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Original Article

Comparison of peak oxygen consumption in patients with idiopathic hypertension treated with beta-blockers and other antihypertensives

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ABSTRACT

Objective: To investigate whether the use of beta-blockers (β-blockers) in patients with idiopathic hypertension compromises exercise performance.
Materials and Methods: Retrospectively, patients with well-controlled hypertension, who had received cardiopulmonary exercise testing (CPET) and pulmonary function testing, were consecutively enrolled. Their medical histories were reviewed. They were grouped into those receiving β-blockers and those receiving other antihypertensives. The heart rate (HR), blood pressure, oxygen consumption ($\dot{V}O_2$), oxygen pulse, ventilatory anaerobic threshold, and respiratory exchange ratio were measured during CPET. The forced vital capacity and forced expiratory volume in 1 second were also collected from pulmonary function testing. Peak values of the CPET indices were compared between the two groups for each index separately by the Mann-Whitney *U* test. A *p* value less than 0.05 was considered statistically significant.
Results: No significant differences were observed in basic characteristics, such as age (59 ± 9 years *vs.* 62 ± 9 years), and peak oxygen pulse (11 ± 3 *vs.* 11 ± 4), between the groups receiving β-blockers and other antihypertensives, respectively. Their resting systolic pressures were well controlled under antihypertensive medication (114 ± 13 mmHg *vs.* 118 ± 19 mmHg). A significantly lower maximal HR and maximal systolic blood pressure during peak exercise was observed in the β-blocker group compared with those in the other group (129.5 ± 17.0 beats/min *vs.* 146.1 ± 18.3 beats/min, $p = 0.008$, and 159.0 ± 22.2 mmHg *vs.* 172.6 ± 29.8 mmHg, $p = 0.028$, respectively). The exercise capacity of the β-blocker group was reduced, as shown by a lower measured peak $\dot{V}O_2$/predicted peak $\dot{V}O_2$ ($\dot{V}O_2$%) (84.2% ± 9.6% *vs.* 96.2% ± 14.6%, $p = 0.003$) and a higher exercise heart rate reserve percentage (19.8% ± 10.3% *vs.* 7.8 ± 10.3%, $p = 0.001$).
Conclusions: The maximal HR, systolic blood pressure during peak exercise, and $\dot{V}O_2$% were lower, whereas the exercise heart rate reserve percentage was greater in patients treated with β-blockers than in those taking other antihypertensives.

1. Introduction

Hypertension is one of the most important independent risk factors of cardiovascular disease. Patients with a blood pressure (BP) greater than 110/75 mmHg have been shown to have increased risks of mortality and morbidity [1]. The most widely used antihypertensive agents are beta-blockers (β-blockers), thiazide diuretics, calcium channel blockers (CCB), angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin II receptor antagonists (ARBs). β-Blockers are only recommended for the initial treatment of heart failure, a history of coronary heart disease, or a hyperadrenergic state [2]. Regular aerobic exercise of moderate intensity can not only lower mean systolic BP (SBP) by 6.9 mmHg and mean diastolic BP by 4.9 mmHg [3,4], but also achieve weight loss, enhance the sense of well-being, improve functional health status, and reduce the risk of cardiovascular disease [5]. β-Blockers are supposed to diminish myocardial contractility and attenuate the heart rate (HR) responses to dynamic exercise. Prior studies [6–8]

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have compared the use of β-blockers with a single agent (CCBs, alpha-blockers, ACEIs) on exercise performance in physically active or general hypertensive populations. Most studies revealed that patients on β-blockers achieved a lower maximal HR and maximal SBP. The maximal work rate and maximal oxygen consumption ($\dot{V}O_{2max}$) were significantly lower in patients on β-blockers than those taking ACEIs. However, in clinical treatment, combination therapy is often needed for adequate control of BP. The aim of this study was to compare whether the use of β-blockers in addition to other antihypertensive regimens during exercise influences $\dot{V}O_{2max}$, the BP response, and exercise capacity in sedentary patients with idiopathic hypertension.

