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Hepatology Highlights

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Transthyretin Familial Amyloidotic Polyneuropathy: Histopatological Study on the Explanted Liver, by Amante M et al.

This paper reports on the hystopatological findings observed in 10 livers explanted from patients affected by Familial Amyloidotic Polyneuropathy (FAP). This rare disease (gene frequency 1 in 10^5-10^6) is related to the synthesis of an altered Transthyretin (TTR, formerly pre-albumin) due to a Val to Met substitution at position 30. What is intriguing is the number of patients with FAP observed which actually accounts for about 5% of the indication for liver transplantation. This gives the opportunity to have a very privileged observatory to better define the pathological alteration of this disease. Both the gross appearance and the histology of the liver were normal with the exception of minor deposition of TTR fibrils in intrahepatic septa. On the contrary, heavier deposition was observed in lymph nodes and in the nerves of hilum hepaticus, confirming that the disease is not affecting the liver itself. This study raises the interesting issue of why patients with FAP should be transplanted and if the explanted liver can be used in other patients (the so called "Domino effect"). Transplanted liver will remove the TTR alteration but the sick liver will start producing the altered protein in the recipient. Though it is true that FAP needs time to develop, how happy would be a young subject with advanced liver disease to face FAP within the next 20 years? This points even more for the need of gene therapy where cells rather organs are transplanted.

Ketorolac Pharmacokinetics in Experimental Cirrhosis by Bile Duct Ligation in the Rat by Rivera-Espinosa L et al.

Cirrhosis is frequently associated with a severe impairment of the metabolism of several drugs thus making the treatment of these patients even more complicated. Several reports investigated how a reduced liver function may affect the metabolic fate of drugs. This study adds information on how cirrhosis in the rats (induced by bile duct ligation) affects the pharmacokinetic of ketorolac, a potent, extensively used non steroidal anti-inflammatory drug. When administered intravenously, the disposition and the metabolism of ketorolac was unaffected by cirrhosis. Conversely, when administered orally, the pharmacokinetic was altered and most important, the bioavailability reduced by about 50% in cirrhotic rats. This was mainly due to a reduction in the absorption resulting in a lower plasma concentration and a reduced plasma clearance of the drug. The findings are intriguing but, unfortunately, the reason(s) for the discrepancy between the two administration routes is not fully unraveled. Is cirrhosis per se responsible for the discrepancy in pharmacokinetic or is the portal hypertension related to the condition? Do other types of experimental cirrhosis (such for example that following CC14 administration) have the same pharmacokinetic pattern? Answering these questions will provide these data a much more relevant clinical significance and application.

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