Lactose and Calcium Metabolism: A Review[1, 2]

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INTRODUCTION

Milk-replacer diets for infants and newborn animals are of much interest. More balanced milk replacers could be developed undoubtedly if more were known about the specific functions of milk constituents. Lactose, among these constituents, has unique physiological effects, some of which are due to the galactose moiety when lactose is hydrolized. Other effects are specific to the lactose molecule itself, however, and the relationship between lactose and calcium falls in this latter category.

This paper summarizes previous reviews (5,10,25,51) on the general physiological effects of lactose and discusses current hypotheses on the mechanism(s) of action of lactose on calcium metabolism. The four main hypotheses are: A, the intestinal acidity theory; B, the chelation theory; C, the metabolic theory: and D, the osteogenic theory.

CALCIUM ABSORPTION AND LACTOSE

Three hypotheses have been presented relating the beneficial effects of lactose to enhance intestinal absorption of calcium. The mechanism(s) by which calcium absorption is increased by lactose feeding, however, ranged from pure physico-chemical concepts within the intestinal lumen to complex enzymatic involvement in the intestinal walls.

INTESTINAL ACIDITY THEORY

A relation between lactose and calcium absorption was observed first by Bergeim (7), who reported that the addition of 25 percent lactose to the diet increased absorption of calcium and sometimes phosphorus, with and without cod liver oil. In a comparison of lactose to glucose, dextrin, sucrose, maltose and starch, lactose was found to be the most active carbohydrate to increase calcium absorption. Bergeim concluded that the effect of lactose in increasing calcium absorption was the result apparently of the tendency of this sugar to maintain a higher hydrogen ion concentration throughout the intestional tract.

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Mitchell (60) found that lactose as the sole source of carbohydrate promoted the best growth of acidophilous bacteria and the poorest growth of the animal. Robinson et al. (66) suggested that the action of lactose in promoting calcium absorption was independent of its effect on the pH of the intestine in calves. Robinson and Duncan (67) found that lactose reduced the intestinal pH in rats on vegetable diets but not in those receiving meat, and calcium absorption was improved with both diets. Kline et al. (51) were not able to establish a relation between increased calcium absorption and increased acidity in the intestine in young chicks as a result of lactose ingestion. They stated that whether the change in the intestinal reaction was the cause of increased calcium absorption or the result of removal of calcium from the tract was questionable. However, they reported that lactose had a favorable effect upon calcium absorption and ossification when added as 40 percent of a rachitic diet for young chicks.

Fournier (21,22) reported that the beneficial effects of lactose on calcium metabolism were more direct than the simple favoring of the acidification of the intestinal tract content. Fournier and others (23,24,39,40) showed that a group of sugars which they designated as structural sugars all showed the same beneficial effect on calcium absorption. These sugars were lactose, D-galactose, D- and L-xylose, D- and L-arabinose, mannose, melibiose, and raffinose. The structural sugars were all attacked to a lesser extent by the intestinal bacteria. Fournier and Dupuis (30,31) offered a definition for the structural sugars which stated that these sugars are numerous and interchangeable, and that their biological role is independent of their chemical nature. Dupuis and Fournier (14) found that the favorable effect of lactose on calcium absorption did not change by adding aureomycin to the diet. Wasserman and Lengemann (77) reported that lactose and/or neomycin improved calcium absorption in the growing rat. Lactose decreased the pH of the ileum with or without neomycin added to the dosing solution. They concluded that the effect of lactose on calcium metabolism could not be attributed to a direct effect on intestinal fermentation pattern.

The presence of both lactose and neomycin in the ileum failed to improve calcium absorption over that of lactose and neomycin when given separately. If the effect of lactose on calcium absorption was independent of the fermented lactose in the ileum, the combination of lactose and neomycin in the dose, should have increased calcium absorption over that of lactose alone. The slight increase in the ileal pH when neomycin was added in the presence of lactose indicated only partial inhibition of lactose fermentation and calcium absorption in the ileum.

