Plasma Levels of Branched Chain Keto Acids in Nephrotic Patients

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Patients

All the values are expressed as nmol/ml. KIVA = α -Ketoisovaleric acid; KIMVA = α -Keto- β -methylvaleric acid.

Dear Sir,

Experimental evidence suggests that branched chain amino acids (BCAAs) and their ketoanalogues (BCKAs) exert important effects on muscle protein metabolism and on serum albumin synthesis. Namely, leucine stimulates protein synthesis, whereas α -ketoisocaproic acid (KICA) reduces muscle protein breakdown [1] and exerts a nitrogen-sparing effect [2]; a mixture of BCKAs can increase albumin synthesis [3].

In patients affected by nephrotic syndrome, BCAAs seem quite normal [4] but, to our knowledge, BCKAs plasma levels have never been measured.

Fasting levels of BCAAs and BCKAs were evaluated in 12 patients (8 males, 4 females, aged 16-62 years) affected by primary, steroid-resistant nephrotic syndrome. BCKAs were found to be reduced in early and late chronic renal failure [5], and, to avoid the interference factor of renal failure, only patients with normal or slightly reduced renal function were studied.

Serum creatinine, creatinine clearance and other biochemistries are shown in table 1. Light microscopy and immunofluorescence revealed membranous glomerulonephritis in 9 cases, focal glomerular sclerosis in 1 and membranoproliferative glomerulonephritis in 1 case. One patient refused kidney biopsy. No patient was treated by immunosuppressive or steroid therapy during the study. All of them were following a low-sodium diet with no limitation in protein intake.

All the plasma samples were obtained after a fasting period of 12 h and stored at -20°C. The analysis of plasma amino acids and plasma keto acids were performed as previously described [5]. The reference ranges were obtained from determinations of plasma amino and keto acids in 100 healthy volunteers [5].

The results are shown in table 2. In these nephrotic patients, the fasting levels of valine, leucine and isoleucine were normal. Instead, all three BCKAs were strongly reduced. In 8 of 12 patients, KICA plasma levels were below the lower limit of the normal range (mean - 2 SD).

We can thus confirm that fasting plasma levels of BCAAs in nephrotic patients are within the normal limits, whereas the BCKAs levels are abnormally low.

The question then arises if this abnormality can negatively affect protein metabolism in nephrotic patients and if dietary supplementation with BCKAs may correct it.

Table 2. Fasting plasma levels of BCAAs and BCKAs in 12 patients with nephrotic syndrome (mean $\pm$ SD)

References

Mitch WE, Clark AS: Specificity of the effect of leucine and its metabolites on protein degradation in skeletal muscle. *Biochem J* 1984; 222: 579-586.

Mitch WE, Walser M, Sapir DG: Nitrogen sparing induced by leucine compared with that induced by its keto analogue, α -ketoisocaproate, in fasting obese man. *J Clin Invest* 1981; 67: 553-562.

Kirsch RE, Frith LC, Saunders SJ: Stimulation of albumin synthesis by keto analogues of amino acids. *Biochim Biophys Acta* 1976; 442: 437-441.

Table 1. Biochemistries of the 12 studied patients

Serum creatinine, mg/dl 0.9 $\pm$ 0.2

Creatinine clearance, ml/min 80 $\pm$ 19

Serum urea, mg/dl 24 $\pm$ 14

Urinary urea, g/day 13.2 $\pm$ 3.2

Urinary protein, g/day 7.6 $\pm$ 1.9

Serum total proteins, g/dl 5.0 $\pm$ 0.6

Serum albumin, g/dl 2.5 $\pm$ 0.3

Serum cholesterol, mg/dl 297 $\pm$ 66

Serum triglycerides, mg/dl 234 $\pm$ 98

Reference range

Don BR, Wada L, Kaysen GA, Schambelan M: Effect of dietary protein restriction and angiotensin converting enzyme inhibition on protein metabolism in the nephrotic syndrome. *Kidney Int* 1989; 27: S163-S167.

Langer K, Frohling PT, Diederich J, Brandl M, Lindenau K, Fekl W: Plasma amino and keto acids in chronic renal failure. *Contrib Nephrol. Basel, Karger*, 1988, vol 65, pp 55-59.