Dose-response Curve to Exercise in Hypertensive Individuals: Analysis of the Number of Sessions to the Hypotensive Effect

Paulo Ricardo Nazário Viecili, Daiana Cristine Bündchen, Cleusa Maria Richter, Thiago Dipp, Daciano Bastos Lamberti, Angela Maria Reis Pereira, Luciana de Castro Barbosa, Angélica Cunha Rubin, Evanilda Goulart Barbosa, Tiago Facchini Panigas

Instituto de Cardiologia de Cruz Alta, Universidade de Cruz Alta (Unicruz), Cruz Alta, RS - Brazil

Summary

Background: The effect of exercise on blood pressure (BP) is already known; however, the dose-response curve of the hypotensive effect of exercise in hypertensive individuals is yet to be clarified.

Objective: To evaluate the dose-response curve of the number of sessions that are necessary to cause a hypotensive effect in hypertensive individuals.

Methods: 88 individuals, aged 58 ± 11 years, divided in Experimental group (EG), with 48 that participated in a physical exercise program (PEP), which consisted of 40 minutes of aerobic exercises performed 3x/week, for 3 months, at 70% of the VO\textsubscript{2}max, and muscular exercises at 40% of the maximal voluntary contraction (MVC) and Control Group (CG) with 40 individuals that did not participate in the PEP. The systolic (SAP) and diastolic (DAP) arterial pressures were measured before each of the 36 sessions in the EG and assessed by ambulatory blood pressure monitoring (ABPM) in the CG. Differences in BP, the variation rate (D%) and the maximum hypotensive effect (MHE%) were observed between sessions. The data were expressed as means ± SD; the t test and correlation were used, with p<0.05 being considered significant.

Results: There was no difference regarding BP values in the CG. The EG showed an important decrease of 15 mmHg in SAP and 7 mmHg in DAP, with a large part of this effect occurring as early as the first session and the majority up to the 5\textsuperscript{th} session. There was a strong inverse correlation (R:-0.66) with the number of sessions.

Conclusion: An important hypotensive effect was observed from the 1\textsuperscript{st} session on and it was observed that the dose-response curve can be abrupt and decrescent, instead of flat. (Arq Bras Cardiol 2009;92(5):361-367)

Key words: Hypertension; exercise; motor activity; period effect.

Introduction

The systemic arterial hypertension (SAH) disease is especially significant, as approximately 20% of the adult Brazilian population is affected and represents one of the main risk factors for cardiovascular morbidity and mortality\textsuperscript{1}. For this picture to change, pharmacological and non-pharmacological antihypertensive measures must be systematically applied and among them, the life style modifications, including the regular practice of physical exercise, which currently has an important role within the clinical approach of arterial hypertension (AH)\textsuperscript{2-6}.

In spite of the variability of the results, in general, almost all are unanimous in describing that the aerobic physical activity shows relevant efficacy in the treatment of hypertension, by causing some type of hypotensive effect\textsuperscript{3-10}. Another important point, in this complex discussion, is that there seems to be not only one responsible mechanism, but a series of complex and integrated mechanisms that can result in small but significant decreases of 2 mmHg up to higher ones of 15 mmHg in SAP\textsuperscript{7-9}.

Studies have reported that the time necessary for the hypotensive effect to take place is very variable, as it can be short, such as two weeks after the start of the activity, or longer periods can be necessary, such as 12 to 16 weeks, generally coinciding with the study period itself\textsuperscript{7-9}.

It has also been reported that there is no association between the weekly frequency of training, duration or intensity of the training session, with the magnitude of the blood pressure decrease, consequently suggesting that the dose-response curve for the exercise and the pressure is a flat one\textsuperscript{11}.

Therefore, although much is known about the effects of exercising, there is a scarcity of data demonstrating the association between the significant hypotensive behavior with the number of exercise sessions performed, so that this non-pharmacological measure can become more known.
Thus, the association between the BP behavior and the minimum number of exercise sessions to achieve the significant hypotensive effect is the objective of the present study investigation.

Methods

Population and Sample

Eighty-eight sedentary and hypertensive individuals stage I were selected and divided in two groups: 48 (57.7 ± 9 years) participated in a physical exercise program (PEP) and were called the experimental group (EG), whereas the other 40 (61 ± 6 years) did not participate in the program and were called the control group (CG).

