MICROCIRCULATION IN HYPERTENSIVE PATIENTS

Jung F[1], Pindur G2, Ohlmann P3, Spitzer G4, Sternitzky R4, Franke RP5, Leithäuser B6, Wolf S7, Park JW8

Abstract

Regardless of the mechanisms that initiate the increase in blood pressure, functional and structural changes in the systemic vasculature are the final result of long-standing hypertension. These changes can occur in the macro- but also in the microvasculature. The supply of the tissues with oxygen, nutrients, and metabolites occurs almost exclusively in the microcirculation (which comprises resistance arterioles, capillaries and venules), and an adequate perfusion via the microcirculatory network is essential for the integrity of tissue and organ function. This review focuses on results from clinical studies in hypertensive patients, which have been performed in close cooperation with different clinical groups over the last three decades. Intravital microscopy was used to study skin microcirculation, microcatheters for the analysis of skeletal muscle microcirculation, the slit lamp for conjunctival microcirculation and the laser scanning ophthalmoscope for the measurement of the retinal capillary network. The first changes of the normal microcirculation can be found in about 93% of patients with essential hypertension, long before organ dysfunctions become clinically manifest. The earliest disorders were found in skin capillaries and thereafter in the retina and the skeletal muscle. In general, the disorders in the different areas were clearly correlated. While capillary rarefaction occurred mainly in the retina and the conjunctiva bulbi, in skin capillaries morphological changes were rare. A significant decrease of capillary erythrocyte velocities under resting conditions together with a marked damping of the postischemic hyperemia was found, both correlating with the duration of hypertension or WHO stage or the fundus hypertonicus stage. Also the mean oxygen tension in the skeletal muscle was correlated with the state of the disease. These data show that the microcirculatory disorders in hypertension are systemic and are hallmarks of the long-term complications of hypertension. There is now a large body of evidence that microvascular changes occur very early and may be important in their pathogenesis and progression.**[Biorheology. 2013;50(5-6):241-55. doi: 10.3233/BIR-130645] PMID:24398607**

[1] Institute of Biomaterial Science and Berlin-Brandenburg Center for Regenerative Therapies, Helmholtz-Zentrum Geesthacht, Teltow, Germany.
[2] Institute for Clinical Haemostasiology and Transfusion Medicine, University Saarland, Homburg/Saar, Germany.
[3] Marienkrankenhaus Papenburg, Akademisches Lehrkrankenhaus der Medizinischen Hochschule Hannover, Papenburg, Germany.
[4] Praxisklinik Herz und Gefäße, Dresden, Germany.
[5] Department of Biomaterials, University of Ulm, Ulm, Germany.
[6] Neuro-Kardiologie im Zentrum, Hamburg, Germany.
[7] Department of Ophthalmology, Inselspital, Bern University Hospital, and University of Bern, Bern, Switzerland.
[8] Asklepios Klinik Harburg, 1st Medical Department, Cardiology, Hamburg, Germany.

CARDIOVASCULAR BENEFITS OF PHLEBOTOMY: RELATIONSHIP TO CHANGES IN HEMORHEOLOGICAL VARIABLES

Holsworth RE Jr[1], Cho YI, Weidman JJ, Sloop GD, St Cyr JA

Abstract

Renewed interest in the age-old concept of "bloodletting", a therapeutic approach practiced until as recently as the 19th century, has been stimulated by the knowledge that blood loss, such as following regular donation, is associated with significant reductions in key hemorheological variables, including whole blood viscosity (WBV), plasma viscosity, hematocrit and fibrinogen. An elevated WBV appears to be both a strong predictor of cardiovascular disease and an important factor in the development of atherosclerosis. Elevated WBV through wall shear stress is the most direct physiological parameter that influences the rupture and erosion of vulnerable plaques. In addition to WBV reduction, phlebotomy may reduce an individual's cardiovascular risk through reductions in excessive iron, oxidative stress and inflammation. Reflecting these findings, blood donation in males has shown significant drops in the incidence of cardiovascular events, as well as in procedures such as percutaneous transluminal coronary angioplasty and coronary artery bypass grafting. Collectively, the available data on the benefits of therapeutic phlebotomy point to the importance of monitoring WBV as part of a cardiovascular risk factor, along with other risk-modifying measures, whenever an increased cardiovascular risk is detected. The development of a scanning capillary tube viscometer allows the measurement of WBV in a clinical setting, which can prove to be valuable in providing an early warning sign of an increased risk of cardiovascular disease. **[Perfusion. 2014 Mar;29(2):102-16. doi: 10.1177/0267659113505637]. PMID:24045034**

[1] Southeast Colorado Hospital, Springfield, CO, USA

OXIDATIVE STRESS AND SUICIDAL ERYTHROCYTE DEATH

Lang F[1] Abed M, Lang E, Föller M

Abstract

Eryptosis, the suicidal erythrocyte death, is characterized by cell shrinkage, membrane blebbing, and phosphatidylserine translocation to the outer membrane leaflet. Phosphatidylserine at the erythrocyte surface binds endothelial CXCL16/SR-PSOX (CXC-Motiv-Chemokin-16/Scavenger-receptor-for-phosphatidylserine-and-oxidized-low-density-lipoprotein) and fosters engulfment of affected erythrocytes by phagocytosing cells. Eryptosis serves to eliminate infected or defective erythrocytes, but excessive eryptosis may lead to anemia and may interfere with microcirculation. Clinical conditions with excessive eryptosis include diabetes, chronic renal failure, hemolytic uremic syndrome, sepsis, malaria, iron deficiency, sickle cell anemia, thalassemia, glucose 6-phosphate dehydrogenase deficiency, glutamate cysteine ligase modulator deficiency, and Wilson's disease.

Recent advances

Eryptosis is triggered by a wide variety of xenobiotics and other injuries such as oxidative stress. Signaling of eryptosis includes prostaglandin E_2 formation with subsequent activation of Ca(2+)-permeable cation channels, Ca(2+) entry, activation of Ca(2+)-sensitive K(+) channels, and cell membrane scrambling, as well as phospholipase A2 stimulation with release of platelet-activating factor, sphingomyelinase activation, and ceramide formation. Eryptosis may involve stimulation of caspases and calpain with subsequent degradation of the cytoskeleton. It is regulated by AMP-activated kinase, cGMP-dependent protein kinase, Janus-activated kinase 3, casein kinase 1α, p38 kinase, and p21-activated kinase 2. It is inhibited by erythropoietin, antioxidants, and further small molecules.

Critical issues

It remains uncertain for most disorders whether eryptosis is rather beneficial because it precedes and thus prevents hemolysis or whether it is harmful because of induction of anemia and impairment of microcirculation.

Future directions

This will address the significance of eryptosis, further mechanisms underlying eryptosis, and additional pharmacological tools fostering or inhibiting eryptosis. **[Antioxid Redox Signal. 2014 Jul 1;21(1):138-53. doi: 10.1089/ars.2013.5747]. PMID:24359125**

[1] Department of Physiology, University of Tübingen, Tübingen, Germany.