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CALCIUM FROM A CALCIUM-RICH MINERAL WATER: SUPPLEMENTATION AND BIOAVAILABILITY

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Abstract

The present work highlights the importance of proper hydration with rich mineral water to ensure correct intake of this microelement. Calcium is considered to be inadequate in the various age groups due to an incorrect diet or in the presence of factors that may significantly reduce its absorption such as menopause, age, liver diseases, nephropathy, malabsorption syndrome, hypoparathyroidism, surgical interventions, antibiotic intake and laxatives. This reported data confirm that calcic mineral waters, rather than supplements and fortified foods, can help achieve recommended levels of intake, with key implications in the prevention of pathologies that may result from lower calcium intake. Mineral waters are without calories, and some of them, possess calcium levels above 300 mg, playing an important role as calcium sources.

Keywords: Calcium, Acqua Lete, bioavailability, supplementation

Introduction

Calcium is the most abundant mineral present in the organism, representing about 40% of the total mineral mass. In big quantities is present in the bone where, in combination with phosphorus in the form of hydroxyapatite crystals $Ca_{10}(PO_4)_6(OH)_2$, plays a key role providing mechanical strength to skeleton and teeth. Approximately 99% of body calcium is present in these two structures for a total of about 1200 grams, Calcium is unique among nutrients, in that the body's reserve is also functional: increasing bone mass is linearly related to reduction in fracture risk. The remaining body calcium functions in metabolism, serving as a signal for vital physiological processes, including vascular contraction, blood clotting, muscle contraction and nerve transmission. Calcium deficiency predisposes to various pathologies such as: osteoporosis, kidney stones, cancer, hypertension, obesity and insulin resistance. Dietary calcium may be implicated in the etiology of insulin resistance through the fluctuations in calcium-regulating hormones in states of calcium sufficiency and deficiency. Calcium acts as a second messenger to match intracellular responses with extracellular signals, its deficiency, at different levels of organization, generates: 1) exhaustion of the nutritional calcium reserve; 2) inadequate complexation of undesirable gastrointestinal products; 3) side effects of hormones produced mainly to compensate for low calcium intake. The first mechanism contributes to osteoporosis, the second may cause kidney stones and cancer, and the third leads to hypertension, preeclampsia, obesity and insulin resistance (Heaney 2006; Khazai, Judd et al 2008; Peterlik and Cross 2009; Pilz Et al., 2009).

Clinical studies on adults with controlled and appropriate Ca dose (1000-1500 mg/day) have shown that a correct intake reduces risk of osteoporotic fractures (Fagotti et al., Avenell, et al., 2017), kidney stones, obesity and hypertension (Zemel, 2001). Bonovas et al. (2016) reported the chemopreventive effect of calcium integration against rectal colon adenomas by highlighting recent randomized, placebo-controlled studies, where daily doses of elemental calcium administered ranged from 1200-2000 mg/day with duration of treatment for participants of 36-60 months.

In the Italian population, average daily intake is approximately 500-800 mg of calcium. Only a small part (30%-35%) is absorbed, the remaining amount is eliminated with stools (about 650 mg/day). In our society Calcium (Ca) food intake is deficient in all age groups. In adolescents, milk consumption (which could cover 50%-75% of daily calcium requirements) is often replaced by the use of other drinks or new eating habits. It is reported that only 15% of females and 53% of males achieve adequate calcium intake. In an effort to reduce this trend, and considering that calcium absorption is more efficient if consumed in multiple doses during the day, doctors offer numerous alternative therapies, to which they add the recommendation of drinking calcium-rich water. (Fulgono et al., 2004; WHO, 2005; Straub, 2007).

Recommended consumption values

The ideal calcium intake values are difficult to determine, because there is no single satisfactory approach. The determination of needs at different ages and in different physiological conditions is based on the effect that calcium intake has on the skeletal mass. To assess calcium requirements in children, for example, different techniques are used, including:

- Average calcium rating with different levels of intake.
- Measurement of bone mineral content, with radiographic techniques such as DEXA (dual-energy x-ray absorptiometry), computed axial tomography (CAT) and Magnetic Resonance Imaging (MRI), which allow to directly visualize and measure the variables of body composition (bone tissue and muscle tissue) in groups of children before and after calcium supplementation.
- Epidemiological studies link calcium intake of bone mass in infancy to the risk of fractures in adulthood.

