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Revisión

Calcium ingestion and obesity control

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Abstract

Introduction: **Obesity is a risk factor for other non-transmissible chronic diseases. It has been suggested calcium intake helps to control obesity, but there is no consensus about this.**

Objective: **Analyze the studies published on this topic in order to highlight issues to be further explored in future studies.**

Methods: **A literature review was conducted using the PUBMED, Science Direct, Scielo, Scopus, Medline and CAPES electronic scientific basis. Studies, which evaluated the effect of calcium ingestion in energy metabolism, body weight, and body composition, published from 2000 through 2011, were analyzed.**

Results and discussion: **The results of most of the interventional studies selected suggest that calcium ingestion may favor the reduction of the anthropometric measures and improve body composition. The discrepancy in the results of the observational studies is probably due to methodological differences. It seems that the benefits are only detected when a low calcium habitual ingestion (≈ 700 mg/day or lower) is increased to about 1,200-1,300 mg/day.**

Conclusion: **When assessing the effect of calcium derived from supplements, the investigators should test higher bioavailability compounds. If the calcium source is the dairy product, it is necessary that to consider and isolate the impact of other nutrients present in these foods. Longer term studies should be conducted to assess the effect of calcium on energy metabolism.**

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Key words: *Calcium. Energy metabolism. Body weight. Body composition.*

INGESTA DE CALCIO Y CONTROL DE LA OBESIDAD

Resumen

Introducción: **La obesidad es un factor de riesgo para otras enfermedades crónicas no transmisibles. Se ha sugerido que el consumo de calcio ayuda a controlar la obesidad, pero no hay un consenso al respecto.**

Objetivo: **Analizar los estudios publicados sobre este tema con el fin de destacar los aspectos a investigar en estudios futuros.**

Métodos: **Se realizó una revisión bibliográfica utilizando las bases de datos electrónicas PUBMED, Science Direct, Scielo, Scopus, Medline y CAPES. Se analizaron los estudios que evaluaban el efecto de la ingesta de calcio sobre el metabolismo energético, el peso corporal y la composición corporal, publicados desde 2000 a 2011.**

Resultados y discusión: **Los resultados de la mayoría de los estudios intervencionistas seleccionados sugieren que la ingesta de calcio podría favorecer la reducción de las medidas antropométricas y mejorar la composición corporal. La discrepancia de los resultados de los estudios observacionales probablemente sea debida a diferencias metodológicas. Parece que los beneficios sólo se detectan cuando una ingesta habitual de calcio baja (~ 700 mg/día o menor) se incrementa hasta cerca de 1.200-1.300 mg/día.**

Conclusión: **Cuando se evalúa el efecto del calcio derivado de los suplementos, los investigadores deberían evaluar la biodisponibilidad de los preparados. Si la fuente de calcio son los productos lácteos, es necesario que consideren y aíslen el impacto de otros nutrientes presentes en estos alimentos. Deberían realizarse estudios a largo plazo para evaluar el efecto del calcio sobre el metabolismo energético.**

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Palabras clave: *Calcio, Metabolismo energético, Peso corporal, Composición corporal.*

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Abbreviations

NTSD = Non-Transmissible Chronic Diseases.
PTH = Parathyroid Hormone.
RDA = Recommended Dietary Allowance.
NHANES = National Health and Nutrition Examination Survey.
FAS = Fatty Acid Synthase.
UCP2 = Uncoupling protein 2.
BMI = Body Mass Index.
WC = Waist Circumference.
EAR = Estimated Average Requirement.
DEXA = Dual Energy X Ray Absorptiometry.

Introduction

Non-transmissible chronic diseases (NTSD) are a global health problem.[1] It causes serious impacts on health, leading to several adverse effects on life quality of people, favoring the occurrence of premature deaths and high costs for society.[2] Cardiovascular diseases, cancer, chronic respiratory diseases and diabetes are responsible for 60% of deaths around the world.[3] If effective prevention and control measures are not taken, it is estimated that 41 million people will die from a NTSD by 2015.[2]

Obesity stands out among the NTSD because it is a risk factor for other diseases such as dyslipidemia, cardiovascular diseases, diabetes, hypertension, câncer.[1,2,4-6] Overweight and obesity are responsible for 2.6 million deaths per year.[2] Regardless of its complex and multifactorial etiology,[7] the decrease in the levels of physical activity and the increase in energy intake are strong environmental determinants for this situation.[2,7,8] Many researchers have focused on the identification of the combination of macronutrients capable of regulating body weight, but the effect of micronutrients still needs to be further explored.[9-12] Minerals participate in the energy metabolism and in the secretion and action of insulin,[13] and may interfere in the control of obesity.

Calcium, the most abundant mineral in the human body, is involved in various physiological processes: muscle contraction, cell adhesion, hormones and neurotransmitters release, glycogen metabolism, cell proliferation and differentiation, blood clotting, nerve or synapthetic impulse transmission and structural support of the skeleton.[14, 15] In addition, it has been suggested that it may assist body weight control. Two possible mechanisms of action have been proposed to explain this effect. It seems that when high quantities of calcium is consumed, it binds to dietary fat forming insoluble compounds, reducing fat absorption and hence the amount of calories generated from this absorption.[16,17] Calcium ingestion is also important to maintain normal blood calcium levels, preventing the increase of $1,25(OH)_2D_3$ and parathyroid hormone (PTH), which in turn can promote increased levels of intracellular Ca^{2+}, activating lipogenic routes.[18]

However, there is no consensus in the results of studies evaluating the effects of calcium intake on body weight and body composition,[11,19-29] and in energy metabolism.[11,17,30-32] It is possible that the outcomes may be affected by the source of calcium tested. Although the results of some studies suggest that calcium originated from the supplements has no effect,[20,22,24,27,29] others demonstrate positive effects in controlling obesity.[21,33,34] It has been suggested that dairy products may have a stronger effect than supplements.[18,33] However, exact the reason why this occurs is not known.[17,27,35,36]

