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Editorial

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Angiotensin receptor blocker add-on therapy in portal hypertension: To use angiotensin receptor blocker or not to use, that is the question

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Portal hypertension is one of the most important cause of morbidity and mortality in cirrhotic patients. Over the last decades several randomized controlled trials have led to standard treatment options. As standard of care, the effective therapy for controlling portal hypertension is non-selective beta blockers (NSBBs).[1] These drugs ameliorate portal pressure by lowering splanchnic blood flow and prevent variceal bleeding and re-bleeding in patients with large varices. However, NSBBs have been ineffective in preventing the development of varices and other complications of portal hypertension at early cirrhosis.[2]

It is well known that renin-angiotensin-aldosterone system plays an important role in endothelial function and vascular adaptation in cirrhotic condition. Especially, the role of angiotensin II is predominantly carried out through angiotensin II type 1 receptor.[3] Several experimental studies reported that angiotensin receptor blockers (ARBs) attenuate liver fibrosis. In this perspective, ARBs were expected as a promising strategy in preventing liver fibrosis.[4] In clinical practice, however, the usefulness of ARBs remains controversial in the respect of efficacy and safety in cirrhotic patients with portal hypertension.[5,6] Several reports showed that angiotensin II type 1 receptor blockers were unlikely to fulfill the needed therapeutic efficacy against portal hypertension.

Ten years ago, Gonzalez-Abraldes et al. performed a randomized trial comparing the effects of losartan and propranolol on the hepatic venous pressure gradient (HVPG) in cirrhotic patients with portal hypertension. In this study, losartan reduced the mean arterial pressure (MAP) and GFR, but did not changed HVPG significantly.[5] However, Schneider et al. reported that losartan may produce an important decrease in HVPG in patients with portal hypertension without a clinically important decrease in MAP.[6] It is difficult to explain the discrepant results between the published studies. Therefore, some authors evaluated the role of different losartan doses, and suggested the use of ARBs in selected patients of early cirrhosis with significant portal hypertension. However, the sample size is very small in these articles (less than 40 patients).[7]

In this issue of the *Clinical and Molecular Hepatology*, Kim et al. reported the efficacy of ARB combined with propranolol in 53

Abbreviations:

NSBBs, non-selective beta blockers; ARBs, angiotensin receptor blockers; HVPG, hepatic venous pressure gradient; MAP, mean arterial pressure.

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cirrhotic patients with portal hypertension.[8] As a result, portal pressure declined significantly in both groups (candesartan 8mg + propranolol vs. propranolol monotherapy). However, no difference was observed in the effect of pressure reduction between the two groups. With significant number of patients and prospective, randomized trial, they demonstrated that ARB plus propranolol combination therapy does not show additional efficacy in ameliorating portal hypertension. Although this study may not be new concept, this result provides the need for advanced studies with different doses of ARBs combination therapy for the management of portal hypertension. Hopefully, such studies will improve the treatment efficacy and prevent the progression of portal hypertension.

Conflicts of Interest

The authors have no conflicts of interests to disclose.

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