



## Lipid Profile and Nutrition Counseling Effects in Adolescents with Family History of Premature Coronary Artery Disease

Gislaine A. Mendes, Tania L. Martinez, Maria C. Izar, Olga M. Amancio, Neil F. Novo, Simone C. Matheus, Marcelo C. Bertolami, Francisco Antonio Helfenstein Fonseca  
*Universidade Federal de São Paulo e Instituto Dante Pazzanese de Cardiologia - São Paulo, SP - Brazil*

### OBJECTIVE

To assess lipid profile and nutritional parameters from adolescents with family history of premature coronary artery disease (CAD) and assess the effects of nutritional counseling.

### METHODS

The study included 48 adolescents of both gender and with ages ranging from 10 and 19 years old (case group, n=18; control group, n=30).

### RESULTS

Offspring of young individuals with coronary artery disease showed higher values of total cholesterol ( $189 \pm 30$  vs.  $167 \pm 26$  mg/dl,  $p < 0.01$ ), LDL-C ( $144 \pm 20$  vs.  $100 \pm 27$  mg/dl,  $p < 0.001$ ) and apoB ( $80 \pm 15$  vs.  $61 \pm 18$  mg/dl,  $p = 0.001$ ) and lower values of HDL-C ( $45 \pm 9$  vs.  $51 \pm 13$  mg/dl,  $p < 0.02$ ) than control young individuals. Differences were not found for triglycerides and apoA-I. With a dietotherapeutic counseling, we obtained a reduction in alimentary consumption of saturated fatty acids (pre:  $15.5 \pm 4.7\%$  vs. post:  $6.6 \pm 3.7\%$ ,  $p = 0.003$ ) and an improvement in lipid profile: TC ( $-8\%$ ,  $p = 0.033$ ), LDL-C ( $-18.2\%$ ,  $p = 0.001$ ), TG ( $-53\%$ ,  $p = 0.002$ ) rates in offspring of premature CAD patients who showed hyperlipidemia.

### CONCLUSION

The presence of dyslipidemia was more prevalent among offspring adolescents of premature CAD patients, but it was responsive to nutritional intervention.

### KEY WORDS

Teen health, diet, lipids, lipoproteins, apolipoproteins.

Atherosclerosis starts early, with evidences in the presence of fat streak in the aortas of offspring of mothers with hypercholesterolemia already in intrauterine life<sup>1</sup>. Its occurrence is still much influenced by the presence of risk factors for coronary artery disease (CAD)<sup>2</sup>. Cohort prospective studies carried out in children, such as those from Bogalusa<sup>2-4</sup> and from Finland<sup>5</sup>, evidenced that the presence of a certain risk factor in infancy was associated to a greater probability of its presence also in adult life. Such phenomenon was called “track” and it is observed for most risk factors. Besides, an aggregation of risk factors is observed and the exposure to those factors during infancy and adolescence are associated with the early development of atherosclerosis<sup>6-8</sup>.

Family history of premature CAD is one of the main risk factors in infancy and adolescence, and such youngsters usually show a more unfavorable risk factor profile<sup>7</sup> and that, only recently have been having more attention. In our country, some initial studies have already shown the high prevalence of dyslipidemia in young individuals with or without family history of premature CAD<sup>9-11</sup>, which is a finding that has been more and more described in different countries<sup>12,13</sup>. As opposed to adults, the experience with hypolipidemic medicines, which makes changes in lifestyle, such as nutritional counseling, of high clinical relevance<sup>14-16</sup>.

Nutritional counseling assumes, therefore, a determinant role in implementation of recommendations and it has been shown effective without causing nutritional shortage to children or adolescents<sup>16,17</sup>. Recent American guidelines for handling of children and adolescents concerning hypertension, dyslipidemia and obesity (*AHOY – Atherosclerosis, Hypertension and Obesity in the Young*)<sup>18</sup>

have guided the approach of that population and proposed algorithm, by taking risk factors into consideration, among those with family history of premature CAD, as a situation deserving investigation in offspring. Our study compared risk factors and nutritional aspects between adolescents with or without family history of premature CAD and assessed the effects from a nutritional counseling in those young dyslipidemia patients.

