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EDITORIAL

High salt intake: detrimental not only for blood pressure, but also for bone health?

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Both sodium and chloride are essential nutrients. Notwithstanding, high daily ingestions of sodium chloride (NaCl) can exert adverse health effects. Increasing NaCl intake is associated with rising blood pressure, not only in adults [1], but also in children and adolescents, even in those with blood pressure levels in the low-normal range [2]. While it becomes obvious that the amount of NaCl in daily diet is related to the risk of cardiovascular events, influences of NaCl intake on other health outcomes are less well examined. In this issue of Endocrine, Kim et al. present data from the 2008 to 2011 Korea National Health and Nutritional Examination Surveys, showing that high urinary sodium excretion was significantly associated with low BMD and high prevalence of osteoporosis in lumbar spine in postmenopausal women [3].

This is not the first report on an inverse relationship between salt intake and bone status densitometrically determined as BMD. Similar findings have also been described for young women cross-sectionally [4] and postmenopausal women longitudinally [5]. However, overall evidence is still rather low, due to (i) lacking interventional confirmation and (ii) the fact that several surveys did not find significant inverse relationships between salt intake and BMD. What, on the other hand, is regularly observed along with an increased salt intake, is a rise in renal calcium excretion (for the literature, refer to [3]). In this context, most authors speculate that the corresponding calcium loss is not appropriately compensated by an elevation in intestinal absorption, hence leading to a negative calcium balance with concomitant bone loss. While negative calcium balances cannot be fully excluded, a meta-analysis of few, small-scale nutritional intervention studies (e.g., [6]) on the impact of higher dietary acid loading on the body's calcium balance suggests that the known clear increase in renal calcium loss with elevations in net acid excretion (NAE) is largely intestinally compensated [7].

High sodium intake and high dietary or metabolic acid loading have two important things in common. Both induce a so called low grade metabolic acidosis, i.e., a moderate shift of blood pH and blood bicarbonate buffer to lower levels, usually still within the "normal healthy" range [8, 9]. The high renal sodium excretion following high NaCl ingestion causes an adaptive (renal physiological) reduction in tubular reabsorption of sodium bicarbonate ($NaHCO_3$), thus reducing our most important circulating buffer system $NaHCO_3$. Corresponding $NaHCO_3$ reductions also occur after dietary acid loading, i.e., through increases in potential renal acid loads (PRAL), biochemically measurable as renal NAE increases. The consequences of either form of low grade metabolic acidosis are increases in glucocorticoids, i.e., cortisol levels, as have been reported for high salt intake [10–12] and observed for dietary (orally) acidification in adults [13] as well as in children of our DONALD study [manuscript in preparation]. These glucocorticoid elevations are only of moderate magnitude, however in the long-term, if habitually high PRAL diets or high NaCl amounts are ingested—or even both are combined—an accordingly raised cortisol activity will not be without consequences. Consequences of such mild forms of glucocorticoid increases can be a substantial worsening of cardiometabolic risk factors, e.g., low-density lipoprotein-cholesterol increases or hyperglycemia, as

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recently observed in children with obesity [14]. Various lifestyle, socioeconomic, and environmental causes [15] have additionally been reported to trigger functional hypercortisolism, i.e., moderate glucocorticoid elevations with potential negative skeletal and cardiovascular effects [16]. The mere quantification of cortisol (in blood, urine, or saliva) may not always suffice to appropriately identify functional hypercortisolism. For this, the additional measurement of cortisone can be particularly useful, since cortisone is efficiently activated to cortisol in many tissues and it increasingly emerges as an important player in glucocorticoid-mediated endocrine effects [17–19].

Only recently we could show in healthy children that moderately elevated cortisol and cortisone metabolites—still fully within the normal physiological range—are independently associated with lower BMD and bone strength parameters at the proximal radius [19]. The proof of such subtle long-term effects does usually require a number of sophisticated methodological efforts regarding sample collection (e.g., 24-h urines), dietary recording (e.g., 3-day weighed dietary records), and specific biomarker and hormone metabolite measurements (e.g., gas chromatography–mass spectrometry steroid profiling) which can explain that not every study will uncover corresponding physiological relationships between bone status and moderate elevations of glucocorticoids or other biomarkers. Nonetheless, similar results have been obtained also for healthy young adults [20] as well as elderly [17] showing that even a mild hypercortisolism or -cortisonism may be sufficient to produce detrimental effects on bone health.

Thus, moderate glucocorticoid elevations (definitively not of acute clinical relevance) may represent an important mechanism responsible for detrimental long-term influences of high salt intake (or high dietary PRAL) on BMD, bone health, and later fracture risk [21]. Obviously, such slightly elevated glucocorticoid levels—as potential mediators—could at least partly also explain why high salt diets cause blood pressure increases too.

The question remains at which level of daily intake the detrimental long-term influences of NaCl become relevant. According to the current view, NaCl intakes >5 g/day are already associated with an increased risk for cardiovascular events related to higher blood pressure. In the study of Kim et al., estimated average daily NaCl intake of the studied postmenopausal women was 9 g/day which is almost the same intake level as in a current German survey [22], indicating that at current "normal" NaCl intake levels not only an increased risk for development of hypertension exists, but possibly also for an advancing osteopenia.

The so far obtained results of prospective and cross-sectional studies on varying NaCl intake and long-term bone health are still inconsistent. However, the current study of Kim et al. along with a number of data on bone's susceptibility against only moderate glucocorticoid elevations, which in turn can be induced by high NaCl intake, strongly suggests that high salt ingestion in the long run probably promotes BMD reductions and osteoporosis.

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