2. Materials and methods

2.1. Participants

Participants were recruited retrospectively from another study "Cardiopulmonary Exercise Testing (CPET) in Patients with Preclinical Diastolic Ventricular Dysfunction." From March 2010 to April 2011, patients with idiopathic hypertension, 45–70 years old, under regular antihypertensive treatment, with a well-controlled BP, defined as an SBP less than 140 mmHg and a diastolic pressure less than 90 mmHg for more than 1 month, were enrolled consecutively. All patients received CPET and pulmonary function testing.

Patients were excluded from the study if they had (1) clinical evidence of respiratory disease, including chronic obstructive pulmonary disease, cor pulmonale, parenchymal lung disease, or restrictive lung disease; (2) significant valvular heart disease, arrhythmia, or history of any thoracic surgery; (3) congenital anomalies; (4) recent history of symptomatic myocardial ischemia or exercise-induced myocardial ischemia; (5) anemia (hemoglobin < 10 g/dL); (6) inability to exercise on a cycle ergometer for other reasons (e.g., neurologic or orthopedic diseases); (7) a disease that made exercise risky, for example, suspicion of aortic dissection, aortic aneurysm, cerebral artery aneurysm, deep vein thrombosis, exercise-induced asthma, hyperthyroidism, or history of syncope; or (8) an insufficient ventricular ejection (<50%) proven by echocardiography or a myocardial nuclear scan. Patients were divided into two groups: those who used β-blockers and those who used other antihypertensives, including thiazide diuretics, CCBs, ACEIs, and ARBs.

2.2. Cardiopulmonary exercise testing

CPET was performed with a cycle ergometer (MasterScreen CPX; Cardinal Health, Germany 234 GmbH, Hoechberg). Gas exchange (breath by breath), ventilation, electrocardiography, BP, and oxyhemoglobin saturation by pulse oximetry were recorded during the entire exercise test, which included resting for 3 minutes, unloaded pedaling at a cycling speed of 60 rpm for 3 minutes, an incremental exercise test to symptom-limited maximum, and then a recovery phase for 3 minutes. The work rate increment per minute was estimated according to Wasserman et al's formula [9] in an attempt to keep the total incremental exercise time to about 10 minutes.

The indications for terminating exercise testing were (1) a fall in SBP or mean BP greater than 10 mmHg; (2) development of a significant arrhythmia; (3) EKG readings of an ST segment depression of 3 mm or greater; or (4) inability to maintain a cycling frequency greater than 40 rpm.

The measured data in the testing included (1) the electrocardiogram and HR; (2) BP at baseline and during each exercise step; (3) ventilatory gas exchange; (4) oxygen pulse ($O_2P = \dot{V}O_2/HR$); (5) ventilatory anaerobic threshold, defined as the $\dot{V}O_2$ (mL/min) at the time the respiratory exchange ratio = 1; (6) $\dot{V}O_{2max}$, which was the highest oxygen uptake achieved; and (7) the maximal exercise ventilation. The percent of predicted oxygen consumption ($\dot{V}O_2\%$) is used to compare the tested peak $\dot{V}O_2$ in healthy sedentary individuals. The calculation of the predicted peak $\dot{V}O_2$ for healthy sedentary men or women was done according to Wasserman et al's formula [9]. The HR reserve (HRR) was estimated by the predicted maximal HR (calculated by 220 − age) minus the maximal HR during peak exercise. We calculated the exercise heart rate reserve percentage (ExHRR%) as the percentage of HRR divided by the predicted maximal HR.

2.3. Pulmonary function testing

Pulmonary function testing was conducted by a trained therapist. We collected the forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) at rest before exercise and the maximal voluntary ventilation. Other spirometry data were collected according to American Thoracic Society standards.

2.4. Statistical analysis

Continuous variables are presented as mean ± standard deviation. The Mann-Whitney *U* test was used to compare the two groups for each index separately. A *p* value less than 0.05 was considered statistically significant. All statistical analyses were performed with SPSS (version 18.0; SPSS Inc., Chicago, IL, USA). We used the software, Power and Sample Size Calculations version 3.0.43 to examine the power of our study.

