

HEPATOCELLULAR TRANSPLANTATION, ANTIOXIDANT DRUGS AND CYCLOSPORINE MODIFY LIVER REGENERATION FOLLOWING HEPATIC ISCHEMIA

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In previous Meetings of this Society we have shown our experiences about the hepatotrophic effect of cyclosporine A, and how this effect is not always manifested. Thus, hepatocytes inoculated into the spleen start regeneration following CsA administration, but this drug is not effective to enhance regeneration of these cells induced by partial hepatectomy. On the other hand, we have found that normothermic hepatic ischemia hinders liver regeneration, and that this negative effect can be partially reverted by some antioxidant drugs and cyclosporine. In the present study we test the effectiveness of the same drugs in an experimental model of hepatocellular transplantation plus normothermic ischemia.

Male syngeneic Fisher rats have been used (300 gr.) Twenty million hepatocytes, obtained by collagenase digestion, were inoculated into the spleen 24 hours prior to splanchnic ischemia (15 min. clamping of the superior mesenteric artery, the celiac trunk and the porta hepatis) and 70% partial hepatectomy. Five groups of ten animals have been used: (1) non-treated controls, (2) folic acid (2.5 mg/kg iv.), (3) S.O.D. (6 mg/kg iv.), (4) allopurinol (50 mg/kg iv.), (5) CsA (30 mg/kg i.p.). All of the animals were sacrificed 24 hours after surgery, and hepatocytic DNA content was quantified both in the liver and the spleen.

All the treatments tested clearly improved hepatocytic regeneration in the liver [PHR: 1=42, 2=50, 3=56, 4=56, 5=56 ($p < 0.05$)]. However, the antioxidant drugs did not increase hepatocytic regeneration in the spleen [PHR: 1=25, 2=34, 3=25 ($p > 0.05$)]; more over, allopurinol showed a negative effect [PHR=2.57 ($p < 0.05$)]. CsA, as was observed in previous normoperfused series, has not been able to enhance the hepatocytic proliferation in the spleen, following partial hepatectomy (25 vs. 23; $p = 0.96$).

Antioxidant drugs and cyclosporine, though useful in reverting the negative effect of ischemia upon liver regeneration, are useless for hepatocytes ectopically placed into the spleen.