The new recommendation for calcium intake (Recommended Dietary Allowance (RDA) = 1000 mg/day) is based on its effects on bone health, since there is no consensus on its effects on NTSD.[38] According to some authors, to obtain the beneficial effects on body weight and NTSD calcium intake should range from 1,000 to 1,200 mg/day.[39] It is unclear whether the effects are dose dependent, but the knowledge of the minimal dosage capable of resulting in positive effects is important to improve adherence and effectiveness in response to the mineral intake and to minimize the costs with NTSD.[29]

Due to the increase in obesity prevalence, the effect of diet in its etiology and the limited number of longitudinal clinical studies publish about this topic so far, it is necessary to conduct well-designed studies to assess the effect of high calcium intake on resting energy expenditure, body weight, and body fat control.[12,19] Therefore, the purpose of this review is to highlight issues to be further explored in future studies to clarify the possible effect of calcium intake on anthropometry, body composition and energy metabolism.

Methodology

Articles published from 2000 to 2011, in which the effects/association of calcium intake on/with body weight, body composition and energy metabolism were selected. A literature review was conducted in order to find articles in the electronic databases PUBMED, Science Direct, Scielo, Scopus, Medline and CAPES Journals.

Using the following indexing terms in English or in Portuguese: "calcium intake and obesity", "calcium intake and weight control", "calcium intake and weight loss", "calcium intake and body composition", "calcium intake and energy metabolism," "calcium intake and fat oxidation", "calcium intake and energy intake".

Possible mechanisms through which calcium may favor obesity control

The inverse relationship between calcium intake and body weight was observed since the 1st National Health

and Nutrition Examination Survey (NHANES) in 1984.[40] However, due to the lack of a possible mechanism of action to explain this association made this topic was not explored at that time. Today, the mechanisms by which calcium may control body weight and the magnitude of this effect are not well understood.[22] However, two possible mechanisms of action have been suggested. These mechanisms will be presented below.[30,41,42]

Increased fat excretion

It has been postulated that the interaction of calcium with fatty acids forming insoluble soaps can reduce the absorption and increase the excretion of these fatty acids, contributing to body weight reduction.[16,17,43]

In a crossover study, the effect of two treatment types on fat excretion in adult men was assessed. One of the treatments contained ≈ 410 mg/day of dietary calcium. The other contained 1,800 mg of calcium citrate malate plus 400 mg/day of dietary calcium (total of ≈ 2,200 mg/day). Calcium citrate malate, a soluble form of calcium, was administered together with fatty acids. Saturated fatty acids excretion doubled after the high calcium treatment compared to the low content one.[43] In another study, the effect of the consumption of a diet containing calcium-free chocolate (≈ 950 mg/day) and of another containing chocolate supplemented with calcium (calcium carbonate) was compared (≈ 1,855 mg/day). Once again, the excretion of saturated fatty acids was increased approximately two times after the consumption of the chocolate supplemented diet.[16] The results of these last two studies suggest that fatty acids should be consumed with calcium in the same meal so that fat excretion increase can take place.

Fecal fat excretion was 2.5 times higher after the consumption of a diet containing 1,800 mg/day of calcium and 15% protein compared to two other test diets (500 mg/day of calcium + 15% of protein and 1,800 mg/day of calcium + 23% of protein). According to the authors, a higher protein intake may favor calcium binding to phosphorylated proteins. Therefore, fatty acids would be free to be absorbed in the intestine, reducing the effects of calcium intake on fat excretion.[17]

The results of these studies suggest that calcium consumption ≥ 1,800 mg/day may be effective to reduce fat absorption, and that the joint ingestion of that mineral with fatty acids is important for that effect to occur. It should be noted, however, that this amount is higher than the recommended daily intake of calcium.[38] It has been shown that in some populations calcium intake is less than what is recommended.[41,42,44-48]

It should be emphasized that in two of the previously mentioned studies[17,43] there was an increase in urinary calcium excretion in response to the higher calcium intake, suggesting that the amount of the ingested

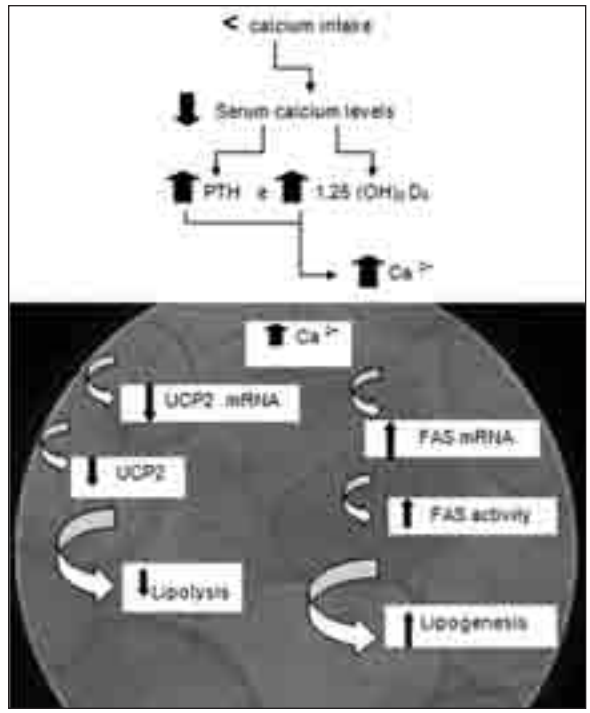

Fig. 1.—Mechanism of action of calcium proposed by Zemel et al., 2000.[18] The low intake of the mineral, reduces the serum calcium levels by stimulating the increase of PTH and 1,25(OH)$_2$D$_3$ levels. As a result there is an incrase in the intracellular levels of Ca^{2+} that can stimulate lipogenesis and distributive lipolysis.