The sample characterization took into account the age, sex, presence of diabetes, cholesterol, body mass index (BMI)13 and the maximum oxygen consumption (VO2max)13, which are shown in Table 1.

As observed, the groups presented similarities. Individuals that performed regular physical activity at least twice a week or more were excluded from the study. All individuals signed the free and informed consent form and were informed of all procedures and possible risks involved. The study was evaluated and approved by the Ethics Committee in Research of Universidade de Cruz Alta/RS.

All individuals were submitted to the assessment of the maximum aerobic capacity through an ergometric test (ET) in Bruce protocol, for the indirect measurement of VO2max13. The ET was carried out in an IMBRAMED treadmill, model Classic, with the computerized program ERGO PC version 2.2, by MICROMED Biotecnologia Ltda.

Experimental group procedures

The 48 individuals from the EG were randomly selected, among those who agreed to participate in the study. After undergoing the ET, the individuals were submitted to the PEP. The sessions lasted up to 90 minutes and consisted of aerobic and muscular-strengthening exercises. The aerobic training consisted of walks on the treadmill, 3 times a week, at 70% of the VO2max, in progressive sessions from 20 to 40 minutes, during 12 continuous weeks. The muscular training program was carried out at 40% of the maximum voluntary capacity (MVC) with three series of 12 repetitions.

The systolic (SAP) and diastolic (DAP) arterial pressures were measured before each of the 36 sessions through the classic auscultation method44. At each session, the individuals remained five minutes at rest to have the pre-exercise BP measured, followed by stretching and after, a 20-minute walk in the first two weeks, 30 minutes from the third to the sixth weeks and 40 minutes from the 7th to the 12th week. The muscular training program was carried out immediately after the aerobic training.

Control group procedures

Forty individuals from the CG were randomly selected among those who did not undergo the exercise program. In these, the BP was measured by ambulatory blood pressure monitoring (ABPM) for 24 hours, pre and post-study, in a DYNAMAPA equipment, according to the recommended method15.

The ABPM method was chosen as it is more effective than the occasional BP measurement, considering that the study adherence would be very difficult if participants had to measure their BP three times a week during three months. Equally, the inaccurate occasional variations in BP were filtered15. Thus, every individual had 120 verifications, 60 in each ABPM, instead of a manual verification at the start and at the end of the study.

Hemodynamic variables

The hemodynamic variables studied were SAP and DAP at rest, between the exercise sessions, from the first to the 36th one, considering the differences between pressures, the percentage variations of pressure differences (D%) and the maximum hypotensive effect (MHE).

The MHE was considered as the maximum hypotensive effect throughout the program, when comparing the first and the last exercise session, accepting this difference as 100% of the hypotensive effect of the exercise, being described as a percentage.

Statistical analysis

The data were analyzed inter- and between groups and expressed as means ± SD. The continuous variables were analyzed with the student’s t test and the categorical variables with the Chi-square test. The association between the pressure behavior and the number of exercise sessions was carried out through linear regression. The level of significance was set at p<0.05.

Results

Experimental group

The BP difference values, the variation index and the MHE between sessions are shown in Table 2. As it can be observed, when comparing the differences in the BP means in the second session with those in the first session, as shown in Table 2, we can verify that there was a significant decrease SAP of 7 mmHg.
demonstrating a MHE of 50%, whereas for DAP, there was a decrease of 5 mmHg (-7%), with a MHE of 80%. No significant variation was observed when comparing the third session with the second and the fifth session with the fourth. However, when comparing the fifth session with the first, there was an important decrease of 12 mmHg in SAP (-9%), which corresponds to 81% of the MHE and 7 mmHg in DAP (-8%), which corresponds to 97% of the MHE. No significant variations occurred from the 5th to the 12th session and the same MHE levels were maintained.

When comparing the SAP and DAP levels on the 12th and the 1st session, we can observe that there was no further decrease in addition to the previously demonstrated one.

When analyzing the two remaining months of exercise, one can observe that the behavior of the values remained similar, except for the fact that there was a lower variability between sessions. Thus, the MHE occurred significantly from the first session on, mostly, up to the 5th session of physical exercise and little was added after that.

