DYSLIPIDAEMIAS IN CHILDREN

Zaburzenia lipidowe u dzieci

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Abstract

Lipid disorders (dyslipidemias) in children have so far been associated with genetically determined lipid disorders (such as familial hypercholesterolemia). Due to unfavorable lifestyle changes in recent years, in addition to congenital forms of dyslipidemia, acquired, environmentally determined lipid disorders are increasingly being found in children, which carries the risk of developing atherosclerosis and future cardiovascular incidents. In 2021, Polish recommendations for diagnosing and treating dyslipidemia were published, for the first time including the pediatric population. The article discusses lipid metabolism in humans and the norms of lipid indices in developmental age. In addition, the most common genetically determined dyslipidemias are presented, as well as forms secondary to kidney disease and diabetes. In addition, the article discusses treatment options for lipid disorders in developmental age. All children with dyslipidemia require non-pharmacological management. The indications for implementing pharmacotherapy, the most commonly used drugs, dosage, and possible complications are also discussed. The use of statins in children is discussed in detail.

Streszczenie

Zaburzenia lipidowe (dyslipidemie) u dzieci były do tej pory kojarzone z uwarunkowaniami genetycznymi (np. rodzinną hipercholesterolemią). W ostatnich latach, ze względu na niekorzystne zmiany trybu życia, poza wrodzonymi postaciami dyslipidemii coraz częściej stwierdza się już u dzieci nabyte, uwarunkowane środowiskowo zaburzenia lipidowe, co niesie za sobą ryzyko rozwoju miażdżycy, a w przyszłości – wystąpienia incydentów sercowo-naczyniowych. W roku 2021 ukazały się polskie rekomendacje dotyczące diagnostyki i leczenia dyslipidemii, w których po raz pierwszy tak szeroko omówiono także populację dziecięcą. W artykule przedstawiono metabolizm lipidów i normy wskaźników lipidowych w wieku rozwojowym. Ponadto opisano najczęstsze uwarunkowane genetycznie dyslipidemie, a także postacie wtórne do chorób nerek i cukrzycy. Omówiono też sposoby leczenia zaburzeń lipidowych w wieku rozwojowym. Wszystkie dzieci z dyslipidemią wymagają postępowania niefarmakologicznego. Przedstawiono wskazania do wdrożenia farmakoterapii, najczęściej stosowane leki, dawkowanie i możliwe powikłania. Szczegółowo omówiono zasady stosowania statyn u dzieci.

Keywords: children; lipids; statins; lipid disorders; non-pharmacological treatment

Słowa kluczowe: dzieci; lipidy; statyny; zaburzenia lipidowe; postępowanie niefarmakologiczne

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Introduction

The problem of lipid disorders in the paediatric population usually arises in the context of inherited dyslipidaemias and the increasing prevalence of obesity among children and adolescents. Due to the underestimation of the problem in this age group and the fact that a large proportion of lipid-lowering agents have not been approved for paediatric patients, paediatricians have long faced the lack of clear guidelines for the management of lipid disorders in children. In recent years, the problem of dyslipidaemia has been increasingly raised by researchers, redefining the magnitude and severity of its consequences, as well as seeking the optimal therapeutic pathways for both adult and paediatric patients. This paper discusses lipid disorders in the paediatric population and summarises the current knowledge and guidelines in this field.

