

Post-exercise hypotension: possible relationship with ethnic and genetic factors

Hipotensão pós-exercício: possível relação com fatores étnicos e genéticos

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Abstract – Post-exercise hypotension (PEH) is characterized by a decrease in blood pressure (BP) in relation to pre-exercise levels and has been intensively studied in different populations after different modes of exercise. Several mechanisms are associated with PEH, which makes it a multifactorial condition. However, over the last decade, some studies aimed to investigate the possible influence of ethnic and genetic factors on PEH. Thus, the purpose of this study was to review the environmental and, mainly, ethnic and genetic factors related to PEH. The studies used herein were obtained from a review of the following online databases: MEDLINE, SciELO and, Portal Capes. In relation to ethnicity, studies appear to indicate an unfavorable trend toward development of PEH in blacks as compared to whites, although this cannot be stated categorically. As for genetic studies and PEH, we stress the importance of these studies and highlight the need for selecting candidate genes for research on the basis of the physiological system implicated in BP regulation. Published studies have basically examined the relationship between PEH and mutations in genes that express proteins involved in the renin-angiotensin-aldosterone system. In this genetic sense, it seems that the greatest decline in PA occurs mainly after low-intensity aerobic exercise performed by normotensive or borderline hypertensive adult men. Further studies on the subject are required.

Key words: Ethnicity; Genetic polymorphism; Post-exercise hypotension

Resumo – A hipotensão pós-exercício caracteriza-se pela redução dos valores pressóricos em relação ao pré-exercício, sendo intensamente estudada em diferentes populações a partir das diversas modalidades de exercício físico. Inúmeros mecanismos relacionam-se à HPE, tornando-a de origem multifatorial. No entanto, na última década, alguns estudos objetivaram investigar possíveis influências de fatores étnicos e genéticos sobre a HPE. Nesse sentido, o objetivo do presente estudo foi revisar os fatores ambientais e principalmente, os étnicos e genéticos relacionados à HPE. Os estudos utilizados nesta revisão de literatura foram obtidos a partir de um levantamento bibliográfico realizado nos seguintes bancos de dados disponíveis na internet: Medline, SciELO e Portal Capes. Com relação à etnia, verifica-se que os estudos apontam desfavorável tendência aos indivíduos negros em obter HPE quando comparados aos de etnia branca, embora ainda não seja possível afirmar de maneira categórica. Quanto aos estudos genéticos e HPE, ressalta-se a importância destes estudos, assim como a necessidade de que a seleção dos genes candidatos à investigação seja feita baseando-se no sistema fisiológico implicado na regulação da PA. Basicamente, os estudos publicados analisaram a relação entre HPE e mutações de genes que expressam proteínas envolvidas no sistema renina-angiotensina-aldosterona. Nesse sentido, parece que o maior decaimento da PA ocorre, principalmente, após exercícios aeróbios de baixa intensidade realizados por homens adultos e normotensos limitrofes ou hipertensos, sendo necessários mais estudos acerca do tema.

Palavras-chave: Etnia; Hipotensão pós-exercício; Polimorfismo genético

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INTRODUCTION

Post-exercise hypotension (PEH), characterized by a decrease in blood pressure (BP) to values below those measured at rest before exercise¹, has been studied for decades in different modalities of physical activities^{2,3}. PEH is seen as an important non-pharmacological resource in the treatment of systemic hypertension³ because the performance of a single physical exercise session may result in a BP decrease that may last for up to 23 hours after exercising, when compared with values on a control day without physical exercise¹.

Numerous mechanisms are associated with PEH, and they are associated with both cardiac output and peripheral vascular resistance. Some of these important mechanisms are the reduction of blood volume, the activation of the cardiac efferent and afferent sympathetic nervous system and of skeletal muscle ergoreceptors, as well as the production of vasopressin, noradrenalin, rennin and angiotensin II (AngII) in addition to the increased release of adenosine, blood lactate, potassium and nitric oxide (NO)^{1,4-6}. The complexity of BP regulation⁷ suggests that PEH has a multifactorial origin⁸, also affected by ethnic and genetic factors.

