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## Azygos and hepatic extraction of atrial natriuretic factor (ANF) in patients with cirrhosis No evidence of reduced disposal

Atrial natriuretic factor (ANF) is a circulating hormone with natriuretic and vasodilating effects, which has been reported to be decreased, normal or elevated in different patients with cirrhosis. Thus, Hollister et al. (1) and Moreau et al. (2) have suggested that decreased splanchnic removal plays a role in the abnormal levels of ANF reported in some patients with cirrhosis. Recently, we found a normal hepato-enteric clearance in patients with cirrhosis ( $274 \pm 46$  vs  $237 \pm 46$  ml/min in controls, n.s.) (3). As pointed out then, our results only accounted for disposal from those parts of the liver and intestine that are drained through the hepatic veins (2). Oesophageal varices are drained through the azygos vein. However, the extraction of ANF in blood drained through this vein has hitherto not been investigated. The present investigation was therefore undertaken to determine azygos extraction of ANF in patients with cirrhosis.

We report results from 9 patients (age 52-68, mean

58 years) with biopsy-verified cirrhosis (8 alcoholic, 1 posthepatitic), who underwent hepatic and azygos vein catheterization. Fluid retention and ascites were present in 7 patients. Patients without fluid retention were not restricted as to diet, whereas those with ascites were put on a sodium diet of 40 mmol/day. Seven patients received diuretics. Six patients with minor disorders and unrestricted diet served as controls. Catheterization procedure, flow measurements, assessment of extraction and clearance, and analysis of ANF have been described in detail elsewhere (3-5).

The mean arterial concentration of ANF in the patients was similar to that of the controls ( $10.0 \pm 1.4$  vs.  $9.6 \pm 2.8$  pmol/l, respectively, n.s.). As illustrated in Figure 1, a substantial arterio-azygos extraction ( $0.35 \pm 0.09$ ) was present in patients with cirrhosis and directly correlated to the arterio-hepatic extraction ( $0.33 \pm 0.10$ ,  $r = 0.86$ ,  $p < 0.005$ ). Azygos and hepato-enteric clearances of ANF were similar (Table 1) and the

TABLE 1

Splanchnic disposal of atrial natriuretic factor (ANF) in patients with cirrhosis and controls

|                 | Azygos blood flow (l/min) | Hepatic blood flow (l/min) | $E_{ANF}$ Azygos | $E_{ANF}$ Hepatic | Azygos ANF clearance (ml/min) | Hepatoenteric ANF clearance (ml/min) | Overall splanchnic ANF clearance (ml/min) | Overall splanchnic ANF removal (pmol/min) |
|-----------------|---------------------------|----------------------------|------------------|-------------------|-------------------------------|--------------------------------------|-------------------------------------------|-------------------------------------------|
| Cirrhosis (n=9) | 0.97 ± 0.09               | 1.29 ± 0.09                | 0.35 ± 0.09      | 0.33 ± 0.097      | 235 ± 75                      | 320 ± 146                            | 552 ± 91                                  | 5.8 ± 1.8                                 |
| Controls (n=6)  |                           | 1.10 ± 0.17                |                  | 0.53 ± 0.09       | 33 <sup>b</sup>               | 347 ± 81                             | 380 ± 90                                  | 3.3 ± 0.5                                 |

Mean ± SEM.  $E_{ANF}$  = arterial-venous extraction ratio of ANF.

<sup>a</sup> $p = 0.1$ .

<sup>b</sup>Estimated from a normal azygos blood flow of 0.15 l/min and an extraction ratio of 0.5.

overall splanchnic clearance and removal of ANF were similar or slightly higher in the patients compared to controls. We did not find any significant relation between ANF extraction, clearance or removal rate, on the one hand, and S-bilirubin ( $r=0.18-0.37$ ), S-albumin ( $r=-0.43$  to  $-0.48$ ) or hepatic venous pressure gradient ( $r=-0.42$  to  $-0.62$ ), on the other.

Plasma levels of ANF in our cirrhotic patients were similar to those in the control subjects. This may be due to the fact that control subjects were studied on an unrestricted diet and most patients were studied on dietary sodium restriction and while being treated with diuretics (which are known to decrease ANF levels). This resulted in comparable arterial ANF in the two groups.

The present study shows substantial and similar extraction of ANF in the azygos and hepato-enteric venous beds in patients with cirrhosis. Thus, a major part of the splanchnic inflow of ANF is cleared through the superior collateral flow. This shows conclusively that the overall splanchnic removal of ANF is not decreased in patients with cirrhosis as Hollister et al. have suggested (1). In fact, the overall splanchnic removal of ANF tended to be somewhat higher in the patients than in the controls.

ANF is rapidly hydrolyzed by endopeptidase 24.11 and cleared by specific receptors identified in most vascular endothelial cells. The high ANF extraction in azygos plasma, as found in the present study, is similar to extraction described in other tissues (1,2). Our finding, therefore, may suggest that the degradation of ANF in blood drained through the azygos venous bed is mediated

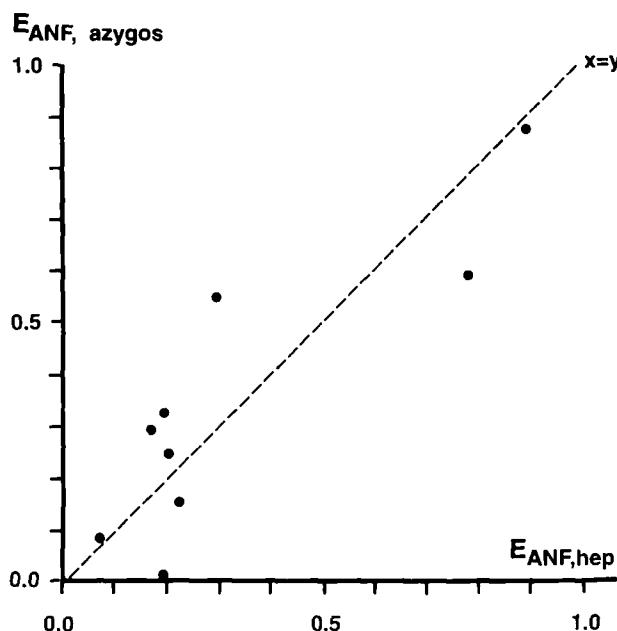


Fig. 1. Relationship between arterial-azygos venous ( $E_{ANF, azygos}$ ) and arterial-hepatic venous ( $E_{ANF, hep}$ ) extraction ratio of ANF in 9 patients with cirrhosis ( $r=0.86$ ,  $p<0.005$ ;  $y=0.83x+0.07$ ).

by the same mechanisms (i.e. related to vascular structures) as those described for other tissues.

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