Characteristics of lipids

Lipids (fats) are a heterogeneous group of chemical compounds sharing two properties, i.e. insolubility in water and solubility in non-polar solvents. Fats play many important roles in the body. They are the most calorie-dense food component, providing about 9 kcal in 1 g (compared to 4 kcal in 1 g for protein or carbohydrates). They are a solvent for vitamins (mainly A, D, E, K). Lipids also act as a thermal insulator, making up the subcutaneous fat tissue and surrounding internal organs, as well as an electrical insulator, as the main component of the myelin sheath. Fats are also an essential component of the cell membrane and enable the transport of other lipids in the plasma. Furthermore, lipids are substrates in the synthesis of other biologically important substances, such as steroid hormones [1]. All these functions require both endogenous and exogenous lipid supply. Acetyl-coenzyme A (acetyl-CoA), which is obtained from carbohydrates and can be converted to free fatty acids through liponeogenesis after excess energy intake with food, is the main endogenous source of lipids. Liponeogenesis and lipogenesis, i.e. conversion of free fatty acids into triglycerides, are stimulated under physiological conditions by, among other things, hyperinsulinemia. The reverse process of extracting energy from free fatty acids takes place through □-oxidation in situations of energy deficiency, for example, under fasting conditions or after stress-induced catecholamine release. Animal or plant triglycerides, sterols and membrane phospholipids, ingested with food and broken down to bioavailable forms by enzymes (salivary and gastric lipase, bile, pancreatic lipase, phospholipase, carboxyl esterase, intestinal lipase and alkaline phosphatase) represent external sources. Short- to medium-chain fatty acids (up to 12 carbon atoms) and glycerol are absorbed in the duodenum and enter the liver via the hepatic vein, while long-chain fatty acids, cholesterol, monoglycerides, phospholipids and glycerol, broken down in the distal small bowel, reach the enterocytes, where two important processes take place, i.e., the resynthesis of triglycerides from free fatty acids and glycerol, and the esterification of cholesterol by acyl-coenzyme A (CoA):cholesterol acyltransferases (ACATs). Triglycerides additionally require the attachment of apolipoprotein (apo) B-48 molecules, followed by apoA-I and apoC-II, forming prechylo- and chylomicrons, respectively. This results in the final assembly of lipids for transport to the liver, where they can undergo further transformation, or to target tissues, where they are metabolised. Triglycerides cannot freely pass from the plasma directly into tissues, but must be broken down by lipoprotein lipase (LPL), which allows their trans-membrane transport. After reaching the target site, the released fatty acids can be used as energy sources or substrates for the synthesis of new triglycerides, deposited in the cytosol, or substrates for cell membrane synthesis [2].

Plasma lipid transport

Cholesterol esters (36%), phospholipids (30%), triglycerides (16%), cholesterol (14%) and non-esterified free fatty acids (4%) are the main forms of lipids found in the plasma. Of these, only the latter are characterised by polarity and, as such, can be transported when bound to albumin. In order for the remaining groups, i.e. non-polar triglycerides and cholesterol esters, as well as amphipathic (i.e. both polar and nonpolar) phospholipid and cholesterol molecules, to be transported in the plasma, they require the attachment of appropriate proteins or, additionally, prior aggregation with each other, i.e. non-polar molecules with amphipathic ones, to form water-soluble lipoprotein molecules. This process enables normal lipid metabolism, in which fats absorbed in enterocytes or synthesised in the liver can, in the form of chylomicrons and very-low-density lipoproteins (VLDL), respectively, reach the appropriate tissues. The extent to which lipoproteins participate in the reverse process, i.e. the "recovery" of lipids stored in adipose tissue, is much more limited, since it is mainly the transport of free fatty acids (bound to albumin), but they play a key role in the transport of cholesterol. Impaired lipoprotein metabolism leads to hypolipoproteinemias or hyperlipoproteinemias, which will be discussed in more detail later in the paper [3]. Lipoproteins differ in their density, depending the ratio of protein to lipid content in the molecule, while the type of these proteins (apolipoproteins) determines the function of a given lipoprotein group. Four classes of the most functionally and diagnostically important lipoproteins may be distinguished: ultra-low-density lipoproteins (ULDL), also known as chylomicrons, derived from intestinal absorption of triglycerides and other lipids; very-low-density lipoproteins (VLDL), formed in the liver to carry triglycerides; low-density lipoproteins (LDL), which are the primary carriers of cholesterol in peripheral tissues; and high-density lipoproteins (HDL), responsible for reverse cholesterol transport (from peripheral tissues to the liver) and involved in the metabolism of VLDL and chylomicrons [2, 4]. These apolipoproteins have many functions in addition to being a component of lipoproteins. They serve as cofactors for enzymes, such as apoC-II for lipoprotein lipase or apoA-1 for lecithin-cholesterol acyltransferase (LCAT), i.e. functional plasma equivalent of intracellular ACAT; they can be enzyme inhibitors, such as apoA-II and apoC-III for LPL, apoC-I for cholesteryl ester transfer protein (CETP); and are ligands for lipoprotein receptors in tissues, such as apoB-100 and apoE for the LDL receptor (LDL-R), apoE for the LDL receptor-related protein (LRP), and apoA-I for the HDL receptor (HDL-R) [5].

