Cardiovascular risk factors in renal artery stenosis

Effects of renal angioplasty and angiotensin II receptor antagonism

Akademisk avhandling
som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademin vid Göteborgs Universitet kommer att offentligen försvaras i Hjärtats aula, Vita Stråket 12, Sahlgrenska Universitetssjukhuset/Sahlgrenska, Göteborg,

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av
Elzbieta Nowakowska-Fortuna

Fakultetsopponent:
Docent Anders Christensson, Institut för Kliniska Vetenskaper, Lunds Universitet

Avhandlingen baseras på följande delarbeten:

I. **Renal angioplasty causes a rapid transient increase in inflammatory biomarkers, but reduced levels of interleukin-6 and endothelin-1 1 month after intervention.**
Alaa Alhadad, Gregor Guron, Elzbieta Nowakowska-Fortuna, Aso Saeed, Ingrid Mattiasson, Gert Jensen, Bengt Lindblad, Anders Gottsäter and Hans Herlitz.
Journal of Hypertension 2007;25(9):1907-14

II. **Lipoprotein abnormalities in patients with atherosclerotic renovascular disease.**
Elzbieta Nowakowska-Fortuna, Hans Herlitz, Aso Saeed, Per-Ola Attman, Gert Jensen, Petar Alaupovic and Gregor Guron.
Kidney Blood Pressure Research 2011;34(5):311-19

III. **Brain natriuretic peptides in atherosclerotic renal artery stenosis and effects of renal angioplasty.**
Elzbieta Nowakowska-Fortuna, Aso Saeed, Gregor Guron, Michael Fu, Ola Hammarsten, Gert Jensen and Hans Herlitz.
Kidney Blood Pressure Research 2013;37(6):657-66

IV. **Effects of candesartan on kidney function and inflammatory biomarkers in hypertensive patients subjected to renal angioplasty of atherosclerotic renal artery stenosis.**
Elzbieta Nowakowska-Fortuna, Aso Saeed, Gregor Guron, Gert Jensen, Anders Gottsäter and Hans Herlitz.
Submitted

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Cardiovascular risk factors in renal artery stenosis
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Abstract

Renovascular hypertension (RVH) caused by atherosclerotic renal artery stenosis (ARAS) is one of the most common forms of secondary hypertension. The prognosis for patients with RVH is much worse compared to patients with primary hypertension, and caused by a high cardiovascular morbidity. The aim of this thesis was to increase our knowledge about the pathophysiology of RVH and to identify novel treatment targets that could reduce cardiovascular risk in these patients. We investigated: 1) whether systemic inflammation and endothelin-1 (ET-1) are increased in patients with RVH and evaluated how treatment with percutaneous transluminal renal angioplasty (PTRA) affected these variables; 2) lipoprotein abnormalities in patients with atherosclerotic renovascular disease (ARVD) and analyzed whether angiotensin II (Ang II) receptor antagonism with candesartan influenced lipoprotein levels; 3) whether plasma levels of brain natriuretic peptides (BNP) are increased in patients with ARAS and may predict favorable outcome of PTRA; and 4) the long-term effects of candesartan on kidney function, inflammatory biomarkers and ET-1 in patients with ARVD and residual hypertension after PTRA.

In patients with significant renal artery stenosis (RAS) we found increased plasma levels of inflammatory biomarkers and ET-1 compared to healthy subjects. Intervention with PTRA triggered a rapid, transient increase in hs-CRP and IL-6. However, one month after PTRA, both IL-6 and ET-1 had decreased compared to before intervention. Patients with ARVD had elevated levels of atherogenic, triglyceride-rich, ApoC-III-containing lipoproteins in spite of ongoing treatment with statins. Treatment with candesartan did not correct these abnormalities. Patients with ARAS had increased plasma levels of BNP compared to healthy controls, but BNP concentrations were not affected by PTRA. Plasma levels of BNP could not be used to predict the outcome of PTRA on blood pressure. Candesartan did not have any significant effects on kidney function, inflammatory biomarkers or ET-1 in patients with ARVD during 35 months of follow up.

In conclusion, patients with ARAS had increased levels of inflammatory biomarkers, ET-1, and ApoC-III-containing lipoproteins that may contribute to progressive atherosclerosis and accelerated cardiovascular disease. Intervention with PTRA reduced plasma levels of IL-6 and ET-1 indicating beneficial effects on inflammation and the endothelin system. Plasma concentrations of BNP could not be used to identify patients with a favorable outcome to PTRA.

Keywords: inflammation, endothelin-1, apolipoprotein C-III, brain natriuretic peptides, angiotensin II receptor antagonism, renal angioplasty, renovascular hypertension, atherosclerotic renal artery stenosis

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