Plasma Levels of 5-Hydroxyindole-Acetic Acid in Chronic Renal Insufficiency and Their Effect on Platelet Aggregation

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Dear Sir,

The manifestation of uremic symptoms in chronic renal insufficiency (CRI) is attributed to the accumulation of toxic organic solutes. However, it is still not completely clear which organic anion or cation causes or contributes to the development of the defined metabolic or systemic disorder [1]. The accumulation of 5-HIAA in the circulation in CRI has been anticipated [2, 3] but not proved up to now because of the lack of adequately sensitive and specific analytical methods.

We determined plasma 5-HIAA levels in healthy subjects, and in patients with CRI treated conservatively and by hemodialysis. Acetate hemodialysis through cupro-phane membrane was performed for 5 h twice a week, and venous blood before dialysis was analyzed. 5-HIAA in platelet-poor plasma was determined by HPLC with electrochemical detection [4]. The results are summarized in table 1, from which it is clear that 5-HIAA accumulates in the plasma of patients with CRI. A correlation was found between 5-HIAA plasma concentrations and the clearance of endogenous creatinine (Ccr) fitting to the equation: $y = 75.32 \times -0.99$; $r = -0.8955$; $p < 0.001$. 5-HIAA levels in plasma start to increase if $CCT < 0.5$ ml/s, which corresponds to the other organic-anion accumulation [5]. The accumulation of 5-HIAA could interfere with other organic anions for the binding capacity of transport proteins and the organic anion transport system in proximal tubular cells of the kidney. Moreover, 5-HIAA added at the uremic concentration of 1 μ mol/l to withdrawn blood from healthy volunteers ($n = 20$) increased platelet aggregation (PA) induced by ADP ($2-8 \cdot 10^{-6}$ mol/l; area under the curve in 5 min; $AUC_5 = 63.30 \pm 7.32\%$ /min without 5-HIAA versus $79.78 \pm 6.78\%$ /min with 5-HIAA; $p < 0.05$), but did not significantly influence PA induced by 5-HT ($5 \cdot 10^{-4}$ mol/l; $AUC = 18.01 \pm 2.60\%$ /min versus $13.64 \pm 2.54\%$ /min). However, the exact role of accumulated 5-HIAA in the development of hypercoagulable state or consumptive hypocoagulation, both characteristic for patients with CRI, remains to be elucidated. In analogy to the metabolic effects of the other cumulated organic anions in CRI, previously considered as simple metabolic end-products (e.g. hippuric acid) [6],

Table 1. Plasma 5-HIAA levels and Ccr in healthy controls, and in patients with CRI treated conservatively and by hemodialysis

gation (PA) induced by ADP ($2-8 \cdot 10^{-6}$ mol/l; area under the curve in 5 min; $AUC_5 = 63.30 \pm 7.32\%$ /min without 5-HIAA versus $79.78 \pm 6.78\%$ /min with 5-HIAA; $p < 0.05$), but did not significantly influence PA induced by 5-HT ($5 \cdot 10^{-4}$ mol/l; $AUC = 18.01 \pm 2.60\%$ /min versus $13.64 \pm 2.54\%$ /min). However, the exact role of accumulated 5-HIAA in the development of hypercoagulable state or consumptive hypocoagulation, both characteristic for patients with CRI, remains to be elucidated. In analogy to the metabolic effects of the other cumulated organic anions in CRI, previously considered as simple metabolic end-products (e.g. hippuric acid) [6],

we expect that 5-HIAA could interfere with metabolic pathways. Further studies should elucidate the metabolic effects of cumulated 5-HIAA in detail.

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References

- Schoots AC, Dijkstra JB, Ringoir MG, Vanholder R, Cramers CA: Are the classical markers sufficient to describe uremic solute accumulation in dialyzed patients? Hippurate reconsidered. *Clin Chem* 1988;34:1022–1029.
- Sebeková K, Raucinová M, Dzúrik R: Serotonin metabolism in patients with decreased renal function. *Nephron* 1988; 53: 229–232.
- Parbtani A, Frampton G, Cameron J: Platelet and plasma serotonin concentration in glomerulonephritis II. *Clin Nephrol* 1980;14:112–123.
- Sebeková K, Fedelesová V, Blazíček P, Dzúrik R: Acute effect of urapidil on peripheral serotonin metabolism. *Cor Vasa* 1990; 32: 274–281.
- Schoots AC, Peeters JAG, Gerlag PGG: Effect of hemodialysis on serum concentration of HPLC-analyzed accumulating solutes in uremia. *Nephron* 1988; 53:208–217.
- Spustová V, Dzúrik R, Geryková M: Hippurate participation in the inhibition of glucose utilization in renal failure. *Czech Med* 1987;2:79–89.