

Evidence for the involvement of ET(B) receptors in ET-1-induced changes in blood flow to the rat breast tumor.

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Structure, growth, and function of the blood vessels in breast tumors are markedly different from those in normal breast tissue due to changes in the production of growth factors such as vascular endothelial growth factor (VEGF), vasoactive substances such as endothelin-1 (ET-1) and cytokines. The role of ET-1 in breast tumor angiogenesis is not adequately understood. Studies have shown that the expression of proET-1, proET-3, and ET(B) receptors is increased in breast tumor. However, it is unclear whether there are any changes in ET-1-induced vascular responses in breast tumor. Hence, in the present study we investigated systemic hemodynamics and regional circulatory effects of ET-1 in rats with breast tumors. **METHODS:** Female Sprague-Dawley rats weighing 180-200 g were divided into the following groups: (1) normal rats treated with saline (n=6), (2) tumor-bearing rats treated with methylnitrosourea (MNU) (n=6), (3) normal rats treated with saline plus the specific ET(B) receptor antagonist BQ 788 (n=5), and (4) tumor-bearing rats treated with MNU plus BQ 788 (n=5). Tumor development was monitored by regular palpation and measurement of tumor size. Once tumors had reached approximately 2-4 cm in diameter, the rats were anesthetized with urethane (1.5 g/kg i.p.) and their cardiovascular parameters were measured using a radioactive microsphere technique. Simultaneously, blood perfusion to the breast tissue was also measured using a laser Doppler technique. **RESULTS:** ET-1 produced a significant increase in mean arterial pressure in normal and tumor-bearing rats. Blood flow to the tumor tissue increased significantly in response to ET-1 as compared to breast tissue in normal rats. This response was accompanied by a concomitant decrease in vascular resistance in the tumor tissue. These results were confirmed by laser Doppler flowmetry, which showed a significant increase in blood perfusion to breast tumor compared to normal breast tissue. This increase in blood perfusion was attenuated by pretreatment with BQ 788, suggesting an ET(B) receptor-mediated vasodilator action of ET-1 in rat breast tumor. **CONCLUSIONS:** The results indicate that ET-1 induced an increase in blood flow to breast tumor tissue mediated through ET(B) receptors.