RESEARCH ARTICLE
Blood pressure reaction to treadmill test in normotensive Indian males with genetic risk of hypertension

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ABSTRACT

Background: Studies have found that individuals with a genetic risk of hypertension may show an abnormal blood pressure (BP) reaction to various stressors and varied exercise protocols. Thus, these individuals may show an abnormal BP reaction in their daily activities. A submaximal exercise test usually mimics dynamic daily activities. This study was done to understand the BP reaction to the treadmill test in these individuals during incremental submaximal exercise testing. Aims and Objectives: The aims and objectives of the study are to compare BP reaction to treadmill test in healthy normotensive males with and without genetic risk of hypertension. Materials and Methods: A total of 100 healthy normotensive males between the age group of 35 and 45 years old took part in the study – fifty men with genetic risk of hypertension and 50 men without genetic risk of hypertension. The reaction of BP to exercise was done by treadmill test using submaximal Bruce protocol. The BP and pulse rate during rest, at the termination of each stage of the treadmill test, and during recovery were measured in each group. Data analysis was done using unpaired t-tests between the groups. Results: The systolic and diastolic BP were significantly increased during each stage of the treadmill test and during recovery in normotensive men with genetic risk of hypertension ($P < 0.001$). Conclusion: Genetic risk of hypertension leads to increased BP reaction to exercise and during recovery in healthy normotensive males. Incremental exercise testing may have predictive value in recognizing individuals with a greater risk of developing systemic hypertension in the future.

KEY WORDS: Blood Pressure Reaction; Treadmill Test; Genetic Risk of Hypertension

INTRODUCTION

Hypertension is the one of most common diseases worldwide and it noticeably upsurges the morbidity and mortality of an individual. It is one of the major modifiable risk factors for ischemic heart disease, stroke, renal dysfunction, peripheral artery occlusive diseases, and congestive heart failure. An early detection of hypertension in the population is of paramount importance so that an early management program can be started. The cause of hypertension is multifactorial with a genetic contribution. A genetic risk of hypertension is known to predispose people to an early development of systemic hypertension. Earlier studies have found that individuals with a genetic risk of hypertension may show an abnormal blood pressure (BP) reaction to various stressors and various types of exercise. A study by Chauhan found an increase in BP responsiveness to exercise in normotensive individuals with a genetic risk of hypertension. Similar findings were reported by another study where they found increased sympathetic activity in normotensive individuals with a genetic risk of hypertension. Measurement of heart rate variability showed an elevated basal sympathetic tone in such individuals.
The BP increases in moderate whole-body exercises, such as running, is the result of the interplay of increased sympathetic response leading to increased cardiac output and peripheral arteriolar vasoconstriction and local metabolic vasodilatation in active muscles. This response may be altered in people with a genetic predilection to hypertension. Thus, an abnormal reaction of BP to exercise may reflect a disturbed neuro-cardiovascular regulation with a genetic predilection to hypertension.\[5\] A study reported a magnified sensitivity of the vasculature to exogenous noradrenaline, an amplified reaction of BP to stress, and high plasma catecholamine concentrations during stress in normotensives with genetic risk of hypertension. Hypertensive families may possibly transfer an aberration in the regulation of arterial smooth muscle cells.\[6,7\] Another study also observed that the activity of the sympathetic nervous system, plasma noradrenaline, and endothelin (ET) levels are amplified in non-hypertensive subjects with familial predisposition to hypertension suggesting an inherently determined atypical regulation of the sympathetic nervous system.\[8\]

Further, exaggerated BP reactions in normotensive people may be an indicator of masked hypertension and a predictor of future hypertension.\[9\] A systemic review by Keller et al. has also found a significant association between exaggerated BP reaction during cardiopulmonary testing and new-onset hypertension on follow-up of 2–14 years.\[10\]

Thus, individuals with a genetic risk of hypertension may show an abnormal BP reaction in their day-to-day activities. A submaximal exercise test usually mimics dynamic day-to-day activities. The objective of this study was to see if the BP reaction to exercise varies in normotensive individuals with and without a genetic risk of hypertension during incremental submaximal exercise testing. The varied reaction of BP to exercise in individuals with a genetic risk of hypertension, if any, may prove to be an early indicator of genetic predisposition to the development of hypertension.

**MATERIALS AND METHODS**

**Inclusion Criteria**

A total of 100 healthy normotensive males between the age group of 35 and 45 years old were included in this study. Fifty men with genetic risk of hypertension (42 with hypertension of one parent and eight with hypertension of both parents) and 50 men without genetic risk of hypertension.

