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INHERITED METABOLIC DISORDERS AND HEART DISEASES

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Abstract

Inherited metabolic disorders can cause heart diseases, cardiomyopathy in particular, as well as cardiac arrhythmias, valvular and coronary diseases. More than 40 different inherited metabolic disorders can provoke cardiomyopathy, including lysosomal storage disorders, fatty acid oxidation defects, organic acidemias, amino acidopathies, glycogen storage diseases, congenital disorders of glycosylation as well as peroxisomal and mitochondrial disorders. If identified and diagnosed on time, some of congenital metabolic diseases could be successfully treated. It is important to assume them in cases when heart diseases are etiologically undefined. Rapid technological development has made it easier to establish the diagnosis of these diseases. This article will focus on common inherited metabolic disorders that cause heart diseases, as well as on diseases that might be possible to treat.

Key words: inherited metabolic disorders, heart diseases, diagnosis, treatment

Introduction

Metabolism (from Greek: μεταβολή *metabolē* – change, substance modification) is a set of chemical processes occurring in a living organism in order to maintain life. These processes allow the organism to grow and reproduce, to maintain its structure as well as to react to its surroundings. Metabolism is classified in two categories, catabolism and anabolism, depending on metabolic reactions. Catabolism breaks down the organic compounds. During

these processes, energy is either being stored in complex molecules or is being released in response to their degradation, ultimately allowing life. Main mode of actions of metabolism are formation of adenosine triphosphate (ATP), reduced nicotinamide adenine dinucleotide (NADH), as well as synthesis of macromolecules of the organism itself. Anabolism, however, uses the energy for cell compartments build-up and for synthesis of organic compounds, i.e. proteins or nucleic acids (1).

Metabolic chemical reactions are divided into metabolic pathways in which a certain chemical compound transfers into another compound using enzymes. Enzymes are key compounds in metabolism due to their catalytic properties that allow the organism to quickly and effectively perform biologically needed chemical reactions. Moreover, enzymes allow the control of metabolic pathways in response to either changes in the cell environment or some other stimulations (1, 2).

Structure of enzymes is encoded in the genes, and their mutations lead to congenital metabolism deficiencies. Clinical manifestation of hereditary metabolic disorders usually occurs during childhood, although some symptoms can be noticed in adulthood.

Many childhood conditions are caused by single-gene mutations that encode specific proteins. These mutations can result in the alteration of primary protein structure or in the amount of protein synthesized. The function of a protein, whether it is an enzyme, receptor, transport vehicle, membrane component, or structural element, may be compromised or abolished. These hereditary biochemical disorders are termed inherited metabolic disorders (3).

Some inherited metabolic disorders are rare; however, it is estimated that all metabolic diseases affect at least 1% newborns overall. As a result of weak knowledge on these diseases it is difficult to recognise them in patients or are established too late. Increasing number of inherited metabolic diseases are rapidly progressive, thus if not recognised they lead to death or other consequences. On the other hand, if identified and diagnosed timely, some of them are successfully treated (4).

Inherited metabolic disorders can cause hearth diseases, cardiomyopathy in particular, as well as cardiac arrhythmias, valvular and coronary diseases.

Exact prevalence of cardiomyopathy in children is still unknown, and neither is the amount of inherited metabolic diseases. Estimates vary mainly because of different age groups in which children are diagnosed and due to the fact that many cardiomyopathies are slowly developed and become recognised in adulthood.

Rapid technological development has made it easier to establish the causes of the disease among the growing number of children suffering from cardiomyopathy. However, it has remained difficult to estimate the number of patients with unrecognisable asymptomatic cardiomyopathies. Data obtained from various researches state that 26% of children with hypertrophic and 16% of children with dilative cardiomyopathies have metabolic disorders (5, 6).