According to Agarwalet al.⁹, genetic mutations, among other physiological and behavioral factors, may affect the capacity to maintain adequate BP and, consequently, favor hypertension and even interfere with PEH. Additionally, the association between the current worldwide epidemics of hypertension and modern lifestyles seems clear, particularly because of high salt intakes and sedentary habits, among other behaviors (also called environmental factors), as well as due to the interaction between these variables and ancestral susceptibility^{5,7,10}, represented by ethnicity and genetics. These factors have become the object of recurrent studies in the last decades, particularly because such susceptibility may affect BP-related phenotypes.

Therefore, considering the multiplicity of factors widely studied and associated with the hypotensive effects of physical exercise, the possible effects of individual, unchangeable characteristics on these responses should be investigated. This study reviewed studies about ethnic and genetic factors and their associations with PEH. Our data search was based on studies retrieved from the following databases, available in the Internet: Medline, SciELO and Portal Capes. The following keywords, both in English and Portuguese, were combined in various ways: post-exercise hypotension, human beings, ethnicity, genetic polymorphism, rennin-angiotensin-aldosterone system, ethnicity and blood pressure. Data used in the review were collected only from studies published in national and international journals, and results of studies (dissertations and theses) not yet published in peer-reviewed journals were not included.

POST-EXERCISE HYPOTENSION AND ETHNIC FACTORS

The tendency towards elevated BP is assigned, in part, to human evolution. Adaptation to climate, first in Africa and then in the rest of the world, may have led to the current patterns of susceptibility to hypertension.

According to Young⁷, populations in hot and humid environments are more susceptible to hypertension than those that live in cold environments because the propensity to retain salt and water may raise BP, as heat loss is fundamental in hot environments. However, as large amounts of water and salt are lost in transpiration, hypovolemia occurs and there is a decrease in the capacity to dissipate heat. Therefore, individuals genetically adapted to a high appetite for salt and the increase of the renal conservation of sodium are better adapted to hot environments due to evolution.

Based on that, evidence suggests that genetic susceptibility may have expanded due to human evolution, as well as a result of population migrations and miscegenation between different ethnicities, which favored elevated BP values⁷ and may be associated with PEH. Moreover, studies about associations based on miscegenation were first published for hypertension phenotypes¹¹, and epidemiological analyses conducted in the United States consistently pointed to a greater risk of hypertension among the African American population¹².

The variations in BP responses due to physical exercise may also be associated with ethnicity, both in its acute and subacute forms. Brandon and Elliott-Lloyd¹³ found a decrease in BP after 16 weeks of walking (subacute effect)¹⁴ among both African American and white American women, and the greatest variation was found in the group of white women. In contrast, Pescatello et al.¹⁵ found a BP reduction after moderate exercise (acute effect) only in white women with hypertension, with no BP fall among white women with normal BP and BP elevations among African American women with hypertension or normal BP.

A study with white and African American men with normal BP found lower values of systolic BP (SBP) at rest, as well as a smaller reduction of SBP after acute exercises of moderate to high intensity before and after training at 55-75% VO_2max for African American men with a specific mutation of the angiotensin gene¹⁶. However, Headley et al.¹⁷ found that young African Americans with normal BP that practiced aerobic exercises of moderate intensity had a prolonged reduction of post-exercise SBP, a results that was probably associated with the changes in cardiac output and total peripheral resistance.

In addition, a recent study conducted with 22-year-old individuals detected a significant reduction in diastolic BP and mean BP in the 15 minutes after exercise, among both African American and white individuals, without any significant difference between the two groups. However, their study also analyzed both central and peripheral vascular stiffness, greater in the group of African Americans, a finding that led the authors to discuss the possible association between stiffness and reduction in sensitivity to β_2 adrenoreceptor¹⁸.

According to Muszkat¹⁹, three polymorphisms identified for β_2 adrenoreceptor blocked it and, consequently, affected vasodilatation. The frequency of these polymorphisms varies according to ethnicity and is greater among black people than among European whites. Finally, Gainer et al.²⁰ reported that the different genotypes of ACE insertion/deletion (I/D)

polymorphism also interacted with ethnicity to define the impact of the endothelium-dependent vascular response of bradykinin.