calcium capable of increasing fat excretion may be lower than the ones tested. However, in one of these studies,[17] the higher urinary excretion was observed only when the high calcium intake was associated with high protein intake (1,800 mg/day + 23% protein). It has been demonstrated that an increase in protein consumption may increase calcium urinary excretion.[49]

Increased levels of intracellular Ca^{2+}

Some authors suggest that the effect in response to calcium consumption would be small to explain the magnitude of the observed effects on body weight and body composition. Besides that the amount to be consumed to possibly lead to these effects is very high.[33,50] Therefore, the mechanism proposed by Zemel et al. (2000)[18] (fig. 1) has been pointed out as the more consistent one to explain how low calcium intake would contribute to excess weight.[42]

The analysis of human adiposities indicated that the levels of 1,25(OH)$_2$D$_3$ and PTH can increase the intracellular levels of Ca^{2+} and inhibit lipolysis.[18] The results of human adipose tissue culture studies showed that the treatment with 1,25(OH)$_2$D$_3$ induced an increase of intracellular Ca^{2+} in a dose dependent form, increased by 40% the activity of fatty acid synthase (FAS), increased from 2 to 2.5 times the expression of mRNA FAS and inhibited the lipolysis in 35%,[51] reducing in

40% the expression of mRNA of uncoupling protein (UCP2), which is involved in the regulation of thermogenesis and energy metabolism and the levels of UCP2 in 50%.[52]

On the other hand, a higher consumption of calcium is capable of preventing weight gain, reducing body fat and increasing thermogenesis. These effects were observed in an animal study, which ate one of the four types of diet. 1) 0.4% of calcium diet, 2) 1.2% of calcium (0.4% dietary calcium + 0.8% from $CaCO_3$ supplement), 3) 1.2% of calcium (0.4% non-dairy source + 0.8% derived from dairy) and 4) 2.4% (0.4% non-dairy source + 2% derived from dairy). Although in terms of quality the effects of calcium from supplement were equivalent to dairy, the effects of calcium from dairy were stronger.[18]

Animal studies also support this evidence.[35,53,54] The consumption of a low calcium (0.4%), high fat, and sucrose diet doubled the concentration of intracellular Ca^{2+}. On the other hand, the consumption of diets containing 1.2 and 2.4% of calcium reduced the concentration to 50%, besides leading to greater reduction on body weight, body fat, mRNA FAS expression, FAS activity, and increased lipolysis, UCP2 expression, and body temperature. A greater increase body temperature, and a greater reduction in body weight, body fat, activity and expression of FAS was observed in response to the consumption of dairy calcium compared to calcium carbonate.[35] Parra et al. (2008)[54] verified that the consumption of a calcium supplemented diet reduced body weight and body fat in laboratory animals. But no changes were observed in the levels of UCP2. The effect of the consumption of a diet enriched with milk serum protein, calcium and vitamin D to that of a diet with low content of these nutrients were tested. Both test diets had high fat and sucrose content. Although food intake and body weight were not affected, it was observed that the animals that were fed the enriched diets had less body fat, and there was an increase in lean body mass.[53] However, the results of this study cannot be attributed to any specific nutrient (protein, vitamin D or calcium).

The consumption of a calcium-rich diet by laboratory animals led to less body weight and body fat gain, increased UCP2 expression, higher lipolysis rates, and higher body temperature than those that consumed a diet with low calcium content. These results suggest that calcium and dairy products may modulate adiposity independently of caloric restriction. In quantitative terms, the consumption of the high calcium derived dairy products diet resulted in the greatest effects than the diet continuing calcium from fortified cereal.[37]

This is useful for explaining the effect of calcium in adiposities and in rodents, but there it is necessary to conduct studies involving human beings to test this mechanism.[19] Although investigations in animals support this hypothesis, there is no homogeneity in the results of the studies in terms of some parameters assessed; for example the expression of UCP2.[35,52,53,54] There is also a study involving animals in which body fat was not affected after the ingestion of diets with low, normal amount of calcium and supplemented with calcium.[55]

The reasons why the effects of dairy products could exert more striking effects, quantitatively, than calcium supplements are not clear.[17,35,50] In animals similar effects were observed in reducing the concentration of intracellular Ca^{2+}. It has been suggested that other dairy products components may act by a route independent of that concentration. However, neither the mechanism of action nor the responsible components of dairy products have been identified,[35] and future studies are needed to determine the effect of these components.[50]

In human studies, the effects of calcium in body weight and body fat are not consistent either.[32] If we think about the proposed mechanism[18] it is important to find out not only the possible effects of calcium but also the role that PTH and $1,25(OH)_2D_3$ may play in humans body weight and body fat regulation.[11]

Effect of vitamin D ingestion and serum levels

There is no consensus on the relationship between serum levels of vitamin D and adiposity. The results of an intervention study indicated that there is no difference between serum levels of vitamin D between obese and normal weight people.[56] However, after being submitted to UV-B, obese subjects showed a more attenuated response to changes in the levels of $1,25(OH)_2D_3$ than the normal weight subjects, regardless of the absence of a significant difference in the production of $1,25(OH)_2D_3$.[56] This result suggests that obese individuals release less vitamin D from the skin to the circulation.[56] It has been claimed that vitamin D is stored in the adipose tissue, and that the higher the fatty tissue, the lower the serum levels of 25(OH)D.[57] In the previously mentioned study,[56] it was verified a negative correlation between body mass index (BMI) and serum levels of $1,25(OH)_2D_3$ only after UV-B radiation treatment. Obese patients had lower serum levels of 25(OH)D. BMI was negatively correlated with 25(OH)D concentrations only after the ingestion of 50000 IU of that vitamin.[56]

These results have been corroborated in other studies. Parikh et al. (2004) verified lower levels of 25(OH)D and $1,25(OH)_2D_3$ in obese compared to normal weight adults.[36] Vitamin D deficiency (levels of 25(OH)D < 20 ng/ml) was considered a predictor of metabolic syndrome in obese patients with BMI > 40 kg/m^2. It was observed a higher occurrence of deficiency between obese patients presenting metabolic syndrome.[58] The levels of 25(OH)D were negatively correlated with body fat,[57,59] BMI,[59,60] waist circumference (WC) and skinfolds.[59]

These data contradict what has been claimed by Zemel et al. (2000),[18] that is high serum levels of

vitamin D would increase the body weight and adiposity. Therefore, further studies are needed to evaluate the influence of serum levels of vitamin D on body weight, body composition and energy metabolism.

