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Hepatology Highlights

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Non alcoholic steatohepatitis (NASH) with diabetes: Predictors of liver fibrosis, by DN Amarapurkar et al

Hepatic steatosis (plus or minus fibrosis and inappropriate ethanol intake) is becoming "the problem" in several liver centers around the world. Several reports now conclude that obesity and diabetes are two of the main risk factors for the disorders. These risks together with high blood pressure, increased insulin resistance and hyperlipoproteinemia are making liver steatosis a landmark for the so call "metabolic syndrome". However still more that tenuous is the border between simple fatty liver and NASH. The distinction is not only taxonomic and academic since the prognosis of the two clinical entities is quite different. The golden standard is liver biopsy which, unfortunately is invasive and may have some, though very limited, risk. Several surrogates have been suggested (fibrotest, fibroscan, others) but all of them still need a definite validation in larger series worldwide. Amarapurkar *et al* tried to answer the issue by analyzing the possible correlation between the degree of liver fibrosis (assessed by biopsy) and several clinical and biochemical variables. The study examined 36 cases with NASH and diabetes suggesting a rather sever metabolic damage and preventing the export of the results in less advanced cases. Surprisingly fibrosis was found only in a third of cases pointing to the need of expanding the number of cases prospectively collected before reaching sound conclusion. Unfortunately none of the variables tested correlated with the extent of fibrosis. This is bad news pointing again to the need a biopsy in the definition of NASH *vs* fatty liver. The time of the needle is not over, yet.

Pentoxifylline does not prevent neither liver damage nor profibrogenetic events in a rat model of non-alcoholic steatohepatitis, by Paula Vial et al

As reported in the article by Amarapurkar, the mechanisms involved in the pathogenesis of NASH are still vague and undefined. One of the problems for this lack of hints, and therefore effective treatment(s), is the lack of animal models sufficiently mimicking what observed in patients. Vial and colleagues tried to address the issue if the fibrosis associated with NASH, and eventually progressing to cirrhosis, may be reversed/ameliorated by pentoxifylline (PTX). PTX was previously suggested to reduce activation of cytokines (TNF-α in particular), the activation of hepatic stellate cells and the collagen production. Rats were given a choline-deficient diet for 8 weeks and developed and initial NASH. NASH was assesses histologically in addition to some molecular markers of fibrogenesis. All animals treated with choline-deficient diet for 8 weeks showed an liver histology compatible with moderate NASH associated with fatty infiltration. Interesting was the observation of an increased level of expression of the gene encoding for procollagen I and TNFβ-1 indicating profibrogenetic activity. Unfortunately PTX did not reduce any of these parameters pointing to the conclusion that the drug is ineffective at least in this model and/or at the dose used. As for the study by Amarapurkar this is bad news but the disappointment should prompt for additional research, possibly with different drugs either alone or in combination. The burden of NASH in the population urges these studies.

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