Bradykinin Receptor Antagonism Attenuates Prolactin-Induced Hypertension Following Cardiopulmonary Bypass

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Background: The administration of prolatin to heparinized patients following cardiopulmonary bypass (CPB) induces hypertension. Prolactin inhibits the cardioprotection mediated by the vasodepressor peptide bradykinin. This study tests the hypothesis that bradykinin mediates prolatin-induced hypertension through its B2 receptor.

Methods: We conducted a prospective, double-blind, randomized study in sixteen adult male patients undergoing elective cardiac surgery requiring CPB and taking an angiotensin-converting enzyme inhibitor propranolol. Subjects were randomized to receive either saline (N=8) or the bradykinin B2 receptor antagonist HOE 140 (100 µg/kg, N=8) prior to the administration of prolatin. Mean arterial pressure (MAP) and tissue-type plasminogen activator (t-PA) activity were measured intraoperatively and before and after prolatin.

Results: Prolatin increased bradykinin concentrations from 6.3±1.1 to 12.1±2.4 fmol/ml (p=0.015). HOE 140 administration did not affect MAP prior to the administration of prolatin. Prolatin significantly decreased MAP in the saline group (from 69.8±4.4 to a mean individual nadir of 56.1±2.6 mmHg, p=0.0031) but bradykinin receptor antagonism blunted this effect (from 74.3±3.7 to a mean individual nadir of 69.6±1.2 mmHg in the HOE 140 group, p=0.0015). HOE 140 administration decreased MAP in the saline group as compared to the HOE 140 group (p=0.0002). T-PA activity significantly decreased following HOE 140 administration (from 0.59±0.10 to 1.67±0.42 µl/ml, p=0.0001), but not during saline (from 2.12±0.46 to 1.44±0.36 µl/ml, p=0.214). Similarly, T-PA activity decreased significantly during prolatin administration in the HOE 140 group (from 1.67±0.42 to 0.77±0.26 µl/ml, p=0.038), but not in the saline group (from 1.44±0.36 to 0.99±0.26 µl/ml, p=0.132).

Interpretation: Increased bradykinin contributes to prolatin-induced hypertension through its B2 receptor. Administration of a bradykinin receptor antagonist may represent a novel therapy for the prevention of prolatin-induced hypertension.

Osteopontin and Plasminogen Activator Inhibitor-1 in Malignant Hypertension: Suppression by p38 MAPK Inhibitors

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Assessment of target organ damage is important in defining optimal treatment of hypertension and blood pressure-related cardio-vascular disease. The aims of the present study were to: 1) quantify the expression of osteopontin (OPN) and plasminogen activator inhibitor-1 (PAI-1) in malignant hypertension and to examine the effects of a potent p38 MAPK inhibitor (SB203580).

Osteopontin and PAI-1 were determined by both real-time PCR and Western Blot in human malignant hypertension samples and normal control samples. Osteopontin and PAI-1 were upregulated in malignant hypertension as compared to normal controls, and SB203580 treatment significantly decreased the expression of OPN and PAI-1 in malignant hypertension.

Conclusion: Osteopontin and PAI-1 expression is increased in malignant hypertension and SB203580 treatment significantly decreases their expression.