Inherited metabolic diseases can cause dilative cardiomyopathy, hypertrophic cardiomyopathy, as well as rare restrictive cardiomyopathy (7). Epidemiological study of Paediatric Department of University Hospital of Zagreb observed that in a period of 28 years, 315 children diagnosed with cardiomyopathy were treated, out of which 42.5% were suffering from dilative cardiomyopathy, 37.1% were suffering from hypertrophic and 6.7% from restrictive cardiomyopathy. The rest were suffering from different and rare entity forms of cardiomyopathy (8). More than 40 different inherited metabolic disorders can cause cardiomyopathy, including lysosomal storage disorders, fatty acid oxidation defects, organic acidemias, amino acidopathies, glycogen storage diseases, and congenital disorders of glycosylation as well as peroxisomal and mitochondrial disorders (9).
This article will focus on common inherited metabolic disorders that cause hearth diseases, as well as on diseases that might be possible to treat (Table1.).

Table 1. Common inherited metabolic disorders that cause hearth diseases

1. LYSOSOMAL STORAGE DISEASES
• Pompe disease • Fabry disease • Mucopolysaccharidosis • Mucolipidosis • Oligosaccharidosis
2. FATTY ACID AND CARNITINE METABOLISM DISORDERS
3. MITOCHONDRIAL DISEASES
4. OTHER INHERITED METABOLIC DISEORDERS
• Glycogenosis • Inherited haemochromatosis • Congenital glycosylation disorders • Disorders of amino acid and organic acid metabolism • Disorders of lipoprotein metabolism • Hyperhomocysteinemia

Lysosomal storage diseases

Lysosomes are cell organelles in which degradation of complex molecules occurs and which take part in metabolic processes or are being removed from the cell. Lysosomes can be referred to as cellular 'digestive system'. Lysosomal storage diseases (thesaurismosis) are defined as a set of inherited metabolic diseases that are characterised with storing of macromolecules that have not previously been degraded in lysosomes due to insufficient activity of the enzymes which are crucial for their breakdown. This storing of non-degraded macromolecule can also be due to disabled secretion of lysosomes into cytosol.

Lysosomal storage leads to cell damaging, as well as to damaging of tissues and organs (10).

Lysosomes are present in almost each and every cell in the human's body, therefore lysosomal storage diseases are multisystemic and progressive inherited diseases that affect different organic systems. Moreover, they tend to widely range and variate among the patients.

Cardiomyopathy is a part of the clinical manifestations of lysosomal storage disease. It is often the first or the main symptom for diseases such as Pompe disease and Fabry disease, but is relatively more frequent in mucopolysaccharidosis, mucolipidosis and in some oligosaccharidosis (11).

Pompe disease, or glycogen storage disease type II, is classified as a neuromuscular disease, primary muscular disease, according to the clinical manifestation. Glycogen is stored in lysosomes of all cells, mainly in cardiac, skeletal and smooth muscle cells due to insufficient activation of 1,4-glucosidase. Gene labelled as 17q25.2, q25.3 is responsible for enzyme synthesis. Depending on the occurrence and clinical expression, Pompe disease is usually classified as either infantile-onset or late-onset, whereas the late-onset is further divided into juvenile and adult Pompe disease (12).

Infantile onset is noticeable in first months of life and is characterised with progressive inactivity of muscles and hypertrophic cardiomyopathy as main symptoms of this disease. Untreated patients are prone to dying within the first year of life, either because of cardiac or respiratory system failure (13). Timely application of enzyme replacement therapy tends to drastically change the disease progression and has shown satisfying results in decreasing cardiomyopathy, and thus allows survival of these patients (14). Thus, when hypertrophic cardiomyopathy occurs, it is necessary to check whether it is, in fact, the Pompe disease, which can be performed by measuring enzyme

activity from dried blood spot (15). Less successful results have been obtained among CRIM-negative patients (CRIM – Cross reactive immunological material) (16).

