Endocrine diseases as causes of secondary hyperlipidaemia

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Abstract

Cardiovascular diseases are among the leading causes of increased morbidity and mortality in developed and developing countries. One of the most important risk factors responsible for atherosclerosis and subsequent cardiovascular diseases is hyperlipidaemia. Currently, hyperlipidaemias are divided into several clinical entities. The greatest risk is associated with hypercholesterolaemia. As a result, modern guidelines for the treatment and prevention of atherosclerosis focus predominantly on the reduction of LDL-cholesterol. Hypertriglyceridaemia and atherogenic dyslipidaemia, which are responsible for a less significant increase in the cardiovascular risk, are nowadays secondary targets of the treatment.

During the work-up for hyperlipidaemia one of the essential actions is the exclusion of secondary causes of the lipid abnormalities. Those include, among others, endocrine diseases, diabetes, drugs, nephrotic syndrome, and pregnancy. Data regarding the impact of endocrine disease and diabetes on the lipid profile are scattered. In this review, the authors aimed to perform a thorough analysis of the available publications regarding the topic and the preparation of a comprehensive review dealing with the incidence, clinical features, and the therapy of hyperlipidaemias in patients with endocrine disease. **(Endokrynol Pol 2019; 70 (6): 511–452)**

Key words: *hypercholesterolaemia; hypertriglyceridaemia; hyperlipidaemia; endocrine disease; diabetes*

Introduction

Lipid profile abnormalities are common in patients visiting general practitioners and endocrinologists, as well as in patients admitted to hospital wards. The importance of this finding is connected with significantly increased risk of atherosclerosis and its complications. Current treatment guidelines focus on the primary and secondary prevention of cardiovascular events and emphasise the importance of adherence to lipid-lowering strategies that consist of therapeutic lifestyle changes and pharmacotherapy [1]. Hyperlipidaemia is subdivided into several clinical subclasses: hypercholesterolaemia, hypertriglyceridaemia, mixed hyperlipidaemia, and atherogenic dyslipidaemia. The primary target for therapy is reduction of the LDL cholesterol (LDL-C) level, and the secondary aim concerns hypertriglyceridaemia. In referral units for treatment of refractory and severe hyperlipidaemias, a significant fraction of patients (nearly 30%) have been found to be suffering from secondary hyperlipidaemias [2]. Therefore, during the clinical work-up, practitioners need to exclude secondary causes of lipid abnormalities. Those include: type 2 diabetes mellitus, alcohol abuse, and several endocrine disorders. Endocrine-related conditions, excluding diabetes (e.g. hypothyroidism, glucocorticoid excess, sex hormones excess, etc.) might be the cause of up to 13% of secondary hyperlipidaemias [2]. For many years it has been established that several endocrine diseases may worsen glucose tolerance or even lead to overt diabetes, but the topic of secondary hyperlipidaemias as a result of primary endocrine disease has not been profoundly explored. The most common endocrine causes of hyperlipidaemias are hypothyroidism, poorly controlled diabetes, and Cushing's syndrome. However, one should remember that there are also less common endocrine diseases that may be responsible for hyperlipidaemias, such as growth hormone deficiency, hyperparathyroidism. Hyperlipidaemia is a major risk factor for atherosclerosis, which in turn is responsible for increased cardiovascular mortality due to cardiovascular events (e.g. myocardial infarctions, strokes) [3]. Secondary hypertriglyceridaemia is connected with increased risk of acute pancreatitis [4]. The prevalence of hyperlipidaemias, certain specific features of lipid profiles, and additional risk of clinical problems resulting from untreated background endocrine disease led us to review the available data and provide a comprehensive

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summary on the topic of endocrine diseases as causes of secondary hyperlipidaemias.

