MANAGEMENT OF OBESITY AND ITS COMORBIDITIES

40. Clinical evaluation of the obese patient

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European guidelines on obesity management recommend to establish multidisciplinary teams and multilevel obesity management networks that include obesity specialists. However, all physicians should be able to clinically assess an obese patient, identify potential genetic, behavioral and environmental factors that may have contributed to the development of obesity and screen for obesity-related complications. More specifically, the physician should be aware of important elements from the family and personal history of the obese patient, as well as of clinical signs that may provide clues as to the aetiology of obesity. A biochemical and hormonal screening is also essential both to identify potential contributing factors and to document the presence of metabolic complications. The presence of other complications of obesity should also be actively explored (e.g. sleep apnea, musculoskeletal problems, psychological symptoms, reproductive disturbances, etc.). Further, it is important that the physician gains the trust of the obese patient by acknowledging the problem and avoiding wording that may be offensive to the patient in order for any intervention to be successful in the long-term. Finally, we should all recognize that obesity is a complex, adiposity-based chronic disease, where management targets both adiposity and weight-related complications in order to improve overall health and quality of life. Individualization of care is essential as well as optimization of health outcomes and safety.

41. Very low energy diets: the past and presence

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Failure to achieve appropriate weight loss, particularly in severely obese patients, by traditional low calorie diets led to implementation of strict calorie restrictions in the weight management. Serious health hazards including sudden deaths associated with semi-starvation and the use of liquid protein diets in the past led to development of very low energy diets (VLEDs). VLEDs were prepared by using proteins of a high biological quality as that of milk or egg white. The whey protein represented the main source of supplied proteins in the first Czechoslovak VLED (Redita®) prepared in the late eighties. Currently used VLEDs are characterized by energy intake about 3500 kJ and provide an appropriate supply of proteins incl. all essential amino acids, minerals, vitamins and trace elements. Amount of fat is substantially reduced and is mainly represented by essential fatty acids. Daily supply of carbohydrate in VLEDs is reduced to 30–80 g. High protein intake and mild ketosis exert protein-sparing and satiating effects. The rapid weight loss, approximately 10 kg after one month of VLED administration, is mainly due to fat loss. In severely obese patients weight loss of 20–25 kg is observed after 4 months of VLED treatment. VLEDs are primarily indicated for weight management, particularly in severely obese, in whom weight loss before surgery is recommended or who cannot undergo bariatric surgery. In addition VLEDs have also been proved an efficient approach to treat type 2 diabetes (T2D), obstructive sleep apnea, arthritis, and non-alcoholic fatty liver disease. VLEDs rapidly reduce cardiometabolic health risks: improve lipid profile and glucose homeostasis, reduce blood pressure and visceral fat. Improvements in steroid profile and SHBG levels were observed after the treatment with Redita®. Some VLEDs significantly reduce carbohydrate intake which leads to a more profound improvement in insulin sensitivity and glucose homeostasis. VLEDs mimic the early beneficial effect of gastric bypass on insulin sensitivity and beta-cell function in T2D. Reversal of T2D in youth who adhered to a VLED was demonstrated. VLED-induced weight loss is associated with improved insulin signaling and with a decrease in intramyocellular lipid content. Replacement of 1–2 daily meals with portion/s of VLED is one of the most effective tools for weight loss maintenance. Look AHEAD trial conducted in overweight/obese patients with T2D clearly demonstrated that the degree of weight loss after 1 year of intensive lifestyle intervention was dependent on the number of daily consumed portions of VLED. Effects of meal replacement (MR) are mostly due to the controlled energy content and to the high protein vs. low fat content. MR also contributes to a more appropriate intake of essential nutrients. Use of VLEDs both as a sole source of nutrition and as MR should be initiated by a physician who should take into account indications and contraindications in individual patients. VLEDs should be included into long-term weight management programs with

diet, increased physical activity and cognitive behavioral intervention. During the follow-up dietitians or trained nurses/counselors may be responsible for the weight management while physicians might play only advisory role.

