

ABSTRACT

Urea Kinetics in Sickle Cell Disease

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When dietary nitrogen intake is inadequate to satisfy the body's metabolic demand for nitrogen, adaptive mechanisms are invoked whereby nitrogen losses are minimised. The most significant reduction in nitrogen loss is effected by reduced urea production and excretion and there is a concomitant increase in the proportion of urea hydrolysed and recycled in the body. This work was designed to explore the mechanisms by which nitrogen equilibrium is maintained in the whole body when the metabolic demands for nitrogen exceed the supply.

Urea kinetics was measured in normal healthy controls (HbAA) and patients with homozygous sickle cell disease (HbSS). HbSS is characterised by an increased metabolic demand for nitrogen for erythropoiesis, which is significantly higher than normal. Urea production (P), excretion (Eu), hydrolysis (T) and recycling (Pr) of hydrolysed urea to urea synthesis, were determined using isotopic urea (urea-30) orally or intravenously, and the two methods compared. The reliability of the methods was examined and demonstrated to be satisfactory.

All aspects of urea metabolism were increased in HbSS compared with HbAA, except Eu which tended to be lower in HbSS. The proportion of urea hydrolysed in the colon was raised in HbSS, regardless of the route by which the isotope was given and the kinetics was measured. Individuals with sickle cell trait (HbAS), were also studied and exhibited rates of urea hydrolysis that were either similar to the HbAA values or raised to values corresponding to the HbSS.

Urea nitrogen was incorporated into haemoglobin in both the HbAA and HbSS. This finding confirmed the utilisation of endogenous urea nitrogen for protein synthesis in the body. The proportion of hydrolysed urea nitrogen is small (10%) compared to a larger pool of enteric nitrogen to which it contributes, suggesting that there may be a more significant contribution of enteric nitrogen metabolism to the nitrogen economy, than of hydrolysed urea alone.

The possibility that glycine may be limited in HbSS has been indicated and warrants more detailed investigation. The metabolism of urea has been shown to be affected by depleting the body glycine pool and alternatively by glycine supplements.

Results from this work support the idea that urea kinetics is modulated by dietary nitrogen intake.