Late-onset Pompe disease type develops less rapidly and it manifests as decreased activity of skeletal and respiratory muscles. Nowadays, different heart diseases are considered to be involved in this onset type as one of the main characteristics of the disease. One of the conditions might include left ventricular hypertrophy, decreased ejection fraction, decreased PR-interval, paroxysmal supraventricular tachycardia, Wolff-Parkinson-White syndrome, as well as dilated ascending aorta (17).

Fabry disease, or Anderson-Fabry disease as first described by authors who discovered it, is the most common lysosomal storage disease after Gaucher disease. This disease is X-linked recessive inherited, although women can also be prone to develop this disease as a result of inactivation of X-chromosomes. This disease is characterised with decreased activity of enzyme α-galactosidase (GLA), leading to glycosphingolipids over-storing in different cell types, particularly in endothelial and vascular muscle cells (18). GLA gene is located on Xq22 chromosome. This disease is usually assumed once the side effects start to manifest, such as kidney failure, heart problems or stroke. However, it is possible to diagnose this disorder in young age. There is a noticeable difference between the classic and the late-onset type of disease. Affected males with the classic phenotype present in childhood with angiokeratomas (telangiectatic skin lesions), hypohidrosis, corneal and lenticular opacities, acroparesthesias, with advancing age develop vascular disease of the kidney, heart, and/or brain. The later-onset phenotype occurs in affected males in the 4th to 8th decade with cardiac disease and/or renal failure. This phenotype is more prevalent than the classic phenotype (19). Heart disease that occurs in Fabry disease is primarily characterised with hypertrophic cardiomyopathy, as well as rhythm disturbances and valvular heart disease (11).

Hypertrophic cardiomyopathy may be the only manifestation of this disease. Therefore, it is vital to check activity of the enzymes responsible for Fabry disease from dried blood spot due to possible treatment using enzyme replacement therapy (20, 21).

Mucopolysaccharidosis are set of rare, but progressive inherited metabolic diseases that are characterised with glycosaminoglycan collection in lysosomes as a result from lack of enzymes that participate in their degradation which ultimately leads to disturbed functioning of the cells, tissues and

organs. Seven different types of mucopolysaccharidosis were described and some of them are divided into their subtypes (22). Clinical manifestations include coarse facial features, recurrent upper respiratory tract and ear infections, noisy breathing, and persistent copious nasal discharge. Obstructive airway disease, notably during sleep, may necessitate tracheotomy. Clinical manifestations also include combined conductive and neurosensory hearing loss and an enlarged tongue, characteristic skeletal dysplasia known as dysostosis multiplex, hydrocephalus, delayed growth and development, as well as mental retardation (11). Heart diseases have been described in all mucopolysaccharidosis types. These include heart valve disease, hypertrophic cardiomyopathy, difficulties in digestion, coronary artery disease, as well as sudden heart death (23). Obstructive airway disease, respiratory infection, and cardiac complications are the common causes of death. Nowadays there are replacement enzymes therapy available for treating mucopolysaccharidosis types I, II, IVA and VI, and some studies have been researching therapies for types IIIA and VII. Patients suffering from type I mucopolysaccharidosis, if diagnosed on time, can effectively be treated by transplantation of haematopoietic stem cells (11). Transplantation of these cells and enzyme replacement therapy decrease hypertrophy of the heart and improve lung function, however no known improvements in treating heart valve disease were noticed (24).

Fatty acid and carnitine metabolism disorders

Mitochondrial β-oxidation of fatty acids is an essential energy producing pathway. It is a particularly important pathway during prolonged periods of starvation, and during periods of reduced caloric intake because of gastrointestinal illness or increased energy expenditure during febrile illness. Under these conditions, the body switches from using predominantly carbohydrate to predominantly fat as its major fuel. Fatty acids are also important fuels for exercising skeletal muscle and are the preferred substrate for the heart. In these tissues, fatty acids are completely oxidized to carbon dioxide and water. The end products of hepatic fatty acid oxidation are the ketone bodies, β-hydroxybutyrate and acetoacetate. These cannot be oxidized by the liver, but are exported to and serve as important fuels in peripheral tissues, particularly the brain, which can partially substitute ketone bodies for glucose during periods of fasting (25). In order to reach a complete use of fatty acids till acetyl coenzyme A and ketone bodies, it is necessary for carnitine cycle