Table 1. Reference lipid parameters in children according to [6] in our own modification

	Range of a given fraction [mg/dL]		
	Normal	Borderline	High/Low
Total cholesterol	<170	170–199	≥200
LDL	<110	110–129	≥130
Non-LDL	<120	120–144	≥145
Triglycerides			
0–9 years	<75	75–99	≥100
10–19 years	<90	90–129	≥130
HDL	>45	40–45	<40
Apolipoprotein B	<90	90–109	≥110
Apolipoprotein A-1	>120	115–120	<115

HDL – high density lipoproteins; LDL – low density lipoproteins

Dyslipidaemias in children

Dyslipidaemia is a general medical term used to describe abnormal blood lipid levels. It includes abnormalities related not only to cholesterol, but also to triglycerides and other lipids. Three ranges for different lipid fractions, i.e., normal, borderline and too high/too low, which are an indicator of the type of dyslipidaemia, have been distinguished in children [6]. Reference values proposed in American guidelines are summarised in table 1.

Dyslipidaemia is classified as secondary (caused by other diseases or conditions) or primary (caused by genetic or environmental factors). There are two main categories of hereditary dyslipidaemias: hyperlipidaemias and hypolipoproteinemias.

To date, the greatest emphasis in the diagnosis of lipid disorders in children has been placed on patients presenting with various forms of familial hypercholesterolemia (FH). It is one of the most common hereditary lipid disorders, characterised by elevated LDL cholesterol levels. The disorder is caused by reduced production of LDL-R due to mutations in genes responsible for cholesterol metabolism, such as *LDL-R* or *PCSK9*, which encodes proprotein convertase subtilisin/kexin type 9 (a protein that regulates cholesterol levels by controlling the amount of LDL-R on the surface of hepatocytes). Children with FH are characterised by elevated LDL levels from birth and, if left untreated, they may be at risk for earlier cardiovascular incidents, which significantly worsens their quality of life and reduces their life expectancy. For this reason, methods for early diagnosis and treatment of FH in children, such as screening programmes, have long been known [7, 8]. However, although the best known and described, FH is not the most common type of hereditary hyperlipidaemia. Other disorders include familial combined hyperlipidaemia (FCH), familial dysbetalipoproteinemia and familial hypertriglyceridemia. The types and subtypes of hereditary hyperlipidaemias are summarised in table 2.

The second group of hereditary dyslipidaemias includes the aforementioned hypolipoproteinemias, which are disorders characterised by a decrease in one or more lipoprotein fractions. Most of them are rare disorders, and their symptoms are rather due to the deficiency of fat-soluble vitamins; for example, in chylomicronemia or abetalipoproteinemia characterised by an impaired transport of chylomicrons from enterocytes to the liver [9]. On the other hand, this category also includes familial deficiency of the above mentioned LCAT, a disorder with high mortality rates due to cholesterol deposition in tissues, including the kidneys, leading to their failure. This is due to the complete or partial absence of LCAT, which prevents efficient esterification of cholesterol and its removal from tissues by HDL [10]. Apolipoprotein B deficiency, which is categorised as a hypolipoproteinemia simply because apolipoprotein B is essential for the synthesis and stabilisation of lipoproteins, including LDL, and therefore its deficiency can impair their function, although the disorder itself progresses with elevated plasma LDL levels, its clinical manifestations are rather similar to those of hyperlipidaemia and it is treated in a similar manner, is an interesting example of another disorder in this group of dyslipidaemias. Selected hypolipoproteinemias are presented in table 3.

Until recently, mainly hereditary forms have been associated with the paediatric population due to strongly expressed symptoms often occurring in childhood, as well as serious complications, such as myocardial infarction or stroke, developing at a very young age. In recent years, however, attention has been drawn to the growing prevalence of primary dyslipidaemia, which is due to poor lifestyle rather than genetic factors, among children. Lipid metabolism disorders co-occur with excess body weight, which in turn results from poor physical activity and excess intake of calories, which cannot be utilised even despite the increased demand during development. The problem seems to be growing, with dyslipidaemia diagnosed in one in five children in some epidemiological studies [11, 12].

