International Journal of Cardiology 202 (2016) 67–72

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Effect of beta-blocker therapy on heart rate response in patients with hypertension and newly diagnosed untreated obstructive sleep apnea syndrome☆

Jacek Wolf [a,c,*], Jacek Drozdowski [b], Krzysztof Czechowicz [a], Paweł J. Winklewski [e,**], Ewa Jassem [b], Tomas Kara [c,d,f], Virend K. Somers [d], Krzysztof Narkiewicz [a]

[a] Department of Hypertension and Diabetology, Medical University of Gdańsk, Gdańsk, Poland
[b] Department of Pneumonology and Allergology, Medical University of Gdańsk, Gdańsk, Poland
[c] Department of Cardiovascular Diseases, International Clinical Research Center, St. Anne's University Hospital in Brno (FNUSA), Brno, Czech Republic
[d] Divisions of Cardiovascular Diseases and Hypertension, Mayo Clinic, Rochester, MN, USA
[e] Institute of Human Physiology, Medical University of Gdańsk, Gdańsk, Poland
[f] Department of Cardiology, University Hospital Olomouc, Czech Republic

ARTICLE INFO

Article history:
Received 16 April 2015
Received in revised form 16 August 2015
Accepted 19 August 2015
Available online 21 August 2015

Keywords:
Beta-blockers
Obstructive sleep apnea
Heart rate control
Bradycardia
Tachycardia

ABSTRACT

Background: Beta$_1$-receptor antagonists (BBs) are commonly administered in the treatment of cardiovascular disease (CVD). The reported benefits of BB use in CVD patients with concomitant obstructive sleep apnea (OSA) may be limited by their impact on apnea-induced bradycardias. Therefore the aim of the study was to test the influence of BBs on periapneic heart rate (HR) fluctuations in hypertensive patients with newly-detected and untreated OSA.

Methods: We studied 88 hypertensive patients (56 on BBs and 32 BB naive) with newly-diagnosed moderate-to-severe OSA who were free of major pulmonary comorbidities and did not require antiarrhythmic therapy. ECGs recorded during sleep were investigated for heart rate (HR) responses to apneas allowing to compare extreme HR accelerations and decelerations between the groups.

Results: Average sleep-time HR was comparable in BB-naive (BB−) and BB-treated (BB+) patients. Direct comparisons showed that HR decelerations were also similar in the two subgroups (53.8 ± 9.6 vs. 54.4 ± 7.8 bpm; P = 0.78, for BB− and BB+, respectively) however, BBs blunted the OSA-induced HR accelerations (82.3 ± 12.2 vs. 74.3 ± 10.0; P = 0.003). After adjusting for baseline HR and magnitude of desaturations, HR decelerations were more evident in BB-naive group whereas tachycardic responses remained blunted in the BB+ group. The incidence of ectopies and conduction abnormalities were comparable across two groups.

Conclusions: Beta-blockers do not potentiate apnea-induced HR decelerations, attenuate apnea-induced increases in heart rate and do not influence incidence of ectopies and conduction abnormalities in patients with hypertension and moderate-to-severe, untreated OSA.

© 2015 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Beta$_1$-receptor antagonists (beta-blockers; BBs) are commonly administered in the treatment of a broad spectrum of cardiovascular diseases (CVD). Large clinical trials showed that irrespective of co-morbidities, 47% [1] to 57% [2] of all treated hypertensive patients receive BBs on a regular basis. However, the role of BBs in the management of hypertensive OSA patients is unclear. Previous studies in patients with OSA report a superiority of BB therapy as a treatment modality for autonomic imbalance and cardiovascular abnormalities commonly seen in these patients [3,4]. Much less is known about the effects of BBs on night-time HR and arrhythmias.