Fournier and Guillman (27) reported that the cecum was the only segment in the gastrointestinal tract of the mouse which increased in dry matter content and size by feeding lactose. Fournier et al. (36) removed the

cecum from rats receiving lactose in the diet and found no change in calcium utilization by feeding lactose. They concluded that the lactose effect on calcium metabolism was independent of the fermentation patterns in the cecum. Lengemann et al. (57) concluded that lactose had a greater effect on calcium absorption from the ileum than from the stomach, duodenum, jejunum or cecum. Ali and Evans (unpublished data Rutgers University) showed that the dry tissue of the small intestine per 100 g. body weight was increased by feeding lactose to the growing rat. This increase in dry tissue was associated with an increased calcium absorption in the ileum.

Ali and Evans (1,3) fed 0- and 12-percent lactose to the growing rat in combination with three different dietary buffering capacities across the dietary calcium levels of 0.19, 0.48 and 0.78 percent. By feeding either lactose in the diet, a lower calcium diet or a more acid diet, a decrease in the pH in many segments of the gastrointestinal tract with the inverse in the absorption of calcium was found. Specifically for lactose, the decrease in pH in the intestinal content was significant in the ileum. These results indicated that the absorption of calcium from the intestine is sensitive to the hydrogen ion concentration. Seki and Goto (69) reported that the lactose elicited its maximum enhancing effect in calcium absorption when calcium intake was low. Lower calcium intake in the presence of dietary lactose activated the transport of calcium across the intestinal wall by exerting an additive increase in hydrogen ion concentration (1,3).

In summary, the intestinal acidity theory relates the effect of lactose and other acid producing conditions to an increased solubility of calcium ions at a lower pH in the intestinal lumen.

CHELATION THEORY

Another aspect of a possible relationship between lactose and calcium emerged from the work of Herrington (48), who found that lactose was more soluble in a molar solution of calcium chloride than in pure water in vitro. The increased solubility of lactose in calcium chloride solutions was due to the formation of a molecular compound of α-lactose and calcium chloride, which they isolated and identified in solution.

Mitchell et al. (59) reported that fecal calcium in the rat was markedly reduced when 60 percent lactose was added to the diet, which they attributed to intestinal conditions more favorable for the absorption of calcium. Roberts and Christman (65), however, presented evidence that lactose did not aid in the absorption of calcium in the fasting rat given a measured dose of calcium lactate and sacrificed 3 hours later for the measurement of calcium absorption.

Wasserman et al. (76) assayed lactose and 18 amino acids for effects on intestinal absorption of calcium-45 in the rat. Lactose was the most potent

organic compound tested and it enhanced calcium-45 absorption when ingested simultaneously. Lengemann et al. (56) contrasted the availability of calcium from milk with that from calcium chloride in rats and rabbits and from calcium chloride with that from grain for cattle, rats and rabbits. Rabbits, young or old, were the only species that showed no increased calcium-45 absorption from milk. Young and old rats absorbed about 150 percent as much calcium-45 from milk as from a solution of calcium chloride or from calcium chloride and grain. Wasserman et al. (75) in a comparative study between normal and rachitic growing rats and chicks concluded that the stimulation of flow of digestive juices by lactose and the subsequent effects of those juices on calcium absorption offered a possible explanation for the lactose effect. Wasserman and Comar (74) confirmed the findings of Fournier and his coworkers (21,22,23,24,39,40) on the effect of the structural sugars in enhancing calcium absorption. They found that galactose, glucose, fructose and sucrose had little or no effect, and concluded that the effectiveness of the structural sugars to enhance calcium and strontium absorption appeared to be positively correlated with a prolonged residence time of these carbohydrates in the gut or the absorption of carbohydrate by a passive mechanism. Thus, both the sugar and calcium should be present in the ileum for enhanced calcium absorption.