3. Results

A total of 45 patients were recruited in this study and were divided into two groups: those taking β-blockers and those taking other antihypertensives. The basic characteristics and medications used by the patients during the study are listed in Tables 1 and 2. Twenty-six patients were treated with a single agent (eight received β-blockers only), 11 patients received two antihypertensive medications, and eight patients had three medications. In both groups, ARBs and diuretics were the most-often-combined medications, whereas ACEIs were less prescribed.

The mean age of the β-blocker group was 58.6 ± 9.4 years ($n = 22$), and the other group was 61.9 ± 9.4 years ($n = 23$). Patients were overweight (body mass index > 24 kg/m^2) in both groups. The mean predicted $\dot{V}O_2$ values in the two groups were almost the same (1653.5 ± 447.5 mL/min *vs.* 1625.2 ± 455.2 mL/min, respectively, $p = 0.699$). The mean SBP values at rest were normal and

Table 1
Baseline characteristics

Characteristics	β-Blockers	Other antihypertensive regimen	*p*
n (%) (female)	22 (59)	23 (52)	
Age (y)	58.6 ± 9.4	61.9 ± 9.4	0.111
Height (cm)	160.8 ± 8.6	162.4 ± 7.9	0.467
Weight (kg)	70.5 ± 14.3	70.3 ± 11.3	0.811
Body mass index (kg/m^2)	27.1 ± 4.3	26.6 ± 3.2	0.856
Predicted $\dot{V}O_2$ (mL/min)	1653.5 ± 447.5	1625.2 ± 455.2	0.699
Maximal exercise ventilation (L)	50.1 ± 16.9	58.1 ± 15.7	0.066
Systolic blood pressure at rest (mmHg)	114.6 ± 13.3	118 ± 19.4	0.768
FEV1 (%)	95.8 ± 14.4	90.2 ± 13.4	0.168
FVC (%)	94.8 ± 13.3	93.6 ± 14.6	0.793
FEV1/FVC (%)	86.5 ± 10.0	88.4 ± 15.9	0.952

Data are expressed as *n* (% of female) or mean ± standard deviation.
FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity.

Table 2
Patient medications

Type	β-Blockers	Other antihypertensive regimen
β-Blockers	22 (100)	0
Angiotensin II receptor antagonists	9 (41)	15 (65)
Angiotensin-converting enzyme inhibitors	3 (14)	2 (9)
Diuretics	9 (41)	15 (65)
Calcium channel blockers	5 (23)	6 (26)

Data are presented as number (percent of total).

comparable between the two groups (114.6 ± 13.3 mmHg *vs.* 118 ± 19.4 mmHg, respectively), which may indicate similar effects in control of hypertension under current medication. The parameters for pulmonary function testing, such as the maximal exercise ventilation, FEV1%, FVC%, and the percent of FEV1/FVC, revealed no other intrinsic factor that would interfere with exercise capacity in our participants.

The mean $\dot{V}O_{2max}$ values in the two groups were similar (1371.5 ± 314.1 mL/min *vs.* 1578.9 ± 544.5 mL/min, $p = 0.34$). The mean achieved $\dot{V}O_2$% was significantly lower in the β-blocker group than that in the other group ($84.2\% \pm 9.6\%$ *vs.* $96.2\% \pm 14.6\%$, $p = 0.003$). There were also significant differences in the mean HR and SBP during peak exercise (129.5 ± 17.0 beats/min *vs.* 146.1 ± 18.3 beats/min, $p = 0.008$, and 159.0 ± 22.2 mmHg *vs.* 172.6 ± 29.8 mmHg, $p = 0.028$, respectively) between the two groups. Patients carried out about the same workload during peak exercise (102.0 ± 31.9 W *vs.* 120 ± 49.6 W, $p = 0.269$). The ExHRR% was greater in the β-blocker group than that in the other group ($19.8\% \pm 10.3\%$ *vs.* $7.8\% \pm 10.3\%$, respectively, $p = 0.001$). There were no significant differences in breathing reserve or peak O_2P (Table 3).

4. Discussion

The present study demonstrated that hypertensive patients treated with β-blockers presented with a lower HR, SBP, and $\dot{V}O_2$% during maximal exercise, but a greater ExHRR% than those taking other antihypertensives.

