Response of Blood Pressure to Maximum Exercise in Hypertensive Patients under Different Therapeutic Programs

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Objective - *To evaluate the behavior of blood pressure during exercise in patients with hypertension controlled by frontline antihypertension drugs.*

Methods - *From 979ergometric tests we retrospectively selected 49 hipertensive patients (19 males). The age was 53±12 years old and normal range rest arterial pressure (≤ 140/90 mmHg) all on pharmacological monotherapy. There were 12 on beta blockers; 14 on calcium antagonists, 13 on diuretics and 10 on angiotensin converting enzyme inhibitor. Abnormal exercise behhavior of blood pressure was diagnosed if anyone of the following criteria was detected: peak systolic pressure above 220 mmHg, raising of systolic pressure ≥ 10 mmHg/MET; or increase of diastolic pressure greater than 15 mmHg.*

Results - *Physiologic response of arterial blood pressure occurred in 50% of patients on beta blockers, the best one ($p<0.05$), in 36% and 31% on calcium antagonists and on diuretics, respectively, and in 20% on angiotensin converting enzyme inhibitor, the later the leastr one ($p<0.05$).*

Conclusion - *Beta-blockers were more effective than calcium antagonists, diuretics and angiotensin-converting enzyme inhibitors in controlling blood pressure during exercise, and angiotensin converting enzyme inhibitors the least effective drugs.*

Keywords: stress test, arterial hypertension, antihypertension therapy

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The purpose of treatment of blood pressure is currently to reduce morbidity and mortality by the least invasive manner possible, which may be achieved either by changes in lifestyle, such as weight loss, exercising, reduction in sodium and alcohol intake, or by association with a pharmacological treatment [1-3].

Moderate exercise, such as walking, biking, and swimming, done regularly, has been shown to be an important ally in the reduction of blood pressure levels in hypertensive persons [3].

Ambulatory blood pressure monitoring in hypertensive patients, has showed higher the percentage of measurements above the normal values within the 24 hours (pressor load) as a result, for instance, of exercise, work, and the act of awaking greater the damage to the target organ or the incidence of medical events associated with hypertension [4]. It is therefore expected that antihypertensive drugs should be able to control blood pressure not only at rest, but also during physical activity.

Because a physical activity program is part of the treatment, the behavior of blood pressure during exercise provides indispensable data for the therapeutic evaluation of hypertensive individuals [5,6]. It is more difficult to obtain reliable measurements by means of ambulatory blood pressure monitoring during the patients' activity, which makes evaluation by means of a exercise test necessary [4,7].

The objective of our study was to evaluate whether any differences existed among the various groups of frontline drugs for the treatment of hypertension, regarding their capacity to control blood pressure during physical activity.

Methods

Nine hundred and seventy-nine exercise tests performed at the Treadmill Stress Test Service of *Hospital Universitário Antônio Pedro* between January 1996 and September 1997 were retrospectively evaluated, and we selected that belonged to patients with primary hypertension under

regular pharmacological treatment with frontline antihypertension drugs, with blood pressure at rest below or equal to 140/90mmHg when being tested, and no other cardiovascular disease. Forty-nine patients (19 males) with mean ages (±SD) of 53±12 years met the selection criteria. Twenty-four percent of patients (n=12) were using antihypertension medication belonging to the beta-blockers group, 29% (n=14) used calcium antagonists, 27% (n=13) diuretics, and 20% of the patients (n=10) were using medication belonging to the group of angiotensin-converting enzyme inhibitors (Table I). Mean systolic and diastolic blood pressure at rest and mean ages were similar in all groups (Table II). The behavior of blood pressure under stress was considered abnormal, if one of the following three criteria [8] existed: systolic pressure on the peak of stress higher than 220mmHg, variation in diastolic pressure under stress higher than 15mmHg, or variation of systolic pressure/MET (metabolic equivalent) higher than or equal to 10mmHg. All tests were performed on a treadmill, following the Bruce or modified Bruce protocols, and symptom-limited. Blood pressure was measured in a noninvasive manner by means of a mercury-column device (Tycos, USA), whereby the blood pressure at rest was obtained on the left arm, the patient being in an orthostatic position on the treadmill.

