Amino Acids (1992) 3: 223–228

Amino
Acids

Are prealbumin plasma levels linked to amino acid supply from peripheral tissues in liver cirrhosis?

P. Amodio, S. Bellon, C. Merkel, M. Bolognesi, and **A. Gatta**

Institute of Clinical Medicine, University of Padua, Italy

Accepted November 25, 1991

Summary. Prealbumin plasma level is considered a good index of liver function in liver cirrhosis. However, plasma protein levels depend not only on liver function, but also on amino acid supply which is consequent to nutritional status.

In 12 cirrhotics we measured prealbumin plasma levels and the lower limb venous-artero difference of amino acid plasma levels in blood samples taken from femoral vein and femoral artery in post-absorptive conditions considered as a direct index of protein release from peripheral tissues and an indirect index of protein nutritional status.

In arterial and in venous plasma amino acid sum was 1.86 ± 0.40 (mean + sd) and 2.00 ± 0.04 mMol/l respectively.

Prealbumin plasma levels were found directly correlated with the venous-artero difference of amino acid plasma levels ($r = 0.57$ $p < 0.05$) and of glutamate + glutamine levels ($r = 0.73$ $p < 0.007$).

In conclusions, these data suggest that prealbumin plasma levels are linked to amino acid supply from peripheral tissues in cirrhotics.

Keywords: Amino acids – Prealbumin – Nutrition – Liver function

Introduction

The evaluation of liver function is a complex task. First of all, liver has many functions: it is implied in the metabolism of glucids, lipids, proteins and foreign substances; it is involved in the biliary excretions of many molecules and drugs, and, eventually, in the plasma clearance of colloids, antigens and immune complexes via the hepatic reticulo-endothelial system.

Dynamic quantitative liver function evaluations by clearance studies, or by the evaluation of the maximal liver capacity to metabolize substances (e.g. galactose) are generally used in pathophysiological studies and in clinical research (Burnstein 1981; Lindskow, 1982; Merkel, 1989).

However, in clinical practice the evaluation of liver function is mainly based on the measuring of bilirubin, albumin plasma levels and prothrombin time which are the paramethers used to calculate the Pugh-Child score (Albers, 1989).

Prothrombin and albumin are proteins synthetized by the liver: their plasma levels reflect the extent of liver protein synthesis, provided that their plasma clearance is not increased.

Theoretically, the lower the half-life of a plasma protein synthetized by the liver, the higher is the reliability of its plasma level as an index of the present liver synthetic ability.

For this reason, recenty plasma proteins with a lower half-life than albumin have been proposed to evaluate liver function: prealbumin (Hutchinson, 1981; Rondana, 1987) and blood coagulation factors II, V and VII (Forster, 1989).

However, some evidence suggest that plasma protein levels in liver disease do not depend only on liver function, but also on nutrition, in particular on protein supply. In this regard Smith (1982) found that a protein-calorie dietetic enrichment increases albumin plasma levels in alcoholic liver disease.

Till now data are not available concerning the relationship between plasma protein levels and amino acid release from peripheral tissues in post-absorptive conditions in chronic liver disease.

We therefore undertake a research in cirrhotics to evaluate if prealbumin and albumin plasma levels are linked to the venous-artero differece in amino acid concentrations in the lower limb, considered as a direct index of amino acid release from peripheral tissues in post-absorptive conditions and as indirect index of protein nutritional status.

Material and methods

The study comprised 12 patients (3 females and 9 males) aged 43–60 years suffering from liver cirrhosis. The diagnosis had been made by case history, clinical and laboratory findings and confirmed by liver biopsy or peritoneoscopy in 8 patients. Seven patients had alcoholic cirrhosis, 2 posthepatitic cirrhosis and 3 cryptogenic cirrhosis. No one had ascites, all of them had esophageal varices and bled in the past. However, no one had bled in the month preceding the study. One patient had non insulin dependent diabetes. Ten cirrhotics were in Pugh-Child class A, two in class B.

In all patients prealbumin plasma level was measured by radial immunodiffusion, according to Mancini (1965).

The main clinical and laboratory data are shown in Table 1.

All patients received a free hospital diet containing about 1600 Cal. with 60 g. of proteins.

