The Nutritional Relationships of Calcium

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Introduction

Calcium is found in every cell throughout the body. However, over ninety percent of calcium is stored in the bones and teeth. The osseous tissues of the body serve not only as structural support but also as a reservoir for calcium and other minerals. These minerals can be drawn upon by the body as the need arises. Calcium is distributed in other tissues as follows: the brain with approximately 4-5 milligrams per 100 grams; the heart, 7-8; kidney, 19; liver, 7; muscles, 7-8; skin and spleen, 9-10. The RDA for calcium are infants, 350-540 milligrams per day; adults, 1000 milligrams per day; and lactating women, 1200 milligrams per day.

Calcium Functions

In conjunction with other elements, calcium is the major constituent of the skeletal structures and teeth. Osseous tissues provide a reservoir for calcium, which can be withdrawn as required in order to maintain extraskeletal functions such as acid-alkaline balance.

The importance of calcium as a potential biological messenger was observed by Ringer in 1883. Shortly afterwards it was determined that calcium is essential for cardiac muscle contractility. It is now known that calcium is involved as a messenger, carrying signals to target activities within cells through specific calcium channels.[1] Calcium ions are essential for activation of enzymes required for normal blood clotting, glycolytic enzyme activation and stability, and influencing cell division and differentiation. Calcium is also involved in secretory processes. Insulin release, for example, is dependent upon adequate calcium being available. Calcium can stimulate insulin release as well.[2]

Calcium Regulation

Calcium is regulated in tissues and

serum at the expense of skeletal structures. Parathyroid hormone (PTH), calcitonin, and vitamin D are the major hormones involved in calcium homeostasis. Their influence on calcium regulation is through their effects upon the kidneys, bone resorption, and intestinal absorption. Other hormones also affect calcium, positively or negatively.

Insulin has a positive influence on calcium retention. Insulin therapy reduces the urinary loss of calcium.[3] Estrogen and prolactin also decrease urinary excretion[4][5] due to their stimulation of active vitamin D metabolites.

Increased calcium excretion can be caused by overactivity of both the thyroid[6][7][8] and adrenal cortical glands. Adrenal glucocorticoids reduce intestinal calcium absorption due to their anti-vitamin D effects.[9] Excessive aldosterone secretion also increases urinary calcium excretion.[10]

Many medications interfere with calcium absorption. Some of the most common include anti-convulsants such as pheno-barbital and diphenylhydantoin, which are known to contribute to osteomalacia.[11] Antacids containing aluminum hydroxide bind calcium in the intestine and have also been documented to contribute to osteomalacia. Cortisone therapy substantially increases the excretion of calcium. Diuretics, except for thiazides, contribute to calcium loss.

Foods containing oxalic and/or phytic acid bind with calcium preventing intestinal absorption. High protein intake can, in some cases, lead to a decrease in calcium absorption or increased urinary excretion.

Malabsorption syndromes that result in increased transient time and diarrhea impair calcium absorption. This can be caused by gastrointestinal surgeries such as jejunoileal bypass and subtotal gastrectomy. Renal failure, nephrotic syndrome, poorly controlled diabetes mellitus, and juvenile diabetes are conditions associated with poor calcium status.

Hypocalcemia

Hypocalcemia is a relatively rare clinical problem. The nervous system is particularly sensitive to the effects of low serum calcium. When the ionic form of calcium falls below 4 milligrams percent (mg.%), or the total serum calcium falls below approximately 7 mg.%, the nervous system can become hyperirritable. Hypocalcemia can eventually lead to sensory disturbances, tetany, and myocardial dysfunction. The major manifestation of low serum calcium is tetany, which usually consists of muscular cramps, laryngeal stridor, seizures, and, if severe, death due to respiratory failure.[12] Causes of true hypocalcemia include chronic renal failure, malabsorption, and hypoparathyroidism. Hypoalbu-minuria is not always associated with depressed ionized calcium and therefore may not give rise to tetany even with hypocalcemia. A positive Chvostek sign is usually indicative of hypocalcemia; however, hypocalcemia does not always give rise to a positive Chvostek sign. It has been reported to be absent in 73% of patients with hypocalcemia.[13]

Calcium deficiency has been associated with conditions not necessarily related to hypocalcemia. These include:
Allergies (histamine)
Adrenal hyperactivity
Hypertension
Hyperkinesis
Anxiety
Hyperthyroidism
Insomnia (type I)
Osteomalacia
Sympathetic dominance Rh. arthritis

Osteoporosis is also associated with calcium deficiency and will be discussed later in more detail.

