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Haemodynamic and renal effects of tadalafil in patients with cirrhosis

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Abstract

A recent report introduced the phosphodiesterase-5 inhibition by vardenafil as a novel treatment of portal hypertension in patients with cirrhosis. In the herein presented "letter to the editor", the administration of tadalafil did not influence portal haemodynamics but impaired systemic haemodynamics in patients with cirrhosis. Our observations concur with the results of a report in a previous issue of *World Journal of Gastroenterology* (October 2008). Moreover, tadalafil adversely affected renal function in patients with decompensated liver disease.

Key words: Tadalafil; Portal hypertension; Cirrhosis; Ascites; Phosphodiesterase-5 inhibition

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TO THE EDITOR

We read with interest the article by Clemmesen *et al*[1] in a previous issue of *World Journal of Gastroenterology* (October 2008) regarding the effects of sildenafil in patients with cirrhosis and hepatic venous pressure gradient (HVPG) above 12 mmHg. Sildenafil had no effects on HVPG but significantly reduced the mean arterial pressure. We would like to add our experience with the use of tadalafil, a long-acting phosphodiesterase-5 (PDE-5) inhibitor[2], in treatment of patients with cirrhosis.

Six patients with and 6 patients without ascites and oesophageal varices (Child-Pugh class A/B/C: 6/0/0 and 0/2/4, respectively) were studied at baseline and 2 h after oral administration of 10 mg of tadalafil. All patients were included after written informed consent was obtained from them and after the local scientific-ethical committee approved the study. The inclusion criteria were the same as in the study of Clemmesen *et al*[1]. Portal vein velocity (PVV) and portal flow volume (PFV) were evaluated as described by Deibert *et al*[3]. Cardiac output (CO) detected by Doppler ultrasound, mean arterial pressure (MAP) measured with an automatic sphygmomanometer, and systemic vascular resistance (SVR) expressed as the ratio MAP/CO were also evaluated. All patients received a continuous infusion of dextrose water at a rate of 2 mL/min for 4 h before and after the administration of tadalafil to

Table 1 Effects of tadalafil on portal and systemic haemodynamics and renal function in patients with cirrhosis (mean ± SE)

	Compensated (n = 6)		P^1	Decompensated (n = 6)		P^1	P^2
	Baseline	2 h		Baseline	2 h		
PVV (m/s)	0.103 ± 0.016	0.102 ± 0.019	0.9	0.186 ± 0.011	0.18 ± 0.015	0.8	0.6
PFV (L/min)	0.611 ± 0.116	0.543 ± 0.125	0.2	1.194 ± 0.169	1.175 ± 0.198	0.7	0.5
MAP (mmHg)	93.9 ± 3	87.5 ± 2.9	0.02	84.8 ± 2.4	76.9 ± 2	0.001	0.02
CO (L/min)	5.56 ± 0.23	5.7 ± 0.24	0.04	6.91 ± 0.3	7.35 ± 0.25	0.002	0.03
SVR (dynes.sec.cm^{-5})	1708 ± 116	1555 ± 101	0.02	1243 ± 84	1056 ± 59	0.001	0.03
ClCre (mL/min)	98.6 ± 8.1	95.6 ± 7.4	0.09	71.6 ± 2.4	64 ± 2.8	0.001	0.01
UNaV (μmol/min)	102 ± 15.9	97 ± 13.7	0.09	29.6 ± 7.3	20.6 ± 4.6	0.02	0.01

[1]*vs* baseline values; [2]*vs* basal and final results in two groups of patients. PVV: Portal vein velocity; PFV: Portal flow volume; MAP: Mean arterial pressure; CO: Cardiac output; SVR: Systemic vascular resistance; ClCre: Creatinine clearance; UNaV: Urinary sodium.

sustain diuresis, and urine was collected over the two periods of time for estimation of creatinine clearance (ClCre) and sodium excretion.

Tadalafil did not significantly change the PVV and PFV but significantly reduced the MAP and SVR and significantly increased the CO in both study groups (Table 1). More significant systemic haemodynamic changes together with a significant decrease in ClCre and natriuresis were noted in the patients with decompensated cirrhosis.

Our observations concur with the results of Clemmesen *et al*[1] and previous series of compensated[4] or mixed compensated and decompensated patients with cirrhosis[5], showing that PDE-5 inhibition by sildenafil has no effect on portal pressure and impairs systemic haemodynamics. Furthermore, the present results confirm those of Thiesson *et al*[6] in that PDE-5 inhibition may adversely affect renal function and natriuresis in patients with cirrhosis and ascites, possibly due to deterioration of the hyperdynamic state. Although a recent report introduced PDE-5 inhibition by vardenafil as a novel treatment of portal hypertension, the present and previous data[1,4,5] strongly question the portal hypotensive efficacy and safety of PDE-5 inhibitors in patients with cirrhosis.

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