DNA FRAGMENTATION IN PERIPHERAL BLOOD LYMPHOCYTES OF PATIENTS WITH LIVER CIRRHOSIS RELATED TO ALCOHOL ABUSE OR TO HEPATITIS B OR C VIRUSES

Grossi Sarah, Mattioli Francesca, Manfredi Valeria, Sumberaz Alessandro*, Testino Gianni*, Martelli Antonietta

Department of internal Medicine, Pharmacology Unit, University of Genoa, I-16132 Genoa, Italy
* Gastreoenterology Unit – St. Martino Hospital - Genoa

Both alcohol abuse and hepatitis B or C virus infections are implicated in the development of hepatocellular carcinoma, but it is still controversial whether the pathogenetic mechanism is epigenetic or genotoxic. Considering that alcohol promotes the generation of reactive oxygen species and both viruses infect peripheral lymphocytes, we investigated the occurrence of DNA fragmentation in peripheral blood lymphocytes from patients with alcoholic cirrhosis and from patients with cirrhosis related to B or C viruses. In addition, the correlation between the degree of DNA fragmentation and the Child-Pugh score used to assess the degree of hepatic insufficiency was analysed.

The study population consisted of two groups; one group of 12 patients with alcoholic cirrhosis, and one group of 25 patients with hepatic B virus (HBV) or hepatic C virus (HCV) cirrhosis. The control group consisted of 20 healthy individuals of similar age and smoking habit, The degree of DNA fragmentation in peripheral blood lymphocytes was determined with the alkaline Comet assay that provides two indexes of the frequency of DNA single-strand breaks and alkali-labile sites, the tail length (TL) and the tail moment (TM).

Mean values of both TL and TM were significantly increased ($p<0.001$) in lymphocytes from the 12 patients with alcoholic cirrhosis (TL=2.96±1.79; TM=258±162) and in lymphocytes from the 25 patients with HBV or HCV cirrhosis (TL=2.81±0.94; TM=233±83) as compared with mean values of the 20 healthy individuals (TL=1.54±0.49; TM=141±45). The lower degree of DNA fragmentation present in lymphocytes of healthy individuals cannot be ascribed to differences of age or smoking habit. A significant positive correlation was found to exist between the degree of DNA fragmentation present in lymphocytes of each of the 37 cirrhotic patients and the corresponding value of the Child-Pugh score.

The occurrence of DNA fragmentation in peripheral blood lymphocytes further supports the hypothesis that a genotoxic mechanism may operate in the liver of patients with alcoholic cirrhosis or HBV and HCV cirrhosis and therefore contribute to hepatocarcinogenesis.