and -oxidation of fatty acids to function properly. Carnitine, whose availability is dependent on a carrier that transports it to the cells, is a crucial factor responsible for successful carnitine cycle functioning. Lack of this carrier, of enzyme of carnitine cycle or lack of enzyme that participates in -oxidation of long chained fatty acids can cause cardiomyopathy with possible heart muscle failure and/or potentially deadly disturbance of heart rhythm (11). Clinical manifestations characteristically involve tissues with a high β-oxidation flux, including liver, skeletal, and cardiac muscle. The most common presentation is an acute episode of life-threatening coma and hypoglycaemia induced by a period of fasting because of defective hepatic ketogenesis. Other manifestations may include chronic cardiomyopathy and muscle weakness or exercise-induced acute rhabdomyolysis (25). Some chronic types can endanger a newborn with cardiac and muscle weakness, hypotonia, as well as with liver failure, disturbances of consciousness, hypoglycaemia and with hyperammonemia. Clinical symptoms and disorder signs are noticed only during metabolic crisis provoked by starving, infections and other stressful situations.

However, if metabolic crisis does not occur, the signs can hardly be detected or can appear as a slight muscle weakness, hypotonia, as signs of cardiomyopathy or liver dysfunction, as well as in a form of frequent disturbance of consciousness in different combinations (4, 25).

Due to impossibility of adequate forming of ketones, nonketotic hypoglycaemia is characteristic of this set of diseases. Analysis of organic acids in urine taken during the crisis periods can provide findings of dicarboxylic acid, the end product of incomplete degradation of fatty acids. During the crisis, it is common to notice increased amount of free fatty acids as well. Concentration of total and free carnitine is decreased, while the analysis of specific acylcarnitines can provide information regarding various diseases of this type (4, 25).

Treatment consists of sufficient calories intake with increased amounts of carbohydrates and decreased amounts of fats that are mainly composed of medium-chained fatty acids. In cases where carnitine carrier is lowered, carnitine is being given (4, 26).

Mitochondrial diseases

Mitochondria are responsible for creating more than 90% of total energy in the body necessary for living and maintaining organ functions. Mitochondrial diseases are primarily characterised with insufficient forming of adenosine

triphosphate (ATP) – energy rich compound that is used in the body for different functions. Cardiac muscle is the main user of this compound in the body. Mitochondriopathies are quite common diseases of inherited metabolism failure and it is estimated that it prevails in 1 out of 5000 (27).

Disturbances and failures of complex processes in mitochondrion can occur due to different mutations in nuclear and mitochondrial DNA responsible for synthesis of approximately 1500 proteins used for maintaining mitochondrion structure and its function.

Organs that require extra energy for their work, such as heart, brain, muscles, liver and kidneys, tend to manifest the symptomatology the most.

However, this can affect many organs and organic systems. Failing to form energy in mitochondrion leads to cardiomyopathy development in majority of patients due to the nuclear DNA gene mutation, whereas the rest of cardiomyopathies occur as a result of mitochondrion DNA mutations (28). Combination of cardiomyopathy and other disorders affecting different organs can often be assumed as mitochondriopathies. It is estimated that cardiomyopathy is found in 20-40% patients with inherited mitochondrial disturbances of forming energy.