Characteristics of hyperlipidaemias

The Frederickson classification of lipid disorders is considered as a reference in the diagnosis of hyper-lipidaemias. It is based on the electrophoresis and centrifugation of serum, and defines six types of hyper-lipidaemias [5]. However, in everyday clinical practice, due to its cumbersome methodology, it is rarely used. Nowadays a simplified approach, based on the mea-surement of fasting lipids [total cholesterol, triglycerides (TG), HDL-cholesterol (HDL-C), and LDL-cholesterol (LDL-C)], is routinely used. This clinical classification divides hyperlipidaemias into: predominant hyper-cholesterolaemia, predominant hypertriglyceridaemia, mixed hyperlipidaemia, and atherogenic hyperlipi-daemia (Tab. I) [1]. The reasoning for that is based on results of clinical trials showing varying levels of cardiovascular risk connected with elevations of lipid fractions. Nowadays LDL-C is considered as a major participant in the progression of atherosclerosis and its complications. Cardiovascular events are respon-sible for a substantial proportion mortality among people overall. Therefore, the majority of efforts in the therapy of hyperlipidaemias are focused on elevated LDL-C. The priority of the LDL-C-lowering approach is changed toward hypertriglyceridaemia in patients with severely (> 500 mg/dL) elevated triglycerides, which is based on the fact that such an elevation in triglycerides is a strong risk factor for a potentially fatal acute dis-ease – acute pancreatitis. But one must remember that when the reduction of TG has been achieved (by proper therapeutic lifestyle change — TLC or diet), the target should be switched again toward LDL-C. In mixed hyperlipidaemia both TG and LDL-C are elevated, and, unless the concomitant TGs are > 500 mg/dL, the LDL-C is a primary target. Atherogenic dyslipidaemia is a clinical entity that, at a first glance in lipid profile, seems like a mild mixed hyperlipidaemia. It is char-acterised by mild elevation in TG, low level of HDL (< 40 mg/dL in males and < 50 mg/dL in females), and normal or slightly elevated LDL-C. In fact, these

changes are more profound than they appear. It was shown that atherogenic dyslipidaemia is often develop-ing in patients with concomitant insulin resistance, loss of lipoprotein lipase activity, and increased activity of CETP [6]. This leads to abnormalities in reverse choles-terol transfer from arteries (low HDL-C), a change in LDL-C particles that become severely atherogenic, and an increase in TG level. All these phenomena greatly accelerate atherosclerosis (Fig. 1).

When diagnosing hyperlipidaemias it is essential to make sure that the results obtained from the laboratory are valid. While the certification of the majority of labo-ratories greatly ensures clinicians that intra-laboratory errors should be minimised, more effort should be put on the pre-laboratory part, especially preparation of the patient for blood sampling. The patient should provide a fasting blood sample. The fasting status should be minimally 12 h, preferably 16 h. It is crucial especially in respect to TG, which in some patients tends to be elevated for prolonged periods of time due to persistent postprandial chylomicronaemia [7].

Endocrine disorders affecting lipid profile

Endocrine disorders and poorly controlled diabetes are responsible for nearly a quarter of cases of hyperlipi-daemia. Therefore, during the work-up of an abnormal lipid profile, efforts toward exclusion of endocrine causes should be made. In the following paragraphs a description of lipid abnormalities in endocrine dis-ease is provided. The majority of such causes may be diagnosed or clinically suspected based on focused anamnesis and physical examination. In selected cases detailed laboratory studies should be considered, to confirm the diagnosis of secondary hyperlipidaemia.

Hypothyroidism
Thyroid hormones play an important role in the metabo-lism of lipids (Fig. 1). They increase the number of LDL receptors in the liver, increase synthesis of bile salts, re-duce absorption of cholesterol from the GI tract, improve reverse cholesterol transfer from peripheral deposits (by the augmentation in ABCA1 and CETP), and increase the amount and activity of lipoprotein lipase and hepatic

Table I. *Clinically important types of abnormal lipid profile*

Type of hyperlipidaemia	Total cholesterol	LDL-cholesterol	Triglycerides	HDL-cholesterol
Hypercholesterolaemia	↑	↑	N	N
Hypertriglyceridaemia	N	N	↑	N
Mixed hyperlipidaemia	↑	↑	↑	N
Atherogenic dyslipidaemia	↑ / N	↑ / N (small dense)	↑	↓