There are also secondary dyslipidaemias, which arise in the course of other disorders. Diabetes mellitus, in which hyperglycaemia occurs by various mechanisms, leading to increased triglyceride production, is an example. Diabetic patients may also present with decreased LPL activity, which inhibits triglyceride removal from the blood, as well as insulin resistance, increasing hepatic fatty acid synthesis, which results in hypertriglyceridemia [13]. Patients with diabetic kidney disease or other conditions causing renal damage may develop chronic kidney disease (CKD), which can also lead to dyslipidaemia. Loss

Table 2. Hereditary hyperlipidaemias

Type		Full name	Impairment	Elevated fraction	Primary symptoms	Treatment	Symptom onset
I	a	Familial hyperchylomicronaemia/ Buerger-Gruetz syndrome	↓ LPL	chylomicrons	AP, *lipemia retinalis*, eruptive xanthomas, hepatosplenomegaly	Diet	Childhood (abdominal colic and eruptive xanthelasma)
	b	Familial apolipoprotein C-II deficiency	Abnormal apoC2				
	c	–	Plasma LPL inhibitor				
II	a	Familial hypercholesterolemia	↓ LDL-R	LDL	Xanthelasma/ flat xanthelasma, *arcus senilis*, tendon xanthelasma	Ion exchange resins, statins, niacin	From birth
	b	Familial combined hyperlipidaemia	↓ LDL-R ↑ apoB	LDL VLDL	–	Statins, niacin, fibrates	Childhood to adulthood
III		Familial dysbetalipoproteinemia	Impaired apoE2 synthesis	IDL	Nodular xanthelasma, palmar xanthelasma	Fibrates, statins	Typically 30–60 years of age
IV		Familial hypertriglyceridemia	↑ production VLDL ↓ elimination VLDL	VLDL	AP (with high TG levels)	Fibrates, niacin, statins	Adolescence
V		–	↑ production VLDL ↓ production LPL	VLDL chylomicrons	–	Niacin, fibrates	Childhood to adulthood

apo – apolipoprotein; IDL – intermediate-density lipoproteins; LDL – low-density lipoproteins; LDL-R –LDL receptor; LPL – lipoprotein lipase; HDL – high-density lipoproteins; AP – acute pancreatitis; VLDL – very-low-density lipoproteins

Table 3. Hereditary hypolipoproteinemias

Disorder	Mechanism	Fraction	Manifestations	Treatment
Familial lecithin cholesterol acyltransferase (LCAT) deficiency	↓ LCAT	↓ HDL ↑ LDL ↑ VLDL ↑ TG	Corneal opacity, renal failure, hepatic failure, anaemia, premature atherosclerosis (rare)	Diet, cornea transplant, dialysis
Tangier disease	*ABCA1 mutation*	↓ HDL ↑ TG	Hepatosplenomegaly, peripheral neuropathies, corneal opacification, orange discoloured tonsils	Diet, niacin, gemfibrozil
Chylomicronaemia syndrome	*SAR1B mutation*	↓ LDL	Abdominal pain, diarrhoea, fatty stools, hepatomegaly, cardiomyopathy	Diet, vitamin supplementation
Abetalipoproteinemia	↓ apoB-48 ↓ apoB-100	↓ TG ↓ LDL ↓ VLDL ↓ chylomicrons	Steatorrhea, vitamin A, D, E, K deficiency, acanthocytosis, polyneuropathy, retinitis pigmentosa	Diet, vitamin supplementation
Apolipoprotein B deficiency	↓ apoB-100	↑ LDL	Xanthelasma/flat xanthelasma, *arcus senilis*, tendon xanthelasma	Niacin, statin, ezetimibe

apo – apolipoprotein; LCAT – lecithin-cholesterol acyltransferase; LDL – low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; VLDL – very-low-density lipoproteins

of filtration function, which prevents the kidneys from efficiently removing VLDL and chylomicrons, such as through reduced clearance and accumulation of apoC-III in the blood, is the main cause of dyslipidaemia in CKD and leads to inhibition of triglyceride breakdown by LPL in plasma [14]. Another reason is the reduced LCAT activity in CKD, especially in end-stage renal failure [15], which leads to decreased HDL, as in hereditary deficiency of this enzyme. It is these two fractions, namely HDL and triglycerides, that are found at abnormal levels in CKD patients, while the LDL fraction generally remains within normal limits. Nephrotic syndrome, which is a disorder of the glomerular filtration barrier, is another nephrological condition typical of the developmental age. This disorder results in the loss of albumin in the urine and a compensatory overproduction of VLDL and LDL, although this view is questioned due to a lack of conclusive evidence from experimental studies [16]. In addition to albumin,

apolipoproteins, such as apoA-I and apo-II, which make up HDL particles, are also lost, which may reduce blood levels of this lipid fraction [17]. Nephrotic syndrome may be also associated with increased production of PCSK9, which increases LDL fraction [18].