Apart from cardiomyopathy, some patients suffering from mitochondrial disturbances of forming energy in heart can suffer from another disorder, such as heart rhythm disturbances, pulmonary hypertension, coronary disease, pericardial effusion and other heart symptoms (11). Mitochondrial diseases clinically manifest between newborn to adult ages and are result of many rare described syndromes. These are hard to diagnose due to various metabolic changes in mitochondria and due to the wide range of variability of clinical manifestations with unpredictable, progressive disorder. As glucose cannot be used to the maximum levels, lactate concentrations are increased which is considered to be one of the causes of congenital lactic acidosis. Disturbances in function of respiratory chain cause increased ratio between lactate and pyruvate, while this ratio is considered to be normal during lack of pyruvate dehydrogenase, meaning the concentration of pyruvate is correspondingly increased. Due to secondary changes in enzyme deficiencies in the respiratory chain the ratio between 3-hydroxibutyric acid and acetoacetic acid is increased. Alanine concentration can be found to be increased in the plasma, while urine can show higher secretion of all amino acids. Organic acid analysis in urine indicate presence of 3-methylglutaconic acid or citrate cycle metabolites. Using histological muscle analysis, it is possible to find ragged red fibres, mitochondrial myopathy specific.

Diseases of this type can be established with specific analysis such as histochemical analysis, use of oxygen measurements and activities of some components of respiratory chain, measuring activities of some enzymes, nuclear and mitochondrial DNA analysis, etc. (4).

Treatment options are limited. It is rarely that results can be positive and if so, it is achieved with ubiquinone and idebenone. Other patients are usually, but not effectively, treated with vitamins, antioxidants and medications that influence resistance development and development of some mitochondrial functions (29).

Other inherited metabolic disorders and heart diseases

Glycogenosis

Apart from Pompe diseases (generalised glycogenosis type II) that have previously been discussed, there are other glycogenosis types that can cause heart disorders. Even though they are classified as primary liver glycogenosis, type 0, III, IV, VI and IX, can provoke muscle weakness in some patients as well as hypertrophic cardiomyopathy (26, 30, 31). Basic treatment of these glycogenosis is a special diet and using glucose polymer aiming to prevent hypoglycaemia and lactacidemia. Nowadays, research studies show that ketogenic diet combined with increased amount of proteins can result in opposite of progressive cardiomyopathy in patients with glycogenosis type III (32).

Inherited haemochromatosis

Inherited haemochromatosis is a result of uncontrolled iron absorption and its over-collection in the body, as well as cell and tissue damaging. Symptoms are expected to appear in childhood among patients suffering from juvenile haemochromatosis, while first signs of patients that developed haemochromatosis due to HFE gene mutation are more noticeable in adulthood (33). Symptoms include cardiomyopathy, arrhythmia, liver disease, endocrinopathy, arthritis and increased skin pigmentation. Apart from the above stated symptoms, diagnosis is also characterised with increased ferritin concentration, high saturation of transferrin with iron, as well as increased iron collection in the tissues. Treatment includes frequent phlebotomy and using iron chelator (34). Cardiomyopathy in haemochromatosis is dilative and is also preceded by diastolic dysfunction and digestion difficulties (35).

Congenital glycosylation disorders

Inherited glycosylation disorders can cause pericarditis and cardiomyopathy that can either be dilative or hypertrophic. This set of diseases usually affects more organic systems so this disorder should be taken as it is, especially if neurological system has been affected too. Standard analysis that prove this set of diseases is isoelectrophoresis of sialotransferrin (11, 36).

Disorders of amino acid and organic acid metabolism

Inherited metabolic disorders of amino acids and organic acids are not common causes of cardiomyopathy, although there are some exceptions. In the long run, cardiomyopathy presents a frequent complication in propionic and methyl-malonic acidemia, therefore such patients should be often controlled. Heart disorders are even more rare in malonic acidemia, β-ketothiolase deficiency, mevalonic acidemia, tyrosinemia and oxalosis (9, 11).

Disorders of Lipoprotein Metabolism

Clinical manifestations of atherosclerosis occur in adulthood when most of the changes in blood vessels are irreversible. Atherosclerosis is a process that starts in young age and is, therefore, possible to act on early in order to prevent its development and the side effects.

