THE ROLE OF THE LIVER AS A SIGNIFICANT MODULATOR
OF THE SERUM GUANIDINOACETIC ACID LEVEL IN MAN

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INTRODUCTION

The metabolism of guanidinoacetic acid (GAA) may be affected
by the status of both the kidney and the liver, as GAA is synthe­sized in the kidney and metabolized to creatine in the liver\(^1\).
Little attention has been focused on GAA metabolism in patients
with liver damage, although there have been many studies on GAA
metabolism in uremic patients\(^2\),\(^3\),\(^4\).

To examine the role of the liver in modulating the serum GAA
level, we studied changes in the serum levels of guanidine compounds
in renal failure patients with liver damage in comparison with renal
failure patients without liver damage and patients with liver
cirrhosis.

MATERIALS AND METHODS

Blood samples were obtained from 38 patients with acute renal
failure (ARF), 111 with chronic renal failure (CRF), 17 with liver
cirrhosis and 60 healthy subjects in the fasting state or before
hemodialysis (HD) sessions. For measurements of serum concentra­tions of GSA, methylguanidine (MG) and GAA, each serum was pre­treated for deproteinization with trichloroacetic acid at a 10 %
final concentration\(^5\), and then, 0.5 ml aliquots of the supernatant
was applied to an automated guanidine analyzer, JASCO model G-520
(Japan spectrophotometric Co., Tokyo, Japan)\(^6\). Serum concentrations
of urea-N and creatinine were determined by an autoanalyzer using
a part of the same blood samples described above.
The ARF group included 38 patients, all of whom had such severe renal failure as to require HD therapy. Although 27 of these ARF patients had no liver dysfunction, 11 patients had liver damage, which was deduced from the following findings: an elevation of the serum transaminase level above two times the normal value, or marked jaundice giving serum bilirubin levels above 4 mg/dl, both or either of which were combined with an abnormality of the hepaplastin test or thrombo test below 40% of the normal value. No patients with liver damage were included among the CRF patients. The CRF patients were divided into three subgroups according to the stage of renal disease: CRF-nondialyzed included 28 patients under conservative treatment; CRF-initial HD, 24 patients at the initiation of HD therapy; and CRF-regular HD, 59 patients undergoing regular dialysis for more than three months. None of the 17 patients with liver cirrhosis had renal failure.

RESULTS

Serum levels of urea-N, creatinine, GSA, MG, GAA and arginine in patients with ARF and CRF

The mean serum values of urea-N, creatinine, GSA, methylguanidine (MG), GAA, and arginine in patients with ARF and CRF in various stages are summarized in Table 1.

The mean serum urea-N level in ARF patients was almost the same as that in CRF-initial HD, and was higher than that in CRF-nondialyzed and CRF-regular HD. The mean serum creatinine level in ARF patients was significantly lower than CRF-initial HD and CRF-regular HD.

The mean serum GSA level in the ARF patients was 274.4 ± 43.5 μg/dl, and was significantly lower than that in CRF-initial HD and CRF-regular HD, although it was higher than that in CRF-nondialyzed. Although the GAA level in ARF patients seemed to be the lowest among the four groups, no significant difference was found except for CRF-regular HD. The serum MG level in the same group was significantly lower than that of CRF-initial HD and CRF-regular HD, with same tendency as seen in the serum GSA level. The mean serum arginine level in ARF patients was the lowest among these groups.

The serum profile of nitrogen metabolites and the guanidino compounds in ARF patients with liver damage in comparison with ARF patients without liver damage and patients with liver cirrhosis:

Serum levels of these measurements in the ARF patients with liver damage are summarized in Table 2 with reference to the presence or absence of liver damage.