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Original article

Serum homocysteine and cysteine levels and changes in the lipid profile of children and adolescents over a 12-month follow-up period

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SUMMARY

Introduction: There is evidence of associations between high serum homocysteine (Hcy) and cysteine (Cys) levels and changes in the lipid profile of adults; however, little information is available with respect to these associations in the pediatric age group.
Objective: To identify the effect of high baseline serum Hcy and Cys levels, alone or in conjunction, on the lipid profile of children and adolescents over a 12-month follow-up period.
Methods: A cohort study involving 540 boys and girls of 7–15 years of age was conducted over 12 months. The outcome variables were the lipid indicators and the principal exposure variable was serum Hcy and Cys levels. A generalized estimating equation (GEE) approach was used to identify the associations of interest.
Results: Irrespective of age, sex, socioeconomic status, diet or anthropometric status, when serum Hcy levels were above the 5th quintile of distribution at baseline, HDL-cholesterol decreased by a mean of 2.91 mg/dl ($p < 0.01$), while triglyceride levels increased by a mean of 1.58 mg/dl ($p < 0.01$) over the 12-month follow-up period. In individuals with high baseline Cys levels, there was a reduction of 1.95 mg/dl ($p < 0.01$) and an increase of 1.76 mg/dl ($p < 0.01$) in mean serum HDL-cholesterol and triglyceride levels, respectively, over the 12-month period. When serum Hcy and Cys levels were both above the 5th quintile of distribution at baseline, there was a reduction of 3.65 mg/dl ($p < 0.01$) in mean HDL-cholesterol and an increase of 3.53 mg/dl ($p < 0.01$) in mean triglyceride levels in the 12 months of follow-up.
Conclusions: High baseline serum Hcy and Cys levels resulted in a reduction in mean HDL-cholesterol levels and an increase in mean triglycerides levels over the 12 months of follow-up in children and adolescents, with these alterations being greater when these two biochemical parameters were simultaneously high at baseline.

1. Introduction

Significant changes have been registered in the lipid profile of children and adolescents worldwide, with prevalence rates of dyslipidemias ranging from 3% to 40% [1–4]. In recent decades, studies have reported an association between lipid disorders and high serum homocysteine [5–7] and cysteine levels [8,9] in adults. In children and adolescents, cross-sectional and case-control studies have also found a positive association between negative changes in the lipid profile and high serum homocysteine [10,11] and cysteine levels [12].

Few studies have been conducted to evaluate the combined effect of high serum homocysteine and cysteine levels on changes in the lipid profile of children and adolescents. A cross-sectional study involving a sample of 2059 adults in China reported lower

Abbreviations: FFQ, food frequency questionnaire; HPLC, high performance liquid chromatography; HCY, homocysteine; CYS, cysteine.

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HDL-cholesterol (HDL-c) levels in the participants whose serum homocysteine and cysteine levels were simultaneously high [13]. To the best of our knowledge, no longitudinal studies have yet been conducted on abnormal Hcy and Cys levels, alone or in conjunction, in any age group.

In view of the scarcity of data on this subject, principally in the pediatric age group, this study seeks to consolidate information on these associations through the use of a robust epidemiological design. The results found here may contribute towards the prevention and control of early changes in the lipid profile. Consequently, the objective of the present study was to identify the influence of high baseline serum homocysteine and cysteine levels, alone or in conjunction, on changes in the lipid profile of children and adolescents over a 12-month follow-up period.

2. Materials and methods

2.1. Study design, population and sample size

This was a cohort study conducted over a 12-month period including 540 boys and girls of 7–15 years of age, from 10 public, urban and part-time schools. It was conducted a simple random sampling, selecting 54 students for each school from a list of elementary school children registered with the Municipal Education Department of a municipality of Bahia, Brazil, in 2006. The primary study was conduct aiming to evaluate risk factors for cardiovascular disease in children and adolescents. Baseline results are described in another publication [14].

The present sample size had a power of 95% for detecting a change of 10% in total cholesterol over 12 months of follow-up, considering mean cholesterol levels of 158.0 mg/dl (SD 30.4). For detecting a 10% change in LDL-cholesterol (LDL-c), the power was 94% considering a mean of 91.4 mg/dl (SD ± 25.9), while for HDL-c the power was 99% considering a mean of 47.5 mg/dl (SD ± 10.5). In the case of triglycerides, the study had a power of 96% for detecting a change of 10% over 12 months, taking into consideration a mean of 92.1 mg/dl (SD 10.5) [15].