Hypercalcemia

Hypercalcemia is an elevation of serum calcium above 10.5 mg.%. Primary hyper-parathyroidism and malignancies are major causes of hypercalcemia.[14] Acute immobilization, hypervitaminosis D, or increased tissue sensitivity to vitamin D, and Paget's disease are also associated with elevated serum calcium. Other causes of high serum calcium include Addison's disease (crisis), myxedema, thyrotoxicosis, milk alkali syndrome, and the use of thyazide diuretics.[15 16 17 18]

Conditions associated with hypercalcemia due to hyperparathyroidism include:
Excessive thirst
Dryness of mouth and throat
Dysphagia
Muscle aches
Recent memory loss
Calcific tendinitis
Chondrocalcinosis
Depression
Hearing difficulties
Fatigue
Joint stiffness
Weakness
Restless leg syndrome
Constipation
Dyspepsia
Conjunctivitis

Hyperparathyroidism can contribute to a number of symptoms associated with the gastrointestinal and urinary tracts. A classical and appropriate history of hyperparathyroidism has been described as consisting of "moans, bones, groans, and stones".[19 20] Some investigators have indicated that specific muscle groups are found weak in patients with primary hyperparathyroid-ism. These include the psoas, gluteus medius, hamstrings, deltoids, and biceps.[21]

Factors Contributing to
Calcium Deficiency

Many factors adversely affect calcium status and can lead to a negative calcium balance without associated abnormalities in serum calcium.

Figure 1 shows the minerals that are antagonistic to calcium. Excessive intake of any one or combination of these minerals can contribute to poor calcium status. Calcium is also considered antagonistic to these elements. Calcium can be helpful in reducing the absorption and adverse effects of heavy metals such as lead and cadmium and of excess tissue iron absorption and storage.

Sodium has long been recognized as contributing to hypertension. Some societies, however, consume large amounts of sodium and yet have a low incidence of hypertension while others consume little dietary sodium and suffer from hypertension. In the U.S., studies have shown a distinguishing difference in the consumption

Figure 1.

Figure 2.
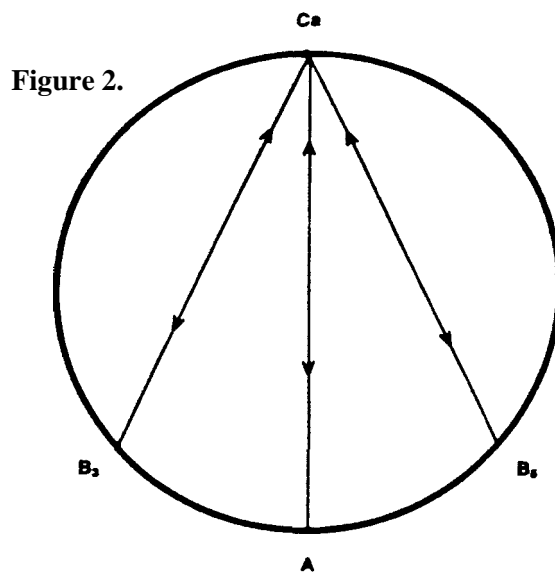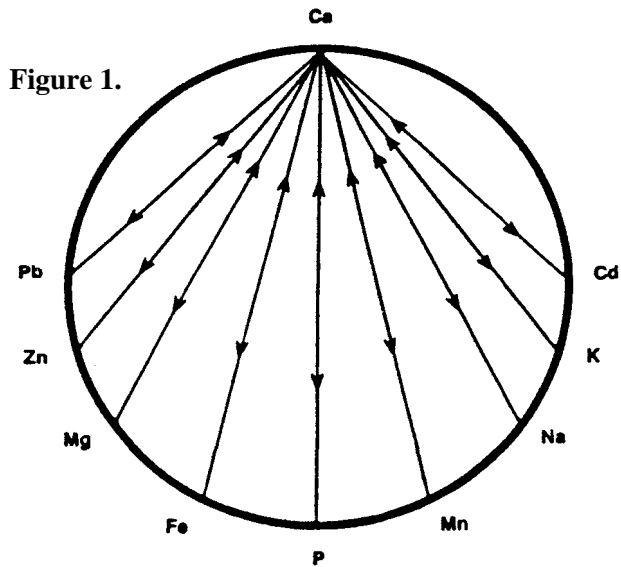
of calcium among hypertensive and normotensive individuals. Hypertensive persons were found to consume 18% less calcium than normotensive persons. Of 17 nutrients analyzed, reduced calcium intake consistently distinguished the hypertensive from the normotensive group.[22] Calcium supplementation has been shown to lower blood pressure in individuals suffering from essential hypertension. The effect is attributed to the natriuresis effects of calcium.[23]