Early discovery of dyslipoproteinemia is one of the most important achievements for successful and effective prevention of atherosclerosis development. Inherited genetic diseases are the main causers of primary disorder of lipoprotein metabolism. They can be divided into hypercholesterolemia, hypertriglyceridemia and combination of hyperlipidemia with some other genetically caused dyslipidemia. Out of disorders of lipoprotein metabolism it is hypercholesterolemia that affects the development of atherosclerosis in particular, as well as family lack of apolipoprotein B, polygenic hypercholesterolemia, family dysbetalipoproteinemia, family combined hyperlipidemia and hypoalphalipoproteinemia (37). One third of patients with early myocardial infarction (50 years ago in men and 60 years ago in women) also suffer from hyperlipoprotenimia, while half of the patients have some kind of inherent dyslipoprotenimia (38). Performing cholesterol screening allows establishment of atherogenic lipoprotein levels in serum (total cholesterol, LDL cholesterol, HDL cholesterol). Dyslipoproteinemia is diagnosed regardless of whether it is caused because of excessive and inadequate die, or is caused by primary or secondary disorders of lipid metabolism (39). Cholesterol screening reliability is noticeably increased when universal screening of lipid

profile is being carried out among population (40). This screening can be performed any time after the 2nd year of life, but is mostly preferable to be done in pre-school period, then at the age of 10, and in adolescent age, and should be carried out every 5 years if the results are positive. Universal cholesterol screening carried out among children provides information of which family members are prone to develop coronary disease, and this eventually requires treatment of older family members for coronary disease. Researches show that grandparents death in families where kids have increased cholesterol is up to 2.5 times higher than in families in which kids do not have increased cholesterol (40). Hypercholesterolemia treatment is performed using titrated diet nutrition in children older than two years. It is vital to strictly pay attention to child's body weight and to insist on increased body activity, to control blood pressure regularly and to avoid other potential causers of atherosclerosis development. Therapy also includes medications depending on hypocholesteraemia and depending on results obtained from diet measurements and life habits. Moreover, some ionic exchangers and statins are also used, however their showed variable effects, usually among children above the age of 10 (37).

Hyperhomocysteinemia

Homocysteine is an amino acid that contains sulphur and it occurs due to methionine metabolism. Moderate hyperhomocysteinemia is clinically significant as it provokes dysfunction of endothelium arteries and provokes development of atherosclerosis with side effects such as early infarction, osteoporosis, thromboembolism and is also related to development of schizophrenia, as well as Parkinson's disease. Hyperhomocysteinemia is also provoked by decreased levels of folate in serum, and decreased levels of vitamin B_{12} due to insufficient input resorption of the same compounds, for instance, in chronic inflammatory bowel disease, short bowel syndrome and due to inadequate diet. Polymorphic genes for some enzymes that participate in methionine metabolism can also cause increased levels of homocysteine in serum. The most common are mutations C677T and A1298C on gene for 5,10-methylenetetrahydrofolate reductase (MTHFR). Incidence for the named polymorphs varies in different populations, i.e. for C677T from 9% in North India up to 59% in Mexico. For A1298C, for example, it starts from 17% in China up to 36% in Europe and Canada. Screening and systematic prevention are not carried out. Given the importance and prevalence of hyperhomocysteinemia, as well

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as the possibility of successful treatment, universal screening is advised to be carried out already in childhood (4, 37, 41, 42).

Diagnosis

Inherited metabolic disorders that can cause heart diseases are noticeably different. It is important to assume them in cases where heart diseases are etiologically undefined mainly because some of them can possibly be treated. Tandem mass spectrometry used for newborn screening can provide findings regarding inherited metabolic diseases that provoke heart diseases. However, this is dependent on the number of screening tests performed on the newborn.