Statistical analysis was based on ANOVA. Once significance was reached, *post-hoc* analysis was made using Student's *t* test with the Bonferroni correction for variables having a normal distribution (age, systolic blood pressure). For variables that did not have normal distribution (diastolic blood pressure), the Mann-Whitney test was used, and the Chi-square test was used to compare proportions (tensional response). Values of $p<0.05$ were considered statistically significant.

Table I – List of most used drugs in each group

Beta-blockers	Calcium antagonists	ACEI	Diuretics
83% propranolol	65% phenylalkilamines	70% captopril	62% hctz
17% atenolol	35% dihydropyridines	30% others	38% clort

Hctz- hydrochlorothiazide; clort- chlorthalidone; ACEI- angiotensin-converting enzyme inhibitors.

Table II - Age and blood pressure (BP) in each drug group. Systolic blood pressure under maximum stress was significantly lower in the group of beta-blocker users (*p<0.05) as compared to with that in the other 3 groups. No significant differences occurred between groups with regard to the other variables.

Variables	Beta	Calcium antagonists	ACEI	Diuretics
Age (years)	51±13	52±11	54±12	54±14
SBP rest (mmHg)	131±8	125±10	132±9	134±9
DBP rest (mmHg)	83±7	83±10	80±5	85±7
SBP stress (mmHg)	179±20*	198±32	203±17	204±22
DBP stress (mmHg)	92±11	84±15	87±17	90±19

Beta- beta-blockers; ACEI- angiotensin-converting enzyme inhibitors; SBP- systolic blood pressure; DBP- diastolic blood pressure; stress- maximum under stress. Data are presented as mean ± standard deviation.

Results

The groups were similar in age and systolic and diastolic blood pressure at rest (Table II). The mean systolic pressure upon maximum exercise was lower in the patients using beta-blockers than in the other groups ($p<0.05$), the values being the following: 179±20mmHg for the beta-blockers, 198±32mmHg for the calcium antagonists, 204±22mmHg for the diuretics and 203±17mmHg for the angiotensin-converting enzyme inhibitors. No difference occurred among the four groups regarding the mean values of diastolic pressure upon maximum exercise ($p>0.05$) (Table II).

No significant difference existed in the blood pressure response to exercise between the groups of patients using diuretic drugs and those using calcium antagonists. Thirty-one percent of the patients in the group with diuretics and 36% of the patients in the group with calcium antagonists showed a physiological response in blood pressure ($p=0.40$). In the group of patients using beta-blockers, 50% showed a physiological response of blood pressure to exercise, this difference being statistically significant as compared with that in the other three groups ($p<0.05$). In the group of patients using angiotensin-converting enzyme inhibitors, we found that only 20% had a physiological response of blood pressure to exercise, which was significantly lower as compared with that in the other drug groups ($p<0.05$) (Fig. 1).

Discussion

Some authors have shown that the use of the angiotensin-converting enzyme inhibitor captopril does not reduce blood pressure under maximum stress [9,10]. Manhem et al.[10] studied the effect of captopril on catecholamines, renin activity, angiotensin II, and aldosterone in plasma during

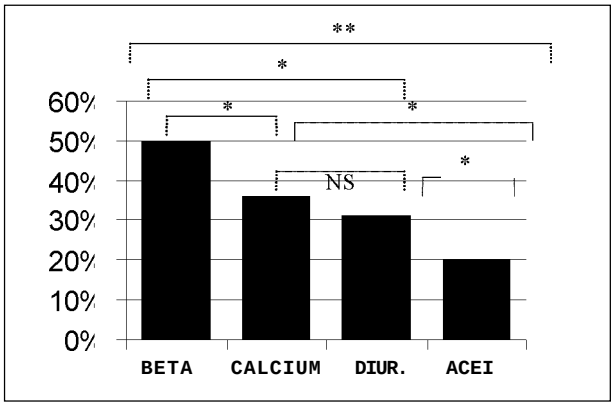

Fig. 1 - Physiological response of blood pressure to stress. Values of p are significant between groups, except for the calcium antagonists and diuretics groups. Beta- beta-blockers; Calcium- calcium antagonists; Diur.- diuretics; ACEI- angiotensin-converting enzyme inhibitors. *p<0.05; **p<0.001; NS- p>0.05.

