Effect of Tetrahydrobiopterin on Coronary Microcirculation in Healthy and Hypercholesterolemic Subjects

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Background: Tetrahydrobiopterin (BH4) is an essential co-factor of the NO-synthase which regulates vasomotion. It has been shown to normalize endothelial dysfunction in the forearm of hypercholesterolemic patients. br/To determine the acute effect of intravenous BH4 on myocardial blood flow (MBF) in hypercholesterolemic patients and in healthy controls at rest as well as during endothelial-dependent (exercise) and -independent (adenosine, Ado) hyperemia.

Methods: 150-labelled H2O and PET was used to measure regional MBF (mI/min/g) at rest, during Ado (0.14mg/kg.min) and immediately after supine bicycle exercise in 10 healthy male volunteers with normal cholesterol levels (mean workload 199 Watts, 71% predicted) and in 8 hypercholesterolemic subjects (102 Watts, 71% predicted). Both groups had no history of and low clinical probability for CAD. Sixty minutes later all MBF measurements were repeated after intravenous BH4-infusion (10mg/kg over 30 min).

Results: Resting MBF and Ado-induced hyperemic MBF are not significantly affected by intravenous BH4. Exercise induced hyperemic MBF increases significantly (p<0.05) after BH4 in both groups.

Conclusions: In healthy men as well as in hypercholesterolemic patients, BH4 increases the post-adrenergic vascular response to exercise but does not affect the endothelial-independent response to Ado. This provides evidence for a role of BH4 in the regulation of coronary microcirculation during physical exercise.

Detection and Reproducibility of Mental Stress Induced Ischemia Utilizing Tc-99m Sestamibi Single-Photon Emission Tomography in Normal and Coronary Artery Disease Population

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Background: Mental stress induced ischemia, as detected by equilibrium radionuclide angiography studies, has yielded reversible ischemia in only 30-50% of patients with exercise induced ischemia. The purpose of this study was to evaluate the sensitivity and reproducibility of mental stress induced ischemia in patients with coronary artery disease (CAD) and in normal controls (with a low likelihood of CAD) using sestamibi single-photon emission tomography (SPECT) imaging.

Methods: 15 patients with CAD and typical angina or reversible ischemia (positive exercise treadmill study or positive adenosine thallium study) and 21 normal controls underwent mental stress testing (public speaking task.) Myocardial perfusion imaging was performed at peak stress (one minute) and compared to rest images obtained on a separate day. Images were read by 2 experienced readers using a 20 segment model scored for the presence or absence of ischemia.

Results: Resting MBF and Ado-induced hyperemic MBF are not significantly affected by intravenous BH4. Exercise induced hyperemic MBF increases significantly (p<0.05) after BH4 in both groups.

Conclusions: In healthy men as well as in hypercholesterolemic patients, BH4 increases the post-adrenergic vascular response to exercise but does not affect the endothelial-independent response to Ado. This provides evidence for a role of BH4 in the regulation of coronary microcirculation during physical exercise.

Evaluation of Peripheral Blood Flow During Exercise: A Complement to Exercise Myocardial Perfusion SPECT for Prognostic Assessment

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Background: Coronal artery disease (CAD) patients (pts) often manifest a paradoxical reduction in finger pulsewave amplitude (PWA) during exercise (EX). Since the clinical significance of this finding is unknown, we compared EX PWA responses to a sensitive measure of functional disease severity: summed reversibility score (SRS) on EX Tc-99m Sestamibi myocardial perfusion SPECT studies.

Methods: 128 CAD pts (mean age 61 ± 11 years, 86% male) had PWA assessed by peripheral arterial tonometry (PAT) during EX SPECT. PWA for each minute of EX was compared to a reference database for each minute of EX and grouped according to PWA ratios. Pt with the lowest PWA ratio (≤ 0.7) had a high likelihood (HL) of CAD (> 60%) with a low likelihood (LL) of CAD (< 40%) were used as a referent group.

Results: The conventional quantification of the uncorrected studies yielded the following accuracy: CAD 91% (39/43), LAD 72% (31/43), LCX 77% (33/43), and RCA 88% (37/43). The gender-combined quantification of the corrected studies yielded the following accuracy: CAD 93% (40/43), LAD 72% (31/43), LCX 77% (33/43), and RCA 88% (37/43). Conclusions: Quantification of attenuation corrected EX Tc-99m sestamibi myocardial perfusion SPECT studies demonstrated a trend towards improved detection and localization of CAD over quantification of uncorrected EX SPECT studies.

Parameter:

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<tr>
<th>PARAMETER</th>
<th>HIGHEST PWA</th>
<th>MIDDLE PWA</th>
<th>LOWEST PWA</th>
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<tr>
<td>ISCHEMIC SPECT (%)</td>
<td>19.1</td>
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<td>NUMBER OF REVERSIBLE DEFECTS</td>
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<td>SUMMED DEFECT</td>
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<td>4.7 ± 6</td>
<td>8.8 ± 10.8</td>
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