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Correspondence

Insulin-like growth factor 1 (IGF-1) in liver cirrhosis: a marker of hepatocellular dysfunction?

To the Editor:

The metabolic effects of IGF-1 and the alterations in the growth-hormone-IGF-1 axis in patients with liver cirrhosis have recently been extensively reviewed in the pages of this journal (1). IGF-1 is a polypeptide mainly synthesized in the liver, which mediates most of the anabolic effects of growth hormone, particularly on skeletal and muscle tissues. IGF-1 has been found to be related to nutritional status, both in physiological conditions and in several diseases. In patients with liver cirrhosis, however, its nutritional significance is controversial (2,3).

In a recent study in a group of 64 patients with cirrhosis, we found that plasma IGF-1 is not correlated with the presence or the severity of energy malnutrition (2). IGF-1 was not different in patients with or without signs of energy malnutrition, and it did not correlate with indicators of fat and fat-free mass. Hypercatabolism and increased IL-6 levels during intercurrent infections could also contribute to the reduction of IGF-1 (1). Our study, however, does not support this hypothesis, as subjects with infectious disease and other acute complications were excluded (2). Other mechanisms, such as portal hypertension and hyperestrogenism, have also been suggested.

While the relations of IGF-1 to metabolic and nutritional alterations characteristic of cirrhosis (4) remain controversial, there is growing evidence to show that IGF-1 represents a good marker of liver dysfunction. In our study we confirmed that low concentrations of IGF-1 correlate with the degree of liver failure. IGF-1 correlated directly with serum albumin ($p<0.001$) and other proteins (transthyretin, retinol-binding protein, transferrin and prothrombin), and inversely with Child-Pugh score ($p<0.01$). Despite these correlations, the reduction of IGF-1 was much greater and more frequent than that of serum proteins. Moreover, IGF-1 was found to be a good predictor of survival. Patients with $IGF\text{-}1_{z\text{-}score} < -2.5$ (median value) showed lower survival rates compared with patients with $IGF\text{-}1_{z\text{-}score} > -2.5$ ($p<0.01$) (2). In another recent study of 337 patients with alcohol-induced liver disease, Møller et al. demonstrated that IGF-1 and its major binding protein (IGFBP-3) are independent predictors of survival (5). Taken together, these data suggest that IGF-1 may be an indicator of liver dysfunction. Plasma IGF-1 changes after liver transplantation (OLT) could contribute to better defining the relationships of IGF-1 with liver function. Liver function normalizes immediately after successful OLT, while no changes in nutritional status are detectable in the first month. Moreover, a negative nitrogen balance has been found to persist at least 1 month after surgery (6).

We measured plasma IGF-1 in nine cirrhotic patients immediately before (1 ± 6 days) and 1 month (30 ± 9 days) after successful OLT. None of the patients had evidence of infection at the time of transplantation. As shown in Fig. 1, IGF-1 dramatically increased above normal values in all patients after OLT (mean IGF-1 before OLT$=51.4\pm51.5$ ng/ml; mean IGF-1 after OLT$=404.8\pm145.6$ ng/ml). The normalization of liver function rather than an improvement in nutritional status or catabolic state is likely to account for the IGF-1 increase after OLT. This observation therefore confirms the hypothesis that IGF-1 represents a true marker of liver dysfunction. Measurement of IGF-1 with the available commercial kits is easy and inexpensive, and so in clinical practice it may be useful both to improve the prognostic accuracy of the commonly used tests and in the detection of liver dysfunction.

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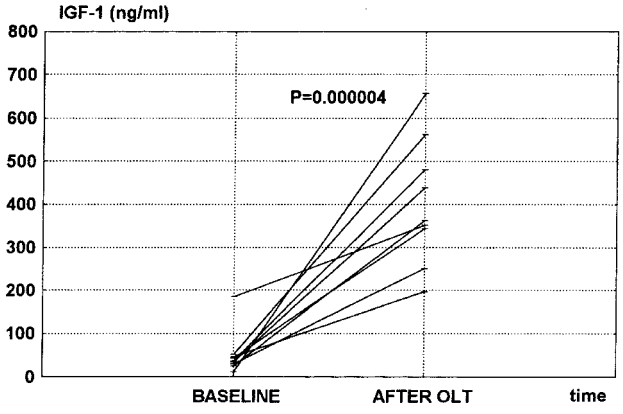

Fig. 1. IGF-1 changes after orthotopic liver transplantation (OLT) in nine cirrhotic patients. Baseline$=1\pm6$ days before transplantation. After OLT$=30\pm9$ days after transplantation.