Furthermore, dyslipidaemia may be induced by medications, such as non-selective beta-blockers, thiazide diuretics, mammalian target of rapamycin (mTOR) pathway inhibitors and neuroleptics, used in children [19].

The importance of dyslipidaemia

Atherosclerosis is the primary condition associated with elevated plasma LDL. Although the disorder mainly affects adults, especially those with multimorbidity, it is increasingly common in children, primarily due to the growing problem of poor nutrition and lack of physical activity, which, in addition to excess body weight, can also lead to hypercholesterolemia.

Atherosclerosis begins when the inner layer (endothelium) of the blood vessel is damaged. This can be caused by various factors, such as cigarette smoking, hypertension, diabetes or hyperlipidaemia.

Damaged endothelium secretes chemical factors such as adhesion molecules and cytokines that attract leukocytes to the site of damage. LDL can then pass through the damaged endothelium into the tunica media, where it is oxidized by free radicals, and thereby modified and transformed into the so-called damaged LDL. Such LDL particles are more likely to adhere to endothelial cells and monocytes, which are also attracted to the damaged tissue. Monocytes transform into macrophages, which take up the damaged LDL, but being unable to digest it, transform into foam cells, which accumulate and form an increasingly thick layer of atherosclerotic plaque. A growing atherosclerotic plaque narrows the lumen and increases its stiffness, which can eventually lead to serious hemodynamic complications, such as myocardial infarction or stroke [20, 21].

Hypertriglyceridemia, which often leads to acute pancreatitis, is another disorder that may develop in the course of dyslipidaemia. This occurs due to an excess of free fatty acids (released from triglycerides), which exceed the ability of plasma albumin to bind them and, after combining with calcium, may cause fat embolism in pancreatic blood vessels. This in turn leads to vascular damage, inflammation and, consequently, acute pancreatitis (AP) followed by many complications, mainly diabetes, but also infections and multiple organ dysfunction [22].

Treatment of dyslipidaemia in children

The 2021 guidelines for the diagnosis and treatment of lipid disorders, developed by many Polish scientific societies dealing with this issue, provided paediatricians with clear recommendations for the management of children with dyslipidaemia in their daily clinical practice [23]. This is the first comprehensive study in a relatively large group of patients, as until now familial hypercholesterolemia was the only lipid disorder with definite diagnostic and therapeutic recommendations [24].

Non-pharmacological treatment

All >2 year-olds with LDL cholesterol levels >100 mg/dL and/or increased triglycerides, defined as ≥100 mg/dL in children <10 years and ≥130 mg/dL in those 10–19 years of age, require education on the causes and consequences of dyslipidaemia, risk factors for cardiovascular disease, as well as the principles and importance of therapy. This should apply to both the patient and all family members. Lifestyle recommendations are similar to those for adults and include proper diet, increased physical activity and, consequently, normalisation of body weight. When used effectively, these measures do not cause major LDL reduction, but significantly reduce triglycerides and increase HDL [23].

Diet

Patients with increased LDL levels are recommended to limit total fat-derived energy intake to 30%, with saturated fats accounting for less than 7% and being replaced by unsaturated fats, and with recommended daily cholesterol intake < 200 mg. Furthermore, efforts should be made to increase the daily intake of dietary fibre to about 10 g at 5 years, 15 g at 10 years, and 20 g at 15 years, as well as to increase the proportion of marine fish (at least once or twice a week), vegetables, fruits, nuts and seeds, as well as plant sterols and stanols in the diet (to about 2 g per day). Patients with increased triglycerides are recommended to reduce the proportion of simple sugars in their diet in favour of fibre and complex sugars, as well as normalise their body weight. It is also advisable to limit food thermal processing techniques to grilling and water or steam cooking [25].

Physical activity

In children <2 years, the therapeutic goal should be to completely or partially reduce the screen time. For children >2 years of age, this time should be a maximum of 2 hours per day. Additionally, the recommended daily physical activity in this age range should be at least 90 minutes [26].

Stimulants

Underage patients who admit to alcohol and cigarette use should, like adults, be strongly advised to discontinue these stimulants. Alcohol cessation has a proven beneficial effect on triglyceride reduction [27], while discontinuing nicotine raises HDL levels [28].

