

ABSTRACT

Glutamine is the major source of urinary ammonia and this study examines the metabolism of that amino acid in rats under varying acid-base conditions.

Other workers have shown that in acidosis there is enhanced renal oxidation of glutamine, which requires increased amounts of acetyl CoA. The present study has shown that during acidosis there was no change in the activity of oxaloacetate decarboxylase and malic enzyme, two enzymes capable of increasing the formation of acetyl CoA.

This study also showed that 3-mercaptopycolinic acid inhibited PEPCK - the rate limiting enzyme of gluconeogenesis - and thereby inhibited ammoniogenesis from glutamine mainly by inhibiting deamination.

Metabolic acidosis was induced with NH_4Cl or HCl . In rats given NH_4Cl there was an immediate increase in blood ammonia levels and urinary excretion of ammonia, but this did not occur with rats fed HCl which showed no change in urinary ammonia but a decrease in urea excretion. Rats fed either NH_4Cl or HCl had similar increases in the plasma concentrations of glutamine, renal PEPCK activity, ammonia and glucose production by renal cortical slices.

The time course of changes in metabolic intermediates was measured in rats given NH_4Cl or HCl . NH_4Cl caused a striking decrease in renal levels of malate, 2-oxoglutarate and phosphoenol pyruvate. Similar changes were observed with

HCl, but in addition the levels of glucose and glucose-6-phosphate were elevated.

The results of the studies with 3-mercaptopycolinic acid and the metabolite profile in response to acidosis are both consonant with the theory that displacement of the glutamic dehydrogenase equilibrium is an important mechanism in the control of glutamine utilisation and the ammoniagenic response to acidosis.