EFFECT OF SIMVASTATIN ON PORTAL HEMODYNAMICS IN EGYPTIAN HCV CIRRHOTC PATIENTS AND ITS RELATION TO SERUM ENDOTHELIAL NITRIC OXIDE SYNTHASE LEVEL

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INTRODUCTION

Insufficient nitric oxide production inside the liver contributes to increased intrahepatic vascular resistance (IHVR), which plays an important role in pathogenesis of liver cirrhosis. Statins are proposed to have a promising role in reducing portal hypertension by increasing intrahepatic nitric oxide level, without having the unfavorable effect of systemic vasodilatation, through their upregulating effect on endothelial nitric oxide synthase (eNOS) enzyme.

AIM OF THE WORK

Evaluating the effect of simvastatin on portal hemodynamics in Egyptian HCV-positive cirrhotic patients and its relation to serum eNOS level.

SUBJECTS AND METHODS

Subjects:

40 patients with compensated HCV-liver cirrhosis and portal hypertension received 40 mg of simvastatin daily for 3 months. They were identified based on clinical and laboratory evaluation, abdominal ultrasound, Doppler study of portal vein and upper gastrointestinal endoscopy.

- Patients with liver cirrhosis due to etiologies other than HCV, liver decompensation, non-cirrhotic portal hypertension, hepatic or extrahepatic malignancy, history of direct acting antiviral therapy and history of hypersensitivity to statins were excluded from the study.
- Serum levels of CPK and transaminases (TA) were evaluated at baseline and after one week of starting statin therapy. Patients with levels more than three folds the upper limit of normal (ULN) were excluded from the study.

Methods:

All patients were subjected to the following before and after statin therapy:

- History taking, clinical examination and Child-Pugh classification.
- Baseline laboratory investigations (liver profile, renal functions, CBC, CPK level)
- Abdominal ultrasound and Doppler study of portal vein (PV) hemodynamics with calculation of the portal vein congestion index as follows:

$$\text{Congestion index} = \frac{\text{cross-sectional area of portal vein}}{\text{Blood flow velocity}}$$

- Upper GI endoscopy: to assess the grade of esophageal and gastric varices and the presence of portal hypertensive gastropathy.
- Serum nitric oxide synthase level by ELISA.

RESULTS

No significant change in Child-Pugh score occurred after simvastatin therapy. Muscle pain was the main reported side effect, but was statistically non-significant. Serum CPK and TA levels were significantly elevated after simvastatin compared to baseline values ($p < 0.001$), but didn't reach three times the ULN. Doppler study of the PV revealed significant reduction of the mean values of PV diameter, cross sectional area and congestion index after simvastatin ($P<0.001$). No significant change occurred in the endoscopic findings after simvastatin. No significant difference was found between serum eNOS levels before and after treatment.

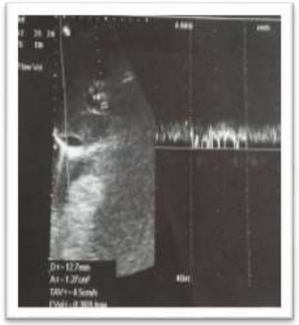

Figure 1: "Doppler of portal vein before statin therapy"

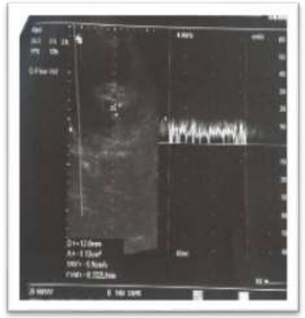

Figure 2: "Doppler of portal vein after statin therapy"

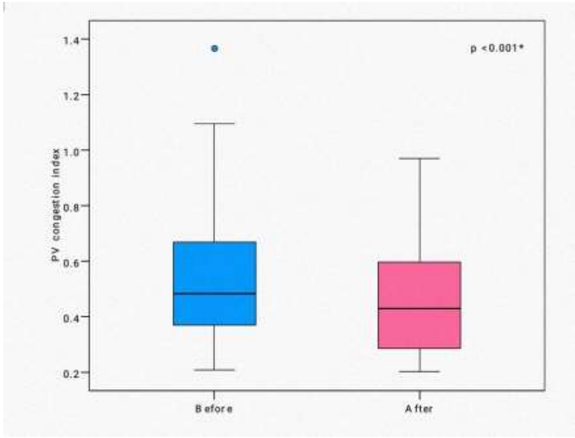

Figure 3: PV congestion index of patients before and after simvastatin

CONCLUSION

- Simvastatin reduces portal hypertension in HCV-cirrhotic patients, as proved by significant reduction of portal vein congestion index. Its use is relatively safe in patients with compensated cirrhosis. However, it has no direct beneficial effect on endoscopic features of portal hypertension. It doesn't affect the serum level of eNOS, so this should not be used as a serum marker for monitoring the effect of simvastatin on portal hypertension.