Important to mention is the fact that most studies about different ethnicities and BP after physical exercise, or even after training, were conducted using observation and/or self-report questionnaires about skin color and ethnicity. No specific laboratory techniques seem to have been used to confirm the estimates of individual genomic origins. For that purpose, it would be necessary to use informative markers of ethnicity selected from literature according to the differences in allelic frequencies and the European, African and American Indian parental populations.

The summary of the studies discussed in this topic, which investigated ethnicity and the reduction of post-exercise BP values, is shown in Box 1.

Box 1. Summary of the studies about ethnicity and acute and chronic effects of physical exercise on BP

| Study | n | Age (years) | Sex | Clinical Condition | Ethnicity | Physical Exercise | Main Results |
|---|-----|----------------------------------|-----|------------------------------------|----------------------------|---|---|
| Brandon and Elliott-Lloyd ¹³ | 75 | 18 to 50 | F | Body fat \geq 27% | White and African American | 16 weeks; Intense walking | \downarrow In BP for both ethnicities by $>$ for W |
| Pescatello et al. ¹⁵ | 33 | 19 to 45 | F | Normal and high BP | White and black | One session; Cycle ergometer; 40 minutes; 60% VO_{2max} | \downarrow BP among W volunteers with hypertension |
| Rivera et al. ¹⁶ | 737 | W: 36 \pm 12 B: 34 \pm 15 | M | Normal and borderline hypertension | White and black | Submaximal and maximal tests before and after 21 weeks of training using cycle ergometer 30 to 50 minutes; 55-75% VO_{2max} | Lower \downarrow of SBP for B angiotensin gene polymorphism |
| Headley et al. ¹⁷ | 19 | 25 \pm 1 | M | Normal BP | Black | One session; Treadmill; 40 minutes; 50 to 60% HR reserve | \downarrow SBP |
| Heffernan et al. ¹⁸ | 24 | 22 \pm 1 | M | Normal BP | White and African American | Maximal aerobic exercise test | \downarrow DBP and MBP for both ethnicities; greater vascular stiffness among African Americans |

F: female; M: male; W: white; B: black; BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; \downarrow : decrease; $>$: greater

POST-EXERCISE HYPOTENSION AND GENETIC FACTORS

Studies with families, twins and model organisms estimate that 30% to 60% of the variability found in BP phenotypes are explained by genomic variation^{21,22}. According to a review conducted by Arora and Newton-Cheh²³, the heritability of high BP may be found in 50% to 60% of the population.

According to Cowley²⁴, hundreds of BP-related phenotypes and genomic regions have been mapped for human beings and rats. However, the total number of genes and alleles that contribute to the hypertension phenotype, as well as other BP-related phenotypes, remains unknown. The

identification of genes segregated in a Mendelian way in cases of familial hypertension and, more recently, the genomic scanning techniques based on single nucleotide polymorphisms (SNP) have both made important contributions to the study of BP-related phenotypes²⁵.

According to Binder²⁵, candidate genes should be selected for investigation according to the physiological system implicated in BP regulation. The rennin-angiotensin-aldosterone system (RAAS), one of the components of the complex network that regulates BP, has been extensively studied, as well as aldosterone synthesis and the genes that express the proteins of this system, such as rennin, angiotensinogen, angiotensin II (AngII) type 1 receptor and angiotensin converting enzyme (ACE)^{9,26}.

However, few studies evaluated the association between genetic mutations and essential hypertension²⁷⁻³⁰. Blanchard et al.²⁷ analyzed the interaction of three RAAS polymorphisms (I/D ACE, A/C AT₁R and W/C Int2) with BP for 14 hours after low and moderate intensity exercises in adult men with borderline normal BP or hypertension (stage 1). Surprisingly, significant differences in essential hypertension were only found after low intensity exercises (40% VO₂max) for SBP and DBP of the volunteers that had three or more of the alleles theoretically favorable to BP increases. Moreover, Pescatello et al.²⁸ stressed that the BP response after aerobic exercises may be modulated by the interactions between dietary calcium intake, exercise intensity, and RAAS polymorphisms. More marked SBP decreases were found in the group that had a low dietary calcium intake, as well as after the performance of light (40% VO₂max) and moderate (60% VO₂max) intensity exercises for the groups with greater and lower risk of heart disease due to genotype combinations, which referred to the same gene mutations studied by Blanchard et al.²⁷.