LDL — low density lipoprotein; HDL — high density lipoprotein

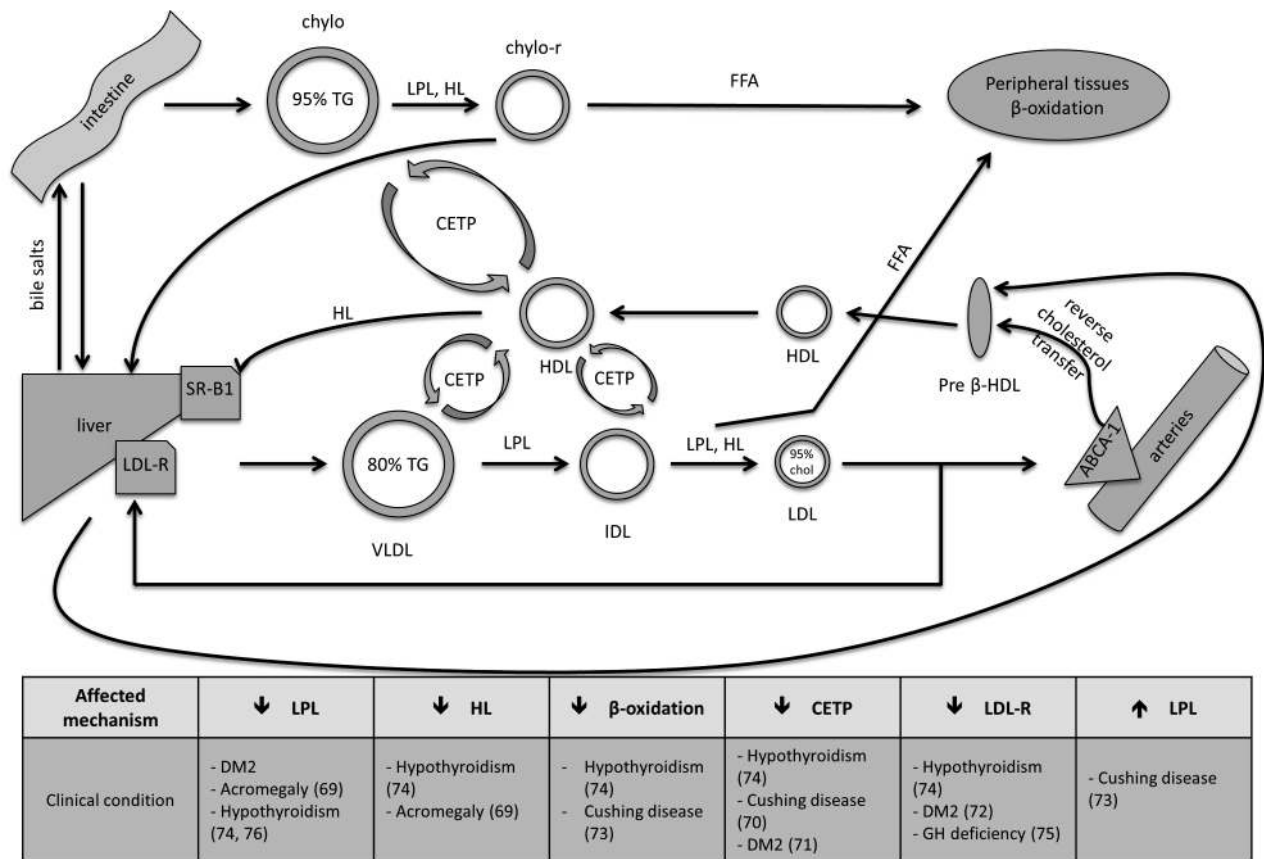| Affected mechanism	↓ LPL	↓ HL	↓ β-oxidation	↓ CETP	↓ LDL-R	↑ LPL
Clinical condition	- DM2 - Acromegaly (69) - Hypothyroidism (74, 76)	- Hypothyroidism (74) - Acromegaly (69)	- Hypothyroidism (74) - Cushing disease (73)	- Hypothyroidism (74) - Cushing disease (70) - DM2 (71)	- Hypothyroidism (74) - DM2 (72) - GH deficiency (75)	- Cushing disease (73)

