SERUM ACUTE PHASE PROTEINS AFTER ORTHOTOPIC LIVER TRANSPLANTATION

A. M. BURNS, M. P. SHELLY, S. WALKER AND G. R. PARK

SUMMARY

Acute phase proteins were measured in six patients before liver transplantation and for 72 h after orthotopic liver transplantation. The ability of the donor liver to mount an acute phase response was demonstrated, although the response was less than that seen in other groups of patients in whom this has been studied. Because of the reduced response to stress, the value of these measurements as indicators of liver function in this group of patients is limited.

KEY WORDS

Liver: transplantation. Liver function: acute phase protein synthesis.

Surgical trauma induces an acute phase reaction in which the liver is stimulated to switch from synthesis of albumin to production of a series of acute phase proteins [1]. These changes include normally a rapid increase in the synthesis of C-reactive protein and α1-antichymotrypsin, with a consequent increase in serum concentrations. Synthesis of α1-acid glycoprotein (AAG) is increased also, but to a smaller extent. Serum concentrations of pre-albumin decrease during an acute phase reaction more rapidly than those of albumin, and it may be regarded therefore as a "negative" acute phase reactant.

Immediately after orthotopic liver transplantation, the function of the donor liver is impaired because of the stress of two surgical procedures (donor and recipient) in addition to the cold and warm ischaemic damage sustained during the period between these operations. This study has investigated the ability of the recently transplanted donor liver to mount a stress response and synthesize acute phase proteins, and to assess their value as indicators of liver function immediately after liver transplantation.

METHODS AND RESULTS

The study was approved by the District Ethics Committee and informed consent was obtained before operation from seven consecutive patients. Patients received routine postoperative care in the intensive care unit and had an uncomplicated postoperative course, except for one patient who bled excessively and was excluded from further study.

Serum samples were collected immediately before orthotopic liver transplantation and after operation on arrival in the intensive care unit, then at 4-h intervals over a period of 24 h. Two further samples were collected at 48 h and 72 h. Subsequent analysis for C-reactive protein, α1-antichymotrypsin, AAG and pre-albumin was performed using specific immunoassay methods [2-5].

Changes in serum concentrations of the acute phase proteins in the 72 h after liver transplantation are shown in figure 1. There was a marked and sustained increase in serum concentrations of C-reactive protein and α1-antichymotrypsin after surgery. The increase in AAG concentration was not as rapid, with the maximal mean values being just above the upper limit of the normal range. Although serum concentrations of pre-albumin increased after operation, they remained well below the lower limit of the normal reference range.

Correspondence to G.R.P.
LIVER FUNCTION TESTS

Fig. 1. Mean (SEM) concentrations of the acute phase proteins C-reactive protein (CRP), α1-antichymotrypsin (ACT), α1-acid glycoprotein (AAG) and pre-albumin (PA) before surgery (pre) and in the first 72 h after orthotopic liver transplantation (tx) in six patients. Normal ranges: CRP < 10 mg litre⁻¹; ACT 0.35–0.63 g litre⁻¹; AAG 0.5–1.0 g litre⁻¹; PA 150–355 mg litre⁻¹.

COMMENT
Monitoring of liver function after operation is important to detect adverse trends. This is particularly important after liver transplantation in patients who, in addition to the usual problems faced by the critically ill, may have episodes of rejection, infarction or infection. Conventional liver function tests are measured routinely, but alterations in enzyme and bilirubin concentrations may be relatively non-specific, and their interpretation following liver transplantation may be complicated by several factors [6].

Stress is a complex series of metabolic, endocrine and physiological processes. The acute phase response includes the de novo synthesis and secretion of proteins by the liver; the rate of production might be used to assess liver function. The stimuli for the hepatocyte to synthesize these proteins, and the underlying cellular mechanisms, are not understood fully and the role of the stress response, particularly its prognostic significance, remains unclear. However, the stress response may reduce tissue injury and promote healing in association with enhanced host resistance [1].

In the immediate period after liver transplantation, when the stress response is still present, serum concentrations of acute phase proteins might be expected to provide an indicator of the synthetic function of the liver, improving liver
function being associated with increased serum concentrations of proteins and deterioration with decreased serum concentrations. This study demonstrated that the donor liver appears to be able to synthesize acute phase proteins, despite the ischaemic damage sustained before transplantation. However, the response was less than that reported previously in association with major tissue injury or bacterial infection. The moderate increases in acute phase proteins in our patients may reflect both dilution of the acute phase proteins by transfused blood and ischaemic damage to the donor liver resulting in a less than maximal response. Alterations in liver function may be associated with only minimal changes in protein concentrations and therefore their prognostic value as indicators of liver function is limited. Acute phase proteins may be used to complement conventional liver function tests as a guide to the function of the donor liver. However, further studies are necessary to define their exact role.

REFERENCES