

Endothelium-dependent vasodilatation produced by the L-arginine/nitric oxide pathway in normal and ischemic bone

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Abstract:

We used an experimental model of the perfused isolated rabbit tibia to investigate the vasodilatation produced by nitric oxide in the circulation of bone. Tibiae were perfused at a constant flow rate while the perfusion pressure was monitored continuously. Perfusion pressure was raised by the addition of noradrenaline to the perfusate, and dose responses were measured for bolus doses of acetylcholine and sodium nitroprusside. N omega-nitro-L-arginine methyl ester (L-NAME), an inhibitor of nitric oxide synthesis, was then added to the perfusate at a concentration of 10^{-4} M, and the dose responses to acetylcholine and sodium nitroprusside were repeated. Measurements were performed on groups of bones after 0, 6, 12, and 24 hours of normothermic ischemia (n 5, 4, 6, and 9, respectively). Both acetylcholine and sodium nitroprusside produced significant vasodilatation after 0 and 6 hours' ischemia, but no significant response was observed after 12 or 24 hours of ischemia. The vasodilatation produced by acetylcholine was significantly attenuated when L-NAME was added to the perfusate, but the vasodilatation produced by sodium nitroprusside remained unchanged. These findings confirm endothelial production of NO by stimulation of muscarinic receptors on the endothelial cells in bone and indicate that vasodilatation via the L-arginine/NO pathway remains viable for 6 hours after normothermic ischemia