

association. Another explanation could be the higher prevalence of ACE inhibitor-induced cough in Chinese subjects, as shown by CHAN *et al.* [6]. It is possible that ACE inhibitors are also protective in non-Asian populations. However, larger populations may be necessary to confirm such an effect.

Further studies on the relationship between angiotensin-converting enzyme and pneumonia in predominantly white populations are currently being undertaken in our department.

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## PDE-5 inhibitors lower portal and pulmonary pressure in portopulmonary hypertension

To the Editors:

Several studies have proved that inhibitors of phosphodiesterase (PDE)5 are potent compounds for lowering pulmonary pressure in pulmonary arterial hypertension. With great interest we read the study conducted by REICHENBERGER *et al.* [1] about the effect of sildenafil on portopulmonary hypertension (PPHTN). This is a specific condition characterised by an elevated pulmonary arterial pressure (PAP), increased pulmonary vascular resistance and a normal wedge pressure in a setting of underlying portal hypertension. Effective medical therapy is of great importance, as a markedly increased pulmonary pressure has a very poor prognosis in cirrhotic patients and is a contraindication for liver transplantation. The results of the studies by REICHENBERGER *et al.* [1] and others [2, 3] show that in these patients, inhibitors of PDE5 also lower PAP. However, REICHENBERGER *et al.* [1] focused on the effect of sildenafil on PAP; the potential effect of this drug on portal pressure was not investigated.

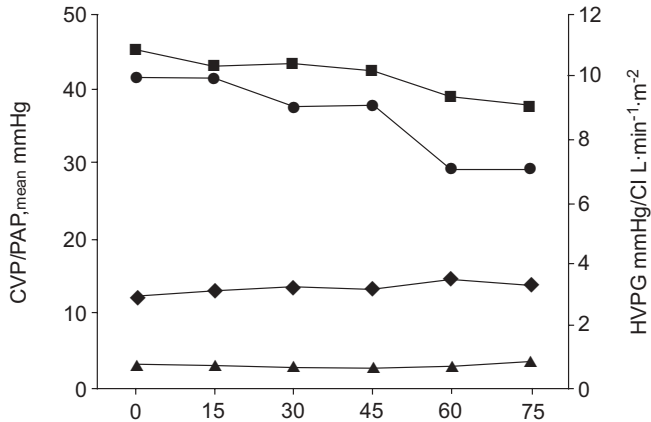
In a recent study, we showed that the PDE5 inhibitor vardenafil lowers portal pressure and increases portal blood flow in healthy subjects as well as in patients with liver cirrhosis [4]. We also found that sildenafil and tadalafil had similar effects (unpublished data). Recently, we investigated the acute effect of tadalafil on portal and pulmonary haemodynamics simultaneously in a patient with PPHTN.

In the 55-yr-old patient, alcoholic Child A cirrhosis had been diagnosed 7 yrs before. Alcohol consumption had stopped since cirrhosis was diagnosed. The reason for admission was increasing dyspnoea at physical exercise. The patient was taking no medication at the time of the study. The patient was obese (186 cm, 108 kg, body mass index 31.2), his blood

pressure was 140/105 mmHg and his cardiac frequency was 79 bpm. ECG and Doppler echocardiogram showed right heart enlargement with systolic PAP ~75 mmHg. Spirometry showed a normal vital capacity (5.3 L, 103%) and forced expiratory volume in one second (3.3 L, 86%). Abdominal duplexsonography showed a slow (9 cm·s<sup>-1</sup>) and reduced portal flow, ~0.15 L·min<sup>-1</sup> with intrahepatic retrograde perfusion. The umbilical vein was reopened and a large splenorenal shunt was detected. Second-grade oesophageal varices were found on endoscopy.

After counselling the local ethics committee, we investigated the effect of tadalafil, a selective inhibitor of PDE5, on portal and pulmonary haemodynamics. Catheters were introduced into the pulmonary artery and one of the liver veins simultaneously. Haemodynamic parameters were recorded every 15 min for 75 min. After 10 mg tadalafil, mean PAP was reduced from 45 to 38 mmHg (fig. 1). Cardiac index increased from 3.02 to 3.24 L·min<sup>-1</sup>·m<sup>-2</sup> and pulmonary vascular resistance decreased from 459 to 351 dynes·s·cm<sup>-5</sup>, while arterial oxygen pressure increased from 70.5 to 78.2 mmHg. Hepatovenous pressure gradient decreased from 10 to 7 mmHg and systemic arterial pressure decreased from 167/89 to 152/87 mmHg. Our results show, that PDE5 inhibition reduces portal venous and PAP in this patient with PPHTN.

Portal hypertension in liver cirrhosis is caused by multiple factors, *e.g.* regenerative nodules and sinusoidal fibrosis, hyperdynamic splanchnic circulation, vasoactive substances and increased sinusoidal tonus due to diminished nitric oxide production and increased cyclic guanosine monophosphate (GMP) degradation [5, 6]. Inhibitors of PDE5 increase portal venous flow and lower portal pressure by inhibiting the degradation of cyclic GMP [4]. Pulmonary arterial hypertension has



**FIGURE 1.** Reduction in mean pulmonary arterial pressure (PAP; ■) and hepatovenous pressure gradient (HVPG; ●) under inhibition of phosphodiesterase 5 in a patient with portopulmonary hypertension. ◆: cardiac index (CI); ▲: central venous pressure (CVP).

been described in up to 16% of patients with portal hypertension (portopulmonary hypertension) [7]. In these patients the application of beta-blockers for therapy of portal hypertension may cause deleterious side-effects [8]. Use of inhibitors of PDE5 in patients with PPHTN would be a reasonable alternative if they prove to be effective in long-term studies. Inhibitors of PDE5 exert a direct dilating effect on pulmonary arteries in PPHTN. In addition, it may be speculated that a reduction of the portal pressure and improved hepatic perfusion diminish circulating vasoactive substances deteriorating pulmonary vascular remodelling.

In conclusion, by using inhibitors of phosphodiesterase 5 in portopulmonary hypertension, a double goal may be achieved: a reduction of elevated portal and pulmonary pressure simultaneously.

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