Figure 1. *Schematic representation of metabolism of exogenous and endogenous lipids, which includes the involvement of enzymes and receptors that are affected in endocrine diseases. CETP — cholesterol esters transfer protein; chol — cholesterol, chylo — chylomicrones; chylo-r — chylomicron remnants; DM2 — type 2 diabetes mellitus; FFA — free fatty acids; GH — growth hormone; HDL — high--density lipoprotein; HL — hepatic lipase; IDL — intermediate-density lipoprotein; LDL — low-density lipoprotein; LDL-R — receptor for LDL; LPL — lipoprotein lipase; SR-B1 — scavenger receptor B1; TG — triglycerides [69–76]*

lipase [8]. Therefore, significant elevations in total and LDL cholesterol (reaching 30% compared to the healthy population) and less prominent rise in triglycerides are seen in patients with overt hypothyroidism. In patients with subclinical hypothyroidism the change in the lipid profile is generally not evident. The magnitude of lipid abnormalities correlates with TSH level. In some studies it was shown that even in euthyroid patients the TSH level correlates positively with total cholesterol, LDL-C, and triglycerides but negatively with HDL-C [9].

In patients with overt hypothyroidism, the introduction of treatment with levothyroxine has led to a reduction in total and LDL cholesterol and triglycerides. On the other hand, in patients with subclinical hypothyroidism, clinical data have shown less promising results [8]. Generally, in patients with TSH > 10 mIU/L the impact of levothyroxine on abnormal lipid profile is clear, which is concordant with other studies showing greater benefit in this group of patients with subclinical hypothyroidism [10].

Nowadays, it seems reasonable to perform TSH estimation in all patients with hyperlipidaemia on a regular basis because hypothyroidism, especially subclinical, is a relatively common disease (1.4–11.2% of the population) [11], may negatively affects patients' quality of life, and might be a cause of increased morbidity [10]. What is more, the treatment of the disease is generally well tolerated, not cumbersome, and, especially in people with overt hypothyroidism, it improves the lipid profile. However, the normalisation of the lipid profile may not be achieved during the therapy with levothyroxine, which may be the result of background hyperlipidaemia. In such cases, a specific, lipid-lowering therapy should be introduced. In the majority of cases the drug of choice is a statin. Due to the increased risk of rhabdomyolysis, the initiation of lipid-lowering therapy with statins is not recommended until euthyreosis is achieved [12].

Hyperthyroidism

Hyperthyroidism is not the cause of hyperlipidaemia, but a very low LDL-C level, especially with signs and symptoms of hyperthyroidism, should urge clinicians to exclude subclinical or overt hyperparathyroidism.

Despite lipid-lowering effects of the excess of thyroid hormones, patients' overall prognosis is worsened [13].

Poorly controlled diabetes

Contrary to hypothyroidism, uncontrolled diabetes leads to hypertriglyceridaemia and features of atherogenic dyslipidaemia [14]. Despite statin therapy, it is estimated that as many as 50% of patients with diabetes have increased level of TG [15]. This results from multiple factors. Generally, patients with bad glycaemic control do not adhere to an appropriate diet, which in many cases contains simple carbohydrates and saturated fats. Dietary fat is transported from the intestines in triglyceride-rich chylomicrons, responsible for a high level of postprandial triglycerides. In the liver, due to an excess of food and insulin resistance, the increased synthesis of TG and its excretion in VLDL is also seen. The TG level is further augmented by the loss of activity in LPL due to increased production of apoCIII (a physiological inhibitor of LPL). What is more, due to alterations in lipid transfer by CETP, LDL cholesterol particles in those patients become very atherogenic — "small dense LDLs" [16]. Finally, in patients with significantly elevated glycaemia, an ongoing glycation and oxidation of lipoproteins is responsible for the acceleration of atherosclerosis and its complications [17].

