Grand Rounds

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Beta adrenergic blockade and decompensated cirrhosis

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Summary

Non-selective betablockers (NSBBs) remain the cornerstone of medical treatment of portal hypertension. The evidence for their efficacy to prevent variceal bleeding is derived from prospective trials, which largely excluded patients with refractory ascites and renal failure. In parallel to the increasing knowledge on portal hypertension-induced changes in systemic hemodynamics, cardiac function, and renal perfusion, emerging studies have raised concerns about harmful effects of NSBBs. Clinicians are facing an ongoing controversy on the use of NSBBs in patients with advanced cirrhosis. On the one hand, NSBBs are effective in preventing variceal bleeding and might also have beneficial non-hemodynamic effects, however, they also potentially induce hypotension and limit the cardiac reserve. An individualized NSBB regimen tailored to the specific pathophysiological stage of cirrhosis might optimize patient management at this point. This article aims to give practical recommendations on the use of NSBBs in patients with decompensated cirrhosis.

Keywords: Beta blockers; Ascites; Liver cirrhosis; Decompensation; Hypertension, portal; Esophageal and gastric varices; Gastrointestinal hemorrhage.

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Key point

Non-selective betablockers (NSBBs) represent the cornerstone of pharmacological treatment of portal hypertension.

Clinical vignette

Clinical scenario 1

A 42-year-old male patient with cirrhosis due to hereditary hemochromatosis with large esophageal varices at endoscopy has been treated with propranolol 120 mg/d for primary prophylaxis of variceal bleeding for 4 years. The patient is undergoing regular phlebotomies to maintain serum ferritin levels of 50–100 μg/L. He presents at the outpatient clinic and reports dizziness and reduced exercise capacity together with weight gain. Edema and new-onset ascites were noted at clinical examination. The heart rate was 58 beats per minute (bpm) and the arterial blood pressure was 95/52 mmHg. Investigations (including diagnostic paracentesis) revealed no evidence of bacterial infection. The patient tells the physician that dizziness is most pronounced after propranolol intake.

Q1: Should the primary prophylaxis with propranolol be interrupted or discontinued in this patient with new-onset ascites and symptomatic arterial hypotension?

Clinical scenario 2

A 55-year-old female patient with cirrhosis due to alcoholic liver disease was referred for evaluation for liver transplantation, as she had developed refractory ascites. Following a variceal bleeding two years ago, the patient has been receiving propranolol 160 mg/d and repeated endoscopic band ligations (EBLs). The last EBL was performed 3 months ago, and the last upper gastrointestinal (GI) endoscopy two days after referral only showed small varices and portal-hypertensive gastropathy. Blood pressure and heart rate were 125/80 mmHg and 59 bpm, respectively. A therapeutic large volume paracentesis was performed and the ascitic fluid polymorphonuclear (PMN) cell count was 78 cells/μL. The patient had a stable serum creatinine of about 1.3 mg/dL over the past 12 months.

Q2: Should the propranolol dose in secondary prophylaxis be lowered or treatment discontinued in this patient with refractory ascites?

Pathophysiology (Fig. 1)

Both increased intrahepatic vascular (sinusoidal) resistance and increased portal blood flow contribute to the elevated portal pressure in patients with cirrhosis. Clinically significant portal hypertension (CSPH) is defined by a hepatic venous pressure gradient (HVPG) of ⩾10 mmHg. In these patients, porto-systemic collaterals (e.g., esophageal varices)

