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References

1. Nakamura T, Inagaki H, Seto M, Nakamura S. Gastric low-grade B-cell MALT lymphoma. J Gastroenterol 2003;38:921–9.
2. Nakamura S, Matsumoto T, Nakamura S, Jo Y, Fujisawa K, Suekane H, et al. Chromosomal translocation t(11; 18)(q21; q21) in gastrointestinal mucosa-associated lymphoid tissue lymphoma. J Clin Pathol 2003;56; 36–42.
3. Liu H, Ye H, Dogan A, Ranaldi R, Hamoudi RA, Bearzi I, et al. T(11; 18)(q21; q21) is associated with advanced mucosa-associated lymphoid tissue lymphoma that expresses nuclear *BCL10*. Blood 2001;98:1182–7.
4. Motegi M, Yonezumi M, Suzuki H, Suzuki R, Hosokawa Y, Hosaka S, et al. *API2-MALT1* chimeric transcripts involved in mucosa-associated lymphoid tissue type lymphoma predict heterogeneous products. Am J Pathol 2000;156:807–12.

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Use of aerosolized inhaled iloprost in the treatment of portopulmonary hypertension

To the Editor: Portopulmonary hypertension (PPHT) is a well-recognized and characterized complication of endstage liver disease.[1] Intravenous administration of epoprostenol (prostacyclin; PGI_2) on a short-term or long-term basis decreases pulmonary arterial pressure (PAP) in the setting of PPHT.[2] Reports on prostanoid inhalation in these patients are scarce. We report the successful treatment of PPHT with inhaled iloprost, a carbacyclin analogue of PGI_2, in a patient with liver cirrhosis related to alcohol consumption and pulmonary arterial hypertension (PAH).

A 39-year-old man with PPHT was admitted to our hospital with exertional dyspnea that markedly limited his physical activity (New York Heart Association class III). Portal hypertension with esophageal varices, grade II, and hypertensive gastropathy had been diagnosed previously.

On presentation, he showed no clinical signs of right heart or liver decompensation. INR, bilirubin, albumin, creatinine, and hepatic aminotransferase were within normal ranges. The Child-Pugh score was 5 points (Child A). He was able to walk 225 m in 6 min. Echocardiography revealed no pulmonary shunting as a possible sign of hepatopulmonary syndrome, and right ventricular systolic pressure was estimated at 75 mmHg. Ventilation-perfusion scan showed no evidence of pulmonary thrombembolism. Initial right-heart catheterization showed precapillary pulmonary hypertension, with a mean PAP (PAPmean) of 44 mmHg, a total pulmonary resistance (TPR) of 514 dyn*s*cm^{-5}, and a cardiac index (CI) of 3.3 l/min per m^2.

Table 1. Cardiopulmonary hemodynamics and 6-min walk distance at baseline and after 6 months of inhaled iloprost therapy

Parameters	Baseline value	After 6 months of therapy
PAPm (mmHg)	44	35
TPR (dyn*s*cm^{-5})	514	431
CI (l/min per m^2)	3.3	3.3
RRm (mmHg)	88	85
SVR (dyn*s*cm^{-5})	1010	1017
RAP (mmHg)	5	2
PCWP (mmHg)	8	3
SaO_2 (volume%)	98	97
6 MWD (m)	225	350

PAPm, mean pulmonary arterial pressure; TPR, total pulmonary resistance; CI, cardiac index; RRm, mean arterial pressure; SVR, systemic vascular resistance; RAP, right atrial pressure; PCWP, pulmonary capillary wedge pressure; SaO_2, arterial oxygen saturation; 6 MWD, 6-min walk distance

Regular inhalation of an aerosolized dose of about 17 μg iloprost, given six times per day (total daily dose 100 μg), with treatment on-hold during the night, was initiated after the first right-heart catheterization. Iloprost (Ilomedin; Schering, Berlin, Germany) was administered with a jet nebulizer system (Ilo-Neb/Aerotrap; Nebu-Tec; Elsenfeld, Germany) combined with a Pulmocar Akku compressor (Sanesco Medizintechnik, Vienna, Austria). After 6 months, repeated right-heart catheterization after nocturnal on-hold treatment showed improved pulmonary hemodynamic parameters at trough level (PAP mean, 35 mmHg; TPR, 431 dyn*s*cm^{-5}; CI, 3.3 l/min per m^2). The distance in the 6-min walk test improved to 350 m. These and other parameters at baseline and after the 6-month therapy are shown in Table 1. No side-effects of inhalation with iloprost were complained of by the patient.

Inhaled iloprost was proven to be effective in the treatment of disease-related symptoms and in slowing down disease progression. It was well tolerated in a placebo-controlled trial in patients with primary pulmonary hypertension, in PAH associated with appetite-suppressant drugs and with connective-tissue diseases, and in inoperable chronic thromboembolic pulmonary hypertension.[3] Recently, the short-term efficacy of inhaled epoprostenol on pulmonary hemodynamics was reported in one patient with PPHT.[4] To our knowledge, this is the first report of the long-term efficacy and safety of inhaled iloprost in a patient with PPHT.

We conclude that inhaled iloprost should be considered for the treatment of PPHT, as well as its use as a bridging strategy before liver or lung transplantation. A phase II trial with inhaled iloprost is warranted to establish its efficacy and safety in patients with PPHT.

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References

1. Kuo PC, Plotkin JS, Johnson LB, Howell CD, Laurin JM, Bartlett ST, et al. Distinctive clinical features of portopulmonary hypertension. Chest 1997;112:980–6.
2. Kuo PC, Johnson LB, Plotkin JS, Howell CD, Bartlett ST, Rubin LJ. Continuous intravenous infusion of epoprostenol for the treatment of portpulmonary hypertension. Transplantation 1997;63:604–6.
3. Olschewski H, Simonneau G, Galie N, Higgenbottam T, Naeije R, Rubin LJ, et al. Inhaled iloprost for severe pulmonary hypertension. N Engl J Med 2002;347:322–9.
4. Schroeder RA, Rafii AA, Plotkin JS, Johnson LB, Rustgi VK, Kuo PC. Use of aerosolised inhaled epoprostenol in the treatment of portopulmonary hypertension. Transplantation 2000;70:548–50.

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