

ABSTRACT

EFFECT OF AEROBIC EXERCISE TRAINING ON THE
ENDOTHELIAL PROGENITOR CELLS DERIVED FROM BONE MARROW
OF SPONTANEOUSLY HIPERTENSIVE RATS

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Aerobic exercise training (ET) has been established as an important non-pharmacological treatment for hypertension, since it counteracts microvascular rarefaction and decreased blood pressure; however, underlying mechanisms remain to be further determined. We investigated for the first time if the endothelial progenitor cells (EPC) number and the functional capacity, impaired in hypertension; are improved after ET potentially contributing to neovascularization and disease regression. The effect of ET on blood pressure, heart rate, exercise tolerance, peak VO_2 and skeletal muscle morphology and biochemistry was studied in twelve-week old male Spontaneously Hypertensive Rats (SHR, n=28) and Wistar Kyoto (WKY, n=28) assigned into 4 groups: SHR, trained SHR (SHR-T), WKY and trained WKY (WKY-T). The ET promoted a decrease in blood pressure in SHR and resting bradycardia, an increase in exercise tolerance, peak VO_2 and citrate synthase activity in trained groups. In parallel, the ET repaired the skeletal muscle fiber type shift and capillary rarefaction in SHR, at least partly, by enhancing protein levels of VEGF, VEGFR-2, eNOS and deactivated apoptosis pathway. Numbers of EPC (CD34+/Flk1+) in the peripheral blood (PB) quantified by FACS analysis were

enhanced 115% in WKY-T of control levels. In contrast, the SHR group decreased 39%, but ET normalized in the SHR-T. Similar results were found in the EPC quantification of the bone marrow (BM) by double positive cells to Di-acLDL and Lectin-FITC. BM-EPC senescence was increased 126% in SHR and this process was reduced 72% by ET. Moreover, EPC functional assay by colony-forming units showed an increase of 40% to BM and 70% to PB in WKY-T of control levels. In contrast, the SHR group reduced 35% to BM and 45% to PB; however the ET repaired EPC dysfunction in hypertension. In fact, the ET corrected failure in the capillary-like tube formation on matrigel. The present findings reveal that the vascular remodeling accompanied by reduction of blood pressure induced by ET occurs in synergy with the restoration of the BM and PB- EPC number and functional properties, as well as of their mobilizing and angiogenic factors. These results suggest that the ET can participate in the vascular repair by means of the EPC, promoting the peripheral revascularization in hypertension. In this way, there is perspective of therapeutic potential of the EPC in treatment of hypertension after ET.

Key words: aerobic exercise training, angiogenesis, hypertension, endothelial progenitor cells, skeletal muscle.