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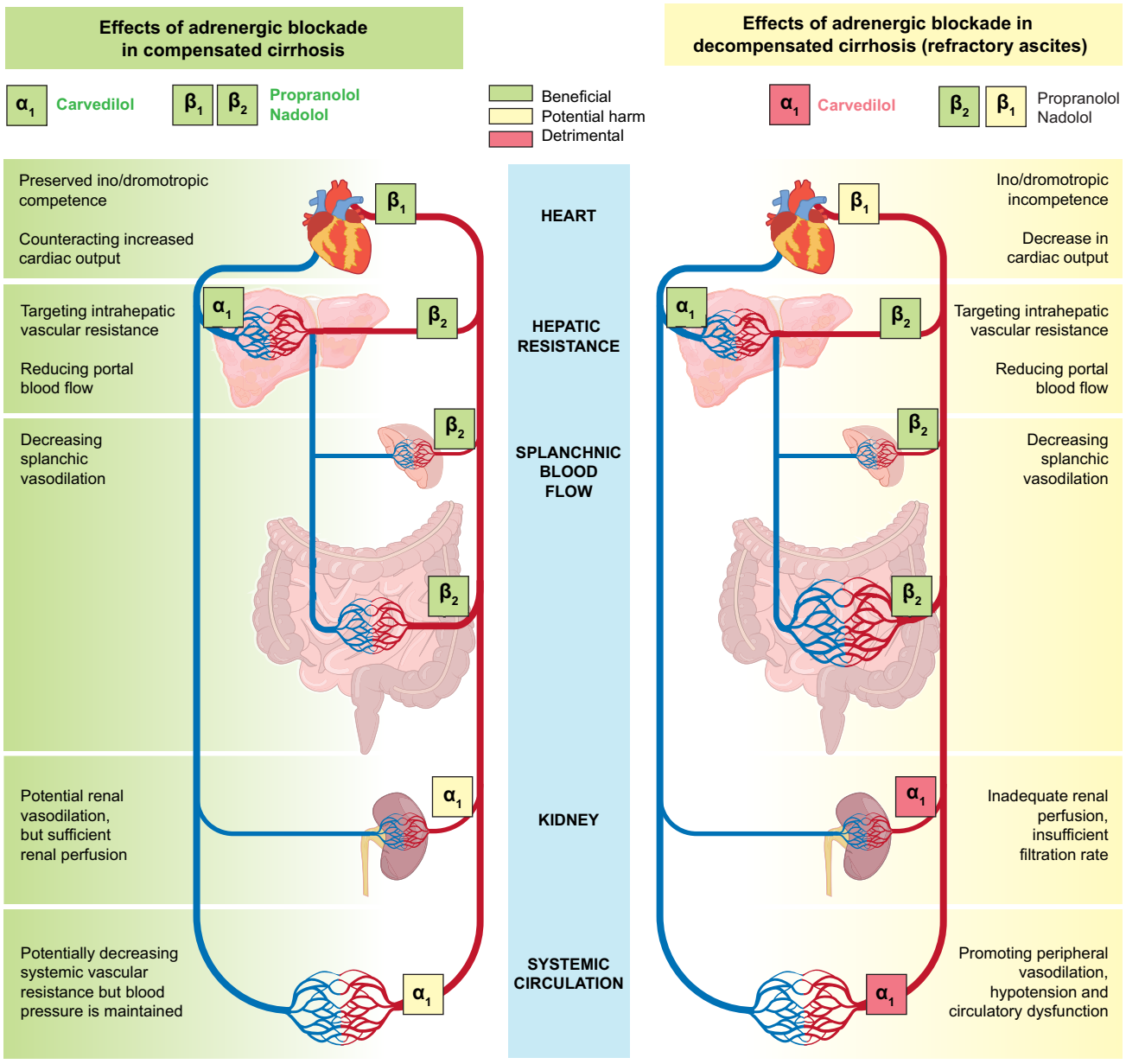

Fig. 1. The effects of adrenergic blockage in compensated and decompensated cirrhosis.

and ascites may develop. Due to progressive splanchnic and peripheral vasodilation, portal hypertension ultimately leads to a hyperdynamic circulation with compensatory increases in heart rate and cardiac output. These changes characterize the hyperdynamic (or hyperkinetic) portal-hypertensive syndrome [1,2].

Importantly, β-adrenergic blockade leads to a more pronounced decrease in HVPG in patients with CSPH, since these patients have splanchnic vasodilatation and hyperdynamic circulation [3]. This explains why NSBBs are not generally effective in preventing the development of varices in patients with cirrhosis [4,5], but might be able to prevent progression from small to large varices in patients with CSPH [6,7]. The hemodynamic effects of NSBBs, thus, depend on the severity of the hyperdynamic state, since mechanistically NSBB act by decreasing heart rate and inhibiting splanchnic vasodilation. This would suggest, that achieving a HVPG-response to NSBBs is more likely in patients with pronounced hyperdynamic circulation (e.g., refractory ascites) [8]. Due to increased resting heart rates, higher doses of NSBBs might be necessary to achieve the same target heart rates in patients with decompensated, when compared to patients compensated disease. This would indeed impact both beneficial effects