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Analysis of arterial hypertension pharmacotherapy in patients with obstructive sleep apnea syndrome

Milan Sova [a,*], Eliska Sovova [b], Milada Hobzova [a], Karel Urbanek [c], Jana Zapletalova [d], Monika Kamasova [b], Denisa Barinova [e], Barbora Gottfriedova [e], Irena Kuca [f], Vitezslav Kolek [a]

[a] Department of Respiratory Medicine, Faculty of Medicine and Dentistry, Palacky University and University Hospital Olomouc, Czech Republic
[b] Department of Internal Medicine I – Cardiology, Faculty of Medicine and Dentistry, Palacky University and University Hospital Olomouc, Czech Republic
[c] Department of Pharmacology, Faculty of Medicine and Dentistry, Palacky University Olomouc, Czech Republic
[d] Department of Biophysics, Faculty of Medicine and Dentistry, Palacky University Olomouc, Czech Republic
[e] Faculty of Medicine and Dentistry, Palacky University Olomouc, Czech Republic
[f] Saba University School of Medicine, Saba, Dutch Caribbean, Netherlands

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ABSTRACT

Introduction: Obstructive sleep apnea (OSA) is often connected with arterial hypertension and it could also be a cause of secondary hypertension. Treatment of arterial hypertension and optimal blood pressure level are important for prevention of cardiovascular complications. It is not well known how to treat patients with OSA and arterial hypertension. Also many patients with OSA suffer from metabolic syndrome which worsen their prognosis.
Aim: The aim of our study was to assess arterial hypertension compensation in patients with metabolic syndrome and moderate to severe OSA and to analyze used pharmacotherapy.
Materials and methods: 85 hypertensive patients (75 men) with metabolic syndrome, average age 53.6 ± 9.3 years, were evaluated using overnight sleep study with diagnosis of OSA, average apnea–hypopnea index (AHI) 56.3 ± 23. Patients underwent 24 h ambulatory blood pressure monitoring (ABPM) and their current pharmacotherapy data were obtained. Appropriate combinations of antihypertensive drugs (patients with metabolic syndrome) were derived from ESH/ESC 2013 guidelines.
Results: Arterial hypertension was well compensated in only 11.8% of the patients. 24.7% patients were treated according to current guidelines. Fisher's exact test with analysis of adjusted residues has found higher rate of blood pressure subcompensation in patients treated with triple+ combination of drugs ($p = 0.035$, 51.4% vs 10%).
Conclusion: Only a small number of patients had optimal blood pressure level and were treated according to current ESH/ESC guidelines. We have to constantly appeal to all physicians to perform ABPM in patients with OSA.

* *Corresponding author at*: Department of Respiratory Medicine, Faculty of Medicine and Dentistry, Palacky University Olomouc and University Hospital Olomouc, I.P. Pavlova 6, 77900 Olomouc, Czech Republic. Tel.: +420 737170392.
E-mail address: milan.sova@email.cz (M. Sova).
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Introduction

Obstructive sleep apnea (OSA) is classified as a sleep breathing related disorder [1]. This disorder is affecting approximately 2–4% of adult population [2] and it represents many risks that could influence morbidity and mortality of patients. OSA is characterized by a presence of more than 5 apneic or hypopneic pauses (at least 10 s in duration) per hour of sleep. Typical symptoms are snoring with apneic pauses and an increased daytime sleepiness as a consequence of repeated microarousals and sleep fragmentation. Patients are often complaining about microsleeps and falling asleep during monotone activities. Patients also suffer from diminished concentration, impaired memory, decrease of intellectual capacities and depression. They feel tired during the morning, polyuria and night sweating are present and sexual dysfunction is also more frequent [1].

During the last few decades of intensive research it was found that the prevalence of OSA is higher in patients with arterial hypertension (30–83%), with heart failure (12–53%), with ischemic heart disease (30–58%) and with cerebrovascular disorders (43–91%) [3].