Diagnosis of inherited metabolic disorders in a child with cardiomyopathy requires thoughtful investigation with respect to evaluation of the diagnostic metabolites, demonstration of deficient enzyme activity in the appropriate cell type or body fluid, and DNA mutation analysis. For the inherited metabolic disorders associated with excessive acid production, the best time for testing is when the child's metabolism is stressed and the underlying metabolic defects are drawn out. Such times include congestive heart failure, infection, illness, post-surgery, fasting, and during a metabolic decompensation (hypoglycemia, metabolic acidosis, acute encephalopathy). At these times, it is good clinical practice to obtain extra serum and urine samples to hold for future metabolic testing rather than waiting until the child is stabilized, as some of the diagnostic metabolites may be transient or present in only small quantities (9). Laboratory examinations include testing of blood, glucose, acid-base status, lactate, aminotransferase, creatine kinase, ammonium, iron, saturation of transferrin and ferritin, cholesterol, triglycerides, HDL and LDL cholesterol, organic acids in urine, amino acids in plasma, total and free carnitine, acyl carnitine profile, free fatty acids, ketones in urine and/or serum, etc. Some of the mentioned tests are not crucial to perform if the clinical picture suggests a set of metabolic diseases that are not of huge importance.

Many disorders can be confirmed by testing the level of enzymatic activity in white blood cells, serum, or plasma, while others are more easily done in cultured fibroblasts from a skin biopsy. However, the latter requires several weeks for diagnosis, which has led to a push towards developing new assays in white blood cells. The enzyme assay for Pompe disease, Fabry disease and mucopolysaccharidosis type I, II and VI can now be reliably performed using a dried blood spot on a newborn screening card, which shortens the turnaround time for diagnosis to just a couple of days. Dried blood spots have the

added convenience of requiring only a small volume of blood, enzyme stability at room temperature, and easy mailing to the laboratory in an envelope (9). Next generation sequencing methods have had an impact on diagnosis, making it easier to establish the diagnosis. This allows quicker etiological diagnosis to be released for many patients, which previously took months or years (43). Modern methods of gene analysis have drastically decreased the need for 'aggressive methods' in diagnostics such as skeletal and cardiac muscle biopsy. Next generation sequencing methods allow massive parallel sequencing of targeted genetic panels for cardiomyopathy. This includes full coding of genome sequences or sequencing of the entire genome (44).

Next generation sequencing has found changes of one nucleotide and small insertions and deletions. In order to discover more complex genetic changes, it is necessary to perform this method coupled with MLPA (multiplex ligation – dependant probe amplification) or qPCR (quantitative real-time polymerase chain reaction) methods (45).

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ANU ВіН АНУ ВиХ

NASLJEDNE METABOLIČKE BOLESTI I BOLESTI SRCA

Sažetak

Nasljedne metaboličke bolesti mogu izazivati srčana oboljenja, i to prvenstveno kardiomiopatije, ali i poremećaje srčanog ritma i bolesti zalistaka. Više od 40 različitih nasljednih metaboličkih bolesti može izazvati kardiomiopatiju, uključivši lizosomalne bolesti nakupljanja, poremećaje oksidacije masnih kiselina, organske acidemije, aminoacidopatije, bolesti taloženja glikogena, nasljedna oboljenja glikolizacije te peroksizmalne i mitohondrijske skupine oboljenja. Ako se dijagnosticiraju na vrijeme, neke se nasljedne metaboličke bolesti mogu uspješno liječiti. Zato je važno posumnjati na njih kod etiološki nerazjašnjenih srčanih oboljenja. Razvoj tehnologije omogućuje brže i uspješnije postavljanje dijagnoza nasljednih metaboličkih bolesti. U radu će se prvenstveno obratiti pažnja na one nasljedne metaboličke bolesti koje izazivaju srčana oboljenja i koje je moguće liječiti.

Ključne riječi: nasljedne metaboličke bolesti, bolesti srca, dijagnoza, liječenje

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