Thus, there has also been evaluated the possible influence of the ingestion of this vitamin on body weight and body composition. In the fourth Tromso Study, the usual intake of vitamin D by adults was negatively correlated with BMI. The odds ratio for obesity was equivalent to 2.24 in men and 1.51 in women. These participants were in the lowest quartile of intake of the vitamin. However, the authors report that cod liver oil the cod fish itself were the highest source of vitamin D habitually consumed by the subjects of that study. Therefore, the effect observed may have been caused by other substances present in these foods.[61] In the Women's Health Study, the usual intake of vitamin D was negatively associated with BMI and WC. However, this association was independent of calcium intake.[62] These results suggest that habitual intake of vitamin D alone has little influence on body weight and body composition.

The effect of vitamin supplementation on body weight, body fat and anthropometric indicators was also evaluated. The addition of 400 IU/day of vitamin D and 1,200 mg/day of calcium associated with caloric restriction (700 kcal/day) did not affect BMI, body weight, body fat and WC in women with excess body weight and obese, which had a habitual calcium intake < 800 mg/day.[63] However, when among women with habitual calcium intake < 600 mg/day, there was a reduction in body weight, BMI and body fat percentage.[64]

In women with lower calcium intake than the recommendations, it was verified that the supplementation with 400 IU of vitamin D associated with 1,000 mg of elemental calcium for seven years reduced the risk of body weight gain.[65] However, weekly supplementation of 20,000 IU (≈ 2,857/day) and 40,000 IU (≈ 5,714/day) of vitamin D associated with 500 mg of calcium/day, did not promote a significant reduction of BMI, body weight, body fat percentage, waist circumference and hip circumference, compared to a placebo containing 500 mg of calcium/day.[60] In another study, the supplementation of 2,000 IU of vitamin D for seven days did not change serum calcium levels, resting metabolic rate and the expression of genes related to lipogenic and lipolytic process such as FAS and UCP2.[66] Despite the increased vitamin D serum levels and reduced PTH concentrations obtained as a result of the daily 3,332 IU vitamin D supplementation for 12 months associated with a body weight reduction program it did not affect the body weight compared to placebo.[67]

These results suggest that the supplementation in higher dosages than the RDA (600 IU)[38] does not result in body weight control. However, the intake of vitamin D in amounts equivalent to the Estimated Average Requirement (EAR = 400 IU)[38] may exert a beneficial effect when combined with calcium supplementation and applied to people with low habitual dietary calcium intake. This data raise questions about which nutrient would be responsible for such benefits (vitamin D or calcium). It is possible that the benefits are due to the combined effect of these nutrients and they are conditioned to the habitual intake of the population evaluated.

Human prospective intervention studies assessing the effect of the adequacy of vitamin D status for NTSD treatment and prevention are still scarce. Therefore, the impact of vitamin D nutritional status in these diseases should be evaluated in future studies.[68]

Effect of PTH serum levels

Some studies have shown higher levels of PTH in obese individuals compared to normal weight individuals.[36,56,59,69] There has been observed a positive association between BMI and PTH levels, PTH and body fat in adults,[37] and between PTH levels and body fat, BMI, waist circumference and skinfold sum in elderly.[59] In the fifth Tromso Study it was observed that each increase of 1 pmol/l in PTH caused an increase of 0.17 kg/m^2 in men and 0.26 kg/m^2 in women in terms of BMI. The relative risk for obesity was 1.40 for men and 1.48 for women, who were in the highest PTH levels quartile.[69] These studies are consistent with the mechanism proposed by Zemel et al. (2000).[18]

In adiposites and skeletal muscles PTH stimulates phospholipids C resulting in an increase in intracellular Ca^{2+}. This increase can impair the ability of catecholamine to activate lipolysis and stimulates cAMP phosphodiesterase, which suppresses lipolysis. The increase in calcium concentration in adiposities can increase the expression of fatty acid synthase and increase lipogenesis.[70]

Although some studies show that both calcium and vitamin D intake and their serum levels may influence the levels of PTH,[69,71] studies involving young adults in Brazil, showed no association between PTH levels versus serum calcium levels and 25(OH)D and calcium intake.[72] Studies involving the supplementation of vitamin D (40,000 IU vitamin D + 500 mg of calcium)[60] and dosage of 3,332 IU of that vitamin caused a reduction of PTH concentrations.[67] These results highlight the controversy as to the triggering factor responsible for the increase in PTH levels. With respect to vitamin D, supplemented quantities capable of reducing the PTH levels are higher (40,000 IU) or close (3,332) to the upper intake levels for this vitamin (4,000 IU).[38]

Observational studies

The results of some studies have suggested the occurrence of possible effects and relationships dosage/effect of calcium intake on body weight and body composition. It has been claimed that calcium intake may explain 3 to 10% of body weight varia-

tion.[73,74] Analyzing the data from NHANES III, it was observed that an increase in calcium intake from 400 mg to 1,000 mg for a year in obese American subjects caused a reduction of 4.9 kg.[18] In middle aged women it was observed that the probability of overweight is reduce from 14.6% to 4.1% and of becoming obese reduces from 1.4 to 0.2%, when calcium intake increases from 10 to 20 mg calcium/g of protein. Besides that the weight gain/year reduces from 0.425 to -0.011 kg when the ingestion increases from 9 to 20 mg calcium/g of protein.[74] According to Eagan et al. (2006), in young normal weight people it is expected a body fat gain of 1.26 kg in 18 months in response to the ingestion of 500 mg of calcium from dairy products/day while in response to an ingestion of 1,200 mg/day it is expected a weight loss of 0.631 kg.[57]

The main features of these observational studies can be seen in table I. Despite the suggestions of the existence of a possible ratio dosage/effect previously mentioned, he analyses of a larger number of observational studies show a non-conclusive scenario in terms of: the existence of effects, dosages and source of calcium (dairy products or supplement). This can be attributed to methodological differences among these studies in term of how the anthropometric data, body composition, and dietary intake were obtained, and even with regards to types of analyses used in these studies.

