction

We describe here the adverse effects on bone in adult humans consequent to their habitual ingestion of typical early 21st century American diets (1–4). We focus on contemporary American diets, but European diets and those of many Westernized countries share the characteristics of American diets relevant to their sodium chloride and acid-base effects. Such diets, their effects amplified by human aging, cause otherwise healthy adult humans to sustain chronic progressively worsening, pathogenically significant, low-grade, hyperchloremic

metabolic acidosis (5–8). The same individuals also suffer chronically from the absence of a chronic low-grade, diet-induced, non-chloride-depleted, potassium-replete, metabolic alkalosis, an acid-base, potassium, and chloride state for which natural selection appears to have optimized human physiology, but one that the contemporary American diet precludes attainment and maintenance (3,9). The same individuals also suffer chronically from the adverse cardiovascular effects of an inverted dietary ratio of potassium to sodium (10,11), inverted in respect to the ratio in the diets consumed by *Homo sapiens* until the agricultural and industrial revolutions began, with the consumption of superphysiologic amounts of sodium chloride.

Contemporary diets and sodium chloride and net acid load

The tonic baseline metabolic acidosis induced by the American diet results from an imbalance in the supply of nutrient precursors of bicarbonate (HCO_3^-) and hydrogen ions (H^+) that causes HCO_3^- delivery to the systemic circulation to lag consistently behind that of H^+. The rate of endogenous generation of HCO_3^- from the metabolism of dietary inorganic, predominantly potassium, salts of organic acids (e.g., potassium
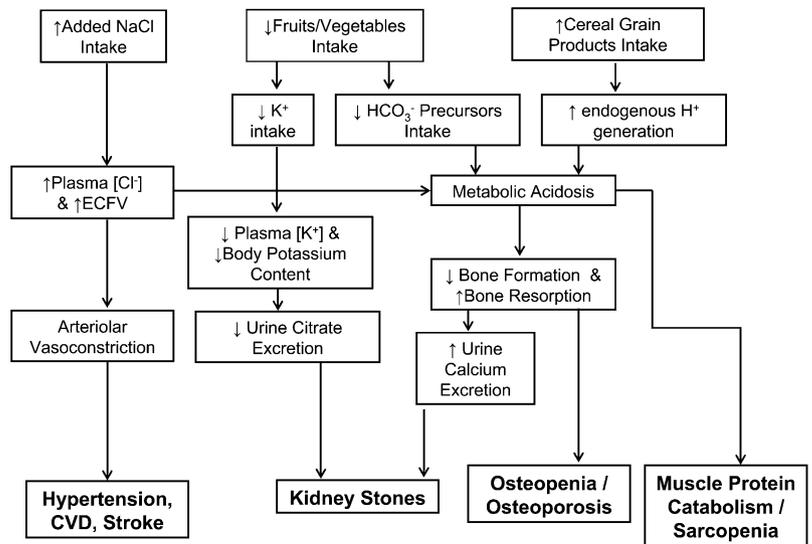
CHARACTERISTICS OF THE MODERN DIET COMPARED TO THE HUMAN ANCESTRAL DIET – AND PATHOPHYSIOLOGICAL CONSEQUENCES

FIGURE 1 Comparisons between the modern and Paleolithic diets and some of the potential pathophysiologic consequences associated with contemporary diets.

citrate) does not keep pace with the rate of generation of H^+ from noncarbonic acids (e.g., sulfuric acid, various organic acids), end-products of metabolism of ingested precursors (e.g., sulfur-containing amino acids yielding sulfuric acid), or incompletely oxidized organic acids (e.g., citric acid). An inadequate dietary supply of plant foods rich in potassium-coupled bicarbonate precursors primarily accounts for the systemic H^+/HCO_3^- supply imbalance (3). Dietary bicarbonate deficiency thus accounts primarily for the tonic metabolic acidosis caused by habitual ingestion of the net acid-producing American diet.

The kidney mitigates, but does not reduce to zero, the severity of the American diet-induced acidemia and hypobicarbonatemia. That mitigating effect wanes, moreover, as renal acid-base regulatory function normally declines progressively with age. The diet's induced acidemia and hypobicarbonatemia progressively increase with age (6). Compounding this trend, the superphysiologic consumption of sodium chloride independently induces a metabolic acidosis. The American diet-induced metabolic acidosis thus constitutes partly a "dietary bicarbonate deficiency" acidosis, partly a "renal" acidosis, and partly a sodium-chloride-induced "dilutional-type" acidosis.

