



Mini Review

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Dyslipidemias in Children and Adolescents

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To Cite This Article: Anita L R Saldanha, André Luis Valera G, Ana Paula Pantoja M, Milena de Sousa V, Giulia Mitsuko Schimit H. Dyslipidemias in Children and Adolescents. *Am J Biomed Sci & Res.* 2023 18(4) AJBSR.MS.ID.002495, DOI: [10.34297/AJBSR.2023.18.002495](https://doi.org/10.34297/AJBSR.2023.18.002495)

Received: 📅 March 29, 2023; Published: 📅 April 21, 2023

Abstract

The prevalence of dyslipidemia in children and adolescents varies worldwide between 2.9 and 33%, adopted as a criterion the level of total cholesterol higher than 200 mg/dL. In Brazil, the prevalence is between 28 and 40% of children and adolescents, when the criterion adopted is serum total cholesterol greater than 170 mg/dL. After 10 years of age, it is already possible to perform tests to trace the lipid profile, because it is easier to keep the child fasting and the rates presented are close to those that will be maintained during adolescence and adulthood. In summary, every child should be screened for dyslipidemias at 10 years of age. For younger children, between 2 and 10 years of age, screening is indicated if: parents, grandparents, siblings and first cousins have dyslipidemia, mainly severe or manifestation of premature atherosclerosis (total cholesterol 300 or triglycerides 400 mg/dL); clinical dyslipidemia (positive history of acute pancreatitis, eruptive xanthomas, eyelid corneal arch, ankle xanthomas, dorsal face of the hands and knees); have other risk factors; there is exposure to other diseases, such as hypothyroidism, nephrotic syndrome, systemic lupus erythematosus, diabetes mellitus, immunodeficiency, etc.; contraceptives, immunosuppressants, corticosteroids, antiretrovirals and other drugs that may induce cholesterol elevation and unknown family history are used.

Keywords: Cholesterol, Triglycerides, Children, Adolescents, Coronary Heart Disease Risk

Abbreviations: ACD: Atherosclerotic Disease; HDL-c: High Density Lipoprotein Cholesterol; LDL-c: Low Density Lipoprotein Cholesterol; NCEP: National Cholesterol Education Program; TC: Total Cholesterol; TG: Triglycerides

Introduction

There is much evidence that the atherosclerotic process begins to develop in childhood [1-6]. Autopsy studies in children demonstrate a strong positive association between pre-death Low Density Lipoprotein Cholesterol (LDL-c) levels and the presence of fatty stretch marks at the aortic level [2]. Although there are controversies, studies focused on the segment of cholesterol levels from childhood to adulthood indicate that children, located at the upper end of the cholesterol distribution curve, have a 40 to 50% chance of remaining hypercholesterolemic 15 to 20 years later [7-8]. This percentage, in addition to genetic influences, is directly linked to the lifestyle adopted by the child and his family [9]. In

addition, in countries where morbidity and mortality rates due to cardiovascular disease are high, both adults and children have cholesterol levels higher than those recommended by the consensus on dyslipidemia [10]. According to the National Cholesterol Education Program (NCEP) [10] and the latest Brazilian Consensus on Hyperdyslipidemia [11], the systematic determination of the lipid profile in childhood is not recommended, and should be performed only in special situations:

1. Grandparents, parents, siblings, uncles and first cousins with presenting atherosclerotic disease (ACD) (ACD and/or cerebrovascular and/or peripheral disease) before the age of 55 for males, and 65 years for females.



2. Close relatives with total cholesterol (TC) > 300 mg/dL or triglycerides (TG) ≥ 400 mg/dL.

3. Presence of acute pancreatitis, xanthomatosis, obesity, or other risk factors for ACD.

At birth, the measurements of TC, LDL-c and High-Density Lipoprotein Cholesterol (HDL-c) are 70, 30 and 35 mg/dL respectively. With the introduction of a higher fat content in the diet, these values tend to increase rapidly. It is recommended to evaluate the lipid profile from the second year of life, because it is around this age that the cholesterol level that should be maintained throughout the first decade is reached [12]. Puberty, due to fluctuations in lipid levels, due to hormonal changes, may offer some degree of difficulty in evaluating the results of lipid profile dosage [13]. It is extremely important that the laboratory results obtained, especially when abnormal, are repeated. A diagnosis of dyslipidemia can generate

a high degree of anxiety. Studies have revealed that a positive laboratory report for dyslipidemia has long-term psychological effects, both in children and in their families, even when it is later reported to be a false positive case [14,15].

We remind you that the isolated dosage of TC, as a way of screening dyslipidemic children, is subject to failures. Children with elevated LDL-c level and decreased HDL-c may have normal TC levels and go unnoticed at screening. In addition, children with elevated TG levels would not be screened. We recall that the most common changes in the lipid profile of obese children are: decrease in HDL-c and increase in TG.

(Table 1) illustrates the reference values for the lipid profile for children and adolescents accepted by the most recent Brazilian Consensus on Hyperdyslipidemia, according to Kwiterovich's recommendations.

Table 1: Reference values of total cholesterol, LDL-c, HDL-c and triglycerides between 2 and 19 years of age.

Lipids	Age (years)	Values (mg/dL)		
		Desirable	Neighbouring	Increased
Total cholesterol		< 170	170 - 199	≥ 200
LDL-c		<110	110 - 129	≥ 130
HDL-c	< 10	≥ 40	-	-
	10 - 19	≥ 35	-	-
Triglycerides	< 10	≤ 100	-	> 100
	10 - 19	≤ 130	-	> 130

Treatment Itself

Once the normal levels and consequently the goals to be achieved are known, we will begin to address the stages of treatment.