After an overnight fast, blood samples were drawn from femoral vein and from femoral artery to measure plasma amino acid levels. The amino acids alanine (ALA), valine (VAL),

Table 1. Summary of the main biochemical data of the cirrhotics studied (mean s.d.)

AST (U/l) = 39 ± 6	ALT (U/l) = 37 ± 5
Prothrombin time (%) = 67 ± 6	Total bilirubin (mg/l) = 13 ± 2
Albumin (g/l) = 38.8 ± 1.4	Prealbumin (mg/l) = 107 ± 12

leucine (LEU), isoleucine (ILE), proline (PRO), phenilalanine (PHE), tryptophane (TRP), glycine (GLY), serine (SER), threonine (THR), cysteine (CYS), tyrosine (TYR), ornitine (ORN), glutamate plus glutamine (GLX), previously isolated by ion exchange chromatography according to Harris (1961), were measured by gas chromatography according to Coulter and Hann (1968). Results are expressed as mean ± s.e.

Results

Prealbumin plasma levels were 107 ± 12 mg/l (mean ± s.e.). In all patients they were below the lower limit of reference used in our laboratory, reported by Rondana (1987).

Arterial and venous amino acid levels are reported in Table 2. The molar ratio between the sum of branched chain amino acids and thyrosine was 1.6 ± 0.7.

A significant correlation ($r = 0.57$ $p < 0.05$) was found between prealbumin plasma levels and the venous-artero difference of the sum of the amino acids that we measured. In particular, prealbumin was found directly correlated with the venous-artero difference of TYR ($r = 0.79$ $p < 0.002$) and GLX ($r = 0.73$ $p < 0.007$) (Fig. 1). Prealbumine plasma levels did not show any link with the venous-artero difference of ALA (Fig. 1) and other amino-acids.

Albumin plasma levels and prothrombin time were not found linked to the venous-artero differences in individual amino acids, or in their sum.

Table 2. Arterial and venous amino acid levels of the cirrhotics studied (mean ± s.e.)

	artery	vein		artery	vein
ALA	192 ± 15	231 ± 21	VAL	133 ± 9	142 ± 12
LEU	97 ± 8	105 ± 9	ILE	46 ± 4	49 ± 4
PHE	92 ± 7	102 ± 8	TYR	111 ± 9	125 ± 8
TRP	57 ± 6	63 ± 7	THR	146 ± 19	151 ± 19
GLY	88 ± 9	93 ± 9	SER	57 ± 6	59 ± 6
PRO	152 ± 10	163 ± 13	CYS	67 ± 7	70 ± 8
ORN	109 ± 15	118 ± 12	GLX	580 ± 53	601 ± 48

Results are expressed as μmol/l

Discussion

Plasma amino acid pattern in our series was the typical one observed in cirrhotics: the molar ratio between the sum of branched chain amino acids and TYR was lower than 5.7 that is the lower limit in normal subjects (Azuma, 1989).

The amino acid venous-artero difference showed the well-known amino acid release from peripheral tissues in post-absorptive conditions. In particular, the difference between femoral vein and femoral artery may be considered a valuable index of the whole muscular amino acid exchange, because the lower limb accounts for one quarter of the total body muscular mass (Malina, 1978).

