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Calcium supplemental use to meet human calcium requirements

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CALCIUM SUPPLEMENTAL USE

TO MEET HUMAN CALCIUM REQUIREMENTS

by

Kelly Jo Shepard Kohls

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TITLE

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BY

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CALCIUM SUPPLEMENT USE TO MEET

HUMAN CALCIUM REQUIREMENTS

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University of Nebraska, 1987

Advisor: Constance Kies

The overall objective of this project was to investigate the effects of consuming several different commercially available calcium supplements. Bioavailability, cost, convenience, physiological responses to each supplement, feasibility and need for a supplement by the targeted population were assesed. Three studies composed the project.

The first study consisted of feeding a controlled diet to two groups of ten young adults. Subjects were fed a laboratorycontrolled diet with one of seven calcium supplements: milk, oyster shell calcium plus vitamin D, calcium lactate and gluconate, mixed calcium source (Mega-Cal), dolomite calcium, or purified calcium carbonate. Calcium carbonate supplementation resulted in the poorest calcium balances and longest fecal transit times while calcium gluconate required the consumption of the largest number of tablets at the highest cost to the consumer. Milk supplementation was fairly expensive, resulted in the highest calcium balance and lower fecal transit time and caused greatest complaints of gastro-intestinal distress.

In Study II, seventy-two retired breeder female mice were fed a basal diet plus one of eight calcium supplements (seven described previously and an additional supplement-purified calcium carbonate plus vitamin D). Highest bone breaking strength was noted in the group

of mice fed purified calcium carbonate plus vitamin D, but the calcium deficient group also had high bone breaking strength. The mice fed calcium gluconate had the best calcium absorption but mice fed purified calcium carbonate had the most positive calcium balance.

In Study III, a survey was conducted to investigate relationship of calcium intake and urinary calcium excretion to other components of the self-selected diets of elderly persons. Only 36% of these elderly subjects consumed 75% or above of the RDA for calcium. Calcium intakes correlated significantly and positively with sodium intakes, phosphorus intakes and protein intakes and tended to correlate ($p<0.101$) with ascorbic acid intake. Urinary calcium excretion correlated negatively and significantly with ascorbic acid intake and tended to increase ($p<0.103$) with sodium intake.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF TABLES (continued)

LIST OF APPENDIX TABLES

LIST OF APPENDIX TABLES (continued)

LIST OF APPENDIX TABLES (continued)

INTRODUCTION

Osteoporosis (brittle bone disease) is not a new disease, but it is a recently publicized one. Possible causes and complicating factors of this debilitating disease have as yet not been defined. Because of the large calcium content of bone, a possible role of dietary calcium is suspected. Calcium nutriture of both sexes has been assessed to determine differences in physiology or intake that might account for preponderence of occurrence of osteoporosis in post-menopausal women rather than in elderly men (Riggs et al. 1981 and Mazess 1982). The U.S. Agricultural Research Service, Consumer and Food Economics Research Division (1972) and the Science and Education Administration (U.S.D.A. 1980 and Riggs, 1967) have reported that calcium intakes are generally lower for women than for men. Although the men consumed significantly more calcium ($p<0.01$) than did women, this was due to their higher total food intake and need for more calories than was the case in the women (Lakshmanan et al. 1984). Also, men and women in this study, regardless of age, excreted the same percentage (90%) of calcium in feces based on their intakes. While urinary calcium excretion did not differ between sexes, calcium balance tended to be higher for men ($p<0.07$).

Selling of calcium supplements for human consumption has become "big business" (Sherman, 1987). From industry sales of calcium supplements by Marion Laboratories, Inc., of $30,000 in 1951 and $7 million in the late 1970's, revenues jumped to $21 million in 1984 and more than $30 million in 1985. Currently, Marian Laboratories Mc's OS Cal supplement is the market leader accounting for 25% of all calcium

supplement sales. The sales of the calcium carbonate antiacid preparation, Tums, marketed by Norcliff Tayer Co., are not included in the calculation of total revenue of calcium supplement sales. However, according to the Tum's marketing director, sales of Tums rose from $34 million in 1984 to $51 million in 1985 to $70 million in 1986 following the publication of an article in <u>Consumer's Report</u> in 1984 which indicated that Tums is actually the cheapest calcium supplement currently available.

If a calcium supplement is going to be used, price is not the sole criterion on which recommendations for a calcium supplement source should be based. Other criteria include effectiveness of absorption, effectiveness of retention and freedom from adverse side effects. These were investigated in research comprising this dissertation.

