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Original article

Influence of nutrition on somatotropic axis: Milk consumption in adult individuals with moderate-severe obesity

Luigi Barrea [a, *], Carolina Di Somma [b], Paolo Emidio Macchia [c], Andrea Falco [a], Maria Cristina Savanelli [a], Francesco Orio [d], Annamaria Colao [c], Silvia Savastano [c]

[a] I.O.S. & COLEMAN Srl, Naples, Italy
[b] IRCCS SDN, Napoli Via Gianturco 113, 80143 Naples, Italy
[c] Dipartimento di Medicina Clinica e Chirurgia, Unit of Endocrinology, Federico II University Medical School of Naples, Via Sergio Pansini 5, 80131 Naples, Italy
[d] Department of Sports Science and Wellness, "Parthenope" University of Naples, Naples, Italy

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SUMMARY

Background & aims: Nutrition is the major environmental factor that influences the risk of developing pathologies, such as obesity. Although a number of recent reviews pinpoint a protective effects of milk on body weight and obesity related co-morbidities, an inaccurate estimate of milk might contribute to hamper its beneficial effects on health outcomes. Seven-day food records provide prospective food intake data, reducing recall bias and providing extra details about specific food items. Milk intake stimulates the somatotropic axis at multiple levels by increasing both growth hormone (GH) and insulin-like growth factor-1 (IGF-1) secretion. On the other hand, obesity is associated with reduced spontaneous and stimulated GH secretion and basal IGF-1 levels. Aim of this study was to evaluate the milk consumption by using the 7-days food record in obese individuals and to investigate the association between milk intake and GH secretory status in these subjects.

Methods: Cross-sectional observational study carried out on 281 adult individuals (200 women and 81 men, aged 18–74 years) with moderate-severe obesity (BMI 35.2–69.4 kg/m^2). Baseline milk intake data were collected using a 7 day food record. Anthropometric measurements and biochemical profile were determined. The GH/IGF-1 axis was evaluated by peak GH response after GHRH + ARGININE and IGF-1 standard deviation score (SDS).

Results: The majority of individuals (72.2%) reported consuming milk; 250 mL low-fat milk was the most frequently serving of milk consumed, while no subjects reported to consume whole milk. Milk consumers *vs* no milk consumers presented the better anthropometric measurements and metabolic profile. At the bivariate proportional odds ratio model, after adjusting for BMI, age and gender, milk consumption was associated the better GH status (OR = 0.60; $p < 0.001$). Among milk consumers, subjects consuming 250 mL reduced-fat milk *vs* 250 mL low-fat milk presented the better anthropometric measurements and metabolic profile. At the bivariate proportional odds ratio model, after adjusting for BMI, age and gender, the consume of 250 mL reduced-fat milk was associated better GH status (OR = 0.54; $p = 0.003$).

Conclusions: A novel positive association between milk consumption, GH status, and metabolic profile in obese individuals was evidenced. Regardless of the pathogenetic mechanisms, this novel association might be relevant in a context where commonly obese individuals skip breakfast, and suggests the need of a growing cooperation between Nutritionists and Endocrinologists in the management of the obese patients.

Abbreviations: BMI, body mass index; GH, growth hormone; IGF-1, insulin-like growth factor 1; IGF-1 (SDS), insulin-like growth factor 1 standard deviation score; SBP, systolic blood pressure; DBP, diastolic blood pressure; PTH, parathyroid hormone; HoMA-IR, homeostasis model assessment – insulin resistance; HDL, High-density lipoprotein; LDL, low-density lipoprotein; AST, aspartate aminotransferase; ALT, Alanine transaminase; γGT, γ-glutamyltransferase; MetS, metabolic syndrome.

* Corresponding author. c/o Unit of Endocrinology, Federico II University Medical School of Naples, Via Sergio Pansini 5, 80131 Naples, Italy. Tel.: +39 081 746 3779; fax: +39 081 746 3668.

E-mail addresses: luigi.barrea@unina.it (L. Barrea), cdisomma@unina.it (C. Di Somma), pmacchia@unina.it (P.E. Macchia), falco.and@gmail.com (A. Falco), cristysav@hotmail.com (M.C. Savanelli), francescoorio@virgilio.it (F. Orio), colao@unina.it (A. Colao), sisavast@unina.it (S. Savastano).

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1. Introduction

Nutrition is the major environmental factor, directly under human control, that interacts with genetic predisposition and influences the risk of developing pathologies, such as obesity and diabetes. Milk, with cheese and yogurt, is one of the three most commonly consumed dairy products. Most countries have quantitative recommendations that usually range from 2 to 3 servings or cups of milk or yogurt or sometimes the equivalent serving of cheese [1]. In Italy it is recommended to consume *per* day 250 mL of milk [2]. A number of recent reviews pinpoint a protective effects of dairy products on health outcomes [1], body weight [3] and obesity related co-morbidities, including type 2 diabetes and cardiovascular disease [4,5]. However, the relative contribution of the nutritional components of milk in these associations still remains inconclusive. In addition, milk consumption is often targeted in obese individuals to reduce saturated fatty acids, the intake of which is commonly discouraged in current dietary guidelines [6]; moreover, eating behavior in obese individuals is often characterized *per se* by skipping breakfast [7], traditionally the main meal of the day where Italians mostly consume milk [8].

