Partial neutralization of the acidogenic Western diet with potassium citrate increases bone mass in postmenopausal women with osteopenia

Chronic acid loads are an obligate consequence of the high animal/grain protein content of the Western diet. The effect of this diet-induced metabolic acidosis on bone mass is controversial. In a randomized, prospective, controlled, double-blind trial, 161 postmenopausal women (age 58.6 ± 4.8 y) with low bone mass (T score −1 to −4) were randomly assigned to 30 mEq of oral potassium (K) citrate (Kcitrate) or 30 mEq of K chloride (KCl) daily. The primary end point was the intergroup difference in mean percentage change in bone mineral density (BMD) at lumbar spine (L2 through L4) after 12 months. Compared with the women who received KCl, women who received Kcitrate exhibited an intergroup increase in BMD (±SE) of 1.87 ± 0.50% at L2 through L4 ($P < .001$), of 1.39 ± 0.48% ($P < .001$) at femoral neck, and of 1.98 ± 0.51% ($P < .001$) at total hip. Significant secondary end point intragroup changes also were found: Kcitrate increased L2 through L4 BMD significantly from baseline at months 3, 9, and 12 and reached a month 12 increase of 0.89 ± 0.30% ($P < .05$), whereas the KCl arm showed a decreased L2 through L4 BMD by 0.98 ± 0.38% ($P < .05$), significant only at month 12. Intergroup differences for distal radius and total body were NS. The Kcitrate-treated group demonstrated a sustained and significant reduction in urinary calcium excretion and a significant increase in urinary citrate excretion, with increased citrate excretion indicative of sustained systemic alkalization. Urinary bone resorption marker excretion rates were significantly reduced by Kcitrate, and for deoxypyridinoline, the intergroup difference was significant. Urinary net acid excretion correlated inversely and significantly with the change in BMD in a subset of patients. Large and significant reductions in BP were observed for both K supplements during the entire 12 months. Bone mass can be increased significantly in postmenopausal women with osteopenia by increasing their daily alkali intake as citrate, and the effect is independent of reported skeletal effects of K.

Jehle S, Zanetti A, Muser J, Hulter HN, Krapf R. *J Am Soc Nephrol* 2006;17:3213–3222. **Reprints:** Dr Reto Krapf, University Department of Medicine, Kantonsspital, CH-4101 Bruderholz/Basel, Switzerland. Fax: 4 161 436 3670. E-mail: reto.krapf@ksbh.ch

Dr Reto Krapf is the head of the University Department of Internal Medicine, Kantonsspital Bruderholz in Basel, Switzerland. During the last several years, he conducted experimental and clinical studies investigating the changes in bone mineral metabolism in bone exposed to acidic environments.

The title of your recent article indicates that citrate is an efficient drug to neutralize metabolic acids and increase bone mass. Please explain the relationship between the so-called Western diet and metabolic acids and how this affects the bone tissues.

The diet consumed in Western societies is dominated by animal proteins and wheat flour. From our own experiments and in accordance with other research groups, it was observed that these nutrients generate a chronic acid load that leads to bone loss by physicochemical dissolution of bone mineral and alteration of bone cell function. The chemical reaction in an acidic environment comprises a reduction in the concentration of systemic bicarbonate, a fall in pH, a negative calcium balance with hypercalciuria and subsequent calcium mobilization from the bone, and an apparent loss of mineral potassium (K). Due to bone degradation, buffering of the additional protons is accomplished, the systemic pH restored, and acid loads absorbed. On a more chronic basis, metabolic acidosis alters bone cell function by suppressing osteoblasts while osteoclasts are activated, resulting in decreased bone formation and increased bone resorption.

Do you believe that osteoporosis is, at least in part, caused by the commonly used acid-generating diet?

Yes, it is assumed that the high prevalence of osteoporosis in Western societies is related to lifestyle factors such as diet. Epidemiologic studies indicate a correlation between acidogenic diets, decreased bone mineral density (BMD), and increased fracture incidence. Age seems to be an important factor due to the exposition to this chronic metabolic acidosis over decades, and additionally, the diminishing ability to excrete metabolic acids due to the normal decline in renal function. Women experience greater loss of bone mass during the first postmenopausal years as a result of the estrogen-related changes in bone metabolism and are at greater risk of osteoporosis with increased incidence of bone fractures.