Figure 1 represents the chart that shows the SAP and DAP means, analyzed session per session, throughout the three months of the PEP, where it takes on a descending and abrupt curve, right within the first five days, with some oscillation between the 6th and the 17th session, however, with a decrescent, slow and progressive feature until it reaches a stable value from the 25th to the 36th session.

This demonstrated behavior differs from the suggested one that the dose-response curve for the exercise and BP would be flat and that there would be no correlation between them.

Finally, Figure 2 shows the BP behavior session by session, presenting a moderately strong negative correlation with the number of physical exercise sessions.

Control group

As for the CG, there were no pressure variations according to the ABPM analyses. The values are shown in Figures 3 and 4, where the EG values are also shown for comparative purposes.

At the start of the study, there was no significant difference in SAP and DAP between the groups. The CG did not show differences in both pressures, verified by ABPM, at the start and at the end of the study. After the PEP, the SAP and DAP levels of the EG were significantly lower when compared to those of the CG.

<table>
<thead>
<tr>
<th>Sessions</th>
<th>mmHg</th>
<th>Difference in mmHg</th>
<th>D%</th>
<th>MHE%</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 x 1 SAP</td>
<td>137 ± 19 X 144 ± 20</td>
<td>-7</td>
<td>-5</td>
<td>50</td>
<td>0.02</td>
</tr>
<tr>
<td>2 x 1 DAP</td>
<td>83 ± 13 X 88 ± 14</td>
<td>-5</td>
<td>-7</td>
<td>80</td>
<td>0.005</td>
</tr>
<tr>
<td>3 x 2 SAP</td>
<td>134 ± 18 X 137 ± 19</td>
<td>-3</td>
<td>-2</td>
<td>-</td>
<td>NS</td>
</tr>
<tr>
<td>3 x 2 DAP</td>
<td>83 ± 13 X 83 ± 13</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>5 x 4 SAP</td>
<td>132 ± 15 X 136 ± 18</td>
<td>-4</td>
<td>-3</td>
<td>-</td>
<td>NS</td>
</tr>
<tr>
<td>5 x 4 DAP</td>
<td>81 ± 9 X 82 ± 10</td>
<td>-1</td>
<td>-</td>
<td>-</td>
<td>NS</td>
</tr>
<tr>
<td>5 x 1 SAP</td>
<td>132 ± 15 X 144 ± 20</td>
<td>-12</td>
<td>-9</td>
<td>80</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5 x 1 DAP</td>
<td>81 ± 9 X 88 ± 14</td>
<td>-7</td>
<td>-8</td>
<td>97</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>12 x 5 SAP</td>
<td>132 ± 19 X 132 ± 15</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>12 x 5 DAP</td>
<td>82 ± 11 X 81 ± 9</td>
<td>-1</td>
<td>-</td>
<td>-</td>
<td>NS</td>
</tr>
<tr>
<td>12 x 1 SAP</td>
<td>132 ± 19 X 144 ± 20</td>
<td>-12</td>
<td>-8</td>
<td>80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12 x 1 DAP</td>
<td>82 ± 11 X 88 ± 14</td>
<td>-6</td>
<td>-7</td>
<td>85</td>
<td>0.0001</td>
</tr>
<tr>
<td>24 x 1 SAP</td>
<td>133 ± 19 X 144 ± 20</td>
<td>-11</td>
<td>-8</td>
<td>74</td>
<td>0.004</td>
</tr>
<tr>
<td>24 x 1 DAP</td>
<td>83 ± 10 X 88 ± 14</td>
<td>-5</td>
<td>-7</td>
<td>80</td>
<td>0.02</td>
</tr>
<tr>
<td>36 x 1 SAP</td>
<td>129 ± 17 X 144 ± 20</td>
<td>-15</td>
<td>-10</td>
<td>100</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>36 x 1 DAP</td>
<td>81 ± 11 X 88 ± 14</td>
<td>-7</td>
<td>-9</td>
<td>100</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SAP: systolic arterial pressure; DAP: diastolic arterial pressure; mmHg: millimeters of mercury; D%: BP variation rate expressed as percentage; MHE%: maximum hypotensive effect expressed as percentage.

