Farmacologia Cardiovascolare dei Donatori di Ossido d'Azoto (NO): Prospettive Terapeutiche
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NITRIC OXIDE AND ANGIOGENESIS

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At cardiovascular level angiogenesis is sought for tissue reperfusion following ischemia and accelerates the healing process. Under the control of chemical mediators and physical forces, the process involves the exit of endothelial cells from quiescence to promote cell migration, to degrade the extracellular matrix and sustain cell proliferation, ultimately leading to differentiation of vascular buds into functional capillaries. Endothelial dysfunction and reduced production of NO are a predominant feature of vascular pathologies as atherosclerosis since a continuous endothelial cell (EC) lining provides a thromboresistant surface and controlled vasorelaxation. Disturbance in endothelial cell function also causes the impairment to mount an adequate angiogenic response during reparative processes. In the last years our group contributed to demonstrate that NO directs endothelial cells in each step of angiogenesis. By investigating the effect of vasoactive peptides and growth factors on cultured endothelium and on the angiogenesis process, we have observed that peptides as substance P and bradykinin, and vasculotropins as vascular endothelial growth factor (VEGF) promote their effects by increasing cGMP levels and PKG activity in endothelium.
In endothelial cells the activation of the NOS pathway brings to the upregulation of the MAPK signaling which in turn increases transcription and production of the growth factor (FGF-2) switching on an autocrine mechanism of cell survival. In this respect the NOS pathway may act as an endogenous limiting step for endothelium to become angiogenic, which cannot be simply overcome by redundance of angiogenic growth factors. Experimental evidences indicate that by these molecular paths, apoptotic events in endothelium are retarded and or prevented by ACE inhibitor and drugs increasing NO production in the endothelium. New highly potent NO donor drugs have been developed and characterized as endothelium-protective agents in cardiovascular disease as well as traditional/consolidated pharmacological approaches.

References:

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