Microdialysis of Prostaglandins, Thromboxane, and Other Eicosanoids: Recall Past Knowledge

To the Editor:

Hansen et al. reported that exercise training alters the balance between prostacyclin and thromboxane, as measured in skeletal muscle microdialysis (MD) samples of essential hypertension patients. Muscle MD prostacyclin and thromboxane concentrations measured by Hansen et al. by ELISA are several orders of magnitude higher than their concentrations in plasma and muscle MD samples, as measured by us by gas chromatography tandem mass spectrometry (Figure). Differences in the MD techniques may have contributed to this deviation. However, in consideration of our knowledge in the eicosanoids research area acquired over the past decades, 2 major methodologic shortcomings are more likely to have led to the discrepancy. First, primary eicosanoids are not suitable as biomarkers of in vivo eicosanoid synthesis because of abundant ex vivo formation. For example, thromboxane can be released from activated platelets during sampling. Prostacyclin and thromboxane synthesis is best assessed by measuring their dehydro and/or dinor metabolites, preferentially in urine. Second, commercially available ELISAs for eicosanoids are artifact prone and lack specificity. In essential hypertension, prostacyclin and thromboxane synthesis is not altered compared with normotension as assessed by gas chromatography-tandem mass spectrometry measurement of their major urinary dinor metabolites. In healthy humans, the same methodology revealed that acute physical exercise shifts the prostacyclin/thromboxane ratio in favor of dilatation. This finding supports the observation by Hansen et al. that acute exercise increases prostacyclin and decreases thromboxane muscle MD concentrations after regular physical training in essential hypertension patients. Yet, chronic training halved prostacyclin and thromboxane MD concentration while leaving prostacyclin and thromboxane synthesis expression unchanged. These opposite observations are difficult to reconcile and may suggest methodologic shortcomings in prostanoid analysis, as mentioned above.

Figure. Chromatograms from the gas chromatography-tandem mass spectrometry (GC-MS/MS) analysis of endogenous prostacyclin (6-keto-PGF1α), thromboxane (TxB2), prostaglandin (PG) E2 and D2, and the externally added internal standard tetradeutero-PGE2 (500 pg/mL) in microdialysis (MD) samples (20 μL) of skeletal muscle. MD was performed in an untreated obese subject with hypertension using CMA MD 107 pumps (2 μL/min, Ringer solution) and CMA 60 MD catheters with a polyarylethersulfone membrane (cutoff, 20 kDa) from CMA/MD (Stockholm, Sweden). The concentration of 6-keto-PGF1α, TxB2, PGE2, and PGD2 in concomitantly obtained MD samples (20 μL) of adipose tissue of the same subject was 1, 21, 25, and 6 pg/mL, respectively.

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Dimitrios Tsikas
Alexander A. Zoerner
Sven Haufe
Stefan Engeli
Dirk O. Stichtenoth
Jens Jordan
Institute of Clinical Pharmacology
Hannover Medical School
Hannover, Germany

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Dimitrios Tsikas, Alexander A. Zoerner, Sven Haufe, Stefan Engeli, Dirk O. Stichtenoth and Jens Jordan

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