A possible source of uncertainty in the beneficial effects of milk in the vast majority of the studies might result from an inaccurate estimate of milk intake due to the use of retrospective methods of dietary assessment or from too demanding food frequency questionnaires. By contrast, 7-days food record provide prospective food intake data. In particular, 7-days food diary are recorded at the same time of consumption, reduce the recall bias and provide extra details about the types and amounts of specific food items. Recently, a prospective study using dietary data from 7-days food record reported the association between the consumption of specific dairy products and a decreased risk of type 2 diabetes [4].

Several studies have consistently shown that high milk intake exerts relevant effects on somatotropic axis, an integrated endocrine system also involved in body weight balance [9]. In particular, milk intake stimulates the somatotropic axis at multiple levels by increasing both growth hormone (GH) and insulin-like growth factor-1 (IGF-1) secretion [10–12]. On the other hand, obesity is associated with reduced spontaneous and stimulated GH secretion and basal IGF-1 levels [13]. Both central and peripheral factors might account for this condition of functional low GH status in obesity, including nutritional-driven components, insulin-glucose homeostasis, and circulating free fatty acids (FFA) [14]. Currently, no studies on the regulation of the somatotropic axis by dietary factors, mainly milk intake, were carried out using a dynamic evaluation of GH secretion and the 7-days food record in obesity.

The aims of this study are twofold. Firstly, to evaluate the intake, frequency, and type of milk consumed, derived from the 7-days food record in obese individuals. Secondly to investigate the association between milk intake and GH secretory status in these subjects.

2. Materials and methods

2.1. Subjects and methods

2.1.1. Design and setting

This is a cross-sectional observational study carried out at the Department of Clinical Medicine and Surgery of the University of Naples Federico II (Italy) from July 2013 to February 2015. The procedures used were in accordance with the guidelines of the Helsinki Declaration on human experimentation. The study was approved by the Ethics Committee of the Federico II University Medical School of Naples (n.5/14). The purpose of the protocol was clearly explained to all the participants. The study was conducted without support from the pharmaceutical industry.

2.1.2. Population study

After obtaining written informed consent, 421 adult individuals (>18 years of age), who were referred to our unit for bariatric surgery evaluation, were consecutively enrolled. Criteria for exclusion from the study were current use of medications affecting calcium homeostasis and fat metabolism, including calcium and vitamin D (8 subjects), corticosteroids (10 subjects), antacids and proton pump inhibitors (15 subjects), bile-acid sequestrants and lipase inhibitors (7 subjects). Moreover, individuals with concurrent medical illness, such as neoplastic diseases (1 subject), renal diseases (2 subjects), malabsorptive disorders (5 subjects), inflammatory bowel diseases (9 subjects) and lactose intolerance (15 subjects), were excluded. Finally, we excluded from the study subjects following a specific dietary regimen for any reason (2 vegan subjects), those reporting to eat dairy foods more than once *per* week (55 subjects), and those drinking special milks, such as goat's and soy milk, and fermented milk as kefir and yoghurt (11 subjects).

Therefore, a total of 281 participants (200 women and 81 men, aged 18–74 years) with moderate-severe obesity (Body Mass Index (BMI): 35.2–69.4 kg/m^2), remained for analysis.

2.1.3. Dietary assessment

Dietary assessment and baseline milk intake data were collected using a 7 day food record [15,16]. Milk consumption was estimated using photographs representing portion sizes and household measures. The day one of the diary nutritionists trained to standardised protocols provided participants with instructions on how to complete the diary at the health check and asked participants to recall the previous day's intake. Participants prospectively completed the remaining 6 days. The subjects returned the records to the nutritionist who asked supplemental questions, if necessary. From these records the total amount of milk consumed was estimated, being the sum of the milk taken in milk containing drinks and with breakfast cereals. According to the Italy Food Guide Pyramid [2], the reference serving size of milk is 125 mL, equal to a glass of milk. It is recommended *per* day to consume 250 mL of milk (2 reference amounts).

The milk consumption was evaluated as: 1. Consumption (yes/no); 2. Type of milk consumed (whole milk, reduced-fat milk, and low-fat milk); 3. Serving of milk consumed (small serving, 125 mL; regular serving, 250 mL and large serving, 375 mL). 4. Daily average of total milk consumed during the seven days (<250 mL/day, =250 mL/day, >250 mL/day); 5. Consumption and type of milk (250 mL reduced-fat milk daily/other servings and types of milk).

Data were stored and processed using a commercial software (Terapia Alimentare Dietosystem® DS-Medica, http://www.dsmedica.info). The data were also compared with the tables of food consumption and recommended dietary intakes of the BDA (Food Composition Database for Epidemiological Studies in Italy) Italian National Institute of Nutrition and Food Composition Database in Italy (www.inran.it).

2.1.4. Anthropometric measurements

All anthropometric measurements were taken with subjects wearing only light clothes and without shoes. In each subject, weight and height were measured to calculate the BMI [weight (kg) divided by height squared (m^2), kg/m^2]. Height was measured to the nearest 1 cm using a wall-mounted stadiometer. Body weight was determined to the nearest 50 g using a calibrated balance beam scale. Waist Circumference (WC) was measured to the closest 0.1 cm with a non-extensible tape at the natural indentation or at a

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