The population reference intake (PRI) and adequate intake (AI) on calcium daily basis are reported in the LARN 2014 Italian edition: children 1-3 years (700 mg), 4-6 years (900 mg), 7-10 years (1100 mg), 11-17 years (1300 mg); Adults between 18 and 29 years (1000 mg), 30-59 years (1000 mg), 60-74 years (1200 mg), ≥75 years (1200 mg); pregnancy (1200 mg), lactation (1000 mg); menopausal women who are not in estrogenic therapy (1200 mg) (SINU, 2014). Moreover the Dietary Reference Intakes (DRIs) established by the United States Institute of Medicine (IOM 1997), are composed of four different values among them the Recommended Dietary Allowance (RDA) is defined as the average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97–98%) individuals in a life stage and gender group. Generally derived from the EAR using a 10% coefficient of variation as a default in the absence of nutrient-specific data on variability in the target population.

Absorption

The absorption of dietary calcium occurs mainly in the upper part of the small intestine, according to two distinct mechanisms. The former is an active transport present in the duodenum and in the small intestine. This mechanism involves a number of calcium-transporting proteins in the intestinal cells whose synthesis is determined by vitamin D, present in some foods and produced by the organism through exposure to the sun. Active absorption is also influenced by homeostatic mechanisms as a response to changes in circulating levels of plasmatic calcium. This absorption increases in case of deficiency or increased needs, such as during adolescence, pregnancy and lactation, is higher in the baby than the adult and elder. The latter mode of absorption of food calcium utilizes passive transport with simple paracellular diffusion along tenuous intestine. In this way it is not saturable and independent from age, vitamin D and mineral calcium needs.

Active absorption becomes prevalent when the meal is poor in calcium. Calcium salts are generally slightly soluble and for this reason their absorption is difficult. Absorption is increased by the presence of proteins (calcium linked to aminoacids is easily absorbed), the acidic environment of the upper digestive tract which solubilizes calcium salts (in fact prebiotic and probiotic are able to increase mineral absorption), the reduced sodium content. In a randomized study of 186 adults 23-76 years, the effects of two dietary models and three sodium levels were evaluated on bone tissue and calcium metabolism. Lower levels of sodium are significantly correlated to a reduction in bone turnover, resulting in improved bone mineral status and reduced calcium excretion in urine (Lin et al., 2003).

The factors that inhibit calcium absorption are a calcium/phosphorus imbalance, a condition that occurs due to excessive intake of animal protein, intestinal alkalinity, which makes calcium salts less soluble, vitamin D deficiency, and presence in meals of anti-nutrition substances such as phytic acid (bran, fiber, whole grains), oxalic acid (spinach, rhubarb, cocoa) and tannins (tea), coffee and alcohol.

Moreover, it should be remembered the reduced absorption occurring in postmenopausal women, amenorrhea, among people who have lactose intolerance, and in vegans with reduced milk derivatives consumption.

It is worth remembering that good intestinal calcium absorption does not necessarily reflect a good bioavailability of the mineral. Once absorbed and poured into the blood, in fact, calcium can be eliminated with urine or deposited in the bones (in addition can participate in the many other functions). In this sense, the greatest stimulus for calcium deposition in the skeleton is given by physical activity and consequent proper hydration.

Food sources of calcium

The group of milk and its derivatives contributes for more than 65% of total calcium intake (540 mg/day), among the richest calcium derivatives there are Grana Padano (1169 mg), Parmigiano Reggiano (1159 mg) and Emmenthal (1145 mg). For vegetarians who do not use dairy products, tofu, prepared with calcium salts or soy milk enriched with calcium (even 500 mg per 250 ml), can represent important sources of calcium. There are a good content in cereals and derivatives, and green leafy vegetables such as spinach and broccoli (120 mg per 100 g of product). Cabbages have high levels of calcium, but its absorption is inhibited by the presence of oxalates. Other sources include some crustaceans and fish (lobster, sardines and salmon), legumes, eggs and almonds. Even mineral waters with high calcium content (over 150 mg/L) and poor sodium (less than 20 mg / L) are a good source of readily assimilable supplemental calcium. Drinking 1.5-2 liters of water per day, preferably out of the meal, provides a quantity of calcium of at least 450-600 mg only from this source.