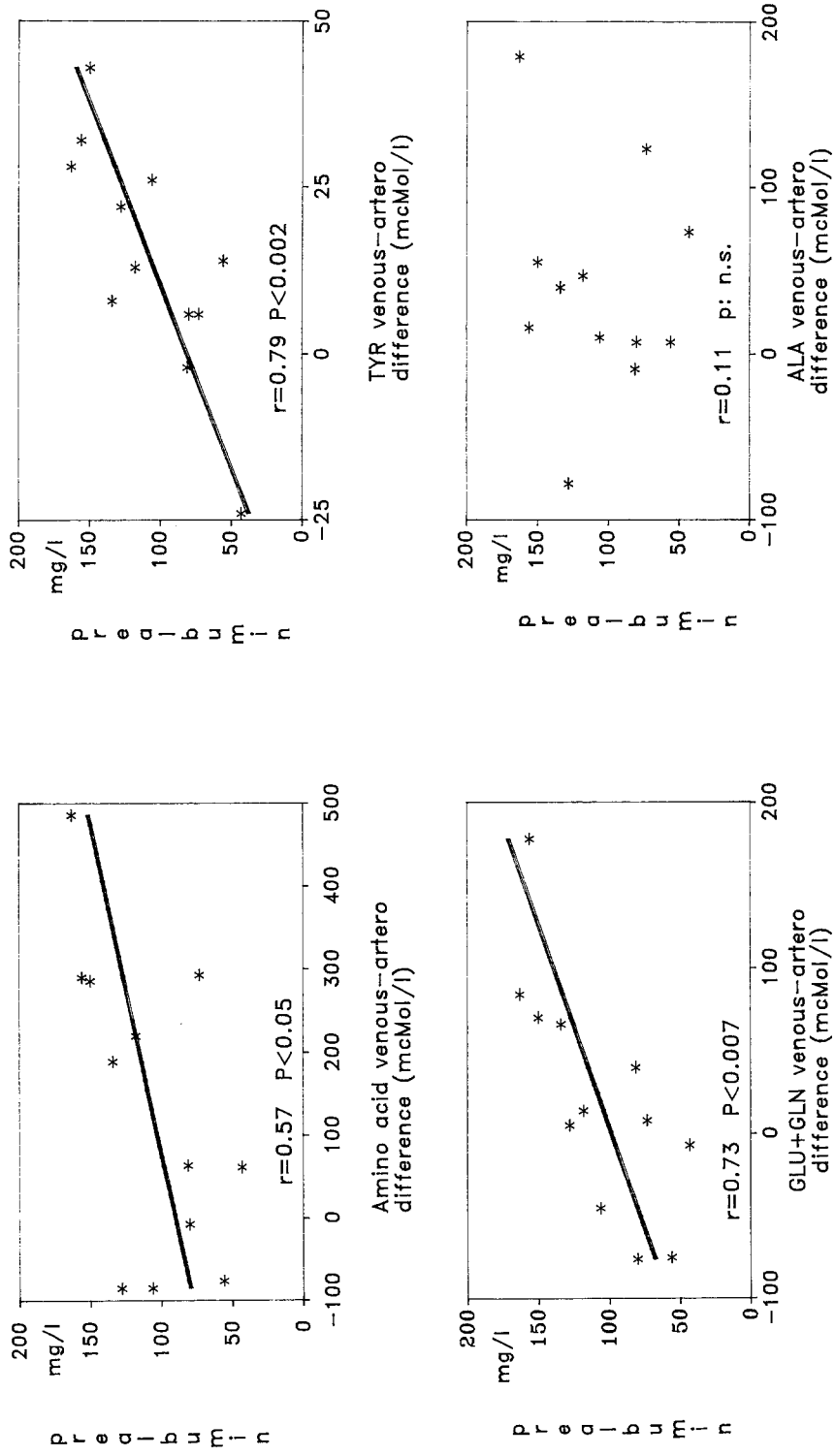

Fig. 1. Correlations between prealbumin plasma levels and amino acid venous-artero differences

Alanine and GLX were the predominant amino acid released, but, since they constitute a small proportion of the amino acid residue in muscle proteins, their predominance in venous outflow indicates in situ synthesis by transamination of their keto analogues. The major nitrogen sources for transamination are the branched chain amino acids which are oxidized prevalently in muscle.

In not hepatopathic subjects liver protein synthesis is limited by protein-calorie malnutrition (Young, 1975; Bernstein, 1989).

In cirrhotics protein synthesis is considered to be limited mainly by liver function and not by the availability of amino acids. This opinion is in keeping with the significant direct correlation that was found by Rondana (1987) between prealbumin plasma levels and galactose elimination capacity that is a valuable index of functional liver mass in liver diseases (Tyngstrup, 1983). Also the significant correlation between prealbumin plasma levels and theophylline clearance in cirrohotics that we recently found (Amodio, 1991) suggests that prealbumin plasma levels are strictly linked to liver function.