## METHODS

The research was approved by the Comissão de Ética em Pesquisa (Ethics Committee in Research) of Universidade Federal de São Paulo/Escola Paulista de Medicina and started after the signing of the term of free and clarified consent (TFCC) and clarifying concerning the objectives of the study, methods and needs of laboratorial exams, by one of the parents or legal responsible person for the adolescents.

Forty-eight (48) adolescents, with ages ranging from 10 to 19 years old, were studied. Eighteen (18) were offspring of premature CAD patients and 30 adolescents composed the control group, which consisted of offspring of parents whose CAD diagnosis was excluded by means of clinical history, electrocardiogram and/or exercise tests without evidences of CAD suggestive changes. The main characteristics of this population are displayed in table 1.

All youths, from both groups, who showed dyslipidemia, had nutritional counseling for a healthy alimentation. However, in order to test the hypothesis that the diet could be effective, only those with family history of premature CAD constituted intervention group. That group consisted of 12 adolescents, offspring of CAD parents

**Table 1 – Demographic characteristics of adolescents studied**

| Variables                             | FH + premature CAD (n=18) | Control (n=30) | p       |
|---------------------------------------|---------------------------|----------------|---------|
| Male sex (%) <sup>1</sup>             | 9 (50)                    | 14 (47)        | NS      |
| Age (years old) <sup>2</sup>          | 15.0 ± 2.8                | 15.3 ± 2.8     | NS      |
| BMI (kg/m <sup>2</sup> ) <sup>3</sup> | 21.5 ± 4.6                | 21.9 ± 3.5     | NS      |
| TC (mg/dl) <sup>2</sup>               | 189.5 ± 29.7              | 166.9 ± 26.4   | < 0.01  |
| LDL-c (mg/dl) <sup>2</sup>            | 144.2 ± 19.8              | 100.4 ± 26.8   | < 0.001 |
| HDL-c (mg/dl) <sup>3</sup>            | 44.5 ± 9.1                | 51.2 ± 12.9    | < 0.02  |
| TG (mg/dl) <sup>3</sup>               | 86.2 ± 46.4               | 76.0 ± 49.0    | NS      |
| TC/HDL-C <sup>3</sup>                 | 4.4 ± 1.2                 | 3.5 ± 1.2      | < 0.001 |
| LDL-C/HDL-C <sup>3</sup>              | 3.3 ± 0.8                 | 2.1 ± 0.9      | < 0.001 |
| ApoB (mg/dl) <sup>2</sup>             | 80.2 ± 15.0               | 61.4 ± 18.2    | 0.001   |
| ApoA-I (mg/dl) <sup>2</sup>           | 132.1 ± 19.2              | 135.0 ± 19.7   | NS      |
| ApoB/Apo A-I <sup>2</sup>             | 0.63 ± 0.12               | 0.47 ± 0.16    | 0.001   |
| Lp (a) (mg/dl) <sup>3</sup>           | 25.8 ± 35.9               | 40.6 ± 32.5    | < 0.01  |
| TEV (kcal/day) <sup>2</sup>           | 2,003 ± 854               | 2,138 ± 737    | NS      |
| Cholesterol (mg/day) <sup>2</sup>     | 217 ± 108                 | 275 ± 143      | NS      |
| Lipids (g/day) <sup>3</sup>           | 34.4 ± 7.9                | 36.5 ± 5.8     | NS      |

TEV- total energetic value; FH- family history; CAD - coronary artery disease; chi-square<sup>1</sup>; t-test of Student<sup>2</sup>; Mann-Whitney<sup>3</sup>

and who showed changes in their basal lipid profile. III Diretrizes Brasileiras de Dislipidemia<sup>19</sup> (3<sup>rd</sup> Brazilian Dyslipidemia Guidelines) provided the criteria used for characterization of premature CAD and family history of premature CAD.

The exclusion criterion was defined due to presence of diabetes mellitus, hypothyroidism, nephrotic syndrome, chronic renal failure, chronic hepatopathies and use of medications that may induce secondary dyslipidemia<sup>19</sup>.