The American diet represents one end of the spectrum of diet patterns that differ from ancestral norms; many countries have similar diet patterns. For ~190,000 y of the ~200,000 y of existence of *Homo sapiens*, people consumed entirely wild animal-source foods and uncultivated plant-source foods but rarely wild cereal grains and legumes. The shift began with the invention of cereal-grain agriculture some 10,000 y ago, spread worldwide ~7000 y ago when agriculture became the dominant source of the food supply of humans, intensified with the industrial revolution and the progressive development of processed foods, and reached extremes with the fast-food revolution of the second half of the 20th century. The American diet's induced metabolic acidosis reflects a shift from net base-producing diets of our preagricultural hunter-gatherer ancestors (3,12), to the net acid-producing diets of our modern agriculturally based, processed-food-based society (2,3). In contemporary diets, the most common plant food ingested, cultivated cereal grains, yields net acid on metabolism (3,4,13,14), and the high energy content of cereal grain products typically ingested in

the American diet, as well as energy-dense nutrient-poor foods (e.g., fats and sugars), results in lower intakes of potassium- and bicarbonate-precursor-rich plant foods. An inadequate dietary supply of plant foods rich in HCO_3^- precursors (and also rich in potassium) primarily accounts for the American diet's induced metabolic acidosis (3). The ratio of potassium organates to sodium chloride inverted with the dietary shift, as potassium- and bicarbonate-precursor-rich plant food consumption fell, and sodium chloride became increasingly mined and utilized as preservative and taste enhancer.

To a considerable extent, humans remain genetically adapted to the potassium-rich, sodium-chloride-poor, net base-producing diet of our ancestral hunter-gatherers, an adaptation that natural selection maintained over some 7 million of years of hominid evolution leading to the emergence of *Homo sapiens* (12). The shift to the contemporary diet occurred too recently for evolutionary forces to have had opportunities to make substantial adjustments in human genetically determined core metabolic machinery (15–19). From an evolutionary perspective, the biologically natural and presumably optimal diet of *Homo sapiens* consists of a potassium-rich, sodium-chloride-poor, bicarbonate-precursor-rich menu (20).

We suggest that the dietary patterns responsible for diet-induced, age-amplified, low-grade metabolic acidosis and the absence of diet-induced, low-grade metabolic alkalosis, coupled with an unavoidably suboptimal dietary K^+ and with superphysiologic dietary sodium chloride, contribute to the pathogenesis of age-related disorders, including osteoporosis, sarcopenia, nephrolithiasis, hypertension, stroke, some types of cancer, insulin resistance, thyroid and growth hormone disturbances, and progressive renal insufficiency (3,4,21–29) (**Fig. 1**).

Bone and dietary sodium chloride

Fractures of the spine and fractures of the hip and forearm, especially related to falls and subnormal bone mass (osteopenia, osteoporosis), impose a substantial health burden on aging women and men. Although many factors other than diet contribute to osteopenia and osteoporosis with aging—hereditary predisposition, insufficient sunlight exposure, hormonal changes—the contemporary diet pattern of inverted ratios of potassium to

sodium and of net base precursors to net acid precursors also plays a role.

As the salt war rages on the blood pressure front, a salt war rages on the bone front: whether to restrict diet NaCl to reduce the risk of age-related osteoporosis (30–32). Cohen interpreted an extensive review of the literature as providing no evidence for dietary NaCl as a risk factor for osteoporosis (30). Teucher and Fairweather-Tait (32) similarly interpreted the literature skeptically. MacGregor, however, interpreted the literature as supporting dietary NaCl as a risk factor for osteoporosis and advocates salt restriction as a preventive measure (31). U.S. Federal agencies have taken no position. The FDA (33) does not advise Americans on their level of NaCl intake; the DHHS and USDA's Dietary Guidelines for Americans 2005 (34) makes no mention of salt intake in relation to bone health; and the NIH Office of Disease Prevention (35) states " … the degree of reduction in Na intake required to protect the skeleton at contemporary Ca intakes is probably not realistically achievable. It is far easier to solve the problem by increasing Ca intake."

A number of studies suggest a detrimental effect of dietary salt on bone. Devine et al. (36), in a longitudinal observational study of the relation of salt intake and bone mineral density using multiple-regression analysis of dietary calcium intake and urine sodium excretion on the change in bone density, showed that both dietary calcium and urinary sodium excretion were significant determinants of the change in bone mass over 2 y at the hip and ankle. In an interventional study, Lin et al. (37) reported that reducing sodium intake complemented the beneficial skeletal effects of the Dietary Approaches to Stop Hypertension diet. Jones et al. (38), in an epidemiological study of salt intake in free-living men and women, concluded, "This study has shown that salt intake is associated with markers of bone resorption in a population-based sample of males and females and appears likely to be a risk factor for osteoporosis …. "

Frassetto et al. (39) also provided evidence of a deleterious effect of dietary sodium chloride. In a cross-sectional study of 166 healthy postmenopausal women habitually consuming typical American diets, they used urine deoxypyridinoline as an index of bone resorption rate, serum osteocalcin as an index of bone formation rate, and urine sodium and chloride as an index of dietary sodium chloride. They interpreted the findings as indicating that dietary sodium chloride magnitude-dependently drives urine calcium excretion, increases bone resorption rate, and increases bone resorption rate relative to bone formation rate. They offered their findings as increasing evidence that the substantial dietary sodium chloride load of the Western diet imposes a significant risk factor for bone loss in adults (36–38).

