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THE CALCIUM CONTROVERSY

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It is often stated that large amounts of calcium are required for strong bones, to calm nerves and for other characteristics of good health. Some nutritionists recommend up to three grams of calcium a day to prevent calcium deficiency. The purpose of this editorial is to review some aspects of Human Evolution, Physiology, Biochemistry and Dietary Habits in order to clarify calcium requirements and its close relationship to intake of other nutrients, mainly magnesium.

EVOLUTIONARY CONSIDERATIONS

Over the past 6000 years or more man evolved in a magnesium and potassium-rich, but calcium and sodium-poor, environment. For survival, the human body had to develop efficient conserving mechanisms for sodium and calcium. To conserve sodium, the Zona Glomerulosa of the Adrenal Cortex secretes a very potent mineralocorticoid, Aldosterone, which increases sodium retention via the kidney [27]. To conserve calcium, the skin developed a synthetic process that manufactures Vitamin D3 from a cholesterol derivative, under the influence of solar ultraviolet radiation. Vitamin D3 is then hydroxylated by the liver to 25-OH-D3. The kidney is the site of the most important step: 1-hydroxylation of 25-OH-D3 to generate 1, 25 (OH)2 D3, the most potent calcium-conserving substance[16]. It increases calcium and phosphate absorption in the small intestine and decreases calcium excretion in the urine:

PHYSIOLOGICAL CONSIDERATIONS

The 1-hydroxylase is located in the kidney as a mitochondrial enzyme. It is sensitive to intramitochondrial calcium and phosphate. Intromitochondrial accumulation of both calcium and phosphate depress the activity of 1-hydroxylase, thereby decreasing formation of 1, 25 (OH)2 D3[22].A low phosphate diet increases and a high phosphate diet depresses 1, 25 (OH)2 D3 production[20].

Besides 1, 25 (OH)2 D3, there are two hormones that play an important role in calcium metabolism: Calcitonin (CT) and Parathyroid Hormone (PTH)[3]. Both hormones are sensitive to serum ionized calcium levels. An increase in serum ionized calcium results in stimulation of CT secretion and suppression of PTH secretion.

CT and PTH regulate skeletal turnover of calcium and availability of cytoplasmic calcium[3]. The major skeletal effect of PTH is to increase bone resorption by stimulating osteoclasts, thereby increasing mobilization of calcium from bone. PTH also favors cellular uptake of calcium by soft tissues and phosphate excretion by the kidney. CT has the opposite effect, that is, it increases deposition of calcium in the bone matrix and blocks cellular uptake of calcium by soft tissues. Magnesium suppresses PTH and stimulates CT secretion[28], therefore favoring deposition of calcium in the bone and removal of calcium from soft tissues. Furthermore magnesium enhances calcium absorption and retention[5, 12], whereas increasing calcium intake suppresses magnesium absorption[2, 25].

BIOCHEMICAL CONSIDERATIONS

Calcium and magnesium are often antagonistic in their effect of biological reactions[7]. For example, the biosynthesis of both phospholipids and proteins involve enzymatic steps which have an obligatory requirement for magnesium and are calcium-inhibited. The glycolytic pathway contains five enzymatic reactions that have an absolute requirement for magnesium and require optimal magnesium/calcium ratio for peak performance.

In order for the cell to maintain the proper magnesium/calcium ratio, several levels of regulation are available, acting on the removal of calcium from the cytoplasm. One such mechanism is the ATP-dependant calcium pump in the cell membrane [9, 10]. The other important mechanism is the transport of calcium inside the mitochondria. The mitochondria uptake of calcium is reversible if calcium concentrations in the microenvironment are kept below certain limits. Above these limits, calcification of mitochondria occurs with subsequent cellular death. In the presence of magnesium, the uptake of calcium by mitochondria can be slowed down. Since ATP utilization is magnesium-dependent, it becomes obvious that the calcium pump at the cell membrane is also magnesium-dependent. The generation of ATP itself through the glycolytic pathway is in part magnesium-dependent and inhibited by calcium.