Food supplements and fortified foods

Another possibility of calcium intake is represented by enriched foods and calcium supplements that can provide from 300 to 600 mg of elemental calcium per tablet. In fact, calcium is found in many multivitamins and multiminerals supplements, in different quantities depending on the specific formulation. There are also dietary supplements that contain a single substance such as calcium or vitamin D. Two of the most popular types of calcium supplements are calcium carbonate and calcium citrate: the former is very cheap and is better absorbed if it is taken with meals. Calcium citrate is expensive and is well absorbed also in an empty stomach. In addition, patients with low levels of gastric acids (most commonly upset among 50 years) absorb calcium citrate more easily than calcium carbonate. Among the other forms of calcium present in supplements and fortified foods we can mention: calcium gluconate, calcium lactate, calcium phosphate. The maximum dose of elemental calcium that should be taken once should not exceed 500 mg (US Pharmacopeia), so supplements containing 1.000 mg of calcium should be taken by dividing into two doses the pharmaceutical form (Fulogoni et al., 2004). Calcium supplements can also cause flatulence, bloating and constipation. Another limit is the possibility that

production and processing do not respect strict quality requirements (Straub, 2007). As for commercial forms, in a clinical trial, commercial calcium supplementation as calcium carbonate, encapsulated calcium carbonate and calcium citrate in 24 postmenopausal women produced the same total serum calcium increase, as well as urinary excretion. Then, there are no significant differences among the products, cost-benefit analysis promotes the less expensive carbonate (Heaney et al., 2001). Calcium lactate and calcium gluconate are less concentrated forms and are not practical as oral supplements. The percentage of absorption of oxides, phosphates and sulphates ranges from 5 to 10%; carbonate from 5 to 20%; gluconates and lactates from 20 to 25%, and 45% citrate.

As for fortified foods, calcium-enriched drinks, which are increasingly present in the market, are a convenient and popular way to increase calcium intake and are especially useful for individuals who have difficulty swallowing tablets and other pharmaceutical forms. Calcium enriched beverages include orange juice, soy drinks and rice milk. The bioavailability of calcium of these fortified foods, however, varies considerably and the nutrition label does not include information about calcium bioavailability. In any case, absorption is lower than that of milk. Calcium in fortified drinks may also precipitate and settle on the bottom of the container depending on the method used for its fortification (Straub 2007).

Calcium mineral water

Food consumption surveys indicate that in the last five years consumption of milk in Italy has decreased by 220 million liters, with a loss of 35 million only in 2015. The decline mainly concerned fresh product, but not only. A cause for concern is that milk consumption has declined particularly in young people (12-19 years), when bone density and growth rates are at their maximum. While the consumption of sodas and juice with high calorific value and calcium enriched has doubled (Heaney, et al., 2005). Moreover, daily consumption of sodas, fruit juices and artificially sweetened beverages intake have been linked to cardiometabolic risk factors, which increase the risk of cerebrovascular disease and dementia, (Pase et al., 2017)

The statistics also report that in the West the diet of young and very young people many a time is very poor in calcium. Apart from occasional ice cream or yogurt, milk isn't on daily table. Cheese is considered as fat and hypercaloric food, and therefore a product to be avoided. In this scenario, mineral waters with high calcium content (over 150 mg/L) and poor sodium (less than 20 mg/L) are a good source of extra calcium that can be easily assimilated and represent a viable alternative to calorie-free drinks and juices.

