Does Tubular Secretion of Creatinine Increase after a Meat

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Dear Sir,

The endogenous clearance of creatinine (Ccr) is widely used to estimate the glomerular filtration rate (GFR) in clinical practice. Consequently it has been used to evaluate the renal functional reserve, that is, the increase in GFR in response to a protein load [1-5]. The usefulness of Ccr for this purpose has been criticized because of the existence of a tubular secretion of creatinine (TScr). TScr has been reported to increase significantly after a meat meal, though in some cases this increase was delayed by 90 min after the meal [6, 7]. Nevertheless, results from studies that analyze the simultaneous changes in Ccr and those of other better markers of the GFR (inulin, sodium iothalamate, EDTA) do not always agree with this role of the TScr. Only a reduced number of studies give enough data (GFR, Ccr, urine and plasma creatinine, urinary volume) to calculate the TScr. We have used the results of three of these studies to analyze the effects of a protein meal on the TScr [8-10]. TScr was calculated according to the formula, $TScr = (Ucr \cdot V) - (GRF \cdot Per)$, where Ucr is the urinary concentration of creatinine, V is the urinary volume, GRF is the renal clearance of iothalamate and Per is the plasma concentration of creatinine.

Rugiu et al. [8] studied 2 groups of patients with solitary kidneys. Group 1 had normal renal function, while group 2 had a GFR of 60 ml/min. Group 3 was the control group (normal subjects). Renal clearances were studied before and 4 h after a meat meal consisting of 100-120 g of protein. Mean basal values were the following.

Group 1: Per 102.5 $\mu\text{mol/l}$ (1.16 mg/dl); Ucr 4154.8 $\mu\text{mol/l}$ (47 mg/dl); V (4 h) 750 ml; Ccr 127 ml/min, and GFR 112 ml/min.

Group 2: Per 145.8 $\mu\text{mol/l}$ (1.65 mg/dl); Ucr 3,270.8 $\mu\text{mol/l}$ (37 mg/dl); V (4 h) 764 ml. Ccr 72 ml/min, and GFR 60 ml/min.

Group 3: Per 68.1 $\mu\text{mol/l}$ (0.77 mg/dl); Ucr 3,138.0 $\mu\text{mol/l}$ (35.5 mg/dl); V (4 h) 700 ml; Ccr 134 ml/min, and GFR 120 ml/min.

Mean values after protein load were as follows.

Group 1: Per 106.0 $\mu\text{mol/l}$ (1.2 mg/dl); Ucr 4,667.0 $\mu\text{mol/l}$ (52.8 mg/dl); V (4 h) 853 ml; Ccr 154 ml/min, and GRF 195 ml/min.

Group 2: Per 159.0 $\mu\text{mol/l}$ (1.8 mg/dl); Ucr 3,624.0 $\mu\text{mol/l}$ (41 mg/dl); V (4 h) 898 ml; Ccr 85 ml/min, and GRF 105 ml/min.

Group 3: Per 76.0 $\mu\text{mol/l}$ (0.86 mg/dl); Ucr 5,481.0 $\mu\text{mol/l}$ (62 mg/dl); V (4 h) 482 ml; Ccr 144 ml/min and GFR 177 ml/min.

TScr before and after the protein load was 1.5 $\mu\text{mol/min}$ (0.16955 mg/min) vs. -4.1 $\mu\text{mol/min}$ (-0.4656 mg/min) for group 1; 1.5 $\mu\text{mol/min}$ (0.1866 mg/min) vs. -3.3 $\mu\text{mol/min}$ (-0.3689 mg/min) for group 2, and 1.0 $\mu\text{mol/min}$ (0.1126 mg/min) vs. -2.4 $\mu\text{mol/min}$ (-0.2760 mg/min) for group 3.

A similar study was carried out in 10 patients with mild renal failure [9]. Mean basal values were: Per 236.0 $\mu\text{mol/l}$ (2.67 mg/dl); Ucr 6,859.8 mg/dl (77.6 mg/dl); Vm (urinary volume in 1 min) 1.86 ml; Ccr 54 ml/min, and GFR 22.6 ml/min. Mean values after protein load were: Per 250.2 $\mu\text{mol/l}$ (2.83 mg/dl; Ucr 4,411.2 $\mu\text{mol/l}$ (49.9 mg/dl); Vm 1.41; Ccr 25, and GFR 60. TScr before and after the protein meal was 0.8399 vs. -0.9944 mg/min.

A third study [10] analyzed the effect of a high protein diet during 4 weeks on the GFR of 31 patients with chronic renal insufficiency.

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Mean basal values were: Per 133.5 $\mu\text{mol/l}$ (1.51 mg/dl); Ucr 8,221.2 $\mu\text{mol/l}$ (93 mg/dl); Vm 0.97 ml; Ccr 51 ml/min and GFR 48 ml/min. TScr before and after the 4-week period was 1.5 $\mu\text{mol/min}$ (0.17 mg/min) vs. -3.0 $\mu\text{mol/min}$ (-0.034 mg/min).

It is widely accepted that Ccr includes glomerular and tubular clearances of creatinine. At normal levels of GFR, the difference between Ccr and GFR is from 10 to 40 ml/min/1.73 m² and this difference appears greatest at lower levels of GFR [11]. Therefore, when Ccr is less than GFR, the possibility that TScr is null is strongly suggested. Some other studies that analyzed the effect of a protein meal also failed to show a major increase in Ccr over GFR [1, 4]. The appearance of TScr seems to be related to time in some studies [4, 7].

In summary, the above data do not support an increment in the TScr after a protein load. The explanation for these findings is unknown. Like cimetidine, could amino acids have an inhibitory effect on TScr?

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