Physiologically, apnea triggers powerful and differentiated co-activation of the sympathetic (SNS) and parasympathetic (PNS) branches of the autonomic nervous system leading to marked peripheral vasoconstriction, and bradycardia. Although SNS/PNS co-activation may potentially increase the risk for arrhythmias [5], apparently the overall benefits of this co-activation outweigh the potential risk. In OSA subjects, each sleep disordered breathing episode may itself evoke reflex

Abbreviations: AHI, apnea–hypopnea index; BBs, beta-blockers; BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; CHF, congestive heart failure; CPAP, continuous positive airway pressure; CVD, cardiovascular disease; HR, heart rate; OSA, obstructive sleep apnea; REM, rapid eye movement sleep; SpO2, mean blood oxygen saturation; T90, cumulative time with blood oxygen saturation below 90%; TIA, transient ischemic attack.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Correspondence to: J.Wolf, Debinki str. 7C, 80-952 Gdańsk, Poland.
** Correspondence to: P.J. Winklewski, Institute of Human Physiology, Medical University of Gdańsk, Gdańsk, Poland.
E-mail address: lupus@gumed.edu.pl (J. Wolf).

http://dx.doi.org/10.1016/j.ijcard.2015.08.139
0167-5273/© 2015 Elsevier Ireland Ltd. All rights reserved.

bradycardia and tachycardia [6–9], as well as frequent bradyarrhythmias [10,11], which might conceivably be potentiated by the negative chronotropic effects of beta-blockade.

In the absence of CPAP, marked increases in heart rate (HR) and cardiac afterload, in the setting of severe hypoxemia, may trigger episodic cardiac ischemia [12] or even infarction [13]. Hence, BBs may mitigate acute neural circulatory responses to obstructive apneas. However, there is a concern that their negative chronotropic effects may potentiate the severity of the acute bradyarrhythmic responses to apnea.

To our knowledge, the effect of BBs on apnea-related cardiac responses has never been systematically studied. We hypothesized that BBs may diminish SNS driven reflex HR acceleration episodes in OSA subjects. Concurrently, we speculated that when PNS driven bradycardia prevail, BB influence might be limited, as the SNS is already effectively blocked by powerful vagal activation.

2. Material and methods

We studied 88 consecutively recruited hypertensive patients screened for OSA at the Medical University of Gdańsk Hospital (Hypertension and Diabetology Clinic, and Pneumonology and Allergology Clinic) in 2009 (Fig. 1). All experimental procedures were performed in accordance with the Declaration of Helsinki on the treatment of human subjects and the Ethical Committee of the University of Gdansk approved the study (NKEBN/48/2011). Informed written consent was obtained from each subject.

2.1. Sleep data

The polygraphic recordings (Embletta X30, X100™) were reviewed and scored according to standard rules [14]. Only apneas and hypopneas (≥30% reduction in the amplitude of airflow) were analyzed if accompanied with ≥4% oxygen desaturations compared to pre-event baseline. The respiratory events included in the analyses were 10 s long at minimum. AHI was defined as the average number of apneas plus hypopneas per hour of study.

2.2. Exclusion criteria

Exclusion criteria were as follows: AHI < 15; other than obstructive sleep-disordered breathing e.g., predominantly central sleep apnea; Cheyne–Stokes respiration during sleep; hypoventilation syndromes; implanted cardiac pacing devices; arrhythmias without evident relation to sleep disordered breathing episodes (sustained supra-, and ventricular arrhythmias incl. atrial fibrillation, sustained 2° or 3° atrio-ventricular block); moderate or severe bronchial asthma or chronic obstructive pulmonary disease (COPD); ongoing therapy with negative chronotropic agents other than BBs including non-dihydropyridine calcium channel blockers (verapamil, diltiazem), ivabradine, digoxin and amiodarone; ongoing treatment with antiarrhythmic agents i.e. sodium channel blockers. ECG signal loss. Following these criteria we excluded 62 patients (Fig. 1).

2.3. Group dichotomization

Patients were assigned to 2 groups with regard to whether or not BB treatment was administered. The distribution of specific BBs was random and reflected the actual distribution of BB use in patients with hypertension in our Center (bisoprolol, n = 24; metoprolol, n = 20; betaxolol, n = 10; carvedilol, n = 2). All patients with coronary artery disease (CAD) and heart failure received beta-blockers.