However, the correlation between prealbumin plasma levels and amino acid venous-artero difference suggests that amino acid supply could be a limiting factor for prealbumin synthesis in cirrhotics too. The direct correlation between prealbumin plasma levels and GLX release from peripheral tissues seems emphasize the link existing between protein calorie nutritional status and prealbumin plasma levels. This is because GLX outflow reflects the oxidation of amino acids in muscle, because its release is the expression of amino group transfer from amino acids to alpha-ketoglutarate which is the principal acceptor of amino groups (Lehninger, 1970). These findings are in keeping with those of Sachs (1986) and Bernstein (1989) concerning prealbumin value as one of the most sensitive and accurate index of energy-protein malnutrition. Moreover, this is also in accordance with the report by Smith (1982) who could increase albumin levels in patients with alcoholic liver disease giving them a protein rich diet.

The direct correlation between prealbumin plasma levels and TYR venous-artero difference suggests that prealbumin plasma levels are linked to muscular mass. This is because TYR is not oxidized in muscle, so that its release reflects the whole amino acid release from muscle protein catabolism which depends on muscle mass and hormonal factors.

However, the direct correlations between prealbumin plasma levels and amino acid release could also suggest that the more severe liver insufficiency, the lower muscle protein mass able to release amino acids.

Albumin levels were not correlated with peripheral amino acid release. In our opinion this is the consequence of the relatively long half-life of albumin which can not, therefore, accurately reflect either liver function, or the present nutritional status of a patient, in accordance with the observations by Shetty (1979), Sachs (1986) and Bernstein (1989).

In conclusion, prealbumin plasma level, well-known index of liver function, is also directly linked to amino acid release from peripheral tissues in post absorptive conditions. This may indicate that prealbumin plasma levels in cirrhotics are limited not only by liver function, but also by nutritional status. Alternatively, it may indicate that the higher the liver impairment in cirrhotics, the lower the amino acid release from peripheral tissues.

References

Albers I, Hartmenn H, Bircher J, Creutzfeld W (1989) Scand J Gastroenterol 24: 269–276
Amodio P, Lauro S, Rondana M, Crema G, Merkel C, Gatta A, Ruol A (1991) Respiration 58: 106–111
Bernstein LH, Leukhardt-Fairfield CL, Pleban W, Rudolph R (1989) Clin Chem 35: 271–274
Burnstein AV, Galambos JT (1981) Dig Dis Sci 26: 1078–1083
Coulter JR, Hann CS (1968) J Chromatogr 36: 42–49
Forster J, Greig PD, Glynn MFX, Poon A, Levy G, Superina RA, Langer B (1989) Transplant Proc 21: 2308–2310
Harris CK, Tigane E, Hanes CS (1961) Can J Biochem Physiol 39: 439–451
Hutchinson DR, Smith MG, Parke DV (1981) Clin Chim Acta 114: 69–74
Lehninger AL (1970) Biochemistry. Worth Publishers, New York, p 437
Lindskow J (1982) Acta Med Scand 212: 295–302
Malina RM (1978) Growth of muscle tissue and muscle mass. In: Falkner F, Tanner JM (eds) Human growth, vol. 2. Balliere Tindall, London, pp 273–294
Mancini D, Carbonara AC, Hermans JF (1965) Immunochemistry 2: 235–237
Merkel C, Bolognesi M, Finucci GF, Angeli P, Caregaro L, Rondana M, Gatta A (1989) J Hepatol 9: 16–22
Rondana M, Milani L, Merkel C, Caregaro L, Gatta A (1987) Digestion 37: 72–78
Sachs E, Bernstein LH (1986) Clin Chem 32: 339–341
Shetty PS, Watrasiewicz KE, Jung RT, James WPT (1979) Lancet ii: 230–232
Smith J, Horozitz J, Henderson JM, Heymsfield J (1982) Am J Clin Nutr 35: 56–72
Tyngstrup N, Vilstrup H (1983) Lab Res Meth Biol Med 7: 17–41
Young VR, Steffee WP, Pencharz PB, Winterer JC, Scrimshaw NS (1975) Nature 253: 192–194

Authors' address: Dr. P. Amodio, Clinica Medica II, Università di Padova, via Giustiniani, 2, I-33126 Padova, Italia.

Received August 20, 1991