Would you please give us a short synopsis of your latest research published in 2006?

We investigated the effect of oral potassium citrate on BMD after supplementation over 1 year. Nonvegetarian women diagnosed for osteoporosis (T scores -1 to -4) were recruited for the study, as long as they were at least 5 years postmenopausal and had, therefore, reached a more stable situation in terms of the dynamics of bone loss. The test group received a relatively low dose of K citrate (30 mmol daily), while the control group got the same amount of potassium (kalium) as K chloride (30 mmol daily) to control for a possible confounding

effect of excess potassium. All participants received calcium carbonate ($CaCO_3$) (500 mg calcium) and vitamin D_3 (400 IU) to ensure a sufficient daily intake. Data revealed that the daily alkali supplementation with Kcitrate resulted in an increase in bone mass, and that this effect was independent of the co-administered potassium. In the test group, calcium excretion was significantly reduced after 6, 9, and 12 months compared to the control with KCl. Another observation was that blood pressure was reduced in both K supplements during the entire study period.

Do you think that the increase in BMD following citrate administration was mainly caused by new bone formation?

Our results demonstrated divergent changes of 2 commonly used markers of bone formation. In both test and control groups, bone-specific alkaline phosphatase increased, thus indicating an enhanced osteoblastic acitivity in the early stages of bone formation, possibly due to a stimulation of osteoid production by potassium. Serum osteocalcin, a marker for bone formation and turnover, exhibited a decrease in both groups. Hence, we concluded that the observed increase in BMD following prolonged alkali administration was related to a suppression of bone resorption and an enhanced matrix mineralization, rather than increased bone formation.

How was the compliance of the participants? Did they report any side effects of the administrated drug?

The compliance of the participants was high in both groups, at 93% (K citrate) and 94% (K Cl). Only few subjects reported gastrointestinal discomfort from fullness or indisposition.

How realistic is the citrate alternative to the traditional pill-prescription approach?

The results of our study clearly indicate that alkali administration facilitates an increase in BMD by neutralizing the diet-induced acid production. The observed lumbar spine BMD increase of 1.9% is large and compares favorably with the 1-year increase following intake of selective estrogen-receptor modulators (ie, Raloxifene, 1.7% BMD increase as reported by Delmas et al in 1997). Kcitrate has the potential to be a beneficial alternative to the common medications in osteoporotic patients and for subjects requiring any osteoporosis prophylaxis. The BMD increase observed in the present study following acid neutralization predicts efficient reduction of fracture prevalence similar to that of approved pharmaceutical agents.

Do you think that a change back to the ancestral diet forms would cure our society from the burdens of osteoporosis and have beneficial systemic effects, such as blood pressure reduction?

Yes, dietary acid loads are a causal risk for bone loss, particularly in postmenopausal women with osteopenia. The metabolic acidosis can be lessened by an increase in vegetable proteins, fruits, and grains like spelt and barley.

In addition to bone degradation and high blood pressure, are there other systemic effects of metabolic acids?

It is further assumed that chronic acidic load over decades also induces the mobilization of proteins from the musculature leading to myoatrophy. Hence, we are planning further investigations within the frame of a Swiss National Fonds project (NSF 53) investigating musculoskeletal health in elderly subjects.

What are your current critical queries and your interests for further research?

There are still several open questions, eg, about the detailed mechanisms responsible for the reduced bone resorption under citrate supplementation in humans, whether this medication has a long-term effect on the prevalence of bone fractures in osteoporotic patients, and whether this medication has beneficial effects in different populations for prophylaxis of osteopenia and muscular dystrophy. So, we are planning further investigations applying increased doses of oral citrate in multicenter studies.

These promising projects will hopefully help to improve the general health situation of diseased patients and we wish the research group a successful continuation. Despite all of the progress and advancement in the treatment and medication of osteopenia and associated diseases, we have to keep in mind that thorough information of young subjects related to healthful and beneficial diets must have a high priority parallel to the curing achievements.