In studies conducted with different mineral waters, intestinal calcium absorption was similar to that found in milk (Dokkum et al., 1996). In one of the first studies (Haney and Dowell 1994), availability calcium content in calcite mineral water was evaluated in 18 healthy women versus calcium availability by ingestion of milk using 45Ca as tracer in a cross-over randomized experimental design. Absorption fractions, compared with a calcium charge ingested by 2.5 mmol, were 0.433 for milk and 0.475 for water. These authors conclude that calcium from mineral water is highly bioavailable, at least, and equally bioavailable as calcium from milk. Subsequently, Heaney (2005) reports that calcium absorption from mineral waters is comparable or higher than that found in milk and in a recent meta-analysis containing data published until 2005 (Heaney, 2006), reports several studies under similar experimental conditions, which demonstrate the high bioavailability of Ca^{2+} in calcite mineral waters. In a recent meta-analysis that reported 6 studies, calcium absorption after mineral water administration was significantly higher than that found by taking milk.

Increased urinary calcium and the positive effect on bone resorption of calcium show significant increases in several clinical trials. In a study on calcite mineral water (Bacciottini et al., 2004), the bioavailability of calcium contained in calcium mineral water was measured in 27 healthy subjects. In 8 subjects this availability was compared with the availability of calcium ingested with milk. The results showed with an absorbed calcium load of 3.18 mmol, a water absorption percentage 22.53 (± 2.53) for men, 22.57 (± 2.10) for pre-menopausal women and 21.62 (± 3.12) for postmenopausal women compared to a calcium absorbed by milk of 23.15 (± 4.06). Calcium from mineral water is therefore highly bioavailable and comparable with the absorption of calcium from food sources.

Natural sparkling mineral water Lete

Natural sparkling mineral water Lete is carbon dioxide, bicarbonate-calcite water and can be considered a calcium diet source (330 mg/L), with adjuvant action in osteoporosis therapy, preventing pathologies related to calcium deficiency and maintaining effects on state of health. Free carbon dioxide at source is present in quantity (1950 mg/L) that determine pH variations towards acidity. Acidic waters have bicarbonates that release CO_2, while at alkaline pH (>8.5) prevail bicarbonates (HCO_3^-) and carbonate (CO_3^{2-}). In Natural sparkling mineral water Lete, average pH is 6.2 and there are HCO_3^- and CO_2. After its consumption there is a tendency to intestinal acidity that can solubilize calcium salts with increased absorption of the mineral (Wood and Serfaty-Lacrosniere1992).

Several authors report the positive action on the digestive system by bicarbonate-carbon waters, in particular the phenomena regulating secretion and tone of the gastric walls, coleretic and buffer activity (mainly due to the action of bicarbonates) (Rastrelli et al., 2009). In literature is reported CO_2 vasodilating action, in the gastric mucosa with consequent increased absorption of water and its minerals, including calcium, and increased diuresis (Holm et al., 1998). As for the bicarbonates, Natural sparkling mineral water Lete has 1080 mg/L. HCO_3^- anion and possesses a specific protective activity on the gastric mucosa with excess acid secretion, in fact calcium and magnesium appear to be implicated in the release of gastrin and other enteric hormones (Hearty et al., 1981). At duodenal level, bicarbonate waters favor the action of pancreatic enzymes. Numerous studies have shown positive activity on calcium and magnesium of cholecystokinin a peptide hormone of the gastrointestinal system responsible for stimulating the digestion of fat and protein (Miller et al., 2016). A further study has shown that daily administration for 10 days of Acqua Lete mineral water induces a significant reduction of functional dyspepsia symptoms (Tarocchi et al., 2006).

For people with hypertension, it is advisable, in addition to low-sodium water (Lete = 4.9 mg/L), to consume bicarbonate-calcium water. In fact, inadequate calcium intake has been associated with an increase in the incidence of hypertension more specifically, in male subjects, the incidence of hypertension increases three times when calcium diet is less than 500 mg/day (Rylander and Arnaud, 2004). It has also been found that a consistent intake of recommended levels of calcium contributes to reducing the risk of cardiovascular diseases (Schoppen et al., 2004). Lower levels of sodium correlated significantly with higher calcium absorption (Lin et al., 2003).