The ability of increased gastrointestinal absorption of calcium to compensate for the hypercalciuria of increased dietary sodium chloride may be related to age and menopausal status. In young men and premenopausal women, increased dietary sodium chloride and consequent hypercalciuria induce an increase in 1,25-dihydroxyvitamin D levels and intestinal calcium absorption (40). However, postmenopausal women do not demonstrate increased 1,25-dihydroxyvitamin D levels (41), suggesting that older women may be unable to compensate for urinary calcium losses induced by sodium chloride.

In part the mechanism of increased bone resorption with dietary sodium chloride may result from the low-grade metabolic acidosis that correlates with the amount of sodium chloride in the diet. In a cross-sectional study of healthy men and women, Frassetto et al. (42) found that dietary chloride strongly correlated positively with dietary sodium ($r = 0.84$, $P < 0.001$) and was an independent negative predictor of plasma bicarbonate concentration after adjustment for diet net acid load, blood carbon dioxide tension, glomerular filtration rate, and positive and negative predictors, respectively, of blood acidity and plasma bicarbonate concentration after adjustment for diet acid load and blood carbon dioxide tension. Those data provide the first evidence that, in healthy humans, the diet loads of sodium chloride and net acid independently predict systemic acid-base status, with increasing degrees of low-grade hyperchloremic metabolic acidosis as the loads increase. If we can assume a causal relationship, over their respective ranges of variation, sodium chloride has ~50–100% of the acidosis-producing effect of the diet net acid load.

Sellmeyer et al. (D. E. Sellmeyer, S. R. Cummings, F. Tylavsky, D. C. Bauer, S. Kritchevskey, A. Newman, S. Rubin, E. Simonsick, T. Harris, and A. Sebastian, unpublished observations, 2005) found in older individuals that P_{CO_2}-adjusted serum bicarbonate associated positively with hip bone mineral density and negatively with the rate of bone loss measured by interval bone mineral density. This is the first report directly linking systemic acid-base status to bone status in humans. Because previous investigations have shown that, under ordinary physiological conditions, the diet's sodium chloride load independently of net acid load determines systemic acid-base status, that discovery provides perhaps the most solid support to date for the hypothesis that the low-grade metabolic acidosis of the American diet contributes to the pathogenesis of age-related osteoporosis.

Not surprisingly, then, the adverse effects of increased dietary sodium chloride on urine calcium excretion and bone turnover markers in postmenopausal women might be preventable by coadministration of potassium alkali (citrate). Sellmeyer et al. (43) adapted 60 postmenopausal women to a low-salt (87 mmol sodium/d) diet for 3 wk, then randomized them to a high-salt (225 mmol sodium/d) diet plus potassium (90 mmol/d) or to a high-salt diet plus placebo for 4 wk. Urine calcium increased 42 ± 12 mg/d (11 ± 3 mmol/d, mean ± SEM) on the high-salt-plus-placebo diet but decreased 8 ± 14 mg/d (2 ± 4 mmol/d) in the high-salt-plus-potassium-citrate group ($P < 0.008$, potassium citrate vs. placebo, unpaired t-test). N-Telopeptide increased 6.4 ± 1.4 nmol bone collagen equivalents/mmol creatinine in the high-salt-plus-placebo group and 2.0 ± 1.7 nmol bone collagen equivalents/mmol creatinine in the high-salt-plus-potassium citrate group ($P < 0.05$, potassium citrate vs. placebo, unpaired t-test). Thus, the addition of oral potassium citrate to a high-salt diet prevented the increased excretion of urine calcium and the bone resorption marker caused by a high salt intake.

From the above considerations, it would behoove us to consider both the inordinate dietary sodium chloride load and the habitual dietary net acid load of contemporary American diets among the many factors contributing to the pathogenesis of osteopenia and osteoporosis in the aging population. To what extent Americans realistically will restrict sodium chloride intake remains uncertain, and to what extent such restriction is necessary if Americans will substantially increase potassium intake and its associated bicarbonate precursors remains uncertain. However, both decreasing sodium chloride intake and increasing potassium- and bicarbonate-rich precursors may likely not just help the aging skeleton but provide other potential health benefits as well.

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