Lifestyle Changes

Diet

Diet is the cornerstone of the treatment of dyslipidemias in childhood. We must remember that nutritional errors are responsible for most of the changes in the lipid profile found in children and adolescents [11,16,17]. The introduction of nutritional modifications in childhood is related to greater adherence, since eating habits and patterns are in formation [10,16]. However, during the elaboration of the diet and the orientation given to the family, some care should be taken.

a. Nutritional guidance should always be individualized. The calculation of daily caloric intake aims to keep the child at an adequate weight and ensure their growth and development. Extremely restrictive diets have deleterious effects [18].

b. Nutritional adequacy must be achieved through a wide variety of foods. Food monotony can lead to unwanted transgressions.

c. The guidelines given to the child should be incorporated by the family. This measure, in addition to being vital for adherence to treatment, has a positive psychological effect: the child does not see himself sick, but rather acquiring new eating habits like the other members of his family.

d. When prescribing the diet, the professional should prove himself safe. Some parents, alarmed by the report of dyslipidemia, tend to exceed the guidelines given [19].

According to the NCEP, dietary therapy is divided into two phases [10]. The phase 1 diet is prescribed when LDL-c levels are 130 mg/dL. If lipid levels have not normalized, after adequate adherence to the guidelines given for at least 3 months, a more restricted diet is prescribed.

Physical Activity

When performed on a regular basis, it promotes the reduction of TC and an increase in HDL-c levels. In addition, it contributes to the acquisition/maintenance of ideal weight [13].

Other Lifestyle Modifications

Smoking should be discouraged. Since its effect is dose dependent, it is clear that the magnitude of the risk it provides is

exacerbated when the habit of smoking begins in childhood. In the Pathobiological Determinants of Atherosclerosis in Youth Program (PDAY) it was demonstrated that smoking (assessed through the level of thiocyanate in serum) is able to promote atherogenic process in adolescents up to 15 years old [20]. Many authors consider obesity to be an independent risk for ACD [21]. This condition is associated with lipid changes, which usually normalize with weight loss. In addition, the presence of obesity in childhood has a predictive value for its maintenance in adulthood [22], so it should be treated as early and as possible.

Contraceptive use is associated with changes in lipid profile. As the use of this type of medication is a reality among our adolescents, guidance should be given regarding the choice of the pill. Ideally, one should opt for one that has low estrogen and progestogen dosages, and that the progestogen in question does not contain androgenic activity.

Drug Therapy

When lifestyle modifications are not sufficient to reverse dyslipidemia, then the use of lipid-lowering drugs is associated with the therapeutic plan. According to the recommendations of the NCEP, it is only recommended in children over 10 years of age and, in general, should only be introduced if, after a period of 6 months to 1 year of adherence to lifestyle modifications, there is no normalization of the lipid profile [10]. That is, when after the period described, cholesterol levels remain ≥ 190 mg/dL or > 160 mg/dL in children with a family history of premature cardiovascular disease and in those with two or more risk factors for cardiovascular disease.

Bile acid scavengers (cholestyramine and colestipol) make up the most accepted group of drugs for pediatric use and the only ones approved by the NCEP. The light questran (cholestyramine) is the only representative of this group of commercially available drugs in Brazil. These medications are not absorbed and exert their action at the intestinal level. By binding to bile acids in the gut, they reduce their enterohepatic circulation, leading to an increase in LDL-c receptors in the liver [23]. Side effects are less prominent in children than in adults. Intestinal constipation, the most common of them, can be minimized by introducing fiber into the diet. Because they are related to the decrease in the absorption of fat-soluble vitamins (A, D, E) and folate, in addition to concomitantly administered medications, it is suggested that an interval of at least 2 and a half hours be maintained between the use of bile acid sequestrants and meals/use of other drugs [23]. In some cases, folic acid supplementation 5 mg/day may be necessary.

Dosage calculations are based on LDL-c levels and not on children's weight. The suggested starting dose is 4 g/day. The usual

maximum dose is 16 g/day [23]. Nicotinic acid represents another alternative for the treatment of hypercholesterolemic children. However, it should only be prescribed by specialists [10]. In general, its use is made in association with the sequestrant of bile acid, when the same, alone, is not able to reduce LDL-c levels properly. The side effects arising from its use require prior clarification to the patient and his family. The vast majority of patients present with skin reactions (flushing and heat) after its administration. Previous use of aspirin 30 minutes before can minimize these effects [24-26] and its administration should precede that of nicotinic acid about 10 days.

Omega-3 fatty acid should be seen more as a dietary supplement than as a drug itself. Its use is related to the reduction of Very Low-Density Lipoprotein Cholesterol (VLDL-c) and TG levels. However, its action on LDL and HDL-c is controversial [27]. Medications, such as Vastatins, due to the small current experience, can be used in cases of severe familial hypercholesterolemia (TC > 300 mg/dL and/or manifest ACD, in which the use of resins was unsatisfactory) [10].

Conclusion

The evaluation and treatment of dyslipidemias in childhood and adolescence should not be neglected. Early intervention is able to prevent future atherosclerotic manifestations. In addition to the individual approach to dyslipidemia, discussed throughout this chapter, we would like to focus on the importance of the population approach. The adoption of healthy lifestyle habits such as a balanced diet, without excess saturated fat, regular physical activity, maintenance of ideal weight and combating smoking, should be adopted by the general population. Obviously, this type of approach requires the support of groups and entities that can collaborate with the implementation of the proposed measures: health professionals, schools, government agencies, food industries and the media.

Acknowledgments

None.

Conflicts of interest

No conflict of interest.

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