Blood samples were collected to determine total cholesterol, triglycerides, HDL-C, Lp(a), apolipoproteins A-I and B after 12 to 14 hours of fasting. Analyses were carried out in an Ópera (Bayer, Germany) apparatus, through colorimetric method, and LDL-C was estimated through Friedewald equation, for values of TG < 400 mg/dl<sup>20</sup>. Apolipoproteins A-1, B and Lp(a) were dosed through nephelometry, in an automated Beckman Array System – 360 apparatus.

After obtaining body mass index (BMI) in kg/m<sup>2</sup>, adolescents were classified for the presence of obesity (BMI ≥ percentile 95) and overweight (BMI between percentiles 85 and 95)<sup>21-23</sup>.

Investigation on alimentary consumption was performed through a three-day alimentary record<sup>24</sup> and the quantification concerning total calorie consumption (in kilocalories), lipids (in grams) and cholesterol (in milligrams), was carried out with the help from Programa de Apoio à Nutrição (Nutrition Support Program) of UNIFESP<sup>25</sup>.

Adolescents with family history of premature CAD and showed dosages of TC ≥ 170 mg/dl were submitted to individual nutritional intervention (verbal and written counseling), by respecting the conditions of access to previous food and alimentary habits, since they were not harmful to health, based on guidelines<sup>19</sup>, that advise consumption, in relation to the total caloric ingestion, lower than 30% of fats (< 10% of saturated fatty acids;

up to 10% of polyunsaturated fatty acids; up to 15% of monounsaturated fatty acids), besides an ingestion of cholesterol < 300 mg/day, by keeping caloric offering for maintaining the desirable weight.

For statistical analysis, categorical variables were shown in percentages and compared through chi-square test. Numerical variables were displayed as means ± EPM. Case and control groups were compared through t-test of Student for independent groups, or Mann-Whitney test, in the case of non-parametric distribution. Wilcoxon test was used to assess nutritional intervention effect. Alpha risk was fixed in 5%.

## RESULTS

Table 2 shows demographic characteristics, laboratorial variables and alimentary intake that formed analyzed groups. Differences in distribution of patients in groups concerning sex, age and BMI values were not observed. Lipid profile comparison between groups showed higher values for TC, LDL-C, apoB and TC/HDL-C and LDL-C/HDL-C rates between adolescent offspring of premature CAD patients, who also showed lower values for HDL-C and Lp (a), but similar ones for TG and apoA-I. However, apoB/apoA-I rate showed higher values among adolescent offspring of premature CAD patients than those from control group.

Although caloric intake, cholesterol and lipid consumption had not differed between groups, excessive ingestion concerning lipid consumption was observed in 72% of adolescents from both groups.

After nutrition intervention they were submitted to, case group adolescents, with TC > 170 mg/dl, a reduction in TC, LDL-C, TG, TC/HDL-C and LDL-C/HDL-C was observed (tab. 2)

BMI, caloric intake, cholesterol and lipid intake kept similar before and after intervention, but with reduction in saturated fatty acid consumption (tab. 2).

**Table 2 – Effects of nutritional intervention on variables studied**

| Variables          | Units             | Pre-intervention | Post-intervention | p     |
|--------------------|-------------------|------------------|-------------------|-------|
| BMI                | kg/m <sup>2</sup> | 21.9 ± 5.4       | 21.6 ± 4.5        | NS    |
| TC                 | mg/dl             | 206 ± 19.5       | 190 ± 23.9        | 0.033 |
| LDL-c              | mg/dl             | 145.9 ± 16.6     | 119.4 ± 21.9      | 0.001 |
| HDL-c              | mg/dl             | 43.7 ± 10.6      | 42.4 ± 6.1        | NS    |
| TG                 | mg/dl             | 90.3 ± 36.5      | 42.4 ± 6.1        | 0.002 |
| TC/HDL-C           | -                 | 4.92 ± 1.05      | 4.56 ± 1.12       | 0.033 |
| LDL-C/HDL-C        | -                 | 3.48 ± 0.63      | 2.83 ± 0.78       | 0.004 |
| TEV                | kcal/day          | 1,968 ± 876      | 1,757 ± 498       | NS    |
| Cholesterol        | mg/day            | 232 ± 120        | 213 ± 107         | NS    |
| Lipids             | %                 | 35.2 ± 6.9       | 32.6 ± 9.4        | NS    |
| Saturated FA       | %                 | 15.5 ± 4.7       | 6.6 ± 3.7         | 0.003 |
| Polyunsaturated FA | %                 | 7.83 ± 4.9       | 4.4 ± 3.2         | NS    |
| Monounsaturated FA | %                 | 11.0 ± 5.9       | 5.5 ± 3.8         | 0.05  |

