CALCIUM: REQUIREMENTS, BIOAVAILABLE FORMS, PHYSIOLOGY AND RELATED CLINICAL ASPECTS

JAMES MESCHINO DC, MS, ND

Introduction

No other nutrient generates as much controversy in the world of complementary medicine as does the mineral calcium. Statements such as, " the calcium from dairy products does not get absorbed due to the pasteurization process; dairy products, though high in calcium, leech more calcium out of bone than they deposit and are the primary cause of osteoporosis in our society and; calcium carbonate supplements are nothing more than chunks of insoluble chalk that simply travels through the gut like a stone and are not absorbed by the body, are not infrequently encountered beliefs in the world of complementary and alternative medicine. Thus, it seems appropriate that health practitioners should be aware of the peer-reviewed scientific studies that have examined the clinical aspects of calcium requirements, bioavailability and other related factors, in order to best address their patients' interests in this area from an evidence-based standpoint.

The Role of Calcium in Human Health

Calcium is the most abundant mineral in the body. It makes up approximately 2 percent of the body weight with 99 percent of it incorporated into the hard tissue, bones, and teeth. The other one percent is present in the blood and extra cellular fluids and within cells of soft tissue where it regulates many important metabolic functions. In addition to building and maintaining bones and teeth, calcium is necessary for muscle contraction, blood clotting (stimulates the release of thromboplastin from platelets, facilitates conversion of prothrombin to thrombin), cell membrane transport functions, release of neurotransmitters, synthesis and secretion of protein, hormones and intracellular enzymes, nerve transmission and regulation of heart beat. The proper balance of calcium, sodium, potassium and magnesium ions maintains muscle tone and controls irritability and the muscle membrane's electrical potential.

Calcium is present in bones in the form of hydroxyapitite crystals, composed of calcium phosphate, calcium carbonate, magnesium, zinc, sodium and fluoride. These salt crystals are arranged around a framework of softer protein material (organic matrix). The hydroxyapitite crystal provides strength and rigidity to the softer protein matrix of bone. The same crystals are present in the enamel and dentin of teeth; however, the calcium from teeth is generally not reabsorbed into the bloodstream in times of need or in conjunction with low circulation levels of estrogen, progesterone, or testosterone. Bone calcium can be reabsorbed into the blood stream, weakening the skeleton and increasing susceptibility to osteoporotic fractures (often seen in the spine and neck of the femur).

Blood levels of calcium are maintained within a fixed range by various feedback mechanisms. A significant increase in serum calcium can cause cardiac or respiratory failure and a hypocalcemic state leads to tetany (involuntary muscle spasm that can cause asphyxia and death from spasm of airway musculature).

Absorption and Metabolism

Calcium is absorbed primarily via active transport in the duodenum (some via passive diffusion). Active transport requires the assistance of Vitamin D. The body normally absorbs 30-40 percent of ingested calcium, but it can be as low as 10 percent from inorganic sources such as vegetables or grains with a high content of phytic or oxalic acid. Parathyroid hormone (PTH) increases calcium absorption by increasing the conversion of Vitamin D to its active form. In general, factors that increase calcium absorption include: serum levels of Vitamin D, PTH, lactose, intestinal acidity, and possibly fat intake. Factors that hinder calcium absorption include: oxalic acid (chocolate, spinach, beet tops, collard greens, etc.) but this is not of great concern as dietary calcium is usually far greater than dietary oxalate. The

same is true for phytic acid found in whole grains (e.g., wheat bran and whole wheat). Low serum levels of Vitamin D and/or PTH decrease calcium absorption.

Following absorption, calcium enters the bloodstream and is transported to body tissue. The major site of deposition is bone.[1] Unabsorbed calcium (approximately 60-70 percent of intake levels) is excreted in fecal matter, but may provide a protective role in regards to colon cancer prevention by binding to bile acids and other sterols and blocking their conversion to cancer-causing secondary sterols (lithocholic acid, deoxycholic acid).

Calcium and Prevention of Colon Cancer

This role of calcium as a chemopreventive agent in the prevention of colo-rectal cancer is emerging to be of potentially great significance. Colo-rectal cancer is the second leading cause of cancer death in much of the western world, after lung cancer (if which, 87% of cases develop in cigarette smokers). A number of epidemiological reviews, including those by Willett and Doll and Peto, indicate that as much as 70 – 90% of colo-rectal cancers may be avoidable through more health-promoting nutrition and other lifestyle practices (e.g., exercise). A high fat diet, particularly saturated fat, is associated with a higher incidence of the disease in most countries studied. A higher fat intake results in greater secretion of bile acids into the small intestine (to emulsify the fat in the gut), and in turn results in greater concentrations of bile acids reaching the large intestine. These bile acids are metabolized by large bowel bacterial and converted into the cancer-causing secondary sterols mentioned above. Epidemiological studies and experimental animal studies suggest that higher calcium intake can reduce risk of colo-rectal cancer by binding to bile acids in the gut, forming an insoluble calcium soap that is unavailable for conversion to secondary sterols by gut bacteria. Additionally, calcium and Vitamin D have been shown to slow the rate of cell division of colonic epithelial cells, which is another biomarker suggestive of a cancer protective (chemoprevention) effect. A number of small intervention trials involving high-risk human colon cancer and polyp-prone subjects have shown that supplementation with calcium (calcium carbonate), Vitamin D and/or wheat bran fiber, can improve the histological profile of the colonic epithelium of these subjects in a manner which is consistent with a reduction in risk of colo-rectal cancer.