Anthropometric and body composition data have been obtained by self-reports, electrical bioimpedance and anthropometry (weight, height, BMI, WC), computed tomography and dual energy x ray absorptiometry (DEXA). It is clear that the use of some of these methodologies may affect the accuracy of the measurements. It has been shown, for example, that self-report data may differ from the measured data, which may interfere in the nutritional status classification.[75,76] Some authors have reported that bio-impendence may underestimate body fat percentage compared to DEXA in overweight people.[77,78] These methods have different capabilities and applicability of measuring body fat and its distribution.[79]

Food intake data have been obtained through dietary recalls and food frequency questionnaires. The number of recalls and frequency in which they were used vary between studies. The 24-hour recall and food record only represent the habitual diet if applied for several nonconsecutive days.[80,81] The accuracy of these methods depends on the number of days in which they are repeated. According to Willett et al. (1998),[80] these dietary recalls should be applied from 3 to 10 times.

Another important factor to be considered is the need to adjust the statistical analyses regarding the consumption of nutrients such as proteins and vitamin D that may affect results.[23,37,64,82-88]

Nevertheless, the results of these studies suggest that calcium derived from dairy products or from supplements and even the dairy products themselves are associated with body weight and body composition, and that a low calcium intake (≈ 600-700 mg/day) is related to a higher body weight and adiposity. Due to methodological differences and to the fact that observational studies do not prove causality it is necessary to analyze the results obtained in the existing intervention studies.

Intervention studies

Effect of calcium intake on anthropometry and body composition

The characteristics of some intervention studies on the effect of calcium on body weight and body composition are shown in table II. The results of sudies that evaluated the effects of the calcium intake derived from the supplements,[20,22,27] mostly suggest that calcium does not affect body weight and body composition. However, there are some common points in these studies that need to be better explored. It is observed that the tested dosage of the supplements was higher than 1,000 mg/day, which added to the habitual food intake lead to a daily ingestion higher than the recommendation.[38] If calcium affects anthropometry and body composition, there may be a threshold level after which this effect does not occur. Another issue is that in these studies the average habitual intake of the participants was higher than 800 mg/day and results of observational studies[19,25] suggest that there is a strong association when the habitual intake is lower than ≈ 700 mg/day. Therefore, there must be a lower intake threshold where the association can be detected. The administration different forms of supplements can also interfere in the results. According to one of the proposed mechanisms of action of calcium, the ingestion of supplement in association with food is important for the mineral to cause the expected effect.[16,43] Furthermore, the ingestion in association with certain types of foods may increase the calcium bioavailability.[49]

The results of intervention studies[28,33,83] reinforce the assumption that when participants have low habitual intake < ≈ 700 mg/day, calcium seems to really affect body weight and body composition.[19,25] In the study conducted by Kabrnová-Hlavatá et al. (2008)[84] there was no significant effect of calcium. However, in the treatment groups fat free mass was preserved compared to placebo. Furthermore, it is likely that the absence of effects may be attributed to the amount of calcium consumed (850 mg/day), which was lower than the RDA (1,000 mg),[38] or to the short duration of the study.

In a study conducted by Zemel et al. (2004),[33] the effect of calcium derived from dairy products was quantitatively higher than that derived from calcium supplements. The possible reason for this possible superiority remains unexplained. This difference may be due to the bioavailability of the mineral in the supplement. Therefore, it becomes interesting to conduct studies to test the effect of supplements having higher bioavailability such as calcium citrate.[49,89,90] It is

Table I

Characteristics of the observational studies that evaluated the effect of calcium intake on anthropometric measures and body composition

Reference	*Subjects characterisics (number of participants/ gender/age/BMI*	*Observation period*	*Daily habitual calcium intake (mg/day)*	*Results*
Jacqmain et al. 2003[19]	235 ♀ and 235 ♂ 20-65 years old ≈ 25-31 kg/m²	–	< 600 600-1,000 > 1,000	There was a correlation between calcium intake and body fat %, fat mass, BMI, WC in women. Body weight, BMI, fat %, fat mass, WC, and abdominal fat were significantly higher in women with calcium intakes < 600 mg
González et al., 2006[21]	10,591 ♂♀; 53-57 years old	8-12 years (retrospective)	♀ 1,094 ± 558 ♂ (1,115 ± 557) (diet + supplement)	Women who used supplements had lower weight gain than those who did not use. Dosage of supplements > 500 mg was associated with less weight gain.
Rajpathak et al. 2006[24]	19,615 ♂ 40-75 years old ≈ 25 kg/m²	12 years	Baseline-Total: 791 diet: 736 End-total: 899, diet: 765	Increase in calcium intake was not associated with changes in body weight; even when dietary calcium, dairy products, supplements was evaluated separately
Eliat-Adar et al. 2008[25]	2,975♂♀; 47-79 years old ♀ 31.7 ± 0.1 kg/m² ♂ 29.9 ± 0.2 kg/m²	–	♀ 610 + 8.56 ♂ (680 ± 14.11)	BMI (0.80 kg/m² lower) and body fat (1.28% lower) in the highest quintiles of calcium intake (> 1,200 mg) compared to the lowest (≈ 300 mg)
Vergnaud et al. 2008[26]	2,267 ♀♂; ♀ 50.8 ± 4.3 years old; ♂ 51.5 ± 4.4 years old; ♂ 25.2 ± 3 kg/m²; ♀ 23.5 ± 3.7 kg/m²	6 years	♂ 1,048 ± 354 ♀ 909 ± 319	Consumption of milk and yogurt was inversely associated with changes in body weight and WC in men who where overweight at baseline. In women who where normal weight yogurt consumption was positively associated with weight change and changes in WC was positively associated with the consumption of milk in the ones that were overweight. These associations were not explained by calcium intake.
Azadbakht et al. 2005[23]	827 (357 ♂ and 470 ♀); 18-74 years old; 24.9 ± 4-26.8 ± 4.1 kg/m²	–	< 1.7 servings dairy; 1.7-< 2.3 servings; 2.3-< 3.1 servings; > 3.1 servings	Subjects with higher dairy products ingestion had lower BMI and WC. After adjusting for calcium intake this association became weaker. However, when protein intake was adjusted, the associations were not affected
Esteves, Rodrigues & Paulino, 2010[48]	50 ♀; ≥ 25 a ≤ 44 years old; 26.30 ± 6.20 kg/m²	–	438.7	There was no negative correlation between BMI, fat %, WC

