Asymmetrical Dimethylarginine, Oxidative Stress, and Atherosclerosis

To the Editor:

Antoniades et al1 reported on the role of asymmetrical dimethylarginine (ADMA) in inflammation-induced endothelial dysfunction in healthy subjects and in patients with coronary artery disease or rheumatoid arthritis. In patients with chronic inflammatory rheumatic diseases, serum nitrite concentrations were lower compared with healthy subjects but higher in the patients’ synovial fluid, suggesting impaired endothelial NO synthase activity but increased inducible NO synthase activity in the inflamed joint.2 In coronary artery disease patients without rheumatoid arthritis,3 as well as in rheumatoid arthritis patients without coronary artery disease, both ADMA synthesis and dimethylarginine dimethylaminohydrolase activity are several-fold elevated compared with healthy controls (Figure A). Dimethylamine (r=0.66; P=0.07) and ADMA (r=−0.79; P=0.02) correlated with 3-nitrotyrosine (Figure B), a potential biomarker of myeloperoxidase activity.2 These findings support the conclusion by Antoniades et al1 that ADMA may be both a link between inflammation and endothelial dysfunction and a potential therapeutic strategy for the treatment of inflammation-related endothelial dysfunction.

ADMA is a weak inhibitor of endothelial NO synthase (IC50, 12 μmol/L). Also, ADMA plasma concentration only changes a little (by approximately ±15%) on disease or pharmacological treatment. Other more potent mechanisms, such as ADMA-induced suppression/depletion of endothelial progenitor cells,4,5 are likely to be involved in coronary artery disease and rheumatoid arthritis. Systemic inflammation and elevated ADMA synthesis are common to many diseases, but ADMA elimination may vary considerably. Measurements of ADMA and dimethylamine in urine rather than ADMA in plasma may be more useful parameters to optimize treatment of inflammation-related endothelial dysfunction.

Disclosures

None.

Kristine Chobanyan-Jürgens
Vu Vi Pham
Dirk O. Stichtenoth
Dimitrios Tsikas
Institute of Clinical Pharmacology
Hannover Medical School
Hannover, Germany


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Hypertension is available at http://hyper.ahajournals.org

DOI: 10.1161/HYPERTENSIONAHA.111.180984
Figure. A, Creatinine-corrected excretion of dimethylamine (DMA) and asymmetrical dimethylarginine (ADMA) in 8 patients experiencing rheumatoid arthritis (RA) without coronary artery disease (CAD) and in 8 healthy control (HC) subjects. B, Linear regression analysis between creatinine-corrected excretion of DMA or ADMA and creatinine-corrected excretion of 3-nitrotyrosine in the RA patients (B). This study was performed with local ethics committee approval and in accordance with the guidelines of the Declaration of Helsinki and of Good Clinical Practice.
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Kristine Chobanyan-Jürgens, Vu Vi Pham, Dirk O. Stichtenoth and Dimitrios Tsikas

Hypertension. 2011;58:e184-e185; originally published online October 3, 2011;
doi: 10.1161/HYPERTENSIONAHA.111.180984
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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World Wide Web at:
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