TEV- total energetic value; FA- fatty acids; Wilcoxon test

## DISCUSSION

The main contribution from this study was confirming the presence, in adolescence, of dyslipidemia associated to a family history of premature coronary artery disease. Besides, the study showed that the diet can have a relevant role in improving lipid profile found in those young individuals.

Family history of premature CAD is one of the main factors to be considered in the decision of assessing the lipid profile in a child or adolescent<sup>18</sup>. Besides, the important observational PROCAM<sup>26</sup> study, in Germany, has recently showed that the incidence of myocardial infarction per age intervals was associated to a greater difference for serum levels of LDL-C, in comparison to those without CAD, the more premature its occurrence was.

Those aspects reinforce the rationale for the lipid profile exam and other risk factors for CAD among young individuals with family history of premature CAD, once that different studies, inclusive in our milieu, showed a greater prevalence of risk factors for CAD, especially lipid changes, between direct relatives of coronary artery disease patients<sup>10-12</sup>.

Berenson et al<sup>27</sup>, in *The Bogalusa Heart Study*, observed an association of previous risk factors with presence of atherosclerotic lesions in the aortas and coronary arteries in necropsies of individuals with age ranging from 6 and 30 years old. Lesions were more prevalent in male sex individuals, both on the aortas and in coronary arteries, and they were associated with lipid variables, hypertension and BMI.

Bogalusa studies point to track phenomenon, which means, risk factors detected in infancy or adolescence tend to perpetuate in adult life, influencing a more accelerated development of atherosclerotic disease<sup>2-4</sup>.

In our country, family history of cardiovascular diseases has been associated to the presence of altered levels of total cholesterol among students<sup>10</sup>.

In another study, in addition to the high prevalence of dyslipidemia, association with other risk factors were described among offspring of premature CAD patients, which suggested that risk factor aggregation can be more prevalent among those children and adolescents<sup>11</sup>.

It is important to mention that improper alimentary habits, overweight, obesity, physical inactivity, smoking and use of oral contraceptives among girls are among other risk factors prevalent in adolescence.

Nutritional counseling can be started from two years of age<sup>16-18</sup>, meeting the energetic and vitamin needs, besides stimulating intake of fibers and discouraging ingestion of saturated fat- and cholesterol-rich foods, as part of changes in lifestyle, which also may include physical activity and weight adjustment<sup>18</sup>.

A dietary intervention study in children with increased levels of LDL-C, the *"Dietary Intervention Study in*

*Children"* (DISC)<sup>17</sup>, compared, within a period of 7 years, the effects of a dieto-therapeutic counseling on 633 children, by examining its effects on lipid profile, growth and sexual maturation. The diet showed effective, without changes in serum levels of ferritin, folate, retinol and zinc. Besides, growth and sexual maturation did not differ between groups, being regarded as a safe and healthy behavior.

The present study compared lipid profile among offspring of premature CAD patients and healthy parent offspring, besides assessing the effectiveness of nutritional intervention, carried out among dyslipidemic adolescents, offspring of premature CAD patients.

A more atherogenic lipid profile was observed among adolescents with family history of premature CAD, characterized by higher values of TC, LDL-C, apoB, and TC/HDL-C, LDL-C/HDL-C rates, and also apoB/apoA-I rate, which has been recently identified as the main CAD predictor among adults, in developing countries<sup>28</sup>. In our study, higher apoB/apoA-I rate identified, in young individuals with family history of premature CAD, a more atherogenic profile, which may have reflected the prematurity of the diseased. However, such unfavorable profile found among those adolescents was responsive to nutritional counseling, by verifying a reduction of approximately 8% in TC levels, 18% in LDL-C levels, and 53%, in TG levels, with consequent reductions of 7% and 18.5% in rates between TC/HDL-C and LDL-C/HDL-C, after eight weeks of intervention.