Of course many of the nutritional minerals shown in Figure 1 are also synergistic to calcium's metabolic and/or structural functions. The mineral copper is also synergistic to calcium, due to its involvement in collagen production and protein cross-linking.

Figure 2 indicates the vitamins that are considered antagonistic to calcium. Their antagonistic effects may be direct or indirect. As an example, vitamin A antagonizes vitamin D and therefore can indirectly affect calcium. Vitamin A also has a stimulating effect upon the thyroid, which will affect calcium status as well. Some vitamins have a stimulatory effect upon the metabolic rate. Increased sympathetic neuroendocrine activity can contribute to calcium losses.[24] Many of these vitamins have a synergistic relationship to calcium, including vitamin D.

Osteoporosis

Osteoporosis affects over six million people in the U.S. and has probably become the most widely recognized condition associated with calcium deficiency. Calcium supplementation is generally accepted as a course of therapy for this condition. However, studies have shown that calcium supplementation alone over extended periods has resulted in decreased calcium retention,[25] [26] or has had only minor beneficial effects.[27] The causes of osteoporosis are numerous. As can be seen in Figures 1 and 2, a multiplicity of nutritional factors can contribute to the osteoporotic process other than calcium deficiency. Calcium supplementation can even have a potential in contributing to osteoporosis in the presence of other mineral deficiencies, such as magnesium, phosphorus, and copper. As an example, magnesium is deposited on the surface of the bone, and if a person's magnesium status is marginal, then calcium supplementation can further contribute to a magnesium deficiency. Magnesium deficiency will produce cortical thinning of the bone with resulting fragility. When the neuroendocrine factors are included, we find that over 30 different mechanisms can be involved in contributing to osteoporosis. This may explain why the etiology of osteoporosis is controversial.

There are also numerous factors that can contribute to hypercalcuria. Since the majority of osteoporotic patients do not manifest hypercalcuria,[28] urinary calcium excretion alone may not be a reliable indicator of osteoporosis. If increased urinary calcium excretion exists, it should be distinguished from absorptive or resorptive hypercalcuria.The urinary hydroxypro-

line to creatinine ratio, calcium to creatinine ratio, and serum hydorxyproline to creatinine ratios can be good indicators of bone resorption.

As stated previously, osteoporosis usually has multiple origins. However, in some cases the resulting bone loss of calcium may be a non-specific, secondary response to a specific underlying metabolic problem.[29] Parathyroid hormone aids in the physiological response of other hormones dependent upon calcium for their activity. Calcium affects a number of enzymes and mediates the action and release of several hormones. As an example, if an increased amount of insulin is required by the body, parathyroid activity will increase, resulting in calcium resorption. This in turn will supply extra calcium for the release of insulin as well as other hormones demonstrating the need for treating the patient instead of the symptom. If the patient is developing adult onset diabetes, then the treatment of his or her osteoporotic condition will not meet with much success until the diabetic condition is addressed.