As such, the calcium the does not get absorbed into the blood stream from the intestinal tract may as important to human health as is the calcium that is absorbed. This is a good example of how misleading it can be to pay attention to, or over emphasize, the importance of a single aspect of nutrient behaviour (e.g., bioavailability) in the body, without taking into consideration the complete clinical picture. At this time health authorities are reviewing the evidence and planning further studies in order to consider a heath policy that encourages higher calcium intake for the purpose of preventing primary and/or secondary colo-rectal cancer. [2, 3, 4] As will be shown later, calcium citrate is more bioavailable than calcium carbonate if ingested on an empty stomach, but when ingested with food, both have about the same degree of bioavailability. Thus, many of the half-truths extolled by nutrition companies, promoting their proprietary calcium formulations, should be critically examine by practitioners, using the criteria and other data derived from this scientific review.

Daily Calcium Requirement (NIH Recommendations)

The following are the most recent calcium recommendations outlined by the National Institutes of Health for the American population, who tend to have a high animal protein diet. These recommendations are suited to such a society, but one should keep in mind that in society's consuming less animal protein, calcium balance is attainable with much lower intakes of calcium than is suggested by the following chart. Thus, a person's absolute calcium need must factor in a number of variables, such as their animal protein intake, caffeine, alcohol, exercise behaviours, family history of osteoporosis, Vitamin D and parathyroid hormone status, drug use and possibly their risk profile regarding colon cancer. Knowledge of these and other related factors, should help to place the following guidelines into proper perspective:

Age Group and Gender	Calcium (mg)
Under 6 months	400
6–12 months	600
1–10 years	800
11-24 years Male and Female	1200-1500
25–50 years Male and Female	1000
Postmenopausal Women not taking estrogen replacement (ERT)	1500
Postmenopausal Women taking ERT	1000
65+ years Postmenopausal Women taking or not taking ERT	1500
50-64 years Men	1000
65+ years Men	1500[4]

Calcium Preparations and Bioavailability

The bioavailability of various forms of calcium supplements has been evaluated using radio-isotope, calcium excretion and other studies. The following is a summary of the key findings to date:

Type	Absorptive Fraction of Calcium in Normal Subjects
Milk	Approximately 33% on empty stomach
Calcium Carbonate	Approximately 31% on empty stomach
Calcium Citrate	Approximately 40% on empty stomach
Calcium Gluconate	Approximately 26.6% on empty stomach
Calcium Lactate	Approximately 34.5 % on empty stomach
Tricalcium Phosphate	Approximately 25.2% on empty stomach
Calcium Citrate-malate	Approximately 34.9% on empty stomach
Calcium Chloride	Approximately 36.4% on empty stomach
Average Diet	Approximately 32% on empty stomach[3]

It is best to take calcium supplements with food to capitalize upon the other potential benefits regarding bone/health, blood pressure regulation, and possibly chemoprevention of colo-rectal cancer, as well as the improved bioavailability of calcium that occurs when ingested with meals (e.g. calcium carbonate absorption is enhanced by approximately 10 percent when ingested with meals).[3]

Supplementation Studies and Clinical Applications

1. Osteoporosis

   Currently one in four women and one in eight men over 50 have osteoporosis. Nearly one-third of all women and one-sixth of all men will fracture their hips in their lifetimes. Women's mortality rates from osteoporotic fractures are greater than the combined mortality rates from cancer of the breast and ovaries. Up to 20 percent of women and 34 percent of men who fracture a hip die in less then a year from complications secondary to these fractures (e.g., pneumonia).[5]

   A large number of clinical trials have shown that calcium supplementation slows the rate of bone loss after menopause and in conjunction with resistance training, can also increase bone mineral density even in women not taking hormone replacement therapy. Very strict protocols have been established regarding strength training and the accretion of bone density for this age group.[4, 5, 6]

   In general, a variety of calcium supplements (carbonate, citrate, citrate-malate, chloride, gluconate, lactate, Microcrystalline Hydroxyapitite Concentrate (MCHC)) have demonstrated an ability to retard age-related bone loss. The key factors appear to be to meet the NIH calcium intake recommendations from food and/or supplementation, ingest supplements with meals, perform weight bearing or weight resistance exercise 4-6 times per week, and ensure

adequate serum Vitamin D levels. All of these factors enhance calcium absorption and/or calcium retention in bone.[4, 5, 7, 8]

2. High Blood Pressure

   Various clinical studies indicate that calcium supplementation (e.g. calcium carbonate – 1500 mg per day) can reduce blood pressure to a significant degree in sodium-sensitive hypertensive patients. Most of these trials were 8-12 weeks in duration and used 1000-1500 mg of calcium carbonate or citrate.[9,10,11] This subject is currently under intensive study to clarify the potential of calcium supplementation as a natural intervention for specific cases of hypertension.