Lengemann et al. (57) found that lactose enhanced calcium absorption when the latter was given as either the chloride, gluconate, lactate, or acetate salt. Lactose increased calcium absorption in the presence or absence of vitamin D in the rachitic rat and did so as effectively as vitamin D. In the intact animal the enhanced absorption of calcium-45 due to lactose was noted within 2 hours after gavage. The increased gastric emptying time in the presence of lactose alone was not sufficient to account for the lactose action. Addition of the chelating agent, disodium ethylenediaminetetraacetate (Na-EDTA), in equimolar concentration with the calcium ions completely counteracted the action of lactose. It seemed that lactose acted only on ionized or readily ionizable calcium. Solubilization was not a factor in lactose action since calcium-EDTA chelate was, in fact, a soluble complex. The lactose effect was apparent within 30 minutes after injection into the ileum. Without lactose, absorption ended within 30 minutes; whereas in the presence of lactose, it continued for 2 hours. They concluded that apparently lactose had a direct action either on the gut wall or within the intestinal lumen. The mechanism of action could range from purely physico-chemical concepts within the intestinal lumen, for example the binding capacity of lactose for calcium ions as reported by Herrington (48), Nordbö (62) and Jensen et al. (50), to metabolic effects on the mucosal cells of the intestine. Lengemann

(53) found that calcium absorption from the ileum was stimulated if calcium and lactose were present together in the same segment, while no effect was observed if they were in adjacent segments. Rats fed for 2 weeks on a diet containing 10 percent lactose and fasted before a test dose of calcium-45 was administered failed to absorb a greater proportion of the test dose than rats fed a diet containing 10 percent glucose. These workers concluded that the site of action of lactose was in the intestine and not within the body.

Vaughan and Filer (72) reported that lactose, bile, sorbitol, glucose, sucrose, fructose, galactose and xylose did not significantly influence calcium absorption when injected with a test dose of calcium-45 in the duodenum but each of the sugars mentioned above greatly enhanced the absorption of calcium from ileal segments. It was concluded that lactose and all other slowly absorbed sugars owed their enhancing action on calcium absorption to the fact that they were absorbed slowly from the intestinal tract and were available in the ileum for a role, still unknown, in calcium absorption.

Charley and Saltman (8) reported that reducing sugars and polyols formed soluble stable complexes with a series of metal ions, including calcium, at pH 12. They concluded that the mechanism whereby metal ion(s) uptake from the diet was stimulated by such compounds could be explained on the basis of a complex formation. Charley et al. (9) presented evidence that lactose was able to chelate with calcium in vitro and under comparable conditions to that of the small intestine. They suggested that the possible role of this proposed complex was as follows: within the intestinal lumen, calcium enters from the acid environment of the stomach as a free ion. As the pH is raised, a small portion of the metal is directly bound and transported by sites on or in the mucosal membrane. A major fraction is then precipitated as an insoluble salt or complex, such as carbonate, phosphate or oxalate. They suggested that the mechanism by which lactose promoted the absorption of calcium was by the formation of a complex with the metal whereby a soluble form of calcium ion was readily available for transport. A high sugar to calcium molar ratio, 40:1, was a requisite for an effective chelate formation. Rubin (68) stated that it was characteristic of the sugar chelates that their stability was enhanced by a strongly alkaline environment, due to the ionization of protons from the alcoholic groups of the polyol. The lactose-calcium complex was shown by Charley et al. (9) to be stable at pH 7 and was considered a firm one and possibly of the chelate type.

In summary, the chelation theory is based mainly on in-vitro findings that lactose chelates calcium under conditions similar to those of the in-

testinal environment. When the soluble chelate is formed in the lower segments of the small intestine, it is readily available for absorption.

METABOLIC THEORY

Wasserman et al. (75) reported a species difference between the growing rat and the young chick with respect to the effect of lactose on calcium-45 absorption. In normal and vitamin-D deficient rats, the gastrointestinal absorption of calcium-45 was stimulated by lactose or skim milk powder. The rachitic chick, however, did not respond to skim milk powder. They concluded that lactose elicited its favorable effect in the rat by acting on the metabolism of the intestinal tissue rather than by a direct effect on skeletal ossification.