BMI: Body mass index; WC: Waist circumference.

Table II

Characteristics of intervention studies that assessed the effect of calcium intake on anthropometric measures and body composition

Reference	*Subjects characterisics (number of participants/ gender/age/BMI*	*Study duration*	*Habitual calcium intake (mg/day)*	*Treatment*	*Results*
Shapses et al. 2004[22]	100 ♀ pre and post-menopausal ≈ 40-60 years old; ≈ 33 kg/m²	25 weeks	600-1,000	1) 500 kcal + Placebo. 2) 500 kcal + 1,000 mg of calcium (source calcium citrate malate or calcium citrate).	There was no difference in body weight and body fat between treatments.
Reid et al. 2005[20]	1,471 ♀ post-menopausal; ≈ 74 years old, ≈ 26.5 kg/m²	30 months	Placebo = 878 ± 430 Ca = 861 ± 390	1,000 mg of calcium (source calcium citrate). Placebo.	Body weight, BMI, body fat and lean mass did not differ between the groups.
Yanoski et al. 2009[27]	340 ♀♂; 38.8 years old; 33.2 ± 6.8 kg/m² (Ca) and 33.6 ± 6.8 kg/m² (placebo)	2 years	Placebo = 878 ± 430 Ca = 887 ± 350	1,500 mg (source calcium carbonate). Placebo.	Body weight, body fat, BMI, WC, hip circumference did not differ between the groups.
Faghih et al. 2011[83]	85 ♀; ≈ 38 years old; ≈ 31 kg/m²	25 weeks	Control: 512.85 ± 72.71 Ca: 532.29 ± 149.77 Milk: 484.58 ± 131.07 Soy: 509.61 ± 101.19	1) 500 kcal; 500-600 mg of calcium. 2) 500 kcal; 1,300-1,400 mg of calcium (800 mg = source calcium carbonate). 3) 500 kcal; 1,200-1,300 mg of calcium (source milk). 4) 500 kcal; 1,200-1,300 mg of calcium (source soy extract fortified with calcium).	Changes in WC were higher in groups 3 and 4. Changes in body weight and BMI wew higher in the group that ingested calcium from milk.
Zemel et al. 2004[33]	32 ♀♂; 49 ± 6 years old; 34.9 ± 4.3 kg/m²	24 weeks	500-600	1) 500 kcal; 400-500 mg of calcium, placebo. 2) 500 kcal; 1,200-1,300 mg of calcium (800 mg = source calcium carbonate). 3) 500 kcal; 1,200-1,300 mg of calcium (source dairy).	Body weight and body fat, including in the trunk region, reduced after the consumption of the diets with high calcium content. Such effects were higher in the diet in which the calcium was derived from dairy products.
Kabrnová et al. 2008[64]	67 ♀; 49.1 ± 12.1 years old; 32.2 ± 4.1 kg/m²	4 weeks	Not specified	1) 600 kcal; diet with 350 mg of calcium + placebo. 2) 600 kcal; diet with 350 mg of calcium + 500 mg of calcium (calcium carbonate). 3) 600 kcal; diet with 350 mg of calcium + 500 mg of calcium (calcium citrate + phosphate + lactate).	There were no differences between the groups in terms of anthropometric measurements and body composition. In the placebo group, there was reduction in free fat mass, tending to be significant compared to the groups treated with calcium.
Wennersberg et al. 2009[28]	76 ♀ 37 ♂; ♀♂: 56.7 ± 7/51.2 ± 8.1 years old; 30 ± 3.3 kg/m² (control) 30.1 ± 3.6 kg/m² (milk)	6 months	Control: 644 ± 252 mg Milk: 815 ± 364 mg	The participants included in the milk group were instructed to increase 3-5 servings of dairy products daily intake.	Weight, BMI, WC, body fat did not change in the course of the study. When evaluating only the people who had basal ingestion lower than 700 mg there was reduction of WC in the milk group.
Gunther et al. 2005[12]	135 ♀; 18-30 years old; 22.1 ± 3.1 kg/m² (control); 23.3 ± 3.9 kg/m² (average) 22.4 ± 2.6 kg/m² (high)	1 year	Control: 695 ± 263 Average 727 ± 269 High: 693 ± 281	1) Control: keep usual intake. 2) 1,000-1,100 mg of Ca (source dairy). 3) 1,300-1,400 mg of Ca (source dairy).	There was no differents in the group as to weight, BMI, and body composition between treatments.
Reid et al. 2010[29]	323 ♂; ≈ 57 years old; ≈ 26 kg/m²	2 years	1) 800 ± 360 mg 1) 870 ± 470 mg 1) 930 ± 510 mg	1) Placebo. 2) 600 mg of Ca (source calcium citrate) 3) 1,200 mg of Ca (source calcium citrate) divided into two daily doses	There was an increase in fat mass in the groups and reduction in the lean mass with no difference between the groups.