   Calcium supplementation (1000-2000 mg per day, calcium carbonate) may also help to prevent pregnancy-induced hypertension or function to reverse existing hypertension during pregnancy. This function is also presently under review.[12, 13]

Dosage Range to Consider for Calcium Supplements

Most young adult and adult North Americans lack 500-800 mg per day of calcium to match the NIH recommended intake levels. Calcium supplementation represents a viable way to meet the recommendation in many cases.[4, 5]

1. Osteoporosis Prevention and Management - Meet the NIH recommended intake levels for calcium, based upon age and gender. Whatever calcium level is missing from food should be compensated for through supplementation[4]
2. Hypertension - sodium-sensitive hypertensive patients may try 800-1,500 mg of calcium supplementation (8-12 week trial period) to test response.[9, 10, 11]

Side Effects and Toxicity

It is generally acknowledged that calcium intake up to a total of 2000 mg per day appears to be safe in most individuals. The efficiency of calcium absorption decreases as intake increases, thereby providing a protective mechanism to lessen the chances of calcium intoxication. This adaptive mechanism can, however be overcome by a calcium intake of greater than 4000 mg per day.[4] High intake of calcium may increase soft-tissue calcification (4000+ mg or in combination with hyperparathyroidism). In 1981, the FDA cautioned the public to limit its intake of calcium supplements derived from dolomite or bone meal because of the potentially high lead levels in these calcium supplements.[1]

Drug-Nutrient and Other Interactions

Dietary factors such as alcohol, caffeine, sodium and a high protein diet can increase calcium loss from the body. However, studies show that these factors can be compensated for by ingestion of 250-500 mg of additional calcium in most instances.[4, 5, 13, 14]

Drug-Nutrient Interactions

The following drugs have been shown to deplete calcium or reduce its absorption into the body:

EDTA[15]; Tetracycline[16]; Aminoglycosides[17]; Amphotericin B[18]; Anticonvulsants[19,20,21]; Salicylates (ASA, etc.)[22]; Bile Sequestrants (cholestyramine)[23]; Colchicine[24]; Corticosteroid drugs[25,26]; Cimetidine[27,28]; Isoniazid[29]; Loop diuretics[30]; Magnesium and Aluminum Antacids[31]; Potassium-Sparing Diuretics[32]; Digoxin (animal studies only)[33]

Drugs that are interfered with if taken at the same time as calcium

1. Fluoroquinolone Antibiotics – calcium can decrease absorption of these drugs and, therefore, calcium supplements and dairy products should not be taken within two hours of ingesting these drugs.[34,35]
2. Levothyroxine – calcium carbonate can decrease drug absorption if taken at the same time.[36]

Nutrient – Nutrient Interactions

1. Iron - high doses of calcium can reduce iron absorption.[37]
2. Zinc - high doses of calcium can reduce zinc absorption.[38]

Summary

As indicated in this review, there are many factors to consider when discussing calcium needs with patients. It is best to have patients fill out a 7-day diet history to assess their current intake from food. At that point the patient can be instructed to consume additional calcium from food and/or supplements if necessary. Other secondary issues can also be discussed at his time such as exercise habits, Vitamin D, caffeine and alcohol intake, smoking etc. In women over 50 years of age, a bone density test should be performed to assess their current bone mineral density status. In general, the patient's age, gender, history of health, present dietary and lifestyle patterns, family history, medication history and present bone mineral status, all factor into the recommendations regarding calcium intake on a case-by-case basis. Responsible practitioners should be aware of the interaction of these factors and help patients arrive at a calcium intake that best suits their needs. Failure to address calcium and Vitamin D requirements has largely been responsible for the disproportionately high incidence of osteoporosis and osteomalacia seen in modern society. As the population ages these problems are predicted to reach epidemic proportions and thus, health professionals should engage patients in a discussion of these matters and aid patients in identifying their specific needs in this regard, especially practitioners such as chiropractors who are viewed as bone and joint doctors by the general public.

Pregnancy and Lactation

During pregnancy and lactation, the only supplements that are considered safe include standard prenatal vitamin and mineral supplements. All other supplements or dose alterations may pose a threat to the developing fetus and there is generally insufficient evidence at this time to determine an absolute level of safety for most dietary supplements other than a prenatal supplement. Any supplementation practices beyond a prenatal supplement should involve the cooperation of the attending physician (e.g., magnesium and the treatment of preeclampsia.)

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