physical exercise in hypertensive patients and concluded that, despite a pronounced decrease in angiotensin II formation, captopril did not change the response of blood pressure to exercise. In our study, the group of angiotensin-converting enzyme inhibitors was the least effective one in controlling blood pressure under stress. However, we noticed that 70% of patients were using captopril, so it is possible that different kinds of responses might occur with other angiotensin-converting enzyme inhibitors, as in the study of Kinugawa et al. [11] with the angiotensin-converting enzyme inhibitor alacepril, where a decrease in blood pressure under stress was observed.

Kostis et al. [9] evaluated the different effects of captopril and nadolol during exercise and showed that both drugs reduce the increase of diastolic blood pressure during exercise. However, although the systolic blood pressure at rest was lower after captopril use, under stress it was lower with nadolol than with captopril. These data are consistent with those obtained in our study, where a significantly lower systolic blood pressure under exercise was observed in the patients treated with beta-blockers, and diastolic blood pressure was similar in all four groups. These different responses to exercise seem to be related to the antihypertensive mechanism of action of each drug. The decrease in blood pressure after angiotensin-converting enzyme inhibitor use is associated with the decrease in peripheral vessel resistance, without any interference in cardiac output [9] whereas the use of beta-blockers reduces blood pressure by reducing cardiac output [12].

In our study, no significant difference occurred in blood pressure control during exercise between the group using calcium antagonists and the group using diuretics. The calcium antagonists reduce blood pressure through direct vasodilative action on the smooth vascular muscles, with a reduction in peripheral vascular resistance as a consequence [13,14]. However, they constitute a heterogeneous group of drugs, because phenylalkilamines have a negative effect on chronotropism and inotropism, whereas dihydropyridines do not significantly alter cardiac output[15]. Roberts et al. [16] did not find any difference in blood pressure at rest or after exercise between captopril and nifedipine. Yet, our results showed a better control of blood pressure in the group using calcium antagonists than in the group using angiotensin-converting enzyme inhibitors. This may be a consequence of the fact that 65% of the patients in the calcium antagonist group were using phenylalkilamines therefore possibly reflecting a cardiac output decrease associated with a decrease in peripheral vascular resistance in a significant number of patients.

Thiazide diuretics reduce blood pressure at the beginning of treatment through the reduction of volemia and, consequently, of cardiac output. However, after 4 to 6 weeks, their mechanism of action involves mainly the decrease in peripheral vascular resistance [17]. In our study, the time of treatment was not determined, so variations might occur in the diuretics' mechanism of action.

Although the time that elapsed between drug intake and performance of the exercise test was not properly controlled, all patients included in this study had a controlled blood pressure at rest, which allows us to assume that adequate use of anti-hypertension medication occurred.

Blood pressure measurements, mainly of diastolic pressure, during exercise tests may be difficult because of the noise coming from the treadmill and of muscle movement. Nevertheless, Pickering et al. [18] found a close correlation between systolic and diastolic blood pressure for a certain heart rate obtained by ambulatory blood pressure monitoring and those obtained during exercise testing. It is worth pointing out that several authors have evaluated systolic and diastolic pressures under exercise through indirect measurements, in different clinical and therapeutic situations, thus undeniably contributing to a better understanding of the mechanisms involving the behavior of blood pressure during exercise [9-12, 14,15,19,20].

The evaluation of hemodynamic responses of hypertensive patients during a stress test can provide important data for the therapeutic choice, considering that the purpose of the treatment is adequate control of blood pressure, not only at rest, but also during daily activities and exercise. Our data suggest that, in hypertensive patients with an excessive response of blood pressure to exercise, the use of beta-blockers may provide greater benefits in the control of blood pressure than the use of angiotensin-converting enzyme inhibitors.

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