Figure 1 - Behavior of the systolic (SAP) and diastolic (DAP) arterial pressure means during three months of physical exercise practice in hypertensive individuals.
Discussion

The effects of exercise, concerning the late acute effects, are those observed during the first 24 or 48 hours (or even 72 hours) that follow an exercise session and can be identified by a slight decrease in pressure levels. The chronic adaptive effects are those that result from the regular exposition to exercise, representing the morphofunctional aspects of a physically trained individual⁴¹⁶.

In fact, as demonstrated in our series, the observed hypotensive effect lasted more than 24 hours and at least 48 hours, as the sessions were held every 48 hours, i.e., on Mondays, Wednesdays and Fridays, except for the period between Friday and Monday (weekends). However, after a separate analysis that was not the study object of the present investigation, it was demonstrated that in spite of the very early successive, sustained and abrupt decrease in pressure...
levels, the SAP means on Mondays were little higher than the means on Fridays, at least during the first 12 exercise sessions (141.2±20 X 135.2±19 mmHg, p < 0.046) and that after this period, there was no difference from Monday to Friday (134.8±20 X 132.8±19, p < 0.1), with a seemingly hypotensive effect, albeit lower, up to 72 hours after the exercise session.

Thus, it was also demonstrated in our series that the late acute effects had an adding and progressive characteristic, with a great deal of influence during the 48 hours post-exercise and a lesser effect after 72 hours and that its maximum effect is limited, as shown in Table 2 and Figure 2, as it can be noticed that, after the 12th session, there was no significant pressure decrease.

Another observed aspect concerning the chronic acute effect was that the BP decrease occurred in the start of the PEP and was not a slight effect, as it reached 7 mmHg for SAP and 5 mmHg for DAP, as early as after the first session, which corresponds to around 50% and 80% of the MHE, respectively; this was notable, as there are no data in the literature that have demonstrated such behavior.

When one observes the behavior of the pressure response curve throughout the exercise sessions, shown in Figure 01, one can see that there was a descending and abrupt curve, with a correlation between the number of sessions and the pressure level decrease, as demonstrated in Figure 04. This behavior was different from the one suggested in the literature, in which there is no correlation between the exercise volume, in general, and the BP decrease. Therefore, our data demonstrate that the dose-response curve might not be flat.

A very interesting aspect of the present study was that the used intensity of 70% of the VO2 max was sufficient to have contributed to the decrease in BP levels, differently from what was reported by other studies, that high loads could be ineffective or even dangerous, mainly in hypertensive individuals. Fagard reported in a recent meta-analysis of 44 randomized and controlled studies that there are no convincing data demonstrating that the BP response in hypertensive individuals, submitted to aerobic training, differs between the intensities of 40% and 70% of the VO2 max and that they are also very safe. It also mentions that there are insufficient data regarding the effect of exercises with loads < 40 and > 70% of the VO2 max in this type of population.

Another point of great divergence and speculation regarding the magnitude and duration of the pressure decrease caused by continuous exercise is that this effect depends on the exercise duration. However, there are sufficient data showing that there are no differences regarding the effect of exercise practiced between 30 and 60 minutes. In our series, differently from the available consensus, there was a decrease in BP as early as on the first day, after 20 minutes of exercise and there was a progressive increase, which reached 12 mmHg at the 5th session, with a 20-minute duration. From this period on, in spite of the fixed load used, the activity increase up to 40 minutes did not contribute to achieve higher significant hypotensive effects. From a practical point of view, this could increase adherence to the activity, as it requires less time from those individuals that present resistance to exercise.

A recent publication by Takata et al studied hypertensive individuals during 8 weeks of exercise at 50% of the VO2 max, with time periods of 30 to 60 min, 61 to 90 min, 91 to 120 min and more than 120 minutes per week. The magnitude of the BP decrease was higher in the 61 to 90-minute group,
when compared to the others, with no further increase in the BP reduction with the increase in exercise duration.

Another fact, yet to be called attention to, refers to the number of sessions per week that is necessary to achieve the hypotensive effect of the exercise. There is a great deal of evidence showing that, with 3 to 5 sessions, the response is very similar and that there are not sufficient data for other types of weekly schedules\(^8\)\(^{-11}\). The data of the present study demonstrated BP decrease taking place as early as the first session, and that the hypotensive effect lasted longer than 24 hours, reaching approximately 48 or even 72 hours, with an exercise session duration of 20 minutes. This could, in part, explain the similar effect of 3 to 5-times-a-week schedules, as there seems to be a prolonged hypotensive effect.