Pharmacological treatment

If the aforementioned non-pharmacological recommendations do not bring the expected improvement after 6 months, pharmacotherapy should be initiated as part of primary prevention of cardiovascular disease (CVD). For this purpose, lipid testing should be performed in duplicate over a period of 2 weeks to 3 months, on an empty stomach. Also, risk factors for CVD should be assessed. If hypertriglyceridemia is diagnosed, the child should be referred to a specialist clinic for a detailed diagnosis of the cause. In the case of a plasma triglyceride level >500 mg/dL, pharmacotherapy should be initiated in

parallel with the referral for diagnosis as part of prevention of acute pancreatitis. Similar management is recommended when genetic hypertriglyceridemia is suspected. For this purpose, statins, fibrates and omega-3 fatty acids can be used in children.

Statins

Treatment with 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA) inhibitors, referred to as statins, should be considered in:

- children ≥10 years of age, without risk factors and with stable LDL levels >190 mg/dL;
- children with at least one high-risk factor or at least two intermediate risk factors and with LDL >160 mg/dL;
- children with diabetes or FH and LDL ≥130 mg/dL.

High-risk factors include hypertension requiring pharmacotherapy, renal failure, body mass index (BMI) >97th percentile, while intermediate-risk factors include hypertension not requiring pharmacotherapy, HDL levels <40 mg/dL, BMI between the 95th and 97th percentile, chronic inflammatory disease (rheumatoid arthritis, systemic lupus erythematosus) and nephrotic syndrome.

Statin therapy can be prescribed by any doctor, without a specialist consultation, starting with the lowest available dose used once daily, in the evening. Statins are the drugs of first choice in the treatment of hypercholesterolemia. Atorvastatin and rosuvastatin are currently the most widely used treatments. In Poland, medicinal products containing rosuvastatin are registered for patients aged ≥6 years, while atorvastatin is approved for children 10 years of age and older. The activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and serum creatine kinase (CK) levels should be measured before initiating statin therapy. Treatment should not be commenced when the activity of any of these aminotransferases is at least 3 times the upper limit of normal (ULN) for age or CK is at least 4 times the ULN for age. Other criteria for discontinuing statin therapy include hypersensitivity to the drug, active liver disease, renal failure, severe infections, major trauma and surgery, severe metabolic or endocrine disorders, and uncontrolled epilepsy. The recommended daily doses of statins in children are 5–40 mg for atorvastatin, 5–20 mg for rosuvastatin, as well as 5–20 mg in children <13 years and 40 mg in children <18 years for pravastatin. The authors also report a recommended daily dose of simvastatin of 5–40 mg, while not recommending its use.

ALT activity should be measured in patients on statins who develop liver symptoms, such as abdominal pain, weakness or jaundice. If muscle symptoms occur, serum CK levels should be checked. Additionally, a lipid panel should be done 6 weeks after the onset of pharmacotherapy and after any treatment modification to monitor treatment goals. If an increased ALT activity of >3 ULN is found, treatment should be discontinued or the dose reduced, while treatment can be continued if ALT activity is increased but remains at <3 ULN, with repeated measurement in 4–6 weeks. Statin therapy should be discontinued if symptoms of myopathy confirmed by laboratory tests occur [23].

The therapeutic goal for statins in children is to reduce LDL below 130 mg/dL or by 30–50% from baseline. For children with diabetes, familial hypercholesterolemia or a family history of coronary artery disease diagnosed before the age of 40 years, the goal is to reduce LDL to <100 mg/dL or by at least 50% from baseline. Once the therapeutic goal is achieved, lipids should be monitored 1–2 times a year [23, 29].

Other therapies

Co-administration of several lipid-lowering drugs, such as ezetimibe at a daily dose of 10 mg, but also mipomersen, alirocumab and evolocumab (PCSK9 inhibitors), can be considered in patients already put on statins (the authors of the recommendations do not mention the recommended daily doses in children). Given the limited data on the efficacy and safety of such management in children, the inclusion of additional treatments should be supervised by a specialist.

Conclusions

In addition to hereditary dyslipidaemias, acquired, environmentally determined lipid disorders are increasingly diagnosed already in childhood due to unfavourable lifestyle changes in recent years. Every family doctor and paediatrician should be able to correctly interpret a lipid panel in a child. The recommendations published in 2021 provide clear guidelines for the diagnosis and management of dyslipidaemias, also in children. Non-pharmacological approaches remain the cornerstone of the treatment of dyslipidaemia in the paediatric population. Pharmacological management (mainly statins) is used in selected cases clearly defined in the available recommendations.

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