BMI: Body mass index; WC: Waist circumference.

also necessary to consider the way in which the supplement is administrated, that is if it is administrated in association with food or not.

Some authors attribute the stronger observed effect to other nutrients present in dairy products such as vitamin D[64] and proteins (branched chain amino acids, such as leucine).[23,37,82-88] It has been claimed that proteins could increase satiation, thermogenesis and avoid muscular mass loss.

Leucine would lead to greater fat mass loss, would stimulate the recovery of muscle protein synthesis thus reducing the loss of lean body mass.[85-88] In the culture of cells, leucine stimulated fat oxidation in muscular cells and inhibited FAS in adiposites.[82] On the other hand, in the elderly, the ingestion of 1g of protein /kg of body weight, containing 7.5 g of leucine/day did not change body composition.[91]

In general, it is suggested that a high protein intake is required to exert the effect. In a recent review study it was shown that in most studies, there is a reduction in energy intake when 30% or more of total energy intake derives from protein.[87] The comparison of the effect of the consumption of isocaloric and isoglycidic diets containing 15% and 30% of protein showed no difference in adults resting metabolic rate. However, there was a reduction in hunger sensation and energy intake, and an increase in satiety in the group that consumed the diet containing 30% of protein.[92] In contrast, in another study, obese subjects consumed diets containing 30% of protein (1,600 mg of calcium) x 15% of protein (600 mg calcium) and the same fat content (30%). There was no difference in energy intake, body weight and body composition. Only in women who consumed 1.4 g of protein/kg body weight lean body mass was preserved. Furthermore, in the group that consumed 30% of protein there was lower ingestion of fiber and higher ingestion of cholesterol. One cannot distinguish if the observed effects are related to increased intake of protein, calcium or reducing carbohydrate ingestion.[93] Similarly, in studies in which there is great change in the percentage of macronutrients, the effects can perhaps be attributed to these changes.

Besides confirming the effectiveness of increased protein intake on obesity control, future studies should assess how this type of dietary intervention effects renal function, calcium balance, cardiovascular diseases risk and other adverse effects associated with chronic high protein consumption before high protein diets are recommended for weight loss,[87,92] once there is currently no Tolerable Upper Intake Level for protein.[85]

These facts can lead to discussion about the most appropriate distribution of macronutrients to maintain healthy body weight. The current recommended distribution of macronutrients considering the total energy expenditure is: protein - 10 to 15%, carbohydrate - 45 to 65%; fat - 20 to 35%.[94] The distribution of macro nutrients tested by some authors, that is (protein: 16%, fat: 35%, carbohydrates: 49%),[33] (protein: 25,3%, fat: 28,7%, carbohydrate: 46%),[84] and (protein:18%, fat: 27%, carbohydrate: 55%)[83] differ from the current healthy diet recommendations and the ones recommended for weight loss (protein: 15%, fat: 30%, carbohydrate: 55%).[5,95-97] Therefore, the effect of increased calcium ingestion associated with the consumption of a diet presenting the recommended macronutrient distribution is not known.

The results of these intervention studies suggest that a daily intake of about 1,200-1,300 mg/day can affect body weight and body composition.[57] On the other hand, the results of the studies that assessed the association between increased fat excretion versus body composition and anthropometry it seems that the ingestion of large quantities of calcium has no effect, suggesting the existence of an upper threshold quantity capable of controlling obesity.

Effect of calcium intake on energy expenditure and substrate oxidation

The main characteristics of the studies that evaluated the effect of calcium on energy expenditure and substrate oxidation are presented in table III. Although the results of the studies indicate that the highest consumption of calcium or dairy products might increase lipid oxidation, this topic is still controversial.[34]

In the study conducted by Teegarden et al. (2008),[34] there was an increase in fat oxidation only in the group treated with supplement. The authors report that other components of dairy products might prevent the increase in fat oxidation induced by calcium. In that study,[34] the protein content was higher (16% SEV) than the recommendations.[5,94-97] The results of that study[34] contradicts the idea that protein could increase thermogenesis and lipid oxidation.[85,86,88,98] In other studies, the consumption of diets containing 20%[30] and 23%[17] of total energy intake derived from proteins did not affect energy expenditure and fat oxidation. But this aspect should be further explored because in two other studies[17,32] the consumption of a diet containing 15% of protein did not change such parameters. However, in that second study, the percentage of carbohydrate in the diet (60% of total energy intake) may have inhibited fat oxidation, since the carbohydrate is the preferred source of energy.[99] This reinforces the importance to assess how the distribution of macronutrients affects the results of such studies.

In terms of the effects of calcium intake on body weight and body composition a minimum and maximum consumption seems to be necessary for the effects to be detected. It is not known whether these assumptions can be extrapolated in terms of the effects on energy expenditure and substrate oxidation. It has been observed that there is an increase in calcium urinary excretion in participants that are used to consuming that mineral above the RDA (1,000 mg),[17,30] which start consuming a higher calcium dose.[31,32] In a study conducted by Jacobsen et al. (2005),[17] it was

Table III

Characteristics of intervention studies that evaluated the effect of calcium intake on substrate oxidation and energy metabolism