Wasserman and Lengemann (77) studied the mechanism of lactose action. Absorption of calcium-45 was proportional to lactose concentrations in the test dose up to maximum rate at 0.4 mmole of lactose. Metabolic inhibitors, such as phlorhizin, sodium fluoracetate, sodium iodoacetate, 2,4-dinitrophenol and sodium azide, did not inhibit lactose action when given as an integral part of the dosing solution. The enhancing effect of lactose could not be duplicated when hydrostatic pressure within the intestinal lumen was maintained at 10.5 to 12 cm. with distilled water, saline or bovine serum ultrafiltrate. In vitro studies showed that lactose, xylose and glucose at concentration up to 0.5 M were unable to increase the solubility of calcium acid phosphate. The amino acids, lysine and glycine, at the same concentration doubled the solubility of calcium acid phosphate. These workers offered two possibilities for the mode of action of lactose: first, that the lactose effect on absorption was a non-specific membrane phenomenon, resulting in an alteration of the general permeability of the intestinal membrane to alkaline earth cations; this would be conceptually in contrast to acting as part of or as an accelerator to a specific transport mechanism. Secondly, that the lactose operated through an unknown intermediate that in turn regulated or influenced alkaline earth absorption (perhaps phosphate or a phosphorylated compound). Physicochemical considerations such as solubility, complex or chelate formation, or hydrostatic pressure differences could not explain the lactose effect. Lengemann and Comar (54) suggested tentatively that calcium was bound as it was absorbed from the small intestine. The presence of lactose in the intestine inhibited the production of the bound form and caused only ionic calcium to appear in the blood. Wasserman and Belanger (78) injected carbon-14 labeled lactose into ligated ileum of fasted rats and reported that intact lactose molecules were detected in the mucosal cells of the intestinal epithelium. Since lactose was not detected in the blood of lactose-fed ani-

mals, they suggested that it was hydrolyzed intracellularly by β-D-galactosidase as well as by an intestinal exoenzyme.

Lengemann and Comar (55) studied the presence of lactose in the intestinal tissue in more detail. On the basis of relative accumulation of carbon-14-labeled lactose in various segments of the gastrointestinal tract of rats, it appeared unlikely to them that the action of lactose on calcium absorption was due to the formation of a lactose-calcium complex.

Wasserman (73) questioned the chelation theory offered by Charley et al. (9) on the ground that the major buffering ion in the intestine was phosphate and not bicarbonate, that lactose enhanced calcium absorption with much narrower molar ratio of sugar to calcium than 40:1, and that, while chelate formation might take place in vitro, this did not mean that the biological activity of lactose could be linked solely to the chelate. He presented an alternative hypothesis that there existed within the ileal cells or the membrane surfaces of the mucosal cells a metabolically controlled block to calcium absorption. Metabolic poisons or inhibiting conditions relieved that block and allowed calcium to traverse the membrane at a more rapid rate. Lactose and certain other polyols, in some manner, altered metabolic pathways to yield the same effect as metabolic inhibitors. He emphasized that lactose should not be considered as a metabolic poison. The hypothesis only suggested that the end result in regard to lactose effect on calcium absorption in the rat's ileum was similar to that of metabolic inhibitors.

In other words, the metabolic theory proposes that lactose acts as a metabolic inhibitor to a system in the intestinal mucosal cells which controls the absorption of calcium. The inhibition of the system increases the rate of transport of calcium and other alkaline earth metals across the intestinal wall.

CALCIUM RETENTION AND LACTOSE

Givens and Mendel (42) claimed that the calcium contained in milk was more effective than soluble calcium lactate in increasing calcium retention. Robinson et al. (66) reported that the simultaneous feeding of lactose and bone meal doubled the calcium retention from the bone meal, but caused no change in the calcium retention from calcium lactate. They concluded that the calcium in calcium lactate was already so available that the addition of lactose did not add to its availability.

French and Cowgill (41) reported that the degree of maturity of the animal played a role in determining the favorable effect of lactose on calcium retention.

Outhouse et al. (64) observed no alteration in growth when 25 percent sucrose or lactose replaced an equivalent amount of starch in the basal

diet of rats. Of the carbohydrates tested, lactose was the only one which caused an acceleration of bone calcification and calcium retention. A later study by these workers (63) showed that lactose and cod liver oil diets caused greater retention of calcium and phosphorus than did diets containing starch or sucrose. Greater increments in retention, however, were obtained in the cod liver oil-fed animals than in the lactose-fed animals.

