



Endothelin-1-induced vasodilatation in rat breast tumor is mediated through endothelin-B receptors.

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Endothelin-1 (ET-1) causes vasodilatation via its endothelin-B receptors. ET-1, endothelin-3 and endothelin-B receptors are known to be overexpressed in breast carcinoma tissue. However, the functional role of ET-1 in tumor vasculature is still unknown. If ET-1 causes an increase in breast tumor perfusion, it could be used to increase delivery of chemotherapeutic agents to the tumor tissues. Female Sprague-Dawley rats (180-200 g) were treated with either saline or N-methyl, N-nitrosourea (50 mg/kg, intraperitoneally), a chemical carcinogen. Each group was treated with: (a) ET-1 (50 ng/kg/minute, 30 minute infusion) (n = 6); or (b) BQ788, an endothelin-B receptor antagonist (0.33 mg/kg/minute, 20 minute infusion) + ET-1 (50 ng/kg/minute, 30 minute infusion) (n = 5). Blood flow to tumor and normal breast tissue was measured using radioactive microspheres. Blood perfusion to the breast and tumor tissue was measured using laser Doppler flowmetry. Blood flow to tumor tissue increased (153%; $P < 0.05$) and vascular resistance decreased following ET-1 infusion. Blood flow to other organs was not affected. Laser Doppler flowmetry showed an increase (176%; $P < 0.05$) in breast tumor perfusion following ET-1 infusion. The increase in perfusion was attenuated (-25.2%; $P < 0.05$) with the administration of BQ788. Results indicate that ET-1 induced an increase in blood flow to tumors in tumor-bearing rats, which is mediated by endothelin-B receptors.