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Curative treatment of hypertension by physical exercise

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Abstract. – Hypertension, one of the most common chronic and sporadic conditions, figures among the important worldwide public-health challenges, and it is a major risk for heart disease, stroke, kidney disease and other complications, including dementia. Hypertension is neglected by individuals, and the prevalence of this condition continues to rise across the world. A great number of patients receiving medical intervention is not successfully treated, while adequate curative health services are dependent on the exact update data of the countrywide prevalence of known and undetected cases. This renders elusive the possibility of a public strategy to eradicate hypertension. Accordingly, a global preventive approach in considering the known etiology of the disease established two types of hypertension including primary hypertension, which is idiopathic, and secondary hypertension, which is based on a demonstrable organic change in tissues. This is relevant since secondary hypertension remains the most prevalent and it is associated with physical inactivity and bad nutrition. The environmental condition may be counteracting with an active life style. Physical exercise, which promotes hemodynamic and humoral changes in healthy subjects, may positively impact on hypertensive subjects. Indeed, patients with hypertension might improve their blood pressure, plasma lipoprotein-lipid profile, insulin sensitivity, likely to normotensive people, as well as the regression of the pathology of left ventricular hypertrophy. Exercise training is an important initial or adjunctive step that may be highly efficacious in the prevention and treatment of individuals with hypertension. Herein, we study the role of exercise training in the treatment of hypertension.

Key Words:
Physical exercise, Hypertension, Blood flow, Cardiovascular disease.

Introduction

Hypertension is a major risk factor for the development of cardiovascular disease[1]. Data have claimed that the root of hypertension in adulthood extend back to childhood[2]. Childhood blood pressure (BP) track into adulthood; thereby, children with elevated BP are more likely to become hypertensive adults[3-7]. This, not only suggested genetically origin[8-11] providing substantial risk for developing hypertension, but also the possibility of improving the accuracy of the prediction of hypertension later in life[12]. However, data have shown that treatment of hypertensive patients should be based on the outcome of the treatment relatively to overall cardiovascular disease risk since hypertension is only one risk factor for cardiovascular disease, and mortality in patients with the pathology is the result of cardiovascular disease, but not hypertension[13,14]. Indeed, electrophysiological and neurochemical measurements of regional sympathetic activity in lean essential hypertensive patients have demonstrated activation of sympathetic outflow to the heart, kidneys and skeletal muscle vasculature in individual ageing under 45 years old[15]. This increase in sympathetic activity, a mechanism for both initiating and sustaining the blood pressure elevation, confers specific cardiovascular risks, thus promoting the development of left ventricular hypertrophy and contributing to the genesis of ventricular arrhythmias and sudden death[16]. Sympathetically mediated vasoconstriction in skeletal muscle vascular beds reduces the uptake of glucose by muscle, thus being a basis for insulin resistance and consequent hyperinsulinemia[17]. Additionally, different components of the insulin resistance syndrome, including obesity, insulin resistance, hyperinsulinemia, accelerated atherosclerosis as well as abnormal increased plasma lipoprotein-lipid levels, tend to cluster in hypertensive patients. Moreover, this emphasizes the need to cure all these cardiovascular disease risk factors, as opposed to only reducing the BP of the patients[1]. Nevertheless, directs measurements in vascular smooth muscle cells derived from resistance arteries of hypertensive

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patients have shown increased in the levels of ROS at rest after angiotensin II stimulation in comparison with normotensive controls[18]. Furthermore, *in vitro* biopsies of resistance arteries from patients for endothelium-dependent (acetylcholine-induced) and endothelium-independent (sodium nitroprusside induced) relaxations after the preconstriction with noradrenaline[19], have shown significant impairment of endothelium-dependent relaxation of resistance arteries of hypertensive subjects compared with normotensive subjects, due to overexpression of cyclooxygenase-2 (COX-2) and NADPH oxidases (Nox). Consistently, a close association between hypertension and vascular endothelial dysfunctions has been documented[20-22], suggesting that endothelium-dependent vasodilation impairments found in hypertension may be the result of oxidative stress[19], known to play an important role in hypertension[23-25]. Indeed, oxidative stress which impaired nitric oxide (NO) can involve a number of different mechanisms including the reduction in endothelial NO synthase (eNOS), uncoupling of eNOS enzymatic activity, scavenging of NO by ROS, and the oxidation of NO targets[26]. The importance of redox imbalance in the development of hypertension, well demonstrated in animal models[27,28], was demonstrated in many population based-studies[29-31] and appreciated in patients with essential hypertension in which BP is positively correlated with biomarkers of oxidative stress and negatively correlated with level of antioxidants[32-35]. Accordingly, recent studies[36-39] have clearly shown beneficial effects of exercise training on all the risk factors of cardiovascular diseases documented in hypertensive patient, although influence of intrinsic factors such as ageing, gender, and quality of training. The ageing has a great influence on the result of exercise training of hypertensive patients[40,41]. Indeed, the prevalence of hypertension is in general markedly increased with age[42], and middle age patients suffering hypertension (41 to 60 years old) seemed reducing their systolic BP more consistently than younger or older patients with exercise training[43-45]. Another factor that greatly influences the results of exercise training in hypertensive patients is the gender[40,41]; thereby, women may better reduce BP compared to men[46]. However, low to moderate intensity training appears more beneficial as higher intensity training for reducing BP in hypertensive patients[47]. Truly, previous data from human and animal models of hypertension have shown that low to moderate exercise training may be just as effective as higher intensity of training for reducing BP in hypertensive subjects[48-50]. In addition, the use of transportable players or hearing music during the training yield better results than in patients who do not listen any music during exercise[51]. These data are particularly relevant since low to moderate intensity of physical exercise programs are much easier to introduce in preventive and curative public health strategy against hypertension. Indeed, hypertensive patients as well as people with advanced ageing are vulnerable candidates who could easily be initiated and maintained in the low and moderate intensity of exercises, relatively with higher intensity exercise programs. This could result in more injuries and cardiovascular events requiring medical supervision[52]. However, BP response of hypertensive patients in the acute exercise remains interesting for BP regulatory mechanism[53]. In this review, we will emphasize on beneficial effects of exercise training in the treatment of hypertension.

