ALPHA-KETOGLUTARATE VERSUS KETOACIDS AS DIETETIC SUBSTITUTES IN CHRONIC RENAL INSUFFICIENCY

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Introduction

Although ketoanalogues (KA) of essential aminoacids (EA) are metabolised roughly one-third into aminoacids, in chronic renal insufficiency these substances exhibit a more favourable effect as dietary substitutes compared with EA alone. Serum concentrations of Valine, Leucine, Isoleucine, Threonine, Lysine and Tyrosine increase significantly. This observation cannot simply be explained as an alimentary effect of KA. Since α-ketoglutarate is a key substance in the metabolism of aminoacids, in this study the hypothesis was tested that α-ketoglutarate may exert effects similar to KA.

Material and methods

Thirty-six patients (age 34–61 years, serum creatinine > 5mg%) receiving a protein restricted diet (45g non selected protein/day) substituted with KA of EAA (10g), were compared with 10 patients (age 36–57 years, serum creatinine >5mg%) having the same protein restriction but instead of KA of EAA, equimolar quantities of α-ketoglutarate. The observation period was 12 months. Serum concentrations of BUN, creatinine, uric acid, triglycerides, cholesterol, phosphate, glucose, and the haematocrit were determined every month. Concentrations of plasma aminoacids were measured every six weeks using an automatic analyzer (Biotronic LC 6000) for chromatographic analysis.

Results

During and immediately after the observation period of one year, there were no differences with respect to the serum concentrations of BUN, creatinine, uric acid, triglycerides, cholesterol, phosphate, glucose, and the haematocrit in the two groups. Analysis of plasma aminoacids depicted an identical course during the observation period: normalisation of plasma aminoacids except for the branched chain aminoacids valine, leucine, isoleucine.
Discussion

It has been generally accepted for a long time that in chronic renal insufficiency concentrations of plasma aminoacids are in the subnormal range. This refers especially to the branched chain AA. Pathophysiological mechanisms responsible for these alterations are hypothetical. Applications of a protein restricted diet combined with substitution of KA is followed by an improvement of the metabolic state and the plasma aminoacids respectively. Alpha-ketoglutarate instead of KA has similar effects. This may probably be explained by a stimulating effect of $\alpha$-ketoglutarate on protein synthesising enzymes or as a nonselective inhibition of desamination.