Our study reinforces the need for a greater attention to nutrition, as in modern society the excessive offer of industrialized foods with high caloric value and, many times, with high amount of saturated fat, cholesterol, trans fat, simple carbohydrates and salt, seems to contribute in a relevant manner towards risk factor development, such as obesity, hypertension and diabetes.

In our study, dietary ingestion over recommendations for total daily ingestion of lipids was observed in 72% of patients from both groups.

Besides the diet, excessive hours of our children in contact with television or with the computer and lower physical activity, not only their, but the lack of stimulation or example from their parents, also contribute to it.

Recently, in our milieu, Giugliano and Melo<sup>29</sup> assessed weight and height of 528 students between 6 and 10 years of age, of both sexes, observing a prevalence of overweight and obesity in 21.2% of girls and 18.8% of boys.

Concluding, our study identified a more unfavorable lipid profile among young individual offspring of parents with premature CAD. Our results reinforce the importance of atherosclerosis prevention policies in early ages, which could contribute towards a reduction in the incidence of premature cardiovascular disease.

## ACKNOWLEDGEMENTS

To Doctor Yara Juliano, for guidance on statistical analysis. The nutritionist Gislaiane A. Mendes had a scholarship from CAPES (Coordenação de Aper-

## REFERENCES

- Palinski W, Napoli C. The fetal origins of atherosclerosis: maternal hypercholesterolemia, and cholesterol-lowering or antioxidant treatment during pregnancy influence in utero programming and postnatal susceptibility to atherogenesis. *FASEB J* 2002; 16: 1348-60.
- Berenson GS, Srinivasan SR Bogalusa Heart Study Group. Cardiovascular risk factors in youth with implications for aging: the Bogalusa Heart Study. *Neurobiol Aging* 2005; 26: 303-7.
- Berenson GS. Childhood risk factors predict adult risk associated with subclinical cardiovascular disease. The Bogalusa Heart Study. *Am J Cardiol* 2002; 90: 3L-7L.
- Freedman DS, Khan LK, Serdula MK, Dietz WH, Srinivasan SR, Berenson GS. The relation of childhood BMI to adult adiposity: the Bogalusa Heart Study. *Pediatrics* 2005; 115: 22-7.
- Raitakari OT, Porkka KV, Viikari JS, Ronnema T, Akerblom HK. Clustering of risk factors for coronary heart disease in children and adolescents. The Cardiovascular Risk in Young Finns Study. *Acta Paediatr* 1994; 83: 935-40.
- Raitakari OT, Juonala M, Kahonen M, Taittonen L, Maki-Torkko N et al Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. *JAMA* 2003; 290: 2277-83.
- Bao W, Srinivasan SR, Valdez R, Greenlund KJ, Wattigney WA, Berenson GS. Longitudinal changes in cardiovascular risk from childhood to young adulthood in offspring of parents with coronary artery disease. The Bogalusa Heart Study *JAMA* .1997; 278: 1749-54.
- Paul TK, Srinivasan SR, Chen W, Bond MG, Tang R, Berenson GS et al. Impact of multiple cardiovascular risk factors on femoral artery intima-media thickness in asymptomatic young adults (the Bogalusa Heart Study). *Am J Cardiol* 2005; 95: 469-73.
- Giannini SD, Deveriacki BE, Góis JM, Diament J, Forti N, Cardoso RH et al. Prevalência de dislipidemias primárias em indivíduos com e sem história familiar de coronariopatia, tendo como referência os valores do "National Cholesterol Education Program" (NCEP). *Arq Bras Cardiol*. 1992; 58: 281-7.
- Coronelli CL, Moura EC. Hipercolesterolemia em escolares e seus fatores de risco. *Rev Saúde Pública* 2003; 37: 24-31.
- Romaldini CC, Issler H, Cardoso AL, Diament J, Forti N. Fatores de risco para aterosclerose em crianças e adolescentes com história familiar de doença arterial coronariana prematura. *J Pediatr* 2004; 80: 135-40.
