

IFN α 2a INFLUENCE ON THE MITOTIC ACTIVITY IN THE REGENERATING RAT LIVER

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Interferon α (IFN α) induces a variety of cellular responses, including antiviral, antiproliferative and immunoregulatory processes. There are also suggestions that IFN α influences the cell cycle and regenerative processes. The worldwide-accepted experimental model for regeneration study is partial (70%) hepatectomy in the rat.

We attempted to determine the proliferative activity in the regenerating rat liver after IFN α 2a treatment. The impact of a single IFN α 2a dose on hepatocyte mitotic activity was also analyzed.

A subcutaneous injection of IFN α 2a (Roferon, Roche) in the amount of 0.3ml of 6MU/100ml 0.9%NaCl was administered to twenty 3-month old male Wistar rats. 24 hours later, a partial hepatectomy was conducted and the removed liver parts were collected. A second, similar IFN α 2a dose was administered 24 hours after surgery. 48, 72, 96, 120, and 168 hours after the hepatectomy, a group of four rats was killed. The obtained liver sections were fixed in paraffin. Fifteen rats serving as a control group received a subcutaneous dose of 0.3ml 0.9%NaCl 24 hours before surgery. In all of the hematoxylin/eosine stained rat liver slides, hepatocytes undergoing mitosis were identified using a light microscope at 1000x magnitude. The mitotic index, M_i , defined as the number of dividing hepatocytes per 1000 hepatocytes observed, was calculated for each liver specimen.

In the control group, the M_i ranged from 0 to 30×10^{-3} ; $x=10 \times 10^{-3}$. After a single IFN α 2a dose, the M_i ranged from 0 to 50×10^{-3} , $x=16.5 \times 10^{-3}$. After the partial hepatectomy and the second IFN injection, the M_i were in general lower and varied depending on the post-surgical sampling time. At 48h, the mean $M_i = 2.7 \times 10^{-3}$; 72h – 8×10^{-3} ; 96h – 3.6×10^{-3} ; 120h – 1×10^{-3} ; and 168h – 0.95×10^{-3} . All of those events were at a lower level than in the control group and than before the hepatectomy in the study group. Moreover, the highest M_i after hepatectomy was noticed at 72h, while during rat liver regeneration the “mitotic wave” is established 36-48h after surgery.

A single IFN α 2a dose seems to result in mitotic activity increasing, while two doses appear to be potent enough to diminish mitotic activity in the regenerating rat liver.