Conclusions

Food consumption analysis and epidemiological studies show that calcium-deficiency diets are very frequent, with a tendency to grow sharply if compared to a few decades ago. In an effort to reduce this orientation, doctors propose numerous alternative therapies, with a dietary recommendation: drink calcium-rich water.

Several studies in this article show that calcium rich mineral water, with peculiar characteristics, can offer an interesting and effective alternative to the calcium supply provided by milk, dairy products, other foods as calcium sources, enriched products such as soft drinks as well as calcium supplements formulated in tablets. Natural sparkling mineral water Lete is able to provide an adequate absorbable and bioavailable calcium (330 mg/L) intake, high CO_2 and bicarbonate content, acidic pH and low sodium concentration. A habitual consumption of Natural sparkling mineral water Lete can be significantly related to increased calcium absorption.

References

- Avenell, A., Bolland, M. J., Grey, I. R. (2017). Reid Further major uncorrected errors in National Osteoporosis Foundation meta-analyses of calcium and vitamin D supplementation in fracture prevention Osteoporosis International, 28: 733-734.
- Bacciottini, L., Tanini, A., Falchetti, A., Masi, L., Franceschelli, F., Pampaloni, B., Giorgi, G., Brandi, M.L. (2004) Calcium bioavailability from a calcium-rich mineral water, with some observations on method. J ClinGastroenterol. 38(9):761-766.
- Bonovas, S., Fiorino, G., Lytras, T., Malesci, A., Danese S. (2016) Calcium supplementation for the prevention of colorectal adenomas: A systematic review and meta-analysis of randomized controlled trials. World J Gastroenterol. 22(18): 4594-4603.
- Brancaccio, P., Limongelli, F.M., Paolillo, I., Grasso, C., Donnarumma, V., Rastrelli, L. (2011). Influence of AcquaLete® (Bicarbonate Calcic Natural Mineral Water) Hydration on Blood Lactate After Exercise- The Open Sports Medicine Journal, 2011, 5, 24-30.
- Brancaccio, P., Limongelli, F.M., Paolillo, I., D'Aponte, A., Donnarumma, V., Rastrelli, L. (2012). Supplementation of AcquaLete® (Bicarbonate Calcic Mineral Water) improves hydration status in athletes after short term anaerobic exercise. J IntSoc Sports Nutr 26; 9(1): 35.
- Dokkum, B.W., De La Gueronniere, V., Schaafsma, G., Bouley, C., Luten, J., Latge, C. (1996). Bioavailability of calcium of fresh cheeses, enteral food and mineral water. A study with stable calcium isotopes in young adult women. British Journal of Nutrition, 75:893-903.
- Fagotti, L., Balbino, Gonzalez Truffa, T.B., Susanna, C. Calvo-Marin, J., Fuentes J.C., CarrascoRueda, J.M., Villares da Costa, L.G. (2015). A Randomized Double-Blinded Superiority Trial to Compare the Efficacy of Vitamin D3 and

Calcium versus placebo in Prevention of Hip Fractures in Elderly Women PPCR1(4): 97-103.

