prostacyclin analogue, endothelin receptor antagonist, phosphodiesterase 5 inhibitor) from 2012 to 2013. Results: After 1 year of oral triple combination therapy WHO-FC improved from III to II in all three patients and 6 min walking test improved from 273 ± 98 to 553 ± 31 ($P < 0.05$) and mean pulmonary arterial pressure decreased from 52.7 ± 9.5 to 31 ± 6.2 mmHg ($P = 0.05$) and cardiac index increased from 1.5 ± 0.2 to 2.82 ± 0.17 mmHg ($p < 0.001$). All three patients were tolerable with triple upfront combination therapy and had no severe side effect. Conclusions: Oral triple upfront combination therapy improved symptoms, exercise capacity and hemodynamics for the patients with severe I/HPAH in long-term without severe adverse effect.

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Combination therapy of bosentan and ambrisentan for portopulmonary hypertension

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Endothelin receptor antagonists (ERAs) such as bosentan and ambrisentan are principal medicines in the treatment of pulmonary arterial hypertension (PAH). On the other hand, the adverse effects are not uncommon such as liver dysfunction and peripheral edema. These side effects are often intolerable for patients and hinder administration of sufficient amount of ERA. In this report, we present a case of a 56-year-old man with liver chirrosis due to non-alcoholic steatohepatitis. He was referred to our hospital complaining of progressive dyspnea on effort equivalent to WHO FC III. His mean pulmonary artery pressure (mPAP) was 62 mmHg and peak VO2 was 10.9 ml/kg/ min. He was diagnosed as having portopulmonary hypertension (PoPH). Tadalafil, bosentan and beraprost were introduced respectively, and his mPAP ameliorated to 54 mmHg. However, he was intolerant of increasing bosentan more than 125 mg, because of worsening liver dysfunction, while a full dose of ambrisentan was hard to use, as he easily got edematous with various drugs. Finally, we administrated a combination of moderate dose of bosentan (125 mg) and ambrisentan (2.5 mg). Three months after administration of both drugs, his mPAP was reduced to 42 mmHg, and peak VO2 was improved from 14.7 to 17.8 ml/kg/min, with no significant adverse effect of each drugs. To our knowledge, this is the first case report in which a combination therapy of bosentan and ambrisentan was practically tried to the patient of PAH, and satisfactory result was obtained. In this report, we will try to discuss the efficacy of combination therapy of bosentan and ambrisentan, in terms of cross-talk of endothelin receptors, based on relevant literatures.

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Experience in combination therapy for portopulmonary hypertension in the young with intravenous epoprostenol and endothelin receptor antagonists

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Background: Portopulmonary hypertension (PoPH) is an uncommon but devastating complication of liver disease. There is no established medical therapy for PoPH and the condition adversely affects the outcome of liver transplantation. The prognosis of PoPH in the young is still very poor even in the recent era. Methods: We retrospectively reviewed seven pediatric patients with PoPH who were treated with different combinations of vasodilators. Expression of endothelin-1 and its receptors in the postmortem lung specimens were analyzed. Results: Primary diagnoses for liver disease were congenital biliary atresia in 5, extrahepatic portal vein atresia in one and patent ductus venosus in the other. The median age at diagnosis was 14 years old. The onset of PoPH was syncope, dyspnea on exercise and abnormal electrocardiogram. The mean pulmonary arterial pressure was 49 mmHg and pulmonary vascular resistance index was 11.2 wood units-m^2 at the time of diagnosis. Cardiac catheterization revealed no acute response to oxygen, nitric oxide, sildenafil whereas a little response to intravenous epoprostenol (IV-PGI2). IV-PGI2 was administrated in four patients and had chronic effect on hemodynamics. Oral endothelin receptor antagonists (ERA: bosentan or ambrisentan) were administrated in five and there was no evidence of drug-related liver injury. Three patients died and liver transplantation was performed in three. Immunohistochemical staining for the endothelin system revealed increased expression of ET-B receptor in the pulmonary vascular endothelial cells. Conclusion: PoPH in the young was diagnosed at moderately severe stage of PH and carried poor prognosis. Combination therapy with IV-PGI2, ERA and PDE5-I may provide a promising therapeutic option for selected patients with PoPH.

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Peak systolic strain at right ventricular free wall determined by two-dimensional speckle-tracking echocardiography is an independent predictor for pulmonary hypertension

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Background: Right heart catheterization (RHC) is the invasive but the gold standard examination for assessing pulmonary arterial pressure (PAP). Thus, pulmonary hypertension (PH) is usually predicted by using echocardiographic parameters. Regional deformation of the left ventricular (LV) wall detected by two-dimensional speckle-tracking echocardiography is evidently useful for detecting myocardial ischemia, viability and LV function, but its significance of right ventricle (RV) has not been fully elucidated. We investigated the ability of peak systolic strain (PSS) and the post systolic strain index (PSI) of the RV free wall determined by speckle-tracking echocardiography to predict PH. Methods: Thirty-six images (27 images from patients with PH; nine from patients with connective tissue diseases without PH) obtained by speckle-tracking echocardiography were analysed. PSS and PSI at the basal and mid-RV free wall were calculated and averaged. We investigated the relationship of echocardiographic parameters of pressure/volume overload in RV including RV end-diastolic diameter (RVDd) and the pressure gradient calculated from the velocity of tricuspid valve regurgitation (TRPG) with mean PAP (MPAP) measured by RHC. Results: PSS, PSI, RVDd and TRPG were significantly correlated with MPAP. Multivariate logistic analysis identified PSS as an independent predictor of MPAP ≥35 mmHg (odds ratio, 1.62; 95% confidence