The HR_{max} of the β-blocker group was significantly lower, whereas the ExHRR% was greater than that of the other group. Cardiac output (CO) is a product of the HR and stroke volume. At low exercise intensities, CO increases chiefly because of an increased stroke volume, but at higher intensity levels, it increases mainly because of an increased HR. The relationship of exercise intensity with CO is essentially linear [10]. Fahrenbach et al compared the effects of atenolol and doxazosin on physically active, hypertensive men and noted that atenolol reduced HR and CO at rest and during exercise and increased arteriovenous oxygen difference [6]. In our study, there was no significant difference in the peak O_2P between the two groups. We would be able to reject the null hypothesis that the peak O_2P in the β-blocker and other antihypertensives groups were equal with a probability (power) of 0.054. The use of β-blockers leads to a lower HR_{max} and greater ExHRR% than that of other antihypertensives, which would, in turn, limit the potential of patients to perform at higher exercise intensities.

Table 3
Cardiopulmonary exercise testing parameters

CPET parameters	β-Blockers	Other antihypertensive regimen	p
$\dot{V}O_{2max}$ (mL/min)	1371.5 ± 314.1	1578.9 ± 544.5	0.34
$\dot{V}O_2$ (%)	84.2 ± 9.6	96.2 ± 14.6	0.003*
Peak systolic blood pressure (mmHg)	159.0 ± 22.2	172.6 ± 29.8	0.028*
Maximal heart rate (beats/min)	129.5 ± 17.0	146.1 ± 18.3	0.008*
Peak O_2 pulse (mL/beat/min)	10.9 ± 2.9	11.1 ± 3.8	0.776
Breathing reserve (L)	41.9 ± 17.3	34.3 ± 19.6	0.173
Exercise heart rate reserve percentage (%)	19.8 ± 10.3	7.8 ± 10.3	0.001*
Maximal work rate (W)	102.0 ± 31.9	120 ± 49.6	0.269

*$p < 0.05$.

The maximal SBP during peak exercise was also lower in the β-blocker users, which was compatible with those of previous studies. Brion et al studied the exercise capacity of 96 physically active hypertensive patients treated with bisoprolol and nitrendipine for 12 weeks [7]. The antihypertensive activity of bisoprolol on peak exercise SBP was significantly greater than that of nitrendipine.

Although there was no significant difference in $\dot{V}O_{2max}$ in our study, the $\dot{V}O_2$% was significantly lower in the β-blocker group (84% *vs.* 96%). The predicted $\dot{V}O_2$ was almost the same in the two groups, and the lower $\dot{V}O_{2max}$ in the β-blocker group led to a lower $\dot{V}O_2$%, which was statistically significant. Because the $\dot{V}O_{2max}$ could be viewed as the aerobic capacity, we could predict that patients treated with β-blockers would be unable to tolerate prolonged exercise. The present study reported that when a β-blocker was used during prolonged exercise, it lowered the HR, BP, and CO [11], and increased the perceived exertion after 15 minutes of exercise [12]. Aerobic exercise of moderate intensity is recommended for at least 30 minutes a day, at least 5 days a week [13], and it is the key component in hypertension control and prognostic improvement. Houston [14] also recommended that β-blockers should be the last choice for hypertensive patients who are physically active. We suggest that physicians should monitor a patient's exercise tolerance before and after the initiation of β-blocker treatment.

There are several limitations in the present study. First, it is a retrospective study analyzing the effects of β-blockers on a cardiopulmonary exercise test. Second, our sample size was too small to display more significant differences in other exercise capacity parameters, such as the work rate and exercise duration. Third, we did not record the duration of antihypertensive treatment or the hypertension history, because it may influence the results of exercise performance. Fourth, we did not distinguish the effects of selective β-blockers from nonselective ones on exercise performance. Further research could focus more specifically on examining the differences.

5. Conclusion

In conclusion, β-blockers and other antihypertensives can achieve similar effects in lowering BP, but β-blockers limit exercise performance, as measured by the HR, SBP, and $\dot{V}O_2$%, during peak exercise. When choosing antihypertensive drugs, we would suggest agents that do not interfere with exercise capacity.

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