Henry and Kon (47) showed that calcium from milk was more available and was retained more efficiently than from other organic sources. They attributed this to the lactose content of the milk. Mills et al. (58) studied the potency of lactose to influence calcium retention in five boys ranging in age from 5 to 7 years. Throughout the 13 to 16 weeks of the experiment, the children were fed a basal diet supplemented with vitamin D to which calcium acid phosphate was added to raise the level of calcium intake to approximately 500 mg. daily. An additional supplement of lactose (36 g. daily) was given for 6 to 9 consecutive weeks. Lactose caused an average increase of calcium retention by 33.5 percent. Hara (46) used the ratio of calcium accumulated in the body to calcium fed as the coefficient of calcium utilization and obtained the coefficients of 70, 60, 55, 44 and 25 percent for dry milk, bone meal, dried fish meal, calcium carbonate, and calcium oxalate, respectively. Fournier (22) showed that 12 to 20 percent lactose replacing an equivalent amount of sucrose, glucose or maltose gave an increase in calcium retention of 63 to 72 percent.

Forbes (20) found that calcium balance was increased in the rat with the addition of 25 percent lactose in the diet. Interaction between calcium level and lactose significantly affected calcium retention. Evans and Ali (18) reported that the increased calcium retention by feeding lactose was less pronounced than the effect on calcium absorption. The effect on calcium retention seemed to be an indirect one since lactose-fed rats were considered more efficient in utilizing the absorbed calcium according to Atkinson et al. (5), Duncan (10) and Nickerson (61). Tomarelli et al. (71), Ali and Evans (4) and Baker et al. (6) reported that lactose fed rats deposited more total water, protein, ash and calcium and less fat in their body than non-lactose fed rats. Lactose-fed rats were considered to be at a physiologically younger age with respect to their body composition which could explain their being more efficient in utilizing the absorbed calcium.

OSTEOGENIC THEORY

Fournier (23,24) and Dupuis and Fournier (14) presented the fourth hypothesis; that the effect of lactose on calcium utilization was at the ossification sites. They postulated that, in contrast with the energy producing sugars, structural sugars assisted in ossification as precursors of

glycine in the synthesis of osseous matrix. Fournier et al. (37) showed that, judging from histological studies in the young rat, lactose could replace vitamin D in improving calcium deposition and tibia growth in young rats on a calcium adequate diet. Fournier and Dupuis (31) reported that 12 percent lactose and 0.6 percent calcium was the best lactose to calcium ratio in terms of improved bone calcification. They also calculated that the addition of 20 percent lactose was equivalent to one international unit of vitamin D per rat per day (32). The extent to which these effects were identical was not known.

Fournier and Dupuis (33) reported that lactose improved the metabolism and deposition of calcium in bones by acting as a metabolic inhibitor of certain steps in the tricarboxylic acid cycle. Sodium fluoracetate and sodium fluoride gave a similar effect to that of lactose by increasing serum calcium and urinary citric acid concentration in rachitic calcium-deficient rats. Tomarelli and Bernhart (70) did not attribute the increase in excretion of tricarboxylic cycle acids to altered metabolism, but they considered it as a renal acid-base mechanism for neutralization of increased calcium content in the body under the action of lactose.

Fournier and Dupuis (34) reported that when malonic acid was fed to calcium-deficient animals, it gave a blood, urine and parathyroid histology picture similar to that given by lactose. They stated that a certain degree of inhibition to tricarboxylic cycle enzymes seemed to be necessary for optimum calcium metabolism. Vitamin D inhibited the activity of the enzymes aconitase and succinic dehydrogenase in vitro. They postulated that the diminished activity of glucose-6-phosphodehydrogenase due to accumulation of galactose-6-phosphate, a metabolic product of lactose in the intestinal walls, would put lactose and vitamin D in the same category.