This prolonged effect could be, in part, explained by the alterations and modifications in the endothelium; however, there are yet no specific results in the literature\(^2\)\(^{-1}\). Nevertheless, there have been reports that, in healthy individuals, exercise increases the production of endothelium-derived nitric oxide (NO) with a consequent prolonged vasodilating effect in the arterial microcirculation\(^2\)\(^{-2}\). On the other hand, there are still doubts regarding the mechanisms involved in the BP decrease in hypertensive individuals after a PEP, but there is a tendency to accept that the frequent increase of the force exercised by the blood against the vessel wall leads to a continuous increase in the release of NO and, subsequently, to prolonged vasodilation.

This improvement in the endothelium-dependent vasodilating response suggests that the physical training interferes with the endothelial dysfunction, and, consequently, with the BP level of hypertensive individuals, which could somewhat justify the BP behavior in the present study. However, more conclusive studies regarding this mechanism must be more clearly demonstrated\(^2\)\(^{-2}\).

Finally, a recent meta-analysis by Cornelissen and Fagard\(^1\) that analyzed 30 studies, observed a decrease of 7 mmHg in SAP and of 5 mmHg in DAP in hypertensive individuals submitted to physical exercise. Our data demonstrated a very important decrease during the first sessions, which reached 80% of MHE for SAP and almost 100% for DAP and that, from the 5\(^{th}\) session on, i.e., a period shorter than two weeks, little was added regarding the decrease in BP. However, a much higher decrease occurred than the one pointed out by Cornelissen and Fagard\(^1\). The present results indicate that the amount of physical exercises that is necessary to decrease BP in hypertensive individuals can be considerably small, which makes the exercise program much easier to be carried out.

Physical exercise directives recommend that every adult must accumulate at least 30 minutes of moderate physical exercise on most days of the week, mainly for the prevention of coronary atherosclerosis\(^1\)\(^{-2}\)\(^{-2}\). Our findings raise the possibility that the amount of exercises that are necessary to reduce BP in hypertensive individuals is lower than the one indicated by the recent directives.

Therefore, the results of the present study have clinical importance, as it has been estimated that a sustained decrease of 2 mmHg in SAP results in a 6% decrease of mortality by CVA and 4% decrease of mortality by CAD\(^1\). On the other hand, the influence of exercise on the hypotensive response suggests that the prescription of exercise for hypertensive individuals can be simple, starting as early as possible, without the need for prolonged periods, with 20 minute-walks a day, at least three times a week and that it can result in higher adherence to the exercise program as well as to the pharmacological treatment, due to the decrease in costs and that it can be safely performed by all individuals, in any part of the world. However, further studies must be carried out so that the results of this series can be reproduced and thus, support our observations.

**Study limitations**

This study was limited to the evaluation of hypertensive sedentary individuals up to stage I. In order to better assess the participants, individuals with blood pressure levels higher than the aforementioned ones were not included, as well as those undergoing pharmacological adjustment and the refractory hypertensive ones, due to the possibility of result interference. Therefore, other studies with these types of hypertensive individuals must be carried out separately. Another limitation of the present study was the lack of comparison of the blood pressure behavior between genders, although literature data have demonstrated that there is no difference between them\(^2\)\(^{-6}\).

**Conclusions**

The data of the present study demonstrated that physical exercises, such as walking, of moderate intensity, for 20 minutes, carried out in alternate days, resulted in important blood pressure decreases and that most part of the hypotensive effect occurred as early as after the first five sessions and that from the 5\(^{th}\) session on, there was little contribution to such effect, even with longer walking periods, of 30 to 40 minutes, thus demonstrating that the dose-response curve of exercise in hypertensive individuals can be decrescent and abrupt, as early as the 1\(^{st}\) session.

**Potential Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

**Sources of Funding**

There were no external funding sources for this study.

**Study Association**

This study is not associated with any post-graduation program.
Dose-response curve to exercise in hypertensive individuals