Pescatello et al.³⁰ also found substantial differences in hypotensive responses nine hours after aerobic exercises performed at light and moderate intensities by men with stage 1 hypertension. About 60% of the individuals had a reduction in systolic BP after moderate exercise, regardless of the presence of alpha-adducin gene polymorphisms (Gly460Gly vs. Gly460Trp). However, careful analysis revealed that, once more, the difference between the effects of genotype interaction and exercise on BP responses are defined at lower intensities (40% VO₂max). Therefore, BP reductions of 83% and 56% may be recorded for individuals with the Gly460Trp and Gly460Gly genotypes. According to the authors, the best explanation for these results is found in the balance between sodium volume and the vasodilation-vasoconstriction status after stimulation generated during the two exercise sessions (light and moderate), in the case of the polymorphism under study.

The balance mentioned by the authors may also be affected by other factors associated with specific genotypes. For example, a study conducted by Tanriverdi et al.³² found greater blood flow due to endothelium-dependent vasodilation in athletes with genotype II of the ACE I/D polymorphism, probably due to the greater concentration of bradykinin and the bioactivity of nitric oxide. The ACE I/D polymorphism refers to the

absence or presence of an ALU sequence of 287 nitrogen-containing base pairs in intron 16 of chromosome 17³¹. Recently, results of a number of Master's and Doctorate studies conducted in Brazil, although unpublished in journals, suggest a possible association of the DD genotype, or even the D allele of the I/D polymorphism with a weaker hypotensive response after physical exercise.

However, it seems that genetic polymorphism mapping, according to published studies, may facilitate the identification of people that respond better to BP decreases, particularly after low intensity aerobic exercises, which may act as a useful treatment against hypertension. This discovery has great importance for the development of physical activity programs to reduce BP values among individuals with hypertension. The magnitude of the exertion tested by Pescatello et al.³⁰ is compatible with a low intensity walk, which is usually enjoyable and favors adherence³³. Therefore, their findings support the idea that genetic information may and should be taken into consideration when prescribing exercises for individuals with borderline normal BP or with hypertension.

All information described here clearly stresses the complexity of the mechanisms of BP control and requires further investigation. The possible interaction between environmental factors and genetic analyses should also be discussed. Environmental factors are usually characterized by intermediate phenotypes susceptible to human intervention along life²⁶. Guedes and Guedes³⁴ reported that the levels of physical activity and cardiorespiratory aptitude are inversely correlated with BP at rest and with the amount and distribution of body fat, which are associated with possible increases of the risk of heart diseases.

Therefore, environmental factors, and even ageing alone³⁶ (not discussed in this review), affect the functioning of the arterial wall, vascular resistance and, consequently, BP control^{5,10}. Such characteristics may affect the magnitude and duration of essential hypertension and favor the appearance of systemic hypertension.

In summary, gene mutations seem to play a role in essential hypertension, even though few polymorphisms have been studied and there are practically no studies using genomic scanning. However, these studies are important for the better understanding of the interaction between genetics and essential hypertension, as well as the relevance of adequate control of the variables associated with environmental and ethnic factors to avoid spurious associations between polymorphisms and BP reductions after physical exercise. However, adequate control of ethnicity, using estimates of individual genomic history, remains an obstacle in studies conducted in this area.

FINAL CONSIDERATIONS

This review of the literature demonstrated that both BP regulation and the mechanisms associated with essential hypertension have a multifactorial origin and are affected by environmental, ethnic and genetic factors.

Environmental factors act upon endothelial functioning, the maintenance of the vascular tonus and, consequently, BP regulation. Ethnicity reveals that human evolution may favor the elevated BP standards found in Modernity, and studies suggest that black individuals have an unfavorable tendency to have essential hypertension when compared with white individuals.

Finally, genetic studies with human beings suggest that there is a possible effect of some polymorphisms on essential hypertension. Further studies should investigate those possibilities, and the selection of candidate genes should be based on the physiological systems implicated in BP regulation. Attention should be drawn to the mutations associated with the genes involved in the rennin-angiotensin-aldosterone system, which may favor a greater decrease of BP, particularly after low intensity aerobic exercises performed by adult men with borderline normal BP or with hypertension.

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