- Fulgoni, V.L., Huth, P.J., Di Rienzo, D.B., Miller, G.D. (2004). Determination of the optimal number of dairy servings to ensure a low prevalence of inadequate calcium intakes in Americans. JAm Coll Nutr. 23:651-659.
- Heaney, R. P. (2000). Calcium, dairy products and osteoporosis. J Am Coll Nutr 19(2 Suppl): 83S-99S.
- Heaney, R.P. (2006). Absorbability and utility of calcium in mineral waters. American Journal of Clinical Nutrition 84:371-374.
- Heaney, R.P., Dowell, M.S., Absorbability of the calcium in a high-calcium mineral wate. (1994) Journal Osteoporosis International 4: 6.
- Heaney, R.P., Dowell, M.S., Bierman, J. Hale, C.A., Bendich, A. (2001) Absorbability and Cost Effectiveness in Calcium Supplementation. Journal of the American College of Nutrition 20: 239-246.
- Heaney, R. P., Rafferty, K., Bierman, J., June, M. (2005). Not all calcium fortified beverages are equal. Nutr Today. 40:39-44.
- Hearty, R.F., Maico ,D.G., Mc Guigan, E.J. (1981). Role of calcium in antral gastrin release. Gastroenterology, 80: 491.
- Holm, M ., Johansson, B ., Pettersson, A., Fändriks L. (1998). Carbon dioxide mediates duodenal mucosal alkaline secretion in response to luminal acidity in the anesthetized rat Gastroenterology, 115: 680-685.
- Khazai, N., S. E. Judd, et al. (2008). Calcium and vitamin D: skeletal and extraskeletal health. CurrRheumatol Rep 10(2): 110-117.
- Lin, P.H., Ginty, F., Appel, L.J., Aickin, M., Bohannon, A., Garnero. P., Barclay, D., Svetkey, L.P. (2003). The DASH Diet and Sodium Reduction Improve Markers of Bone Turnover and Calcium Metabolism in Adults. J. Nutr. 133 (10): 3130-3136.
- Miller L. J. and Desai A.J. (2016). Metabolic Actions of the Type 1 Cholecystokinin Receptor: Its Potential as a Therapeutic Target, Trends Endocrinol Metab, 27(9): 609-619.
- P. Pase, M.P., Himali, J.J. Beiser, A,S. Aparicio, H.J., Satizabal, C.L., Vasan, R.S., Seshadri, S., Jacques P.F. Sugar- and Artificially Sweetened Beverages and the Risks of Incident Stroke and Dementia. A Prospective Cohort Study. Stroke. 2017; doi.org/10.1161/STROKEAHA.116.016027
- Peterlik, M., Cross, M.H.S. (2009). Vitamin D and calcium insufficiency-related chronic diseases: molecular and cellular pathophysiology. Eur J ClinNutr 63(12): 1377-1386.
- Pilz, S., A., Tomaschitz, Ritz, E., Pieber, T.R. (2009). Vitamin D status and arterial hypertension: a systematic review. NatRevCardiol 6(10): 621-630.
- Società Italiana di Nutrizione Umana (SINU) (2014). LARN IV revisione: livelli di Assunzione di Riferimento di Nutrienti ed energia.
- Schoppen, S., Pérez-Granados, a.M., Carbajal, A., Oubiña, P., Sánchez-Muniz F.J., Gómez-Gerique, J.A., Vaquero, M.P. (2004). A Sodium-Rich Carbonated Mineral Water Reduces Cardiovascular Risk in Postmenopausal Women. J. Nutr. 134: 1058-1063.
- Rastrelli, L., Brancaccio, P., Iride Paolillo, I., Piccinelli, A.L., De Simone, F. (2009) ChemicalCharacterization of Appennino Meridionale waters: tenyearsanalysis (1998/2008) of "Acqua Lete". (2009) Journal of Water & Wellness, 1: 13-20.
- Rylander, R., Arnaud, M.J. (2004) .Mineral water intake reduces blood pressure among subjects with low urinary magnesium and calcium levels. BMC Public Health. 2004; 4: 56.
- Straub, D.A. (2007). Calcium Supplementation in Clinical Practice: A Review of Forms, Doses, and Indications. Nutrition in Clinical Practice. 22: 286-296.
- Tarocchi, M., Dabizzi, E., Ninotta, M.G.O., Casanova, B., Violanti C., Surrenti C. (2006). Effetti della somministrazione di acqua minerale bicarbonato calcica Lete nella dispepsia funzionale. Medicina Clinica e Termale, 61:49-54.
- Zemel M.B. (2001). Calcium Modulation of Hypertension and Obesity: Mechanisms and Implications. Journal of the American College of Nutrition, 20: 28S-435S.
- WHO (2005) Nutrients in Drinking Water. World Health Organization, Geneva, 186 pp.

- (http://www.who.int/water_sanitation_health/dwq/nutrientsindw/en/index.html). Wood, R.J., Serfaty-Lacrosniere, C. (1992) Gastric acidity, atrophic gastritis, and calcium absorption. Nutr Rev. 50(2):33-40.