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Short Communication

Safety of Statins in Patients with Chronic Liver Disease

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Abstract: Statins are most widely used lipid-lowering agents. Their use in patients with chronic liver disease has been limited because of the fear of worsening liver function. However, recently evidence suggests that this class of drugs is safe in patients with chronic liver disease. In this editorial, I will summarize studies performed in patients with chronic liver disease using statins.

Keywords: Statins, drug-induced liver injury, chronic liver disease, hyperlipidemia.

INTRODUCTION:

Statins are the most widely prescribed lipid lowering agents. They reduce cardiovascular morbidity and mortality in high-risk patients with hyperlipidemia (Russo, M. W. *et al.*, 2014). Statins are generally well tolerated. Adverse effects of statins include gastrointestinal (constipation, flatulence, abdominal pain and nausea) occur in approximately 5% of patients, headache (4-9%), rash (3-5%), dizziness (3-5%), and blurred vision (1-2%) are other frequent adverse effects (Smith, K.M. *et al.*,2010). Myopathy and myositis can occur with single therapy and can be associated with mild elevations of CPK. Rhabdomyolysis leading to acute renal failure is a rare complication but occur more frequently when statins are administered concomitantly with gemfibrozil, cyclosporine and niacin >1g/day (Smith, K.M. *et al.*, 2010). Mild elevations in serum aminotransferase levels occur in 2% of patients (Smith, K.M. *et al.*, 2010; Pamillo, R.P. 2010). However, clinically apparent drug-induced liver injury is rare (Russo, M. W. *et al.*, 2014). Most patients who developed hepatotoxicity were in the sixth or seventh decade (Pamillo, R.P. *et al.*, 2010). Hepatotoxicity most often occurs within the first 12 weeks of therapy (Pamillo, R.P. 2010). Prior exposure to the same statin or a different statin has been reported in 20% of cases (Pamillo, R.P. 2010). Data from clinical studies reveal that hepatotoxicity is dose related (Pamillo, R.P. *et al.*, 2010). Liver histology reveals hepatocellular inflammation; however, eosinophils are most often absent (Pamillo, R.P. *et al.*, 2010). The chronic use of these agents has not been associated with the development of cirrhosis (Pamillo, R.P. *et al.*, 2010).

Non-Alcoholic Fatty Liver Disease

The presence of non-alcoholic fatty liver disease or non-alcoholic steatohepatitis should not deter physicians from prescribing statins in patients with hyperlipidemia (Gillet, R.C., & Norrell, A. 2011). Several preexisting conditions that cause elevations in transaminase levels (i.e. chronic viral hepatitis, non-alcoholic liver disease) were considered to be contraindications to statin therapy; however, statins do not worsen liver function in most patients with chronic liver disease (Gillet, R.C., & Norrell, A. 2011). Data from a cross sectional study involving 1201 patients with non-alcoholic fatty liver disease who received statins for at least 6 months reveal that statin recepients had a lower incidence of steatosis, inflammation and fibrosis in biopsy in non-1148M PNPLA3 allele (Ignacio, J.V. *et al.*, 2017).

Cirrhosis

Data from retrospective and epidemiologic studies reveal that statins are not only safe for use in patients with cirrhosis, but are also beneficial in reducing liver decompensation, hepatocellular carcinoma, infections, and death (Ignacio, J.V. *et al.*, 2017; Kaplan, D.E., 2018).

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Portal Hypertension

Data from animal and human models reveal that statins decrease fibrosis and lower portal hypertension through multiple putative mechanisms (Ignacio, J.V. *et al.*, 2017; Arab, J.P., & Shah, V.H. 2016; Abraide, J.G., & Cabrera, L. 2017).

Hepatitis B and C

Data from a retrospective study involving 13492 patients receiving lovastatin and a prospective study involving 320 patients receiving pravastatin revealed no evidence of increased hepatotoxicity among patients with chronic liver disease (including hepatitis B and C infections). Data from a cohort study involving 543 HCV chronic hepatitis patients revealed that statin use was associated with a decreased risk of fibrosis progression ((Ignacio, J.V. *et al.*, 2017)). Moreover, data from a cohort study involving 7248 patients with chronic hepatitis C revealed that statin therapy increased response to interferon based therapy (increased sustained virological responses, decreased cirrhosis development and progression in 10 years and decreased in incidental hepatocellular carcinoma) (Ignacio, J.V. *et al.*, 2017).

Primary Billiary Cholangitis

Data from prospective studies of statins in patients with primary biliary cholangitis revealed safety and efficacy of these agents (Gillet, R.C., & Norrell, A. 2011). Their use in this group of patients was associated with improved lipid profile, vascular function as well as antioxidant status (Ignacio, J.V. *et al.*, 2017).

Alcoholic Cirrhosis

Data from a retrospective case-cohort study involving patients with alcoholic cirrhosis revealed a reduced rate of mortality in participants who received statins regularly (Bang, U.C. *et al.*, 2017).

CONCLUSIONS

Statins were initially thought to be hepatotoxic; however current evidence reveals that this drug class may have beneficial effects in patients with chronic liver disease as well a potentially positive impact on the natural history and complications of cirrhosis. However, additional prospective and randomized studies should be performed to confirm these observations.

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