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Effects of protein on the calcium economy

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Abstract. Studies of the association of dietary protein intake and various components of the calcium economy lead to conflicting conclusions, some suggesting that protein would negatively affect calcium retention and others that it would have a positive effect. Most of the apparent conflict can be explained by two factors: (1) the interdependence of the two nutrients for bone health and (2) probable delayed adaptation to altered intake, such that short-term studies may fail to capture the steady-state relationship between protein intake and calcium balance. At the whole body level, most studies show that high protein intake is osteoprotective, but only if calcium intake is adequate; similarly, metabolic evidence indicates that the protective effect of calcium for the skeleton is evident only when protein intake is relatively high.

Keywords: Calcium retention; Urine calcium; Calcium absorption; Protein intake; Adaptation

1. Introduction

Protein makes up roughly 50% the volume of bone (and about one-third its mass). Both collagen, which constitutes the bulk of bone protein, and the various non-collagenous proteins undergo extensive post-translational modification after their synthesis. As a result, when bone is remodeled and old volumes of are bone resorbed, many of the constituent amino acids released by proteolysis cannot be reutilized. Hence, not only does the primary building of bone during growth require a fresh dietary supply of protein in order to ensure both an adequate mass of protein and an adequate suite of essential amino acids, but the maintenance of bone during adult remodeling does as well. Thus, one would expect a high protein intake to promote skeletal health. There is, in fact, a relatively large body of evidence indicating that that expectation is correct. However, the effects of protein on the

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calcium economy are complex, with many reports suggesting that high protein intake would alter the calcium economy in ways that could lead to negative calcium balance and bone loss.

In this brief overview, I shall summarize the principal effects of protein on the calcium economy, attempt to reconcile the effects of what appear to be countervailing factors, and add previously unpublished data bearing on a critical aspect of the interaction of protein and calcium intakes.

2. Protein intake and urinary calcium excretion

It has been recognized for many years that increased protein intake often leads to an increase in urinary calcium loss [1–3]. Generally, the studies reporting this effect were of short duration and consisted of feeding of pure protein or amino acid sources. The effect has been reproduced in many laboratories and summarized elsewhere [4], but in brief a doubling of protein intake is typically associated with an increase in urinary calcium of about 50% (or roughly 1 mg urine calcium for every gram of diet protein). For this reason, high protein intake, which tends to be characteristic of affluent societies, has often been considered a risk factor for osteoporosis, a conclusion seemingly supported in the Study of Fractures (SOF) project, in which age-related bone loss was directly related to dietary protein intake, and particularly to a high dietary ratio of animal-to-vegetable protein [5].

The rise in urine calcium reported for protein feeding probably has at least three bases: (a) an increase in glomerular filtration rate [6], (b) a lowering of the renal calcium threshold [6] and (c) binding by certain of the absorbed amino acids to calcium-sensing receptors in the renal tubule [7], i.e., a possible partial explanation for (b), above. While this increase in calciuria might be due in part, or at least offset by, greater absorption of dietary calcium, as found by Kerstetter et al. [8,9], several other observations make it clear that the issue is more complex. For example, Bengoa et al. showed that, in patients maintained on total parenteral nutrition (TPN), urinary calcium excretion was directly correlated with the amino acid content of the infusate [6]. This is an important observation in that TPN bypasses the variation in absorption of calcium from the gut which was the focus of the studies by Kerstetter et al.

The degree of urinary calcium loss associated with protein in the infusate reported by Bengoa et al. was quite striking, with negative calcium balances as high as several hundred milligrams per day when infusate protein intake was increased from 1 g/kg/day to 2 g/kg/day. Some of the loss may have been conditioned by the anion content of the TPN solution, since the same investigators showed elsewhere that substitution of bicarbonate for chloride strikingly reduced urinary calcium loss, other components being equal [10]. Nevertheless, these TPN experiments show that, for the same calcium input, urinary calcium output is a direct function of protein intake, at least under the unique circumstances of total parenteral nutrition.

On the other hand, Spencer et al. [11], in controlled feeding experiments under metabolic balance controls, with measurement of all input and output, found no difference in urine calcium between diets containing 200 g of meat or 500 g of meat (a difference of ~50 g protein/day). In my own studies of the calcium economy in mid-life women, using methods identical to those of Spencer et al., my colleagues and I had earlier reported a positive correlation between protein intake and urine calcium in multiple regression models adjusting for calcium and phosphorus intakes [3]. However, more recent analyses from a greatly