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Reappraisal of Plasma Exchange for Acute Hepatic Failure in Cirrhosis Based on Levels of Serum Human Hepatocyte Growth Factor

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Serum human hepatocyte growth factor (HGF) levels increase following aggravation of liver damage and reflect the prognosis in fulminant hepatitis. Using HGF levels, we estimated the indication of plasma exchange (PE) for acute hepatic failure based on cirrhosis.

Patients and Methods

Seven patients all had liver cirrhosis with hepatic compensation. Various events had induced acute hepatic failure for which they received plasma exchange. Hepatic failure was characterized by a rapid increase in the levels of serum bilirubin associated with a change in consciousness. Triggers of hepatic failure in cirrhotic patients are shown in Table 1.

The protocol for PE, using a membrane plasma separator, was as follows: the flow rate of blood was 100 ml/min, with an exchange of 30% of the blood volume. The amount of fresh frozen plasma used as a blood substitution was 50 ml/kg. At priming, 2,000 IU of heparin was administered followed by a continuous infusion of nafamostat mesilate, 20 mg/h, during plasma exchange. The procedure was repeated two to three times each week.

HGF, liver tests (serum levels of bilirubin and albumin, prothrombin time), and grade of hepatic encephalopathy were measured just before each PE. The contribution of variables to the prognosis of acute hepatic failure was estimated by discriminant analysis. The variables for analysis were age, liver tests, HGF level, progressive increase in serum level of bilirubin and that in HGF, and grade of hepatic encephalopathy. The HGF level was determined by an enzyme-linked immunosorbent assay.[1)]

Results

The serum bilirubin level, HGF level, and the progressive increase in HGF level were significant and

Table 1 Patients with acute hepatic failure based on cirrhosis.

Case	Age/Sex	Trigger of AHF	HGF (ng/ml)	Bil. (mg/dl)	Alb. (g/dl)	PT (%)	HT (%)	Grade of HE	No. of PE given	Outcome
1	63/M	TAE	6.70	9.4	3.3	38	22	2	2	Dead
2	61/M	Unkown	0.74	12.6	2.1	23	38	2	20	Alive
3	45/M	Decrease of cyclosporin	1.60	8.0	2.7	38	32	1	5	Dead
4	71/M	Aggravation of hepatitis	0.88	34.7	2.9	42	28	2	8	Dead
5	63/F	TAE	0.97	8.4	2.4	50	24	3	7	Alive
6	67/M	Alcohol intoxication	1.41	6.9	2.5	60	39	1	2	Alive
7	58/M	PEI	0.79	7.1	3.1	48	36	1	2	Alive

AHF: acute hepatic failure, Bil.: bilirubin, Alb.: albumin, PT: prothrombin time, HT: hepaplastin test, HE: hepatic encephalopathy, TAE: transcatheter arterial embolization, PEI: percutaneous ethanol injection.

Table 2 Discriminant analysis for the prognosis of patients with acute hepatic failure.

	Discriminant coefficient	*F*-value
Serum bilirubin levels	−0.266	29.01**
HGF	−1.317	8.756*
Progressive increase in HGF	−4.480	9.055*
Constant	9.637	

Overall error rate was 5.0%. *, $P<0.01$ and **, $P<0.001$.

independent factors for the determination of the prognosis. Discriminant function coefficients and constant are shown in Table 2. The overall error rate was 5%. For example, if HGF increases gradually and reaches over 1 ng/ml, patients whose bilirubin level are higher than 15 mg/dl have a poor prognosis.

Discussion and Conclusion

Artificial liver support may influence the clearance of HGF from the circulation. However, the HGF level rose immediately following PE and this increase disappeared 12 h after the procedures.[2] Therefore, daily measurement of the HGF level is a reliable index for liver function in spite of receiving PE.

The object of an artificial liver is to keep the patient alive until his own liver regenerates. PE is only applicable in patients with potentially reversible acute hepatic failure, and the prognosis can be predicted from repeated measurements of serum levels of HGF and bilirubin. Progressive increase in HGF, especially above 1 ng/ml, together with a high serum bilirubin level above 15 mg/dl indicates a poor prognosis. In those cases, PE will not improve survival.

References

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