The management of the obesity-induced hypertension

Manažment obezitou indukovanej hypertenzie

Michał Holecki[1,2], Magdalena Zawadzka[2]

[1]Department of Internal Medicine and Metabolic Diseases, School of Health Science, Medical University of Silesia, Katowice, Poland
[2]Department of Internal Medicine, District Railway Hospital, Katowice, Poland

✉ **prof. Michał Holecki, MD, PhD** | mholecki@sum.edu.pl | smk.sum.edu.pl

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Abstract
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 years and over are obese. 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). The article will present the impact of obesity on cardiovascular system, some characteristic features of obesity-induced hypertension, the most appropriate management, and finally, the most common mistakes made in the therapy.

Abstrakt
Obezita je epidémiou 21. storočia. V roku 2014 malo viac ako 1,9 miliardy dospelých nadváhu, z toho 600 miliónov osôb bolo obéznych. Obezitou trpí viac ako 42 miliónov detí vo veku nad 5 rokov. V roku 2015 pribudlo celosvetovo ďalších 100 miliónov obéznych dospelých osôb. Riziko rozvoja hypertenzie u obéznych dospelých je 2- až 3-krát vyššie a u obéznych detí dokonca 7-krát vyššie, v porovnaní s jedincami s normálnou hmotnosťou. Obezita a hypertenzia sa súčasne vyskytuje u 78 % (65 %) hypertenzných mužov (žien). Vývoj hypertenzie je u obéznych pacientov spojený s mnohými centrálnymi a periférnymi abnormalitami, ako je aktivácia sympatického nervového systému a systému renín-angiotenzín-aldosterón; poškodenie funkcie endotelu; zvýšená retencia vody spôsobená nadmerným príjmom sodíka, zvýšená resorpcia sodíka v renálnych tubuloch a znížená hladina atriálneho natriuretického peptidu (ANP). Prehľadný článok sumarizuje vplyv obezity na kardiovaskulárny systém, niektoré charakteristické znaky hypertenzie vyvolanej obezitou, najvhodnejšiu liečbu a taktiež najčastejšie chyby v terapii.

Introduction

Obesity, which is a consequence of increased accumulation of fat (over 25 % body fat in men and over 30 % body fat in women), is one of the most prevalent healthcare problems worldwide. According to the World Health Organization (WHO), approximately 1.6 billion adults are considered overweight and 400 million are obese [1]. It is estimated that in the United States, by 2030, 51 % of population will have been obese. Furthermore, the prevalence of severe obesity (BMI >40 kg/m^2), which was 5 % of adults in 2010, is growing much faster than that of moderate obesity and will increase in prevalence to 11 % by 2030 [2]. It is difficult to establish main cause of weight gain, but firstly it is strictly related to imbalance

between energy intake and expenditure. We can also consider other causes including ethnicity, social status, genetic predisposition, and region [3].

Obesity is not only a medical condition, but major risk factor of chronic diseases (including cardiovascular disease, type 2 diabetes mellitus (T2DM), musculoskeletal disorders, and some types of neoplastic disease), and also an essential economic problem. It accounts for 2 %–10 % of national healthcare expenditures in the United States and Western Europe countries [4].

Where does "obesity-induced hypertension" come from?

Obesity (especially visceral type), increases the risk of arterial hypertension (as it is present in 78 % of hypertensive men and 65 % hypertensive women) [5,6]. The risk of hypertension in obese adults is 2–3 times higher, and in obese children even 7 times higher than in normal-weight individuals. Moreover, obese subjects display higher BP levels than non-obese individuals even in normotensive range.

The pathophysiology of obesity-associated hypertension is complex, including the following mechanisms: activation of the sympathetic nervous (stimulated by hyperleptinemia and hyperinsulinemia) and renin–angiotensin–aldosterone systems, endothelial dysfunction (induced by high level of free fatty acids and adipokines), and impaired renal-pressure natriuresis associated with reduced level of atrial natriuretic peptide [7,8,9]. Additionally, obesity raises blood pressure by physical compression of the kidney, especially when visceral obesity is present. According to Framingham study, an increase in body weight only by 10 % over the ideal one results in an increase in systolic blood pressure by 6.5 mm Hg, an increase in cholesterol serum level by 12 mg/dl and an increase in glucose serum level by 2 mg/dl. Additionally, is usually associated with the need for an increased number of antihypertensive medications and an increased likelihood of never reaching blood pressure control [10].

Characteristics of obesity-induced hypertension

In obesity there are observed some characteristic hemodynamic changes, like increased tissue blood flow (as the extra adipose tissue needs and additional blood supply) and increased extracellular fluid volume.

Those two factors result in increased cardiac output and increased heart rate which in turn lead to left ventricule remodeling resulted in increased left ventricule mass (LVM). Additionally, increased LVM impairs both systolic and diastolic heart function, as well as increases the risk of arrhythmias and sudden cardiac death [11].

Obesity-induced hypertension has some characteristic features, such as higher prevalence of proteinuria, increased salt sensitivity, higher prevalence of orthostatic (postural) hypotension, absence of a nocturnal BP decrease, as well as higher prevalence of isolated systolic hypertension [11].

All those factors mentioned above may potentially cause hypertension resistant to the treatment.

Basic rules of blood pressure measurement (usually forgotten)

The measurements must be taken on the left arm, 1h after waking up in sitting position after 2-minute rest. One should never forget that the selection of an appropriate sphygmomanometer cuff size is essential, as the smaller cuff size the higher blood pressure. If the arm circuit is 35–44 cm, the cuff width and length should be16 cm and 38 cm, respectively.