Hypertriglyceridaemia, especially with concurrent atherogenic dyslipidaemia, is a known risk factor for cardiovascular diseases [18]. Therefore, it should be treated according to standards of care. The primary goal of therapy is still the LDL-C level, and TG is considered as a second-line treatment goal. In patients with diabetes the treatment of hyperlipidaemia must be multidirectional. A proper therapeutic lifestyle change (TLC), including regular physical activity and diet, is essential. As a result, LDL cholesterol can be reduced by around 10–15% after TLC [19]. Currently, it is recommended to reduce LDL-C in patients with type 2 diabetes below 70 mg/dL. Therefore, in many cases cholesterol-lowering therapy should be introduced at the initial visit. TG level below 500 mg/dL may be initially dealt with by a three-month watch-and-wait strategy for the effects of TLC (± statin). Due to a proper diet, physical activity, and in some cases statin use, remarkable improvements in lipid profile are seen [20]. Conversely, the treatment with fibrates and/or omega-3 fatty acids should be immediately introduced in severe hypertriglyceridaemia (> 500 mg/dL) or the lack of benefit after TLC or statins.

Cushing's disease

Compared to hypothyroidism and diabetes, secondary hyperlipidaemia due to elevated, autonomous secretion of glucocorticoids is much less common. On the other hand, 52% of patients with hypercortisolism are affected by secondary lipid abnormalities [21]. It may be seen more often as the result of the treatment with glucocorticoids (as immunosuppressive agents or excessive substitution). The risk of developing cardiovascular complications is increased even in subjects with "non-functional" adrenal tumours. It was shown that the higher the level of cortisol in 1 mg dexamethasone suppression test (all results within < 1.8 ug/dL), the higher the likelihood of developing diabetes [adjusted RR = 1.87 (1.17, 2.98)] [22]. The cardiovascular risk is additionally elevated in the group with subclinical hypercortisolism [23]. In respect to the lipid profile, glucocorticoids tend to cause atherogenic dyslipidaemia (high TG and low LDL-C), which is commonly connected with central obesity and metabolic syndrome [24].

Naturally, the treatment of choice is the elimination of hypercortisolism. This can be best achieved by the surgical resection of adrenal or pituitary adenoma (especially in overt hypercortisolism) or fine-tuning the cortisol replacement therapy. As a result, a significant improvement, but generally not normalisation, in the lipid profile, described by reductions in TG and LDL-C and an increase in HDL-C, can be achieved [21]. When curative treatment is not possible, a general approach to treat hypercortisolism, including ketoconazole or mitotane, is introduced. Additionally, significant effort should be focused on the reduction of cardiovascular risk factors. Therefore, a therapeutic lifestyle change is advised. In the majority of cases, the treatment of atherogenic dyslipidaemia must include pharmacotherapy. All standard groups of drugs can be used, depending on the mostly elevated lipoprotein fraction (statins in predominant hypercholesterolaemia and fibrates in predominant hypertriglyceridaemia). It should be kept in mind that in patients treated with ketoconazole, which is a potent cytochrome P450 inhibitor, clinically significant drug interactions with lipid-lowering drugs may occur. In the necessity of combined therapy with ketoconazole and statins, pravastatin should be used as the drug of choice. Additionally, in cases of suspected Cushing's syndrome in patients on lipid-lowering therapy, one should consider cessation of fibrate, because in specific circumstances it can lead to false positive diagnosis of hypercortisolism. Fenofibrate interferes with the assay of free cortisol from urine specimens. If the drug cannot be withdrawn, other confirmatory tests for hypercortisolism should be selected [25].

