Antithrombin III During Liver Transplantation

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ANTITHROMBIN III (AT-III) is a liver-synthesized plasma glycoprotein of moderate size (58 kD) that can inhibit most of the activated serine proteases involved in coagulation (eg, thrombin, activated factor X, VII, etc). The inactivation involves formation of an irreversible complex, probably filtered from the circulation of the RES. The complex formation is a time-dependent reaction requiring minutes for maximum effect. In the presence of heparin, this reaction occurs immediately. The biologic half-life of AT-III has not been precisely determined but is estimated at 3 to 4 days in a patient with congenital deficiency. Congenital AT-III deficiency (0.40 to 0.60 U/mL) is an uncommon disorder leading to arterial or venous thrombosis and embolism in young adults. Acquired AT-III deficiency is much more common. In parenchymal liver cell disease, AT-III is markedly decreased because of lack of synthesis. It is also decreased, and may reach very low values, in the presence of disseminated intravascular coagulation (DIC).

MATERIALS AND METHODS

The electrophoretic immunodiffusion (EID) method with a polyvalent antibody (rabbit, Behring Diagnostics) was used. Well-defined rockets were formed and found to be proportional in height to antigen concentration. The range of AT-III levels in 104 normal subjects was 0.73 to 1.20 U/mL.

For these studies, the tests were performed on frozen plasma samples left over from coagulation tests ordered for patient care. There were eight samples from each of 15 patients; the time schedule of sampling is shown in Figs 1 and 2. Seven patients had postnecrotic cirrhosis (PNC), four had primary biliary cirrhosis (PBC), and four had sclerosing cholangitis (SC).

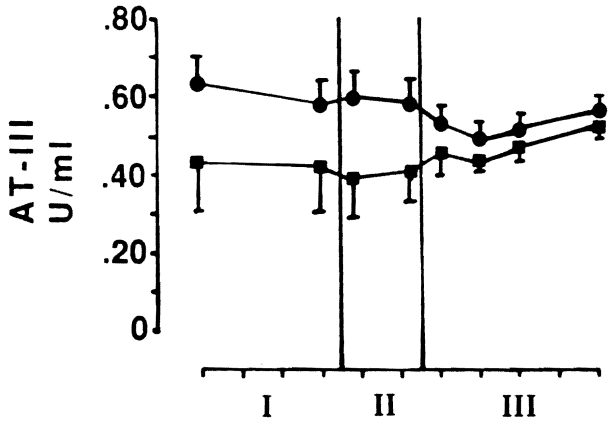

Fig 1. Antithrombin III level during liver transplantation. Solid circles represent mean values of all patients and solid squares represent four patients with rapid lysis. Blood samples were taken after induction of anesthesia, 30 minutes before the anhepatic stage, 10 minutes into the anhepatic stage, 5 minutes before reperfusion, 5 minutes, 30 minutes, 120 minutes after reperfusion, and at the end of surgery.

RESULTS

Fig 1 plots the mean value for the entire group of patients at each time period. Data were replotted from four patients (three with PNC, one with SC) identified as "rapid lysers": at some time during surgery each had a euglobulin lysis time of 15 minutes or less. The baseline for this group is lower than that for the whole group.

Fig 2 shows the mean values for each diagnostic category. As expected, the mean baseline level in patients with PNC (0.39 U/mL) is much lower than those with PBC (0.82 U/mL) or SC (0.77 U/mL). The latter two groups show decreasing AT-III levels during transplantation, whereas those in the PNC group actually increase.

DISCUSSION

These findings confirm the previous observation that baseline levels of AT-III are low in patients with PNC. In PBC and SC, which may be life-threatening without major paren-

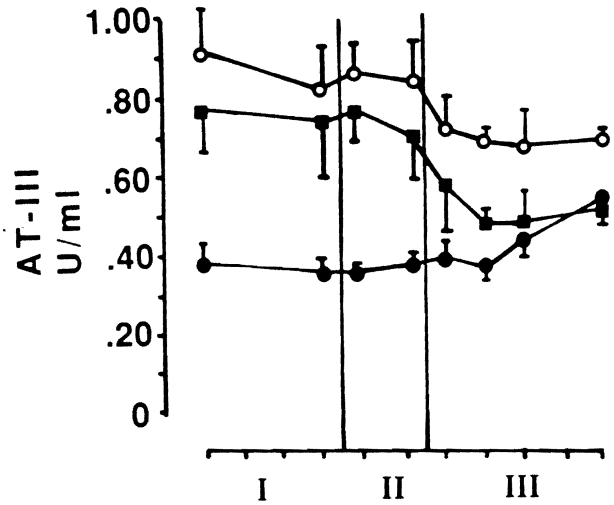

Fig 2. Antithrombin III levels in three groups of patients during liver transplantation. Open circles indicate patients with primary biliary cirrhosis (4), solid squares sclerosing cholangitis (4), and closed circles postnecrotic cirrhosis (7). Blood samples were taken at the same time as those in Fig 1.

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chymal cell involvement, the mean baseline values are normal or near normal. During the anhepatic period, no synthesis can take place. Factors with short half-lives decrease significantly. On the other hand, the AT-III curves for the entire group of patients, as well as those for the rapid lysers, are remarkably flat. AT-III level fluctuates very little presumably because its half-life is relatively long, and a 2 hour period of nonproduction would not be expected to have any effect. The smaller numbers in each group and large standard error of the mean contribute to the lack of statistical significance. However, these findings do not indicate the presence of any active process such as DIC, which is known to reduce AT-III levels significantly. During the entire operation and particularly in early stage III (neohepatic stage), patients receive large amounts of blood. This replacement appears to correct to some degree the defect in AT-III levels of PNC patients.

In summary, AT-III appears not to be involved in any active process during liver transplantation, suggesting that DIC is not a major complication of this surgery.