However, cuff width and length of 20 cm and 42 cm, respectively, should be used when arm circuit equals 45–52 cm. Additionally evaluation of blood pressure control should not be based solely on measurements taken in doctors' offices, after one single measurement of blood pressure. It was proved, that single measurement taken in doctors 'offices overestimates blood pressure in 28 % of patients, previously misclassified as resistant, because of the components of stress accompanying the patient when in contact with medical staff (so called "white coat" hypertension) [12]. That is why „the gold standard" in diagnosing arterial hypertension is ABPM (ambulatory blood pressure monitoring) [13].

Management of hypertension

The treatment of hypertension consists of both non-pharmacological and pharmacological one.
The first should include normalization of body weight, diet modification (low salt and alcohol intake), increased physical activity, and smoking cessation. The most common mistakes that are made are both non-use of non-pharmacological treatment and its discontinuation when starting pharmacotherapy.

When discussing pharmacological treatment, five classes of antihypertensive drugs: diuretics, calcium-channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor antagonists type 1 (ARBs), and β-adrenergic receptor antagonists (β-blockers) are recommended for monotherapy in the treatment of hypertension [14]. It is now emphasized that β-blockers should not be used as the first-line treatment in patients with metabolic syndrome and those at high risk of developing diabetes without other indications. The recommendations also allow the use of lower doses of 2 antihypertensive drugs for the initial treatment of patients with severe hypertension. A combination of a β-blocker and diuretic was removed from the guidelines as the recommended therapy [15].

Even though we have a wide spectrum of drugs and combined antihypertensive therapy is frequently implemented, the effectiveness of hypertension treatment is poor, both in Poland and abroad [16,17,18]. According to Sharma et all, less than 20 % of all patients with elevated BP have well-controlled BP [19]. It is suggested, that among many possible causes, the inadequate antihypertensive regimen is the major reason for

poor BP control [20]. Other factors limiting the proper blood pressure control are: poor compliance, inappropriate drug selection, fluid retention, and secondary hypertension [21].

When discussing antihypertensive therapy, one should remember that monotherapy is less effective than combined one (mean decrease in both systolic and diastolic BP by10/6 mmHg and 18/10 mmHg, respectively) [22]. In the study performed by Żak-Gołąb et al. [23], in the group of 10880 patients observed, ACEIs (40.8 %), β-blockers (21.5 %), ARBs (13.2 %), CCBs (Calcium Chanel Blockers) (13.2%), diuretics (7.7 %), and α-blockers (3.2 %) were used in monotherapy. A total of 69.2% of the patients were prescribed combined antihypertensive treatment, typically including 2 (33.6 % of the respondents) or 3 drugs (25.7 %). A simultaneous use of up to 7 drugs was reported in a small subset of patients. Two-drug combinations usually included an ACEI with β-blocker (26.5 % of the respondents), diuretic (20.9 %), or CCB (8.2 %). A combination of β-blocker with diuretic was prescribed in 7.4 % of the patients. However, it must be pointed out that patient's adherence is „drug-dependent" – slightly above 20 % compliance is observed in patients treated with 8 pills daily [24].

Pharmacotherapy (both mono-, dual or polytherapy) in obese patients should have an influence on volemia, as it is believed that impaired response to antihypertensive drugs in obesity is due to the excessive salt intake (increased volemia). Additionally, in obesity lower serum levels of active forms of drugs are observed when standard doses are used (in other words – obese patients need higher dosage). Moreover, due to the absence of „dipping", long acting calcium channel inhibitors should be used in the evening.

Another common problem in the treatment of obese patients is, that they are commonly treated in contrary to current recommendation. Żak-Gołąb et al. [23] observed the common use of β-blockers in combination with diuretics (7.4 %), which has not been recommended since the results of the ASCOT study had been published in 2005 [25]. What was even more important, 71 % of the patients receiving a β-blocker with diuretic had no clear indication for such regimen (as many as 87.1 % of the patients receiving β-blocker did not have a history of myocardial infarction or revascularization). These drugs were more commonly prescribed in normal-weight women with higher education. The study demonstrated that such combination is less effective than that of an ACEI with (CBB) in the prevention of adverse cardiovascular events. On the other hand, the combination of a β-blocker and CCB, which had been recommended for many years, constituted only 1.5 % of the patients on double therapy, and the combination of ARB and diuretic (2.9 %) also showed limited popularity among practitioners. To summarize, the most common mistake in the regimen of obesity-induced hypertension are the non-use of diuretics (regardless of volemia), suboptimal drug combination and under-dosing. However, on the other hand, it has to be remembered, that effective treatment, that let us achieve the appropriate blood pressure control, is more important than the type of drugs used.

In summary, when treating patients with obesity-induced hypertension, we should remember the following:

- Non-pharmacological treatment is at least as important as pharmacological one
- Diuretics cannot be avoided in hypertensive treatment in obese patients (see: high salt sensitivity)
- Drug dosage must be adjusted for a particular patient
- Due to the absence of „dipping", long acting calcium channel inhibitors should be used in the evening
- β-blockers (with combination with diuretic) should be used primarily in patients with coronary artery disease and heart failure

Learning points

- Educating and encouraging patients to measure their own BP measurements is essential, as it allows a more accurate judgment on the effectiveness of treatment.
- There should be no delay in adding diuretics to multiple drug regimens in hypertensive patients with visceral obesity.
- The use of diuretics in multiple drug regimens may spare an unnecessary number of anti-hypertensive drugs.
- Severe obesity (>35 kg/m2) increases the risk of resistant hypertension.

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