THE ROLE OF ANGIOGENESIS IN ISCHEMIC DISEASE

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Background. Ischemic heart disease, myocardial infarction, ischemic stroke, and peripheral arterial disease are non-communicable, highly disabling conditions with high incidence and mortality rates. It is well recognized that elderly patients may exhibit a relative tolerance to acute ischemic events due to long-standing chronic ischemia and the development of collateral vascular circulation, which provides a biological rationale for exploring therapeutic angiogenesis as a targeted strategy to restore perfusion and improve functional outcomes. Both physiological and pathological angiogenesis use similar mechanisms, but pathological angiogenesis continues after adequate perfusion, hindering the development of new anti-angiogenic agents.
Objective of the study. To elucidate the mechanisms of therapeutic angiogenesis in ischemic disease, in order to elaborate methods of treating and preventing ischemic diseases.
Materials and methods. A review of the literature from 2014-2024 was performed, using 11 articles, including data from ScienceDirect, PubMed Central, Biomed Central, MedScape, and others.
Results. Angiogenesis is the process of new blood vessel formation from pre-existing network through endothelial cell migration and proliferation. It occurs during wound healing, foreign body encapsulation, tumor growth, collateral vessel development, and organ transplantation. In reviewed literature have been mentioned the next methods of therapeutic angiogenesis: recombinant *vascular endothelial growth factor* (VEGF), *angiopoietin-2* (Ang-2), VEGF-encoding plasmid *deoxyribonucleic acid* (DNA), platelet-rich plasma transplantation, mesenchymal stem cells (MSCs) transplantation and mitochondrial transplantation. Transplantation strategies rely on hypoxic, pharmacological or genetic preconditioning to enhance ischemic tolerance and activation of pro-angiogenic pathways like *hypoxia-inducible factor 1 alpha* (HIF-1α)/*vascular endothelial growth factor* (VEGF), *phosphoinositide 3-kinase*/*protein kinase B* (PI3K/Akt), *mitogen-activated protein kinase* (MAPK), *extracellular signal-regulated kinase* (ERK) and *wingless-related integration site* (Wnt)/*beta-catenin* (β-catenin). Current challenges in angiogenesis treatments include difficulties in targeted delivery and precise dosage control. For example, excessive concentrations of VEGF lead to the formation of angiomas and aberrant vessels and may promote carcinogenesis, but suboptimal levels trigger insufficient angiogenesis for restoring perfusion, and the newly formed vessels fail to mature and rapidly regress.
Conclusions. To conclude, pharmacological and transplantation-based angiogenesis therapies hold promise for treating and preventing ischemic diseases; however, optimizing delivery methods, dosing, and pathway activation is critical to ensure effective and mature vascular growth without adverse effects.
Keywords: neoangiogenesis, ischemic disease, VEGF, MSCs.