Pituitary diseases

Hyperprolactinaemia

Hyperprolactinaemia affects various aspects of lipid and glucose metabolism and leads to atherogenic dyslipidaemia, primarily with elevated triglycerides and

LDL-C [26]. The influence on the lipid profile results mainly from the inhibitory effect of prolactin on LPL [27]. Additionally, with the increase in the diameter of adenoma subsequent failure of the pituitary gland occurs, leading to GH deficiency, hypogonadism, and, in severely advanced disease, to hypothyroidism, which are responsible for augmentation of lipid abnormalities. Interestingly, it was noted that in female patients with macroprolactinaemia the HDL-C level is decreased by around 11% compared to healthy women [28]. The therapy of hyperprolactinaemia with dopamine agonists is effective also in the improvement of lipid profile. Total cholesterol and LDL-cholesterol have been significantly reduced following such a therapy [29]. In patients with increased level of TG, further improvements may be achieved by the addition of fenofibrate to the therapy [30].

Acromegaly

Different kinds of lipid abnormalities are diagnosed in 33% of patients with acromegaly [31]. According to data from small-sample observatory studies, 19-56% of patients with acromegaly had increased level of triglycerides, which is significantly more than among age-matched individuals [32, 33]. Conversely, the cholesterol level is generally mildly elevated in the course of the disease [34]. It seems that the elevated TG level is connected with increased synthesis of fatty acids and reduced activity of LPL [35]. This results in the elevation of triglyceride level, which may trigger acute pancreatitis, which is occasionally seen in such patients. Additional risk factors that may aggravate hyperlipidaemia are hormonal insufficiencies of other pituitary endocrine axes (e.g. secondary hypothyroidism, hypogonadism), which are caused by compression trauma in macroadenomas. Lipid abnormalities in patients with acromegaly were shown to be responsible for accelerated progression of subclinical atherosclerosis (intima media thickness and pulse-wave velocity), which in turn may be responsible for increased cardiovascular risk [36]. It was also noted that the risk of cardiovascular complication is considerably elevated and correlates positively with the duration of acromegaly [37].

The greatest improvements in lipid profile are observed in patients after successful surgical treatment of adenoma. Subsequently, the lipid profile improves significantly, which is reflected by a drop in TG concentration. In a paper showing a series of cases of surgically treated patients, the reduction in TG level reached 50.7% (p = 0.004) [38]. The improvement during the treatment of acromegaly is strictly related to the achieved reduction in GH, which leads to increased activity of LPL and finally to the reduction of TG [39, 40]. Recent clinical trials have shown that the lipid profile improvements are the result of the achievement of control of the disease. Somatostatin analogues have led to significant reductions in TG level, which was accompanied by a rise in HDL-C [41]. Lipid abnormalities that are concurrent with acromegaly should be treated according to general guidelines in the treatment of hyperlipidaemias. Therefore, after cardiovascular risk estimation, treatment with statins or fibrate should be introduced. In the case of patients on somatostatin analogues, prior to the introduction of fibrate, gallstones should be excluded. Fibrates are contraindicated in those patients due to increased cholesterol content in bile, which is responsible for increased propensity for gallstone formation [42].

Growth hormone deficiency

In children, growth hormone deficiency leads to growth retardation. The majority of patients are withdrawn from the GH substitution on entering adulthood or when satisfactory height is achieved. Interestingly, adult patients with GH deficiency in many countries have been on hormone replacement therapy to prevent metabolic complication for the last 30 years [43]. The incidence of metabolic syndrome in adult patients with GH deficiency is more than doubled compared to healthy subjects (38.0 vs. 15.7%, p < 0.0001) [44]. Detailed analysis of the lipid profiles of those patients revealed significantly elevated LDL-C and TG (in 85% and 44% of patients, respectively), which were often accompanied by a reduction in HDL-C (in 47% of patients) [45]. Such a lipid profile should be considered as atherogenic dyslipidaemia.