2.2. Exclusion criteria

Children or adolescents in use of anticonvulsants, diuretics, thiazides and corticosteroids, or medications for diabetes mellitus, chronic renal failure, liver disease or hyperthyroidism were excluded from the study since these drugs are capable of altering serum homocysteine or cysteine levels [16]. Pregnancy, breastfeeding and any physical handicaps that would prevent an anthropometric evaluation from taking place also constituted exclusion criteria. Nevertheless, none of the children had any of these conditions.

2.3. Data collection and definition of variables

An appropriately trained team of nutritionists collected the socio-demographic, clinical and anthropometric data, as well as data regarding lifestyle and dietary intake. A laboratory technician experienced in collecting blood from children and adolescents collected all the samples.

The principal exposure variables (serum homocysteine and cysteine levels) were assessed at baseline, whereas the data referring to the outcome variables and the other co-variables of the study were measured at baseline and at 6 and 12 months of follow-up. Adopting this design for cohort studies reduces costs and guarantees the robustness of the results, since the principal exposure is only assessed at baseline and the endpoints are evaluated longitudinally [17,18].

2.4. Anthropometric data

Weight was measured using portable digital scales (Filizola, São Paulo, Brazil) and height using a stadiometer (Leicester Height Measure, SECA, Hamburg, Germany) in accordance with the definitions of Lohman, Roche and Martorell, 1988 [19]. Anthropometric status was evaluated according to body mass index (BMI)-for-age, using the World Health Organization growth reference data for individuals of 5–19 years of age [20]. For the statistical analysis, the BMI-for-Age was classified in healthy weight (<percentile 85) and excess weight (≥percentile 85).

2.5. Dietary intake

Dietary intake was evaluated using a food frequency questionnaire (FFQ) adapted from an instrument previously validated in children and adolescents in the same town [21]. The FFQ consisted of 96 food items with 8 possible answers regarding intake: daily, once a week, 2, 3, 4, 5 and 6 times a week and rarely/never.

Based on the methodology proposed by Monteiro, Riether and Burini (2004) [22], the overall dietary intake of each food item was converted into scores by multiplying the weekly frequency of intake by 4 (the number of weeks in a month) and dividing it by 30 (the number of days in a month). Thus, a mean daily intake score was obtained for each food item. Scores ranged from 1 (daily intake) to zero (rarely or never consumed), and were then classified into tertiles. After these scores were calculated, two dietary groups were constructed, based on the composition of the food items, as follows:

a) Group of food items that increase the risk of high serum homocysteine and cysteine levels: food items poor in complex B vitamins, such as highly processed grains, pasta, cookies, candies, pastry, fries, vegetable oils. For this group, the first tertile was adopted as protection category and the second and third tertile were the risk category.
b) Group of food items that protect against high serum homocysteine and cysteine levels, including food items that are sources of fiber, complex B vitamins and minerals (meats, fish, dark green vegetables, whole and enriched grain products, legumes and citrus fruits). For this group, the third tertile was adopted as protection category and the first and second tertiles were the risk category.

2.6. Demographic, socioeconomic, clinical and lifestyle-related data

These data were obtained by completing a structured questionnaire. The demographic data consisted of the child's sex and age. A socioeconomic index was calculated according to the number of rooms in the house and the number of individuals living in it, the principal form of lighting and the occupation of the head of the family. In addition, an environmental index was calculated based on data collected regarding the water supply to the home, the source of drinking water and how garbage and household waste were disposed. The answers related to these two variables were awarded scores that ranged from 0 to 4, with 0 representing the poorest conditions and 4 the best. Therefore, the socioeconomic and environmental indexes ranged from a minimum of 0 to a maximum of 16 points and were classified into tertiles. The first and second tertile was adopted as the risk category and the third tertile was the protection category.

Since maternal education is also associated with the cultural and dietary aspects of the society in which the individual lives, it was evaluated separately, rather than as a component of the socioeconomic index.

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