The relationship between atherosclerosis and ACE activity is unclear. We tried to establish whether the endothelium bound coronary ACE activity correlates with coronary atherosclerotic burden.

Methods: A single bolus indicator-dilution experiment was performed in 10 patients. Tracer amounts of the specific ACE substrate 125I-labeled-Pre-Ala-Pro (125I-BP) and of the myocardial interstitial space reference 125I-sodium were injected in the left main coronary artery. Serial samples were obtained from the coronary sinus. Plasma concentrations of residual substrate and end-product (3H-BP) were measured. Mean transit time of 3H-BP was computed to obtain the rate constant for 3H-BP hydrolysis by ACE \((K_a)\). Coronary angiograms were scored for atherosclerotic burden according to 2 previously described techniques to obtain the plaque area index (PAI) and Sullivan's extent score (SES). Spearman correlation test was used to calculate \(p\) values.

Results: The atherosclerotic burden extent scores correlated well with each other (\(r=0.82\); \(p<0.002\)). There was a weak correlation between \(K_a\) and measures of atherosclerotic burden (\(r=0.4; p=0.22\)).

Conclusions: The indicator-dilution technique is a safe tool to quantify endothelium bound coronary ACE activity. The weak correlation between endothelium bound coronary ACE activity and extent scores suggests that tissue ACE may play a more important pathophysiologic role in the disease process.

\[
\Phi(\theta^2) \quad K_a \quad PAI \quad SES
\]

\[
\begin{array}{cccc}
1 & 0.04 & 0.12 & 0.53 & 26.50 \\
2 & 0.09 & 0.50 & 2.96 & 96.97 \\
3 & 0.05 & 1.11 & 4.18 & 36.13 \\
4 & 0.50 & 0.95 & 5.75 & 49.21 \\
5 & 0.05 & 0.38 & 0.27 & 4.94 \\
6 & 0.08 & 0.61 & 5.03 & 30.50 \\
7 & 0.05 & 0.63 & 2.77 & 54.08 \\
8 & 0.02 & 0.41 & 3.1 & 64.88 \\
9 & 0.07 & 0.70 & 0.0 & 0.0 \\
10 & 0.06 & 0.84 & 0.0 & 0.0 \\
\end{array}
\]

1199-96

BNP Preserves Endothelial Cell Integrity: Modulation by Atherosclerosis and Vasopeptidase Inhibition


Background: BNP is the most potent natriuretic peptide and mediates its actions by receptors that activate cGMP. We defined anti-atherogenic actions of BNP through preservation of endothelial (EC) impermeability to macromolecules. As atherosclerosis involves damaged EC allowing permeation of oxidized LDL, leading to atheroma formation, we extended our studies to an animal model of atherosclerosis. We located at the ability of omapatrilat (OMA), a vasopeptidase inhibitor, to preserve EC impermeability contributing to inhibition of atheroma formation based on the actions of OMA, namely: cGMP generation was determined by RIA. Aortic EC permeability in vivo was determined using a 0.014" intracoronary Doppler flow wire, were measured, during a) sinus rhythm, b) AF induced by rapid right atrial pacing, and c) atrial tachycardia (AT) induced by atrial pacing at identical heart rate. Volumetric flow rate corresponds to the product of total flow velocity integral, heart rate and cross-sectional area (CSA) of the left descending artery at the tip of the wire. Coronary flow reserve (CFR) corresponds to the ratio of the coronary flow measured during maximal hyperemia to that recorded at baseline.

Results: The induction of AT caused a significantly greater increase in coronary blood flow from 22±4 (control) to 93±18 ml/min, a non-significant decrease in mean blood pressure and a significant decrease in HR from 172±14 to 143±21 bpm, a non-significant increase in MABP from 124±10 to 130±11 mm Hg, and a non-significant decrease in mean pulmonary arterial pressure from 18±2 to 16±1 mm Hg. The induction of AT at a similar heart rate, combined with the fact that the RPP is increased to the same degree, suggests that factors such as the lack of atrial contraction and the irregularity of atrial rhythm prevent the coronary flow increasing to the extent required by the needs of the myocardium. This may have deleterious consequences in patients with coronary artery disease, causing or worsening myocardial ischemia to a greater degree than would an elevated heart rate alone.