**Exclusion Criteria**

Known cases of hypertension, diabetes mellitus type 2, ischemic heart disease, metabolic syndrome, and any acute illness were excluded from the study. Subjects with any contra-indication to exercise testing were also excluded.

**Ethics and Informed Consent**

Institutional ethical committee clearance and written consent from subjects were taken before the start of the study.

**Methodology**

All the participants were asked to sit for 10 min before measuring resting heart rate and resting BP. Resting BP was measured in the sitting posture manually with the help of a sphygmomanometer as per the latest Joint National Committee guidelines. The reaction of BP to exercise was done by an exercise stress test on a treadmill using the Bruce protocol. A submaximal exercise protocol was selected. The protocol started at 1.7 mph speed and a gradient (or incline) of 10%. At every 3-min interval, the incline of the treadmill and the speed were increased. Systolic and diastolic BP with heart rate readings were recorded during treadmill exercise at the end of each stage every 3 min and in the post-recovery period after 5 min and 10 min.

**Statistical Analysis**

The statistical analysis was done by SPSS version 22. The normality of the samples was ascertained. An unpaired t-test was used to compare the inter-group comparison. Statistical significance was considered at $P < 0.05$.

**RESULTS**

The baseline characteristics of the study groups are shown in Table 1. The resting systolic BP and reaction to exercise are shown in Table 2. The resting diastolic blood pressure and reaction to exercise are shown in Table 3.

**DISCUSSION**

Summary of findings of this study are as follows: (a) both BP readings showed significantly greater increase during an incremental submaximal exercise in normotensive subjects with genetic risk of hypertension compared to subjects without

<table>
<thead>
<tr>
<th>Table 1: Baseline characteristics of the study population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
</tr>
<tr>
<td>-------------------------------------------</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Height (meters)</td>
</tr>
<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
</tr>
<tr>
<td>History of smoking (%)</td>
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<tr>
<td>History of alcohol intake (%)</td>
</tr>
</tbody>
</table>

BMI: Body mass index
genetic risk of hypertension and (b) BP was significantly higher in the post-recovery period in subjects with a genetic risk of hypertension compared to subjects without a genetic risk of hypertension.

Similar findings have been found in earlier studies with different stressors and varied exercise protocols. A study by Sinha and Verma found hyperresponsiveness of BP reaction and increased recovery time during cold pressor tests and isometric handgrip exercises.[11] A study by Deyanov and Vangelova also found a similar increase in BP responsiveness to exercise in healthy individuals with genetic risk of hypertension.[12] Further, a similar finding was reported during the post-exercise recovery period in subjects with a genetic risk of hypertension in a study by Mangieri et al.[13]

Mechanisms and Pathophysiology

Various factors and mechanisms may be implicated in increased BP reaction to exercise in subjects with a genetic risk of hypertension.[14] The same has been shown in a flow chart in Figure 1. A study by Boutcher et al. found the presence of higher peripheral resistance consequent to decreased vascular compliance.[15] The decrease in vascular compliance may be due to increased basal sympathetic activity leading to peripheral vasoconstriction,[4] altered balance of vasodilator versus vasoconstrictor paracrine substances such as nitric oxide (NO),[16] increased activity of the renin-angiotensin pathway,[17] and altered arterial structure leading to increased stiffness of arteries.[18]

Various vasodilators and vasoconstrictor substances are known to act in a paracrine manner to modulate arterial tone. Factors that determine both the resting vascular tone and exercise-induced tone include ET, NO, prostacyclin, thromboxane A₂, carbon monoxide, locally released platelet serotonin, and kinins. Vascular tone during exercise is affected by endothelial dysfunction as the endothelium plays an important role in the regulation of vascular tone, in both healthy and ill states. Dysfunction of the endothelium has been described early in life in individuals who develop hypertension later and alterations of the above factors are a known component of endothelial dysfunction.[19,20] ET-1 is responsible for BP regulation by the local mechanism

<p>| Table 2: Systolic blood pressure values in subjects with and without genetic risk of hypertension |
|-----------------------------------------------|-----------------------------|-----------------------------|-----------------------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>With genetic risk of hypertension (n=50)</th>
<th>Without genetic risk of hypertension (n=50)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting</td>
<td>125.66±4.02</td>
<td>124.36±5.14</td>
<td>0.224</td>
</tr>
<tr>
<td>Stage 1 (exercise)</td>
<td>147.86±3.99</td>
<td>141.08±4.97</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Stage 2 (exercise)</td>
<td>166.80±4.45</td>
<td>158.78±4.78</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Stage 3 (exercise)</td>
<td>185.84±5.00</td>
<td>177.12±4.25</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>5 min (post-exercise)</td>
<td>140.90±4.58</td>
<td>131.88±4.27</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>10 min (post-exercise)</td>
<td>127.58±4.10</td>
<td>123.88±3.70</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*Statistically significant

