INFLUENCE OF ESSENTIAL AMINO ACID ANALOGUES ON THE UREA CYCLE ENZYMES AND PROTEIN SYNTHESIS IN THE LIVER OF CHRONIC URAEMIC RATS

M Vlaho, H G Sieberth

Medical Clinic of the University, Cologne, FRG

Introduction

It has been suggested by Walser [1] that the analogues of essential amino acids may be useful in the treatment of chronic uraemic patients. The mode of their action on nitrogen metabolism is not yet completely understood.

Material and Methods

Wistar male rats with initial body weight between 250 and 300 g were used. A 5/6th nephrectomy was performed, removing one kidney and 2/3rd of the remaining kidney 14 days later. The control animals were sham operated. All animals were given a stock diet containing 19% protein. Thirty days after 5/6 nephrectomy, both uraemic and control rats were put on a protein-poor diet containing 8% protein (2 g protein per day). In addition they received a mixture of five analogues of essential amino acids and the remaining essential amino acids themselves (2.1 g per kg body weight/day) through a gastric tube. Three to four weeks after switching to a protein-poor diet and supplementation with essential amino acid analogues, the rats were sacrificed and the liver removed in toto. The activities of the enzymes of the urea cycle were measured by the method of Brown [2], the protein content of rat liver was determined by the method of Lowry [3].

Results

The chronic uraemic rats lost body weight. After switching to the protein-poor diet and keto analogues of essential amino acids, both uraemic and control animals again gained body weight. Blood urea rose significantly in uraemic rats during stock diet. After getting the special diet however, blood urea decreased significantly. Chronic uraemia per se changes the activities of urea cycle enzymes by significantly elevating carbamoylphosphatesynthetase, argininosuccinatesynthetase and argininosuccinateleyase in the liver of chronic uraemic
rats as compared with controls. The protein content of the liver of the chronic uraemic rats is markedly lower than in control animals. After feeding with protein-poor diet and supplementation with analogues of essential amino acids, the enzymes argininosuccinatesynthetase and argininosuccinatelyase were significantly lower in uraemic rats than in controls (Figure 1). The other enzymes of the urea cycle did not differ from that of sham operated rats. No difference was observed in the protein content of the liver between uraemic and normal animals.

Figure 1. Effect of protein poor diet supplemented with keto analogues of essential amino acids on the activities of urea cycle enzymes in the liver of chronic uraemic rats as compared with sham operated rats. The activities of argininosuccinatesynthetase and argininosuccinatelyase are significantly lower in uraemic than in control animals.

Discussion

Uraemic animals on low protein diet alone had significantly higher activities of argininesynthetase than protein restricted controls [4]. Uraemic animals put on a protein-poor diet supplemented with the analogues of essential amino acids had significantly lower argininosuccinatesynthetase activity than controls. The results suggest that such a diet exerts an anabolic effect similar to that observed after treatment with growth hormone [5]. The finding that the protein content in the liver of uraemic rats does not differ from controls supports this concept of anabolic effects of analogues of essential amino acids in experimental chronic uraemia.
References

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