GH replacement therapy in children has shown improvements in lipid profile, which may prevent atherogenic complications in the future [46]. However, the improvements in lipid profile in adults are less evident, showing persistent atherogenic dyslipidaemia during up to five years of the treatment or only minor (5%) reduction in total cholesterol [47]. Interestingly, in patients following effective treatment for acromegaly, who developed GH deficiency, GH replacement therapy seemed to improve lipid profile [48]. In conclusion, the impact of GH itself on lipid profile and long-term benefits in adults are less clear [49]. Therefore, it seems that the active treatment of dyslipidaemia with hypolipidemic drugs should be introduced according to the estimated cardiovascular risk or concomitant diseases to prevent further atherosclerotic complications.

Combined pituitary hormone deficiency

Combined pituitary hormone deficiency (CPHD) is diagnosed when there is a deficiency or absence of at least two pituitary hormones. The genetic background relies

on mutations of several proteins associated with the development of pituitary gland and subsequent secretion of hormones (e.g. Pit-1, PROP-1). Clinical manifestations may vary, depending on major hormone deficiencies, but a rise in total cholesterol and LDL-C is commonly seen [50]. The most probable cause of hypercholesterolaemia in those cases is secondary hypothyroidism. Therefore, successful treatment of hypothyroidism generally leads to the normalisation of cholesterol level. Naturally, in those specific and rare cases, prior to the administration of levothyroxine, a secondary adrenal gland insufficiency must be excluded.

On the other hand, in patients suffering from Sheehan's syndrome, various hyperlipidaemias have been diagnosed, which were connected with the reduced level of lipoprotein lipase and hepatic lipase activity [51]. Reduced activity of both lipases is responsible for various forms of hyperlipidaemias with predominant hypertriglyceridaemia. The introduction of proper hormonal substitution with hydrocortisone and levothyroxine resulted in the reconstitution of lipase activity and normalisation of lipid profile.

Polycystic ovary syndrome

Polycystic ovary syndrome (PCOS) may affect up to 20% of the population of otherwise healthy females. The majority of clinical problems that lead to seeking for help result from infertility and patients changed body appearance due to hyperandrogenaemia. However, due to androgen excess those patients suffer from atherogenic dyslipidaemia [52]. The greatest benefits can be achieved by therapeutic lifestyle change leading to reduced body weight and increased physical activity. Some lipid benefits (reduction in LDL-C and TG) are seen after the introduction of metformin [53]. In the older population or in those with additional cardiovascular risk factors, targeted treatment of lipid abnormalities can be offered. Nevertheless, it should be noted that statin therapy may worsen glucose sensitivity in this specific vulnerable population [54].

Oestrogen/progesterone excess and oral contraception

Combined oral contraception (COC) and progestin-only oral contraception (POC) are methods of contraception used by around 13% of women [55]. Combined oral contraception has been shown to increase triglyceride and total cholesterol (mainly by an increase in HDL-C), whereas POC seemed to have neutral impact on lipid profile. COCs are contraindicated in severe dyslipidaemia, especially in patients with elevated TG, due to the increased risk of acute pancreatitis. In this clinical setting intrauterine devices should be recommended [56].

Hypogonadism

Male hypogonadism may arise from testicular damage (primary hypogonadism) or as a consequence of hypothalamic-pituitary axis insufficiency (secondary hypogonadism). The diagnosis is generally made by the presence of clinical signs and symptoms with concurrent low level of testosterone taken on several occasions [57]. Nowadays, a substantial group of patients, due to obesity, develop secondary hypogonadism [58]. Obesity and metabolic syndrome lead to a mild atherogenic dyslipidaemia. Testosterone replacement therapy improves patients' quality of life and glucose metabolism, but its impact on the lipid profile is less apparent. Reductions in total cholesterol and TG are minute (generally < 5%) [59, 60]. During the therapy, improvements in markers of cardiovascular diseases (e.g. apoB) have been noted [61], but the impact on cardiovascular outcomes remains inconclusive due to the lack of data of sufficient quality [62].