<p>| Table 3: Diastolic blood pressure values in subjects with and without genetic risk of hypertension |
|-----------------------------------------------|-----------------------------|-----------------------------|-----------------------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>With genetic risk of hypertension (n=50)</th>
<th>Without genetic risk of hypertension (n=50)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting</td>
<td>83.74±1.81</td>
<td>81.70±3.39</td>
<td>0.84</td>
</tr>
<tr>
<td>Stage 1 (exercise)</td>
<td>85.82±2.05</td>
<td>79.72±3.42</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Stage 2 (exercise)</td>
<td>87.08±2.34</td>
<td>80.48±3.61</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Stage 3 (exercise)</td>
<td>88.46±2.86</td>
<td>80.86±4.52</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>5 min (post-exercise)</td>
<td>84.82±2.19</td>
<td>78.06±3.63</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>10 min (post-exercise)</td>
<td>82.48±2.05</td>
<td>76.72±3.46</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*Statistically significant

Figure 1: Various factors and mechanisms that may be implicated in increased blood pressure reaction to exercise in subjects with genetic risk of hypertension
of action, i.e., contraction of vascular smooth muscle and by systemic effects (resetting of baroreceptors, enhancing sympathetic tone, and variation of synaptic transmission). Normotensive subjects with a genetic risk of hypertension may also suffer reduced L-arginine transport, which may represent the link between a faulty L-arginine/NO pathway and the beginning of primary hypertension.

Early arterial structural changes in normotensives have been described in individuals with a genetic risk of hypertension. The initial changes in the structure and function of the vessels may involve a reduction in the amplitude and time duration of the pressure waveform. This change reflects a variation in the stiffness or compliance patterns of the arteries.[21] The overall anatomical and physiological changes in the vasculature may contribute to variations in local blood flow, increased atherogenesis, and microvascular anomalies. The changes in the compliance of the vessels are related to arterial endothelial injuries which further increase cardiovascular risks. A constant rise in arterial BP produces mechanical stress which stimulates smooth muscle cell hyperplasia and hypertrophy due to increased collagen synthesis. This results in reduced arterial compliance, which further increases arterial BP and leads to a vicious cycle.[22–21]

Our study also found that normotensive subjects with genetic risk of hypertension exhibit greater elevation of BP in response to a stressor such as incremental treadmill exercise. Further, we have observed that BP was significantly raised during the recovery period in healthy subjects with a genetic risk of hypertension indicating a slower recovery of BP post-exercise. This may be due to factors such as the ET-1 release which has been reported to increase throughout recovery in subjects with genetic risk of hypertension.[31] Furthermore, elevations of circulating epinephrine and norepinephrine, in recovery, have also been reported in such subjects. NO has also been reported to be less in subjects with a genetic risk of hypertension after exercise.[19] It is important to recognize that greater reactivity of the BP reaction to exercise and other stressors in healthy individuals with genetic risk of hypertension because this may unmask a greater likelihood of developing systemic hypertension in the future. Furthermore, repeated short-term increases of BP as seen with exercise in normotensive individuals with genetic risk of hypertension may be implicated in anatomical and physiological changes in vascular wall compliance that predispose to future risk of hypertension, ischemic heart diseases, and the development of stroke.[24,25] Hence, exaggerated BP response to physical exercise also suggests greater BP elevation during daily routine stress activities and hence enhanced sympathetic nervous tone. This is a risk factor for the pathogenesis of hypertension and target organ diseases later in life.[26]

Strengths and Limitations

One of the strengths of the study was that submaximal exercise was the stressor and stimulus for BP change. Submaximal exercise is likely suggestive of BP variations throughout usual dynamic routine activities. One of the limitations was dietary habits and exercise routines of the subjects were not measured. This could have added more value to the study. This study could have also been improved if follow-up of the subjects was done.

CONCLUSION

Genetic risk of hypertension leads to increased BP reaction to exercise and during recovery in healthy normotensive males. Incremental submaximal exercise testing may have predictive value in identifying individuals at greater chances of developing systemic hypertension in the future. This study also emphasizes the importance of genetic influence on the prehypertensive phase of hypertension.

REFERENCES

Yadav et al. Blood pressure response to treadmill test in normotensive Indian males

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