- Sveger T, Flodmark CE, Nordborg K, Nilsson-Ehle P, Borgfors N. Hereditary dyslipidaemias and combined risk factors in children with a family history of premature coronary artery disease. *Arch Dis Child* 2000; 82: 292-6.
- Valente AM, Newburger JW, Lauer RM. Hyperlipidemia in children and adolescents. *Am Heart J* 2001; 142: 433-9.
- Cooperman N, Schebendach J, Arden MR, Jacobson MS. Nutrient quality of fat and cholesterol modified diets of children with hyperlipidemia. *Arch Pediatr Adolesc Med* 1995; 149: 333-5.
- Sigman-Grant M, Zimmerman S, Kris-Etherton PM. Dietary approaches for reducing fat intake of preschool-age children. *Pediatrics* 1993; 91: 955-60.
- Polonsky SM, Bellet PS, Sprecher DL. Primary hyperlipidemia in a pediatric population: classification and effect of dietary treatment. *Pediatrics* 1993; 91: 92-6.
- Obarzanek E, Kimm SYS, Barton BA, Van Horn LL, Kwiterovich Po JR, Simone-Morton DG et al. Long-term safety and efficacy of a cholesterol-lowering diet in children with elevated low-density lipoprotein cholesterol: seven-year results of the Dietary Intervention Study in Children (DISC). *Pediatrics* 2001; 107: 256-64.
- Williams CL, Hayman LL, Daniels SR, Robinson TN, Steinberger J, Paridon S et al. Cardiovascular Health in Childhood. A statement for health professionals from the Committee on Atherosclerosis Hypertension, and Obesity in the Young (AHOY) of the Council on Cardiovascular Disease in Young, American Heart Association. *Circulation* 2002; 106: 143-60.
- III Diretrizes Brasileiras sobre Dislipidemias e Diretriz de Prevenção de Aterosclerose do Departamento de Aterosclerose da Sociedade Brasileira de Cardiologia. *Arq Bras Cardiol* 2001; 77(supl): 1-48.
- Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low density lipoprotein cholesterol in plasma, without the use of the preparative ultracentrifuge. *Clin Chem* 1972; 18: 499-502.
- Must A, Dallal GE, Dietz WH. Reference data for obesity: 85<sup>th</sup> and 95<sup>th</sup> percentiles of body mass index (wt/ht<sup>2</sup>) and triceps skinfold thickness. *Am J Clin Nutr* 1991; 53: 839-46.
- Kuczmarski RJ, Ogden CL, Guo SS, Grummer-Strawn, Flegal KM, Mei Z et al. 2000 CDC Growth Charts for the United States: methods and development. *Vital Health Stat* 2002; 246: 1-190.
- Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999-2002. *JAMA* 2004; 291: 2847-50.
- Basiotis PP. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 1987; 117: 1138-46.
- Anção MS, Cuppari L, Tudisco ES, Draibe SA, Sigulen D. Sistema de apoio à decisão em nutrição – versão 2.5. São Paulo, Centro de Informática em Saúde 1995, Universidade Federal de São Paulo (UNIFESP/EPM).
- Assmann G, Cullen P, Schulte H. Simple scoring scheme for calculating the risk of acute coronary events based on the 10-year follow-up of the prospective cardiovascular Münster (PROCAM) study. *Circulation* 2002; 105: 310-5.
- Berenson GS, Wattigney WA, Tracy RE, Newman WP 3<sup>rd</sup>, Srinivasan SR, Webber LS et al. Atherosclerosis of the aorta and coronary arteries and cardiovascular risk factors in persons aged 6 to 30 years and studied at necropsy (The Bogalusa Heart Study). *Am J Cardiol* 1992; 70: 851-8.
- Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004; 364: 937-52.
- Giugliano R, Melo ALP. Diagnóstico de sobrepeso e obesidade em escolares: utilização do índice de massa corporal segundo padrão internacional. *J Pediatr* 2004; 80: 129-34.

feioamento de Pessoal de Nível Superior) during the development of this study.

No potential conflict of interest relevant to this article was reported.