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42. The renaissance of obesity pharmacotherapy

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The treatment of overweight and obesity is a difficult and lengthy process, requiring both correctly identified causes of these diseases, and implementation of methods, which are adequate to the patient's health status. The mainstay of treatment is lifestyle change leading to a negative energy balance (change in eating habits and increased physical activity). However, many patients in order to facilitate the implementation of recommendations for lifestyle changes require the pharmacological or psychotherapeutic support and a part also surgical procedure. The possibility of using pharmacologic agents to treat obesity is very limited. Orlistat is the only medicinal product, which has been available on the European market for the last 6 years. Mysimba® was authorized by the EMA in March 2015. Mysimba® has been available on the European market since 2016. Mysimba® is a fixed dose combination medicinal product which contains two active substances, bupropion hydrochloride and naltrexone hydrochloride. Due to the additive effect of these active substances in the central nervous system in the arcuate nucleus of the hypothalamus (satiety stimulation) and in the limbic area where the reward system is located (appetite suppressing) the drug raises the hope for increasing efficacy in the treatment of obesity. Clinical studies confirmed efficacy and safety this medicinal product. It should be noted that combination bupropion and naltrexone improves control of eating. The results of LIGHT study confirmed safety use of this medicinal product in the patients with high cardio-vascular risk. The unique mechanism of action this medicinal product is chance for improvement of obesity treatment among subjects with eating disturbances such as binge eating syndrome, night eating syndrome and addictive food consumption.

43. Is obesity a real cardiovascular risk factor?

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The prevalence of weight excess is increasing worldwide and pose serious burden to healthcare systems. It seems to be that obesity is the epidemic of the 21st century. Obesity has strong relationship to hypertension, diabetes, hyperlipidemia, atrial fibrillation, heart failure and OSA. Thus, obesity is a negative determinant for longevity. On the contrary, numerous publications reported better survival among obese patients suffering from heart failure or ischemic heart disease as compared to normal weight patients. This phenomenon is called "obesity paradox". Furthermore, it still exists the term of "healthy obesity" without risk factors and cardiovascular diseases. Long-term observation describes the future outcome of this subjects. Some data suggest that body weight and fat distribution are related to arterial stiffness and early vascular changes. In our earlier observation, an increased arterial stiffness was demonstrated by echocardiography among patients with obesity even in young adults. Increased arterial stiffness is an important risk factor and predictor of cardiovascular mortality. In conclusion, obesity and cardiovascular diseases have strong relationship and these disorders should be considered and treated together.

44. Management of arterial hypertension in obese patients

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Obesity is an epidemic of the XXI century. In 2014, more than 1.9 billion adults had an excessive body weight, of which 600 million were obese. More than 42 million children aged 5 yrs and over are obese. It is estimated that in 2015 there came another 100 million obese adults all over the world. The risk of developing hypertension in obese adults is 2–3 times higher, and in obese children even 7 times higher than in normal-weight individuals. Obesity and hypertension coexist in 78 % of hypertension cases in men and in 65 % of the cases in women. The development of hypertension in obese patients is associated with numerous central and peripheral abnormalities, such as the activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system; impairment of endothelial function; increased water retention caused by excessive sodium intake, increased sodium resorption in the renal tubules and reduced levels of atrial natriuretic peptide (ANP). During the lecture there will be presented the impact of obesity on cardiovascular system, some characteristic features of obesity-induced hypertension, the most appropriate management, and finally, the most common mistakes in the therapy.

