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Hepatology highlights

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Simental-Mendía L, *et al.* The product of triglycerides and glucose as biomarker for screening simple steatosis and NASH in asymptomatic women

Non-Alcoholic Fatty Liver Disease (NAFLD) is considered by many to be the hepatic manifestation of metabolic syndrome, the constellation of obesity, impaired glucose tolerance, dyslipidemia and hypertension that has been associated with a higher prevalence of NAFLD and Non-Alcoholic Steatohepatitis (NASH).[1] Most patients with NAFLD are asymptomatic, with many of them suspected to have fatty liver disease because of elevated liver function tests or abnormal imaging studies, found during evaluation of other medical complains or routine tests.

This study validated the triglyceride and glucose (TyG) index as a screening tool for NAFLD and NASH in asymptomatic women. The TyG index has been found to be comparable or better than scores like triglycerides/HDL cholesterol ratio and the HOMA score as a screening marker of insulin resistance.[2,3] 50 asymptomatic women aged 20 to 65 years with no clinical evidence of chronic liver disease were enrolled. Laboratory data included liver enzymes, fasting glucose, cholesterol and triglycerides. Liver biopsy was performed and results were classified as normal, simple steatosis or NASH. TyG was calculated as Ln (TG [mg/dL] x glucose [mg/dL]/2). Women with simple steatosis and NASH presented the highest percentage of obesity and TyG index, whereas women with NASH had higher cholesterol and triglycerides levels than women with normal liver ($P < 0.05$). The optimal values of TyG index for screening of steatosis and NASH was established on a receiver operating characteristic (ROC) curve, with an index of 4.58 having a sensitivity of 0.94 and specificity of 0.69 for NAFLD, and an index of 4.59 having a sensitivity of 0.87 and specificity 0.69 for NASH.

In recent years, NAFLD has become a worldwide epidemic and a public health concern;[4] however, NAFLD remains unrecognized and the diagnosis delayed. Liver biopsy remains the gold standard to diagnose NAFLD and advanced fibrosis. Nonetheless, liver biopsy is an invasive procedure with potential risk for complications. This study validates results of others that suggest that TyG index can be a useful non-invasive screening biomarker for NAFLD.[5]

Ge, *et al.* miRNA regulation of stellate cell activation

This study provides new information of the role and effects of mir-146 in hepatic stellate cells. MicroRNAs are a class of small non-coding RNA that play an important role in control of gene expression. Prior studies have identified miR-146b as being up-regulated during the development of hepatic fibrosis in the liver. This miRNA has been implicated in inflammatory responses, and is upregulated in response to inflammatory stimuli.

In the present study, Ge, *et al.* show that miR-146b expression was increased in TGF-β1-treated HSCs. TGF-β1 enhanced α-SMA and COL1A1 protein expression and stimulated proliferation of HSC, and these effects were ameliorated by knock-down of miR-146b. In addition, Krüppel-like factor 4 (KLF4) was identified as a direct target for translational inhibition by miR-146b. Forced expression of KLF4 inhibited TGF-β1-induced enhancement of α-SMA and COL1A1 expression, and cell proliferation in HSCs. Moreover, miR-146b expression was negatively associated with KLF4 expression but positively associated with expression of α-SMA and COL1A1 during hepatic fibrosis.

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These results are of interest because they provide a mechanism by which stellate cells can be regulated in response to fibrogenic stimuli. A direct effect of miR-146b on HSC activation through targeting KLF4 is identified. Although the authors postulate that targeted therapy of miR-146b into HSCs could be used to treat hepatic fibrosis, such a conclusion appears premature until the effect of miR-146 on other targets and on other cell types have been elucidated.

Pařízek A, *et al.*
Efficacy and safety of ursodeoxycholic acid in patients with intrahepatic cholestasis of pregnancy

This study assessed the efficacy and safety of ursodeoxycholic acid (UDCA) for the treatment of intrahepatic cholestasis of pregnancy (ICP). This is a common liver disease during pregnancy with a reported incidence of 0.2-2%, and which varies with ethnicity and geographic location. Symptoms usually present in the third trimester with maternal pruritus, abnormal liver function tests and elevated serum bile acids. There is an increased risk of adverse perinatal outcomes, meconium-stained amniotic fluid, and stillbirth.[6] Several studies have reported an increase in fetal complications associated with high levels of maternal serum bile acids (> 40 μmol/L) and early onset of ICP (< 33 weeks of gestation).[7,8] UDCA (10-20 mg/kg per day) improves pruritus and liver function tests in 67-80% of ICP patients, but there is not enough evidence that UDCA improves perinatal outcomes. Even though, UDCA is regarded as the first-line treatment for ICP based on evidence obtained from randomized clinical trials, it has not been widely used by many obstetricians.[9]

Pařízek, *et al.* reviewed the records of 191 pregnant women with ICP who were treated with UDCA, and a control group of 256 healthy pregnant women. They evaluated several parameters such maternal liver function tests, UDCA dosage, therapeutic effect and side effects, gestational age, quality of amniotic fluid, delivery course, and Apgar score of the neonates. With the use of UDCA, liver enzymes improved in 70% and pruritus was ameliorated in 86%. Side effects included negligible skin reactions (0.5%) and mild diarrhea (4.7%). Although gestational age, birth weight, preterm delivery, and neonatal complications were worse in the UDCA-treated group compared to controls, these were attributed to underlying liver disease and related neonatal prematurity. No complications were associated to UDCA treatment, and the authors concluded that UDCA has a good efficacy and is safe for both mothers and neonates.

These findings validate previous studies that reported similar results with minimal side effects.[6,8] UDCA is a FDA category B drug for pregnancy (low fetal risk) and can be use in the second and third trimesters for the treatment of cholestatic liver disease during pregnancy.[10]

CONFLICTS OF INTEREST/DISCLOSURES

The authors have no relevant conflicts of interest to disclose.

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