Dupuis and Fournier (17) suggested that vitamin D acted as an essential regulator and that lactose was required for the perfection of the role of vitamin D in calcium metabolism. In a review, Fournier (25) stated that lactose held the role of indispensable factor in the utilization of calcium, comparable to vitamin D and parathyroid hormones. Automation and nonspecificity were the characteristics of the action of lactose. The remarkable osteogenic power of lactose in the rat may not apply to man. Labat and Tharaud (52) and Fournier et al. (38) reported that lactose feeding to the rat was superior to vitamin D_2 in terms of calcium retention and deposition. Lactose decreased bone catabolism but did not alter the quantity of exchangeable calcium and bone anabolism.

The osteogenic theory suggests that lactose acts mainly at the ossification sites. It proposes that metabolic functions of lactose are similar to those of vitamin D which are essential for proper calcium metabolism and deposition in bones. In contrast to energy producing sugars, lactose provides

precursors required for the synthesis of bone matrix. This theory partially agrees with the metabolic inhibition theory; yet, it considers bones as the target tissue for lactose action.

CALCIUM IN THE BLOOD AND LACTOSE

Inouye (49) reported that lactose-protected parathyroidectomized dogs from tetany by providing a blood calcium level close to normal. Lactose was effective only when ingested and not when injected. Greenwald and Gross (45) concluded that lactose was effective in maintaining close to normal blood calcium only if enough calcium was given along with it in the diet. Robinson et al. (66) showed that the simultaneous ingestion of calcium lactate and lactose caused an increased serum calcium level. They did not report the magnitude of the increase. Dupuis, Fournier and their coworkers (11,12,13,15,16,28,29,32) showed that lactose produced a normal blood calcium level in a rachitic rat in the absence of vitamin D and in the presence of enough dietary calcium in less than 20 days. Ali and Evans (2) reported an increased serum calcium by feeding lactose which reflected the increased calcium absorption in the intestine. Fournier (26) found that simultaneous ingestion of lactose and strontium-85 caused a large increase in radio-activity in the blood.

CALCIUM CONTENTS OF THE BODY AND BONES AND LACTOSE

Kline et al. (51) reported that the feeding of 20 percent lactose to growing chicks resulted in an increase of about 33 percent in tibia ash over the basal diet which contained no vitamin D and lactose. Whittier et al. (79) found that feeding lactose to growing pigs resulted in an increase in the total body ash of about 30 percent over the sucrose-fed pigs. Mitchell et al. (59) reported that replacing glucose with lactose in rat diets resulted in an increase in total body ash and calcium. Tomarelli et al. (71) showed the same trend in total body ash by feeding 52 percent lactose. Fournier and Dupuis (33,35) showed that the increase in calcium retention by adding lactose to the diet resulted in an increase in the density of all bones. The medulla of the femur was narrower in the lactose fed rats. Evans and Ali (18) fed 12-percent lactose diets to rats. An increase in percent femur calcium indicated an improvement in calcium deposition in the bones which was associated with an increase in percent body calcium. Gourvitch (43,44) studied the effect of prolonged feeding of 35 percent lactose on the histology of the long bones. A noticeable thickening of the subperiosteal and perimedullary lamellary system of the tibial diaphysis of 18-month-old rats was evident. Based on histological evidences, Gourvitch (44) concluded that the effect of lactose was probably due to defective bone resorption plus active osteogenesis. Finlayson (19) using calcium-47 reported that

lactose did not increase calcium absorption but increased deposition of calcium-47 in the skeleton.