Reference	*Subjects characterisics (number of participants/ gender/age/BMI*	*Study duration*	*Habitual calcium intake (mg/day)*	*Treatment*	*Results*
Jacobsen et al. 2005[17]	2 ♂, 8 ♀; 24.2 ± 2 years old; 26.5 ± 2 kg/m²	1 week each diet	1,214 ± 264	1) 500 mg of calcium; 15% protein. 2) 1,800 mg of calcium; 15% protein. 3) 1,800 mg of calcium; 23% protein.	The treatments did not promote significant changes in energy expenditure, metabolic rate at rest and energy balance for 24 hours. Protein oxidation higher in the diet with 23% protein.
Boon et al. 2005[30]	12 ♂; 28 ± 2 (20-40 years old): 25.2 ± 0.6 kg/m²	7 days each stage	1,027 ± 82	1) Low Ca/Low Lat = 300-400 mg of Ca. 2) Alto Ca/Low Lat = 1,200-1,300 mg Ca (source calcium carbonate). 3) Alto Ca/High Lat = 1,200-1,300 mg of Ca (source diary).	Energy expenditure in total for 24 hours and at differente times (sleep, at rest, during exercise) did not differ. There was no difference between balances of substrates and in the expression of RNA of genes related to lipid metabolism.
Teegarden et al. 2009[34]	24 ♀; Control/calcium/dairy: 23.3 ± 3.2/22.4 ± 3.7/21.0 ± 2.6 years old; 28.8 ± 2.9/27.1 ± 1.59/ 27.2 ± 1.09 kg/m²	12 weeks	C = 690 ± 85 Ca = 592 ± 104 Lat = 688 ± 85	1) C = 500 mg of Ca/(-500 kcal). 2) Ca = 500 mg + 900 mg of Ca (source: calcium carbonate)/(-500 kcal). 3) Lat = 500 mg + 800 mg of Ca (source: dairy/(-500 kcal).	No differences were observed as to total energy expenditure. There was an increase in fat oxidation in the calcium group.
Bortolotti et al. 2008[31]	3 ♂, 7 ♀; 22.2 ± 1.2 years old; 28.5 ± 1.4 kg/m²	5 weeks each session	586 ± 137	1) Placebo. 2) Supplement = proteins, minerals, lactose and 800 mg of calcium (source: calcium phosphate).	No changes were observed in energy expenditures and significant changes in macronutrients oxidation. No changes were found in the turnover of glycerol and markers of lipid metabolism in fat tissue.
Sampath, Havel & King, 2008[32]	15 ♀; 29 ± 8 years old; 27.8 ± 2.7 kg/m²	12 weeks	616 ± 211	Supplementation with 1,500 mg of calcium (source calcium carbonate).	No changes were observed at the levels of glycerol and in oxidation.
Gunther et al. 2005[11]	19; Low/high calcium: 20.3 ± 2.5/19.4 ± 2.6 years old; 20.2 ± 2.4/24.0 ± 3.3 kg/m²	1 year	1) Low calcium; 643 ± 167 2) High calcium: 663 ± 242	1) Keep usual calcium ingestion. 2) Consume 1,000-1,400 mg/day meals were served with high (> 500 mg) and low (< 100 mg) of calcium on test days.	The acute increase did not affect fat oxidation after low chronic ingestion of calcium. Chronic increase of calcium ingestion increased fat oxidation.
Melanson et al. 2003[9]	21 ♂, 14 ♀; 31 ± 6 years old; 23.7 ± 2.9 kg/m²	24 hours	1,222 ± 116 (485-4,109)	The individuals could select the foods. Average ingestion = 1,046 ± 55 (477-1,768) mg/day.	Acute calcium ingestion was positively correlated with fat oxidation and inversely related to respiratory quotient. Acute calcium ingestion from dairy products was also positively associated with fat oxidation. Total calcium ingestion was a higher predictor than the ingestion of dairy products calcium. Habitual calcium ingestion was not correlated to fat oxidation.

observed an increase in urinary excretion of calcium only when the diet was high in protein content (23%). However, Farnsworth et al. (2003)[93] did not detect differences in excretion when comparing the effect of the consumption of a diet containing 30% of protein (1,600 mg calcium) versus a 15% of protein (600 mg calcium) diet. Data available in the literature are insufficient to define the minimum amount of dietary calcium required to induce a change in energy expenditure and substrate utilization.[32]

The number of human studies in which energy expenditure and substrate oxidation was assessed is small and the duration of these studies is short compared to the number of studies that anthropometry and body composition were evaluated. For example, Boon et al. (2005)[30] tested the effect of the consumption of 1,200-1,300 mg of calcium /day for a period of seven days. On the other hand, it has been suggested that acute changes in calcium ingestion can modify fat oxidation rates. However, these modifications tend revert within a relatively short period of time.[32]

Thinking about the relationship between the effects of calcium intake and study duration, Melanson et al. (2003)[9] and Gunther et al. (2005)[11] obtained different results. In the first study,[9] the authors observed that an acute increase in calcium intake leads to an increase in fat oxidation, whereas if the usual intake of calcium is already high that parameter is not affected. According to Gunther et al. (2005),[11] fat oxidation is only affected when a higher calcium ingestion occurs for longer periods of time. The duration of these two studies and the usual ingestion of the participants were quite different. In addition, both involved normal weight participants. It is not known if the response would differ in overweight people. It has been argued that in normal weight people, the increase in calcium ingestion may cause alter substrate oxidation, without, however, affecting energy expenditure. That would happen as a mechanism to maintain body weight and prevent excessive weight loss due to the increase in fat oxidation.[11]

Final considerations

The results of the studies published so far suggest that the consumption of calcium derived from supplements and dairy products can reduce the anthropometric measurements and favor the achievement of an adequate body composition. However, there is no homogeneity in the results of the observational studies probably due to the differences in the methodologies used. It appears that the benefits of calcium ingestion are only detected in individuals with low habitual consumption of the mineral, and there may be an upper threshold amount of calcium from which this effect is no longer observed. Further studies are needed to confirm this fact and to determine what these values are. It should be emphasized that higher availability supplements should be tested and the administration form must be considered. In the case of dairy products, it is necessary to isolate the effect of other nutrients also present in these foods. It should also be taken into consideration the interference of the distribution of macronutrients in the possible effects of calcium. To better understand the consequences of calcium intake on energy expenditure and substrate oxidation in addition to these factors, longer duration studies should be conducted.

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