With vitamins and minerals, rarely does a single nutrient deficiency develop alone. Usually, other deficiencies co-exist. The same is true of endocrine disturbances. Overactivity or underactivity of a single endocrine gland rarely occurs. As an example, when overactivity of the parathyroid gland develops, a concomitant low thyroid is usually found. Patients with hypothyroidism frequently have elevated parathyroid hormone levels.[30][31] Increased thyroid activity apparently decreases parathyroid activity;[32] therefore, support of the thyroid gland is warranted in patients who develop osteoporosis with hyperpara-thyroid involvement. On the other hand, osteoporosis caused by hyperthyroidism, which usually accompanies increased adrenal activity,[33][34] may improve with parathyroid support.

Tissue Mineral Analysis (TMA) as a Screening Tool for Calcium Status

TMA studies have shown that osteoporosis is found in patients with elevated, as well as decreased, hair levels of calcium. This has led to the typing of osteoporotic conditions (type I and type II).[35] The value of TMA is not to establish a diagnosis of absolute deficiencies but to evaluate relative deficiencies and imbalances. Since minerals are both synergistic and antagonistic, relative excesses and deficiencies can readily be determined from TMA studies in conjunction with the patient's history and other clinical data. Because the endocrine glands govern trace element metabolism and trace elements affect endocrine function,trace mineral patterns found in the hair can serve as an acceptable screening tool for determining body mineral ratio stores and endocrine status. As an example, elevated tissue sodium and potassium relative to low calcium and magnesium suggests increased cellular retention of sodium and potassium as a result of increased adrenal function. Increased epinephrine levels will produce cellular potassium retention,[36][37] which is mediated by Na-K ATPase.[38] Sodium retention occurs as a result of increased adrenal cortical production of aldosterone due to increased potassium retention.[39] Elevated glucocorticoids and aldosterone both increase calcium and magnesium excretion.[40][41] Excessive aldosterone secretion is known to induce magnesium loss,[42] but it is also possible that a magnesium deficiency will promote aldosterone production. This is due to the hyperplasia that develops in the zona glomerulosa in the presence of magnesium deficiency.[43] Increased thyroid activity also promotes magnesium and calcium loss due to the synergistic, reciprocal relationship between the thyroid and adrenal glands.[44] The adrenal steroids, particularly glucocorticoids, antagonize the effects of parathyroid hormone.[45][46]

Some authors feel that TMA sodium and potassium studies are not clinically significant and that they do not reflect adrenal function. However, this is probably due to laboratory preparation and testing techniques that invalidate sodium and potassium results, and lack of interpretation of the sodium and potassium data in relationship to the other elements. Evaluation of mineral levels alone is not as significant as determination of their interrelationships. The adrenals have more significant regulating effects on sodium and potassium than any other gland. An elevated tissue calcium and magnesium

level relative to low sodium and potassium suggests increased parathyroid activity in conjunction with hypothyroidism and adrenal insufficiency. Parathyroid hormone activity influences this TMA pattern due to its increasing calcium and magnesium absorption and renal re-absorption while decreasing renal re-absorption of sodium, potassium, and phosphorus. The parathyroid has a greater influence on calcium; therefore, a relative magnesium deficiency usually exists.[47] As a result of magnesium deficiency, parathyroid hormone activity is increased.[48] In the case of a relative magnesium deficiency, magnesium supplementation will have a sedating effect on the parathyroid. Magnesium supplementation in the presence of an absolute deficiency will enhance parathyroid activity. Decreased adrenal activity is indicated by the elevated tissue magnesium and corresponding low levels of sodium and potassium. Excess magnesium is known to decrease adrenal function.[49] [50] [51]

Conclusion

As with other minerals, calcium is best evaluated in relationship to its other cofactors, whether it is tested through urinary excretion studies, blood, or tissues. When the synergistic and antagonistic nutrients relative to calcium are taken into consideration, fewer conflicting and more fruitful results may be forthcoming with the nutritional treatment of calcium disorders, particularly osteoporosis. Treating the whole person rather than treating the disease or a single nutrient imbalance may also prove more rewarding and beneficial to many of those afflicted with osteoporosis. As stated by Albright, "Osteoporosis is a decreased production of osteoid by the osteoblasts, and is a defect in tissue metabolism." Since TMA is so economically feasible and shows so many nutrient interrelationships, it can be used as the test of choice for screening calcium status. Due to the many factors that contribute to osteoporosis, TMA can aid in developing an eclectic, holistic approach to its treatment.

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