In postmenopausal women, a tendency toward increased levels of total cholesterol and LDL-C triglycerides, and reduced level of HDL-C has been noted [63]. The LDL-C level is increased in more than 48% of patients, low HDL-C level is seen in more than 42% of patients, and high TG in nearly 30% of patients. Lipid profile abnormalities and additional metabolic changes (obesity, arterial hypertension, and insulin resistance) lead to increased risk of cardiovascular events [64]. Despite the change in lipid profile that is attributed to ovarian failure, hormone replacement therapy with oestrogen and progesterone has not reduced the cardiovascular risk and markers of subclinical atherosclerosis in postmenopausal women [65]; nowadays it is not recommended in cardiovascular prevention but merely for symptomatic relief. Therefore, in postmenopausal women with abnormal lipid profile a targeted hypolipidemic therapy (e.g. statin, fibrate) should be introduced.

Hyperparathyroidism

In patients with primary and secondary hyperparathyroidism, a predominant increase in TG level has been noted. More than 52% of patients suffer from some sort of hyperlipidaemia [66], which is 50% higher than the incidence of hyperlipidaemia in the population from the same background. The reason for that is not fully understood, but patients with hyperparathyroidism more often suffer from obesity and diabetes, which may be related to reduced physical activity. However, it has also been shown that the TG level rapidly dropped in patients with primary hyperparathyroidism as soon as seven days after surgery of parathyroid adenoma (1.50 ± 0.11 to 1.19 ± 0.07 mmol/L; p < 0.001) and has been maintained at a lower level for up to 12 months

REVIEW

Table II. *Lipid profile abnormalities in endocrine disorders*

Clinical condition	Total cholesterol	LDL-cholesterol	Triglycerides	HDL-cholesterol
Hypothyroidism	↑	↑		
DM2	↑ / N	↑ / N (small dense)	↑	↓
Hypercortisolism	↑ / N	↑ / N	↑	↓
Hyperprolactinaemia	↑	↑	↑	
Acromegaly			↑	
GH deficiency	↑ / N	↑ / N	↑	↓
CPHD	↑	↑		
PCOS	↑	↑ (small dense)	↑	↓
O/P excess or oral contraception			↑	↑ / N
Hypogonadism	↑ / N	↑ / N	↑	↓
Hyperparathyroidism			↑	

CPHD — combined pituitary hormone deficiency; DM2 — type 2 diabetes mellitus; PCOS — polycystic ovary sendrome; O/P — oestrogen/progestin; GH — growth hormone; LDL — low density lipoprotein; HDL — high density lipoprotein

of follow-up (1.17 ± 0.11 mmol/L) [67]. On the other hand, other researchers have shown that parathyroidectomy did not lead to any significant change in lipid profile [68]. The differences in favour of non-surgically treated patients have been attributed to lipid-lowering therapy. Therefore, the curative method in the treatment of hyperthyroidism is a surgical approach, but it is indicated in patients with clinical or laboratory features that support such treatment. On the other hand, in patients who are not treated operatively, a mild increase in TG or LDL-C level can be successfully treated with lipid-lowering drugs.

Conclusions

Endocrine disorders are relatively common causes of secondary hyperlipidaemia. The wide variety of lipid profile abnormalities makes it nearly impossible to specifically suspect endocrine disease (Tab. II). However, due to the fact that the thyroid function abnormalities and hypercholesterolaemia are often seen in the general population, it is recommended to exclude hypothyroidism in every patient with hypercholesterolaemia (generally, TSH measurement is sufficient). Due to strict recommendations regarding LDL-C levels, the lipid profile in patients with type 2 diabetes is generally regularly checked concomitantly to markers of glucose control (HbA$_{1c}$). Therefore, worsening of lipid profile may swiftly be correlated with glucose levels and proper diet or using pharmacological therapy. In the majority of hyperlipidaemias, the suspicion of endocrine disease should be based on a clinical approach rather than on simple lipid profile estimation (e.g. red stretch marks in Cushing's disease or reduced sexual drive in hypogonadism). The treatment of secondary hyperlipidaemias in many cases is focused on the offending endocrine disease, but in the majority of cases it must be strengthened by specific lipid lowering therapy.

Conflict of interests

All authors state that they have no financial interest in the subject matter or materials discussed in this manuscript.

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REVIEW

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REVIEW