Nitric oxide modulates angiogenesis through an O₂-dependent mechanism

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Background: Angiogenesis is the formation of new vessels from a pre-existing vascular network. Nitric oxide (NO) is an important regulator of endothelial cell function. The prototypical pro-angiogenic agent VEGFA activate eNOS and the VEGFA-NO axis increases angiogenesis but an inhibitory activity of NO on the angiogenic growth has been also described (1). Although hypoxia is a potent inducer of angiogenesis recent evidences indicate that rat aortic rings exhibit a decreased angiogenic response in hypoxic conditions (2). Based on these discrepancies, the aim of the present work was to clarify the role of nitric oxide and hypoxia on the angiogenic growth

Methods: We perform experiments in Matrigel with isolated rat aortic rings or human endothelial cells from aorta, coronary artery or cardiac microvasculature (Promocell, Spain) as previously described (3), and determine the angiogenic growth after 5 days (aortic rings) or 18h (endothelial cells) of incubation in presence or not of L-NAME (100 μ M) or DETA-NO (100 μ M) and under different O₂ concentrations: 0, 1, 3, 12 and 21%.

Results: NO endogenous or exogenous, inhibits the formation of new vessels from rat aortic explants cultured in normoxic conditions. Hypoxia also inhibits the angiogenesis of aortic rings and endothelial cells and this inhibition is more pronounced the lower the availability of O₂. However when aortic rings or endothelial cells were incubated in presence of the NOS inhibitor L-NAME, the angiogenic growth was higher and no differences were found in normoxic or hypoxic conditions.

Conclusions: In presence of NO, a decreased angiogenic growth was observed which was more pronounced as well as the O₂ concentration falls. In absence of endogenous NO the formation of new vessels was not affected by O₂ concentration

(1) Aplin and Nicosia Angiogenesis (2016) 19:133-146

(2) Mistry et al. Free Radical Biology and Medicine (2017) 108: 500-516

(3) Vicente et al. J Cardiovasc Pharmacol (2016) 68 (3): 230-240