GENERAL DISCUSSION

Lactose and calcium levels as well as the overall diet composition exert a profound effect on calcium metabolism. Species and age of the experimental animal contribute to the response of the animal to lactose feeding. The contradicting conclusions reported by different workers on the mode of action of lactose could be attributed to diverse dietary composition and/or experimental conditions employed in such studies. Rats, young or old, proved to be an ideal experimental animal for in vivo studies. In vitro results, on the other hand, are inadequate to deal with such a complex model due to the multitude of factors involved. In the evolutionary process of animals, it seems unlikely that the first food available for the newborn of animal species would be a metabolic inhibitor; yet, this would not disprove the evidences available on that possible mechanism. The inability to isolate the intact lactose moiety from the blood or the ossification centers of lactose-fed rats would question the theory of direct osteogenic effect. Lactose was effective only when ingested and not when injected. Hydrolysis or metabolic products of lactose in the body are not unique in nature, except with galactose which was shown to be not as effective on calcium metabolism as lactose. Physico-chemical effects of lactose within the intestinal lumen seem to offer more logical explanation for the mode of action of lactose on calcium absorption. The availability of calcium for absorption in the intestine is enhanced in the presence of lactose which lowers the intestinal pH and increases the solubility of calcium. Improved permeability of intestinal mucosal cells to calcium and possibly other alkaline earth metals could be the result rather than the cause of increased calcium availability within the intestinal lumen. In the rat, increased calcium retention and improved bone calcification seem to be secondary effects to increased calcium absorption. Rats on lactose-containing diets maintained a physiologically younger body composition, an improvement in calcium absorption, and a better bone ossification when compared to non-lactose-fed rats. The addition of 12 percent lactose to the diet on a dry matter basis improved calcium utilization. However, more applied studies on man and animals are needed before more practical recommendations can be established.

SUMMARY

Four main hypotheses have been presented in the last four decades to explain the mode of action of lactose on calcium metabolism, but not one of these has been widely accepted. Three of them relate the effect of lac-

tose to enhanced calcium absorption and one to improved calcium deposition in bone. These hypotheses listed in chronological order state that the ingested lactose improves calcium metabolism as a result: A, of providing an acidic pH in the intestinal tract which increases the solubility and the availability of calcium for absorption; B, of chelating calcium in the lumen of the small intestine as a soluble chelate which increases calcium absorption; C, of inhibiting a metabolic system which is responsible for controlling the uptake of divalent cations at the absorption sites in the small intestine and results in an increased calcium absorption; and D, of stimulating certain metabolic steps at the ossification sites which increase the deposition of calcium and improve the efficiency of calcium utilization.

Findings by the authors (1,2,3,4,18) agree with hypothesis A and suggest that diet composition affects the mode of action of lactose on calcium absorption. Dietary lactose produced a more acid pH in the intestine, increased calcium retention, raised serum calcium and enhanced bone calcification. The effect on calcium retention and osteogenesis appears to be indirect as lactose-fed rats maintain a relatively younger body composition, i.e., a lower body fat with higher water, protein, ash and calcium, compared to rats receiving no lactose in their diet.

RESUMEN

En el transcurso de las últimas cuatro décadas se han propuesto cuatro hipótesis principales para explicar el modo de acción de la lactosa en el metabolismo del calcio, pero ninguna ha tenido gran aceptación. Tres relacionan el efecto de la lactosa con la intensificación de la absorción del calcio, y la otra con una deposición más efectiva de calcio en los huesos. Estas hipótesis, ordenadas cronológicamente, afirman que la lactosa ingerida mejora el metabolismo del calcio como resultado de: A, proveer un medio ácido en el canal intestinal, el cual aumenta la solubilidad y la disponibilidad del calcio para ser absorbido; B, propiciar la quelación del calcio en el lumen del intestino delgado en forma soluble, lo cual aumenta su absorción; C, inhibir un sistema metabólico regularizador de la absorción de cationes bivalentes en los puntos de absorción en el intestino delgado, lo cual aumenta su absorción; y D, estimular ciertos procesos metabólicos en los puntos de osificación, los cuales aumentan tanto la deposición como la utilización del calcio.

Los autores (1,2,3,4,18) concuerdan con la hipótesis A y a la vez sugieren que la composición de la dieta afecta el modo de acción de la lactosa en la absorción del calcio. La lactosa dietética produjo un pH más ácido en el intestino, aumentó la retención del calcio, aumentó el calcio en el suero y estimuló la calcificación ósea. El efecto sobre la retención del calcio y la osteogénesis parece ser indirecto, ya que en los ratones alimentados con lactosa perduró la composición de un cuerpo más joven, es decir, menos grasa pero más agua, proteina ceniza y calcio, al contrastarse con la de aquellos cuya dieta no contenía lactosa.

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