2.4. ECG analysis

Final analysis was based on ECG tracings (CM5 lead, sampling frequency; f = 200 Hz) extracted from polygraphic studies of 88 eligible patients. As we sought to analyze extreme cardiac responses, we selected and averaged the 50 fastest reflex HR accelerations and 50 slowest reflex HR decelerations associated with apneas/hypopneas from each sleep study. Technically, the raw ECG data along with respiratory channels were exported to the MATLAB-based software (written by K.Cz.), which automatically calculated all associated sinus HR acceleration, and deceleration events. The exact evaluation window for each HR deceleration (longest RR-intervals) assessment was set between the onset of the apnea/hypopnea to the moment of the resumption of breathing (Fig. 2). Similarly, the apnea-related HR acceleration response was analyzed as the shortest RR intervals recorded immediately after the termination of breathing event but no later than the corresponding desaturation nadir (Fig. 2). The average of three RR interval values clustered with extremes entered the analyses. All cardiac responses were manually reviewed (J.W.) and uploaded to the statistical package. Manual reviewing also allowed for artifact exclusion and capturing ectopies such as supra-, and ventricular extrabeats, non-sinus rhythms, atrioventricular blocks, and pauses. If the electrical impulse conduction impairment and/or ectopy occurred the event was classified either as brady-, or tachyarrhythmia, and was excluded from all sinus HR swing analyses.

2.5. Statistical analysis

Statistical tests were computed using Statistica 10.1, Statsoft Inc.®. Skewed data distributions were logarithmically corrected before analyses when appropriate. Descriptive variables were presented as means ± SD or medians (IQR). Chi-squared test (with Yates correction when appropriate) was used to compare co-morbidities, arrhythmia frequencies, and male-to-female ratios. Unpaired, two-tailed t-tests were used to compare continuous variables between two groups, with and without BB treatment. An analysis of covariance (ANCOVA) was performed to assess the differences in periapneic cardiac responses. $P < 0.05$ was considered significant for all calculations.

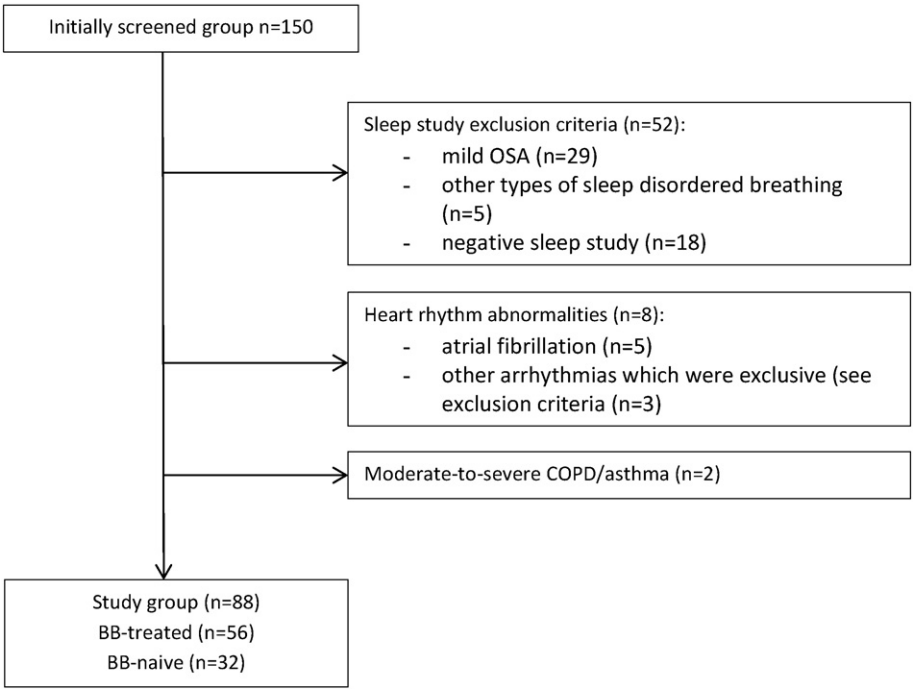

Fig. 1. Study flow-chart.

Download English Version:

https://daneshyari.com/en/article/5965347

Download Persian Version:

https://daneshyari.com/article/5965347

Daneshyari.com