LITERATURE REVIEW

Absorptive efficiency of calcium is inversely related to intake levels but systemic factors influence this relationship (Nicolaysen et al., 1953, Kemm, 1971, and Heaney et al., 1975). Obviously, when an increased urinary calcium excretion it is thought being due to an increased calcium intake, or more calcium is being absorbed (Knapp, 1947). When calcium intake increases but efficiency of absorption is lowered, numerically more calcium is still absorbed. Efficiency of absorption is affected by many factors. Because calcium absorption decreases with age (Bullamore et al., 1970), Tsai et al., 1984, assessed the vitamin D status of elderly and found that the active form of vitamin D 1•25 dihydroxy vitamin D was present in lower concentrations in the elderly than in the nonelderly. Thus, increasing calcium consumption alone might not be as beneficial as increasing calcium plus vitamin D (Ferguson and Hartles 1966 and Kehayoglou et al., 1968).

Osteoporotic patients have been found to require a greater than normal calcium intake to achieve balance (Nordin, 1961). However, these results were not verified by Harrison and Fraser, 1961, or Lutwak, 1969.

It is believed that a negative calcium balance over a long period of time will result in a depletion of skeletal calcium reserves from the body. Researchers interested in finding the cause of this long term negative calcium balance have assessed many aspects of dietary, genetic, environmental, life style effects on individuals inflicted with osteoporosis (Shenolikar, 1970; Pingle and Ramasatri 1978 a & b; Whedon, 1985; Lutz, 1986; Morivchi and Hosoya, 1985; Fujita, 1985).

In America an expansion of the older population is occurring; hence, age related bone loss is becoming a major health problem. Bone density studies over middle and later ages indicate that bone density peaks at age 35-40 and then steadily declines as age increases (Albanese et al., 1975). Earlier L. Riggs et al., 1967, reported a significantly lower ($p<0.05$) estimated dietary calcium intake of osteoporotic patients than of control patients.

Calcium balances of osteoporotic patients and of normal persons were found to be poorer prior to the experimental period in which calcium was supplemented but became more positive during the experimental period (Hioco and Parlier, 1966). A greater change in calcium balance was realized in osteoporotics which suggests that osteoporosis could be slowed in individuals by increasing their calcium intake.

Other studies support this conclusion. Lee et al., 1981, studied 20 elderly osteoporotic females who were supplemented with cheese and a calcium supplement for 6 months. No significant differences in urinary calcium excretion occurred when subjects consumed their self-selected diets containing 452 ± 191 mg Ca or during the experimental time period when they consumed 1152 ± 191 mg Ca. Calcium balance was more positive on the supplemented than on the unsupplemented diet. Heaney et al., 1977 and 1978, demonstrated the same trend. When calcium supplements were given to human subjects, a more positive calcium balance occurred. Lee et al., 1981, also found no correlation between the intake of any single nutrient and changes in bone density; however, they did see an increase in bone density ($p<0.05$) at the end of the experimental period (6 mo.), possibly as a result of combined dietary effects.

Bone mineral disturbances due to dietary mineral imbalances were studied by Ericsson et al. 1986. These researchers found that mineral imbalances caused by Ca, Mg, F, Ca + F or Mg + F supplemented diets were prevented by Ca or Ca + F supplementation. This effect was seen most readily in the femurs of rats. Thus, the theory that dietary calcium supplementation can increase or slow the processes involved in decreased bone mineralization, especially when dietary mineral imbalances exist, is supported (Clark, 1969). If bone density and/or mineral content can be increased by dietary supplementation with calcium or calcium rich foods, which calcium sources would be best suited for this purpose? Calcium exists in a wide variety of forms: as free divalent cations, as specific complexes with enzymes or binding proteins, but largely as inorganic salts in bone and other structural objects. Milk and some milk products such as cheese are the most concentrated sources of naturally occurring calcium.

In 1980 Wong and LaCroix measured femur calcium in response to various dairy products as sources of calcium. Nonfat dry milk, yogurt and rennet-precipitated casein were found to be more efficiently utilized by rats than was the calcium carbonate typically added to the rat diets. They concluded that calcium availability is probably affected by the nature of the calcium complex. Similar results were found in a study of 22 postmenopausal women when one half of these subjects were given an extra 24 oz. of milk per day for two years and the other half received no intervention (Recker and Heaney 1985). They found that the treatment group had a significant increase in urinary calcium, decrease in bone accretion and decrease in bone

resorption. Calcium balance in the milk supplemented group improved and suppression of bone remodeling was less than in a previous study conducted by the same group in 1977, when a calcium carbonate supplement was used. These results suggest milk is a better calcium source than is calcium carbonate because it does not suppress bone remodeling to the extent of calcium carbonates.

During a life-long experiment with female mice, Shaw and Belonje, 1987, found that calcium intake early in life did not affect skeletal calcium in adulthood, but a continuous high dietary calcium intake reduced skeletal turnover rate in old age even when calcium consumption was increased at a later age. This experiment supports the use of calcium supplements even by older patients suffering from osteoporosis. However these patients' vitamin D intake must also be considered.

