Author's response to reviews

Title: Phosphodiesterase 5 Inhibitors Lower both Portal and Pulmonary Pressure in Portopulmonary Hypertension. A case report.

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We thank the reviewers for their comments. The manuscript was revised according to their suggestions.

Reply to reviewers' comments

Reviewer 1: Michael J Krowka
1. The patient's clinical condition actually further improved between 3 and 6 months. Six minutes walking test increased, resting blood gas analysis improved. An invasive hemodynamic examination at 3 months was not done, so we can't comment on that. This is now mentioned in the second last paragraph of the discussion.
2. We agree with the reviewer. Therefore, we modified paragraph # 4 in the Discussion accordingly.
3. In paragraph # 5 of the Case Presentation we mentioned that we gave Sildenafil bid since in liver cirrhosis pharmacokinetics of Sildenafil are changed.
4. Other causes for pulmonary hypertension were ruled out, as mentioned in the text now.
5. Vardenafil refers to our previous study, ref. # 5. In this study pulmonary hemodynamics were not measured.
6. We changed the phrase : This case presentation and recent own results [5] suggest that PDE5 inhibitors are no major risk factor for bleeding from esophageal varices.
7. The effect of limiting right ventricular function of beta blockers is now mentioned.

Reviewer 2: Florian S Fuchs
1. The sentence was changed.
2. The requested information for hepatic encephalopathy is now given in the text. As only abnormal laboratory testing is mentioned, albumin level was not indicated. On the Child-Pough scale the patient had 6 points.
3. Elevated PAP and anamnestic syncopies as mentioned in the text were the indication for an early initiation of therapy. Dose reduction of Sildenafil is now explained in the text (altered pharmacokinetics in liver cirrhosis).
4. Left heart status in echocardiography is now mentioned. PAWP was normal. We included PAWP in Table 1. Holter ECG showed no arrhythmias. Other causes of syncopies were excluded.
5. The primary aim of the present test was not to measure a potential vasoreagibility of the pulmonary vessels but to measure simultaneously the effects of a PDE5 inhibitor on pulmonary and portal hemodynamics. We are aware the fact that vasoreagibility testing with NO or prostacyclin does not have clinical consequences in PPHTN because high dose Ca-antagonist therapy has no beneficial effect in this disease.
6. PAWP is mentioned. The patient was hospitalized in the department of pneumology and underwent complete diagnostics to exclude other kinds of pulmonary hypertension. That is now mentioned in the text (Case presentation).
7. We had planned to start long-term treatment of the patient with Tadalafil, but at that time Sildenafil was approved for PAH. So we decided to give him Sildenafil. The six-months test was done with Sildenafil.
8. We modified # 2 in the Discussion. Some authors speculate that PDE5 inhibitors lead to an increase of
portal pressure in liver cirrhosis and may therefore be a risk for variceal bleeding. However, we show the contrary: PDE5 inhibitors lower portal pressure. See ref. 5.
9. Cardiac output is shown in Fig.1, it refers to the left y-axis. In Table 1 we indicate cardiac index and cardiac output.
10. The patient received no current medication.