45. Mechanisms and potential targets of dyslipidaemia in obesity

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The dyslipidemic state (atherogenic dyslipidaemia) frequently observed in patients with visceral obesity is a key feature of the clustering abnormalities of the metabolic syndrome. Atherogenic dyslipidaemia is characterized by a cluster of quantitative and qualitative changes in the metabolism of lipids and lipoproteins, leading to increased aterogenicity of plasma: increased concentration of the triglycerides and apoC-III-rich VLDL particles, total and LDL cholesterol levels are generally within the normal range, with modified small dense LDL particles, quantitative and qualitative changes in HDL-C particles with loss of cardioprotectivity, increased concentration of remnant lipoporotein particles and the presence of postprandial hyperlipidemia. In a typical clinical setting, hypertriglyceridemia and low HDL cholesterol will, therefore, be the two major detectable blood abnormalities associated with visceral obesity. The increased proportion of small, dense LDL and HDL particles is an important aspect of the atherogenic dyslipidaemia. This phenomenon is due to the remodeling of these lipoproteins in the circulation by enzymes such as cholesteryl ester transfer protein and hepatic triglyceride lipase. In the presence of hypertriglyceridemia, increased concentration of large VLDL1 particles promotes the transfer of triglyceride molecules to LDL and HDL in exchange for cholesteryl ester molecules. As a consequence, both triglyceride-enriched LDL and HDL particles of viscerally obese patients become good substrates for hepatic triglyceride lipase, leading to the depletion of the lipid core of these lipoproteins, thereby forming small, dense LDL and HDL particles. Smaller HDL have reduced cholesteryl ester core content and become more sensitive to degradation and increased clearance from the blood. Each component of the atherogenic dyslipidemia described could contribute, with many other factors, to the development of atherosclerosis. Hypertriglyceridemia per se has been proposed as an independent risk factor for atherosclerosis. Remnants of triglyceride-rich lipoproteins, which are elevated in hypertriglyceridemic states, are highly atherogenic, probably as much as small, dense LDL. Several factors could contribute to the atherogenicity of small, dense LDL particles. In contrast, HDL could be antiatherogenic in a number of ways. The combination of high triglyceride, low HDL cholesterol levels and small, dense LDL particles has been termed the "atherogenic lipid triad"; it has been recognized as a major CVD risk factor. Despite the huge success achieved through statin therapy in reducing LDL-C (primary endpoint) together with the reduction of cardio-cerebrovascular morbidity and mortality still remains high cardiovascular risk. This reflects the rise in obesity, increased metabolic syndrome and type 2 diabetes, which is characterized by high prevalence of atherogenic dyslipidaemia. Targeting the atherogenic dyslipidaemia complex is a next extension of the therapeutic targets. From the existing lipid-lowering agents, we should review the effect of fibrates in combination therapy in patients with atherogenic dyslipidaemia. Near future are selective PPARα modulators, a little further ahead is therapy directly targeting the metabolism of triglyceride-rich lipoproteins. These options represent a new opportunity to reduce cardiovascular risk by influencing the complex atherogenic dyslipidaemia in obese patients.

46. Non-alcoholic fatty liver disease in overweight and obese patients

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Non-alcoholic fatty liver disease (NAFLD) is a major cause of liver disease worldwide. Obesity is a global epidemic contributing to an increasing prevalence of obesity-related systemic disorders. Obesity is a well-established risk factor for the non-alcoholic fatty liver disease. With the increasing epidemic prevalence of obesity, diabetes, and the metabolic syndrome in the general population is increasing the prevalence of NAFLD. Global prevalence of NAFLD is 30 %. The rising prevalence of NAFLD globally may be accounted for by changes in dietary habits and an increase in sedentary lifestyle. The risk of development and progression of NAFLD increases with numbers of components of metabolic syndrome. NAFLD spans a spectrum of hepatic pathology from hepatic steatosis, through steatohepatitis (NASH), to fibrosis and cirrhosis at the opposite end of the disease spectrum. Up to 70 % patients with type 2 diabetes mellitus have NAFLD. Prevalence of NAFLD among obese individuals is up to 76 %, 60 % have NASH, 30 % fibrosis, and up to 10 % liver cirrhosis. NAFLD is associated with a list of hepatic complications considerably adding to morbidity, mortality. NAFLD contribute with a large proportion on cirrhosis, liver failure, and hepatocellular carcinoma. NAFLD is an important and independent risk factor for the development of atherosclerosis and cardiovascular disease (CVD). NAFLD is strongly associated with the clinical features of insulin resistance and is the hepatic component of metabolic syndrome. As the global epidemic of obesity fuels metabolic conditions, the clinical and economic burden of NAFLD will become enormous.

47. Obesity-related nephropathy

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The aim of our study was to clarify the effect of obesity on the genesis of chronic kidney disease. Obesity has a negative impact on the organism. It causes cardiovascular, gastrointestinal, respiratory and other complications, such as chronic kidney disease. We undertook a systematic review of the literature using PubMed database to investigate the relationship between obesity and chronic kidney disease. As key words we used obesity-related glomerulopathy. We searched studies from the last 10 years. 22 studies were corresponding to the above mentioned criteria. Typical abnormalities were confirmed on kidneys such as glomerulomegaly, podocyte malfunction (milder fusion of podocyte pedicels), increased mesangial matrix, vascular changes, tubular atrophy and interstitial fibrosis. Functional changes included hyperfiltration, hyperperfusion, albuminuria and proteinuria. These abnormalities were partially reversible with adequate and on time therapy. The most important, based on these studies, is to change the eating habits, to keep low-calorie diet and to perform more physical activity. Appropriate pharmacotherapy and bariatric surgery is applicable in the case of morbidly obese patients. We should also take into consideration the treatment of obesity complications. In conclusion, there is still a need for further research of therapeutic options, as well as their verification based on series of clinical experiments.