Using the growing pig, Ross et al., 1984, conducted a study comparing sources of calcium (Table 1). Bone breaking strength was used as a criterion of calcium bioavailability. A lower bone breaking strength and % ash in pigs fed dolomite limestone was found ($p<0.05$) in comparison to other calcium supplements. Pigs fed calcium carbonate as the source of calcium consumed more food than those fed other sources of calcium. Calcium carbonate was used as the standard for this study. As shown in Table 1, relative bioavailability of calcium was not affected by source except for the lower availability of dolomite. This trend was seen in rats fed several different calcium supplements (Greger et al., 1987). Rats fed dolomite had the lowest levels of calcium and phosphorus in their tibias. Calcium supplements which contained either magnesium or iron resulted in the lowest apparent absorption

whereas, rats fed milk had diarrhea but highest apparent absorption and tibia calcium and phosphorus (Greger et al., 1987). These researchers reported no significant differences in apparent absorption of calcium existed among the different calcium sources tested (i.e., lactate, amino acid chelate, phosphate or carbonate). One calcium supplement tested in this study by Greger et al., adversely affected the kidneys (calcium phosphate dibasic).

Waldroup et al., 1963, tested the effect of several different calcium sources on bone ash of chicks. Calcium from limestone was more available than calcium from reagent grade calcium carbonate or oyster shell. Thus, calcium carbonate in the purified or non-purified form may not always be the most biologically available source of calcium.

Several studies have shown improved calcium balance when subjects were given an increased calcium level from food sources than when given calcium from calcium salt tablets (Patton and Sutton, 1952). However, other researchers (Steggerda and Mitchell, 1939, McQuarrie et al., 1947, Kempster, 1940, and Sterns and Jeans, 1934) have shown that calcium salts were utilized to approximately the same extent as that from milk. As Americans grow older they often decrease their milk consumption for many reasons: food aversions, allergies, simple likes and dislikes. Thus, it is important to discuss how these individuals can increase their calcium consumption and thus, hopefully, improve their calcium balance via other means.

Recognizing that differences may exist among calcium salt sources in bioavailability and utilization, comparisons of bioavailability and utilization of the commercially available calcium supplements

should be of practical value. Calcium lactate, gluconate, sulfate and carbonate supplements were compared by Patton and Sutton, 1952, using college age women. At a calcium intake of 750 mg/day no significant differences in calcium utilization or calcium absorption among these four calcium supplemental sources were noted. The percent utilization differed somewhat, though not significantly, between the calcium supplements used; Ca carbonate - 10.79%, Ca sulfate - 20.92%, Ca lactate - 11.45% and Ca gluconate was 28.79% utilized. Patton and Sutton noted an interesting trend, in that, no matter what order the supplements were fed to the human subjects at weekly intervals, a decrease in utilization occured after two weeks of the study, suggesting an adjustment period longer than one week may be necessary, especially if randomization of dietary treatments are not made. These calcium supplements were apparently absorbed at a rate of 18%, a rate similar to that found for calcium absorption from food sources in other studies.

The previously described study utilized a controlled feeding regimen in which a constant background diet was used throughout the study. This is important in comparing calcium supplements for bioavailability. Recent literature indicates that protein, fiber, phosphorus, magnesium and naturally occurring substances such as oxalic acid and phytic acids will interfere with calcium absorption (Morrissey and Wasserman, 1971; Pingle and Ramsastri, 1978 a & 1978 b; Anand and Linkswiler, 1974; Chou, 1978; Clark, 1969; Hegsted, 1981; McCance & Widdowson, 1942; Forbes et al., 1979; Rheinhold et al., 1973; and Parker, 1985). Thus, the potential for false results of actual

bioavailability of a supplement is great if constant diets are not employed. For example, a study of nine postmenopausal women given low or high protein diets, equal in calcium and phosphorus showed that the ingestion of a high protein diet significantly increased urinary calcium excretion over that seen when a low protein diet was fed. This effect could be demonstrated whether the added protein was from cottage cheese or from beef (Howe, 1987). Serum phosphorus was altered by protein in the diet (high protein = lower serum phosphorus) but serum calcium was not affected by dietary protein level or by level of dietary calcium intake as shown by Spencer et al., 1969. Hypophosphatemia has been shown to stimulate the synthesis of the vitamin D precursor by the kidney and this in turn enhances intestinal absorption of calcium (Deluca, 1974).

One limitation in studies of calcium nutriture is that efficiency of calcium absorption gradually changes over time as a result of adaptation to new levels of calcium intake (Kemm, 1971, 1972; Benson et al., 1968; and Jeejeebhoy, 1986). It has been suggested that to minimize this problem, a calcium intake similar to that consumed by the subject prior to the experiment should be used (Allen 1982). This is difficult to do since in human feeding studies one must usually devise a diet which meets the NRC RDA (National Research Council Recommended Dietary Allowances). If human subjects received a level of calcium during the experimental periods which was similar to their usual intake, usually it would be much lower than that recommended by the National Research Council (Hanes I and Hanes II).

Most of the calcium found in food is complexed with other food