DIETARY CONSIDERATIONS

Stable civilizations have arisen only when primitive hunting communities have learned to cultivate cereals, such as wheat, rice maize, millets, barley, oats and rye. In many rural areas, cereals provide more than 70% of the energy consumed[9]. Table I shows the magnesium and calcium concentrations in these staple foods. They contain two to eight times more magnesium than calcium, and as much as one thousand milligrams of magnesium could be consumed if two thousand calories were obtained from these sources. One may argue that dairy products contributed to most of the ingested calcium. This is unlikely since 50% of individuals tested so far show allergic

reactions to dairy products and lactose intolerance is common in most ethnic groups, occurring in 70% of Black Americans and over 70% of Orientals, Jews, Arabs, Greeks, Japanese, Eskimos, Indians, Africans and Asians [23, 17, 13, 14, 15, 1, 24, 18, 8, 19 ,30, 31].

TABLE I

MAGNESIUM AND CALCIUM CONCENTRATIONS IN SOME CEREALS

Cereal	Magnesium (mg/100 Cal)	Calcium (mg/100 Cal)	Magnesium/ Calcium Ratio
Millet	50	6.2	8.2
Maize	42	6.0	7.0
Wheat	34	11.0	3.1
Rye	34	11.5	3.0
Brown Rice	25	9.0	2.8
Barley	11	4.6	2.3
Oat	38	18.0	2.1

Considering that 99% of the total body calcium is located in the bones, it is not surprising that academic proponents of high calcium intake have used as an argument the possible role of calcium deficiency in osteoporosis [11, 4, 29]. There is no evidence, however, to support this view. Osteoporosis is not more common in those parts of Asia and Africa where diets are relatively low in calcium (300-500 mg/day) than in Europe and North America where consumption of dairy products contributes to more than1000 mg of calcium/day When patients with severe osteoporosis were given massive doses of calcium they went into positive calcium balance, but radiographic studies revealed no changes in the osteoporotic process Where did that calcium go? Obviously into the soft tissues where it does not belong.

Calcium balance studies have indicated that man can adapt to relatively low calcium intake by increasing calcium absorption and decreasing urinary excretion[10]. There is not such a mechanism for magnesium[26]. The adaptation to low calcium intake is most likely via synthesis of 1, 25 (OH)2 D3 by the kidney. It was previously discussed that high intramitochondrial concentrations of phosphate and calcium in the kidney suppress the formation of 1, 25 (OH)2 D3 [20, 22]. Therefore, mechanisms that increase intracellular and intramitochondrial calcium would prevent adaptation to low calcium intake. Failure of the calcium-pump at the cell membrane and increased uptake of calcium by mitochondria are two such mechanisms which are both magnesium-dependent as previously discussed. Since a low phosphate diet increases formation of 1, 25 (OH)2 D3 [20] and a high magnesium diet would keep calcium out of the mitochondria, it seems therefore that one approach to improving the adaptation to low calcium intake is to ingest a diet low in phosphate and high in magnesium. Such an

approach to the management of osteoporosis would seem more appropriate than the ingestion of massive doses of calcium. The latter approach blocks magnesium absorption and creates a magnesium deficiency, conducive to a failure of the calcium-pump and intracellular accumulation of calcium in soft tissues that eventually leads to irreversible cell damage. Also, magnesium deficiency results in elevated PTH which prevents the utilization of the absorbed calcium for bone formation and favors soft tissue calcification.

Recent studies suggest that calcium requirements are increased by acid-ash, high-protein and high sulfur diet[21]. In order to increase the efficiency of the adaptation mechanism to low calcium intake, every attempt should be made to ingest foods containing a magnesium/calcium ratio of two or more, with neutral or alkaline ash, not excessive in phosphate, sulfur, proteins, refined sugar, fats and other substances that drain the body of both calcium and magnesium. Magnesium deficiency causes a reduced intestinal absorption of calcium and decreased serum ionized calcium.

Magnesium has a calcium-sparing effect and decreases the need for calcium.

Since magnesium suppresses PTH and increases CT, adequate magnesium intake would improve the phosphorous balance from a low phosphate diet by increasing phosphate absorption via the 1, 25 (OH)2 D3mechanisms and by preventing the PTH induced phosphaturia. Furthermore, a high magnesium intake would enhance calcium absorption by the 1, 25 (OH)2 D3mechanisms, increase serum ionized calcium, promote deposition of calcium in the bone matrix where it belongs and minimize cellular uptake and mitochondrial accumulation of calcium.)

With such an approach there would be no need for pharmaceutical companies to develop new and improved calcium blockers in the management of cardiovascular diseases, since magnesium works naturally to produce the same end result.

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