Arterial hypertension is one of the most potent risk factors for cardiovascular diseases. 50% of the patients with OSA also have arterial hypertension and 30% of hypertensive patients suffer from OSA [4]. In OSA patients, arterial hypertension usually has a characteristic of so-called non-dipper type of arterial hypertension [5,6]. In patients with resistant hypertension, OSA is present in up to 83% of the patients [7]. Masked hypertension (MH) is defined as a blood pressure level that is higher during home measurement (24 h blood pressure monitoring (ABPM) or self monitoring) than casual blood pressure level measured in the office [8,9]. An arbitrary threshold of masked hypertension has been defined as blood pressure level during the day >135/85 mmHg measured by ABPM [9]. The prevalence of masked hypertension in general population is estimated to be 10–25% [9–11]. Presence of masked hypertension possibly means worst patient's prognosis [8]. Controversial remains the fact that mere assessment of blood pressure during the day does not detect nocturnal hypertension which then remains unrecognized. Mainly in patients with OSA the prevalence of nocturnal hypertension can be high and it can worsen prognosis of these patients. Only sporadic papers about prevalence of masked hypertension in patients with OSA exist [12–14].

It is not well known, how to treat patients with OSA and arterial hypertension. Few guidelines dealing with this problem have been published (2013 ESH/ESC Guidelines for the management of arterial hypertension [15] and Recommendation for the management of patients with obstructive sleep apnoea and hypertension (2013)) [16], but even in these guidelines is not stated if the pharmacotherapy of arterial hypertension should be modified with respect to obstructive sleep apnea. In the literature, we have found only one paper which was evaluating medication in these patients [17]. Here Nerbass et al. in a group of 186 patients showed that 37% patients were treated with ACEi, 35% with beta-blocking agents, 32% with ARB, and 21% with CCB.

Many patients with OSA also suffer from metabolic syndrome (MS). Coughlin et al. have found up to 9.1 times higher risk of metabolic syndrome development in OSA patients when compared with control group [18]. Treatment of arterial hypertension in patients with metabolic syndrome is well defined in current guidelines. The treatment should start with angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs). It is also possible to use a combination of these drugs together with calcium channel blockers (CCBs). We chose this group of patients because treatment of arterial hypertension is well defined in this group.

The aim of our study was to assess blood pressure compensation in these patients with MS and moderate to severe OSA and to analyze used pharmacotherapy.

Materials and methods

Into this study were consecutively enrolled 85 patients (75 men) with arterial hypertension diagnosed according to current guidelines [15], average age 53.6 ± 9.3 years with diagnosis of metabolic syndrome according to American Heart Association [19] and with OSA (average apnea–hypopnea index 56.3 ± 23) newly diagnosed by standard overnight polysomnography (Alice 5, Respironics, USA or Miniscreen, F+G, Germany). Recordings were manually rescored by an experienced physician with appropriate certification issued by national sleep medicine society. Standard definitions of apnea (flow cessation >10 s) and hypopnea (flow limitation >50% and blood oxygen saturation decrease >3%) were used. Apneas were classified as obstructive, mixed and central according to the presence or absence of respiratory efforts. Following parameters of sleep apnea syndrome were further analyzed – apnea–hypopnea index (AH), oxygen desaturation index (ODI), average night blood oxygen saturation (SpO_2), and percentage of sleep time when SpO_2 <90%.

We performed physical examination including blood pressure measurement according to ESH/ESC 2013 [15] guidelines using standard sphygmomanometer which was regularly calibrated. We have measured anthropometric parameters such as body mass index (BMI = patients weight (kg)/patients height $(m)^2$), and waist, neck and hip circumference. Patients filled Epworth sleepiness scale questionnaire. Ambulatory blood pressure measurement was performed using Spacelabs (Spacelabs Healthcare) device before OSA treatment was started. Following arbitrary values were defined as targets: mean measured blood pressure (mBP) 130/80 mmHg for 24-h interval; mBP 135/85 mmHg during daytime and mBP 120/70 mmHg during night [20].

Patient's pharmacotherapy data were obtained and equivalent doses of chosen substances were calculated using Food and Drug Administration data.

Recommended therapeutic regimes (patients with hypertension and MS) were derived from current European Society of Hypertension/European Society of Cardiology 2013 guidelines [15]. As a first line treatment authors recommended angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB). These two groups of treatment were combined into one group (A) because of easier results reproducibility and because of their similar pharmacokinetic and pharmacodynamic properties. As a second line treatment, the guidelines recommend calcium channel blocker (CCB).