Effects of Physical Exercise on Hypertension

Since hypertension is associated with endothelial dysfunctions, an early feature of vascular diseases in humans, the modification of lifestyle, including good nutrition and physical exercises, are expected as serious effective non-pharmacological therapy for prevention, control and treatment of cardiovascular complications or hypertension[54]. Several studies in both normotensive and hypertensive subjects provided evidence of the decrease of total peripheral resistance by moderate and regular physical activities[20,55], while the mechanisms underlying the antihypertensive effects of exercise have not been fully clarified yet. However, data suggested the improvement of endothelium-dependent relaxation, endothelial adaptation, mainly mediated by a significant increase in vascular NO production and/or decrease in NO scavenging by ROS[54,56] as a product of exercise-induced changes in shear stress[57]. These data suggest that the increase in NO bioavailability, mainly through the reduction of oxidative stress, remains an important contributor to the improvement of endothelial function associated with physical exercises. Moreover, exercise has also been demonstrated to normalize levels and/or expression of pro-inflammatory cytokines that decrease NO bioavailability by stimulation of ROS production[54]. Notably, the

endothelial adaptations were also reported for vascular beds of skeletal muscles and other organs, which are not active or less active during exercise[58]. Furthermore, active muscles are associated with the release of several cytokines and various anti-inflammatory peptides[59], which in turn increase NO bioavailability via decreasing ROS production[54]. In line with these data, exercise-related vasodilation was also associated with the growth of new arterioles and the reduction of sympathetic vasoconstrictor tone to the existing vessels[60-62]. This suggests direct evidence that in humans, physical training lowers sympathetic activity[63-65] supports the involvement of neuronal cardiovascular control in the lowering of blood pressure following training[55]. In addition, in hypertensive patients, physical exercise has clearly shown beneficial effects on various component of the plasma lipoprotein-lipid[66], including the decrease of total plasma cholesterol levels, the significant reductions in plasma low density lipoprotein cholesterol (LDL-C), and the reduction of plasma triglycerides (TG) levels[67,68]. Additionally, physical exercise increased insulin sensitivity and glucose metabolism[69-71]. This is relevant since a large scale of hypertensive patients display insulin resistance that impaired glucose tolerance and metabolism, relatively to their normotensives peers. Also, physical training has a number of other well documented effects of significance for type 2 diabetes patients[72]. Another cardiovascular disease risk factor, particularly critical for both hypertensive and diabetes type 2 patients, is the left ventricular dysfunction namely hypertrophy (LVH). In addition, in this pathology there are endothelial dysfunction[73-76] and chronic low-grade inflammation with raised levels of C-reactive protein[77,78]. Data[79-81] showed significant reduction of LV masse index in hypertensive patients undergoing exercise training and increases endothelium-dependent vasodilatation[82,83], as well as anti-inflammatory effects[84], in type 2-diabetes. These indicate that with exercise training patients can change status from LVH to either a normal LV or undergoing concentric remodeling[85]. Accordingly, reductions of LV mass index were, in general, accompanied by decrease of posterior wall and intraventricular septal thicknesses, together with the substantially reduction of the mortality of hypertensive patients[86]. However, in type 1 diabetes there is no major difference in glycemic control between physically active and inactive patients[87,88] and physical exercise did not bear any improvement[89,90].

Conclusions

The sustained reductions of BP by physical exercise are rapidly evident during 24 h following a single bout of exercise in hypertensive patient, although the tendency for greater reductions for systolic BP is observed with more prolonged training[66]. Overall, changes brought by physical exercise to the body are characterized by cardiac output increase, redistribution of blood flow to muscular territories under activity as well as increase of sympathoadrenergic action[91]. Additionally, substantial benefits carried by physical exercise to hypertensive patients are not only limited in terms of reducing BP, but also by improving a number of risk factors that remarkably increase their risk of developing cardiovascular disease, supporting the use of physical exercise as an effective way that could be combined or not with usual therapy[92]. However, for further research opportunities, including the use of ambulatory monitoring and stratification of patients according to their degrees of hypertension, undergoing different pharmacologic regimens, life style should be undertaken. Nevertheless, training from three to five times per week during 30 to 60 min per session at an intensity of about 40 to 50 of net maximal exercise performance, has been suggested as effective with regards to blood pressure reduction and recommended for hypertensive patients[93].

Conflict of Interest

The Authors declare that they have no conflict of interests.

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