Available online at www.sciencedirect.com
SCIENCE DIRECT
Pulmonary Pharmacology & Therapeutics 19 (2006) 264–271
PULMONARY PHARMACOLOGY & THERAPEUTICS
www.elsevier.com/locate/ypupt

Perfusion lung scan as a prognostic indicator of response to beraprost sodium in idiopathic pulmonary arterial hypertension

So-Yeon Park[a], Dae-Hyuk Moon[b], Yong-Bum Park[c], Ju-Ok Na[a], Heong-Kon Whang[d], Byoung-Sung Lim[d], Sang-Do Lee[a,*]

[a]*Division of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, 388-1 Pungnap-2 dong, Songpa-gu, Seoul 138-736, South Korea*
[b]*Department of Nuclear Medicine, Asan Medical Center, University of Ulsan College of Medicine, 388-1 Pungnap-2 dong, Songpa-gu, Seoul 138-736, South Korea*
[c]*University of Hallym College of Medicine, South Korea*
[d]*Pucheon Sejong Hospital, South Korea*

Received 16 August 2004; revised 15 May 2005; accepted 28 June 2005

Abstract

Study objective: To study whether there is any difference in thfe clinical characteristics between the two patterns of perfusion lung scan of idiopathic pulmonary arterial hypertension (normal vs. diffuse, multiple ill-defined defects) and whether the perfusion lung scan patterns of these patients would predict the effect of long-term use of beraprost sodium.

Methods: We evaluated 27 patients who used beraprost sodium for over 3 months, and noted a diffuse patchy pattern in 13 cases and a normal pattern in the remaining 14 cases. We judged that beraprost sodium was effective when at least two of the following conditions were met: improvement in symptom of dyspnea, more than 10% decrease in peak velocity of tricuspid valve regurgitation by echocardiography (V_{max}), or more than 10% increase in 6-min walking distance.

Results: At baseline there was no difference between the two groups in dyspnea, hemodynamic parameters, and 6-min walking distance. After the use of beraprost sodium, the normal group showed improvement in dyspnea, 6-min walking distance, and V_{max}. But the diffuse patchy group showed no improvement. The use of beraprost sodium in the normal group was effective in 10 out of 14 cases, but was effective in only two out of 13 cases in the diffuse patchy group.

Conclusion: Perfusion lung scan pattern in patients with idiopathic pulmonary arterial hypertension is a useful prognostic indicator of the response to beraprost sodium.

Keywords: Idiopathic pulmonary arterial hypertension; Perfusion lung scan; Beraprost sodium

1. Introduction

Idiopathic pulmonary arterial hypertension (IPAH) is a progressive disease characterized by raised pulmonary vascular resistance without a demonstrable cause and, if untreated progresses to severe pulmonary hypertension and right heart failure [1,2]. The median survival time is 2.8 years after diagnosis. Considerable progress in therapy has been made, such as endothelin receptor antagonists, anticoagulants, vasodilators, calcium channel blockers, and prostacyclin [3].

Beraprost sodium, a chemically stable and orally active prostacyclin analogue, has also shown potential in the management of patients with IPAH [4]. It produces strong vasodilation and inhibition of platelet aggregation, and long-term therapy with beraprost sodium improved exercise capacity and symptoms in patients with IPAH [4–6]. But the response to prostacyclin treatment is not uniform and some

Abbreviations IPAH, idiopathic pulmonary arterial hypertension; NYHA, New York Heart Association; V_{max}, peak velocity through tricuspid valve; MPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; PCW, pulmonary capillary wedge pressure; CO, cardiac output; CI, cardiac; S_VO_2, mixed venous oxygen saturation.

* Corresponding author. Tel.: +82 2 3010 3140; fax: 82 2 3010 6968.
E-mail address: sdlee@amc.seoul.kr (S.-D. Lee).

1094-5539/$ - see front matter © 2005 Published by Elsevier Ltd.
doi:10.1016/j.pupt.2005.06.005

patients with IPAH did not show a favorable response [7–9]. This may be applicable to patients treated with beraprost sodium.

Perfusion lung scan has been used as a method to distinguish IPAH from chronic pulmonary thromboembolism. Two lung scan patterns of normal or diffuse patchy abnormalities are well established in IPAH, and can be easily differentiated from multiple segmental large defects in patients with thromboembolic pulmonary hypertention [10–13]. Lung scan patterns have been reported to be correlated to histologic subtypes [10], however, its clinical significance has not been established. We studied whether there is any difference in the clinical characteristics between the two patterns of perfusion lung scan of IPAH and whether the perfusion lung scan patterns of IPAH patients would predict the effect of long-term use of beraprost sodium.

2. Methods and materials

We evaluated patients enrolled in a prospective study, the first aim of which was to evaluate the effect of beraprost sodium in IPAH and the second was to determine the clinical meaning of different perfusion scan patterns observed in the patients with IPAH. We enrolled all the patients with IPAH from whom written informed consent had been obtained and right heart catheterization was performed. We diagnosed IPAH according to the criteria of the National Institutes of Health Registry on IPAH [1]. In all patients high resolution computed tomography (HRCT) was performed to exclude the possibility of either veno-occlusive disease or pulmonary capillary hemangiomatosis. In patients with diffuse patchy defects in perfusion lung scan, either pulmonary CT angiography or pulmonary angiography was performed to further exclude the possibility of chronic thromboembolism [13]. Two patients had pulmonary angiography and all others had CT angiography. Radiologists experienced in the evaluation of pulmonary vascular disease, particularly thromboembolism and pulmonary hypertension, performed and interpreted the tests. All CT examinations were performed by using a four-row multidetector CT scanner (Light-Speed QX/i; General Electric Medical Systems, Milwaukee, WI) or a single detector CT scanner (HiSpeed CT/I) (Fig. 1). The diagnostic criteria for primary pulmonary hypertension was the absence of any CT findings of chronic pulmonary embolism including (a) complete occlusion of a vessel that is smaller than adjacent patent vessels; (b) a peripheral, crescent-shaped intraluminal defect that forms obtuse angles with the vessel wall; (c) contrast material flowing through thickened, often smaller arteries due to recanalization; and (d) a web or flap within a contrast material-filled artery. In selected cases, multiplanar reformation images in various planes were additionally generated and were reviewed to confirm the absence of eccentric embolus. Connective tissue disease was excluded if the patient had negative antinuclear antibody (ANA) without any clinical manifestation suggestive of connective tissue disease. Five of the 27 patients with IPAH had positive ANA. In patients with positive ANA, further tests including anti-DNA, anti-Sm, anti-RNP, anti-Ro, anti-La, anticentromere, anti-Jo1, and anticardiolipin antibodies were done; all were negative. Thyroid function tests performed on 17 patients were all normal. Among 33 cases of IPAH who were enrolled from March 1998 to December 2002, we evaluated 27 cases who used beraprost sodium for over 3 months. Three patients had not used beraprost sodium for over 3 months and three patients were lost during the follow-up period. This study was approved by an institutional ethics review committee.

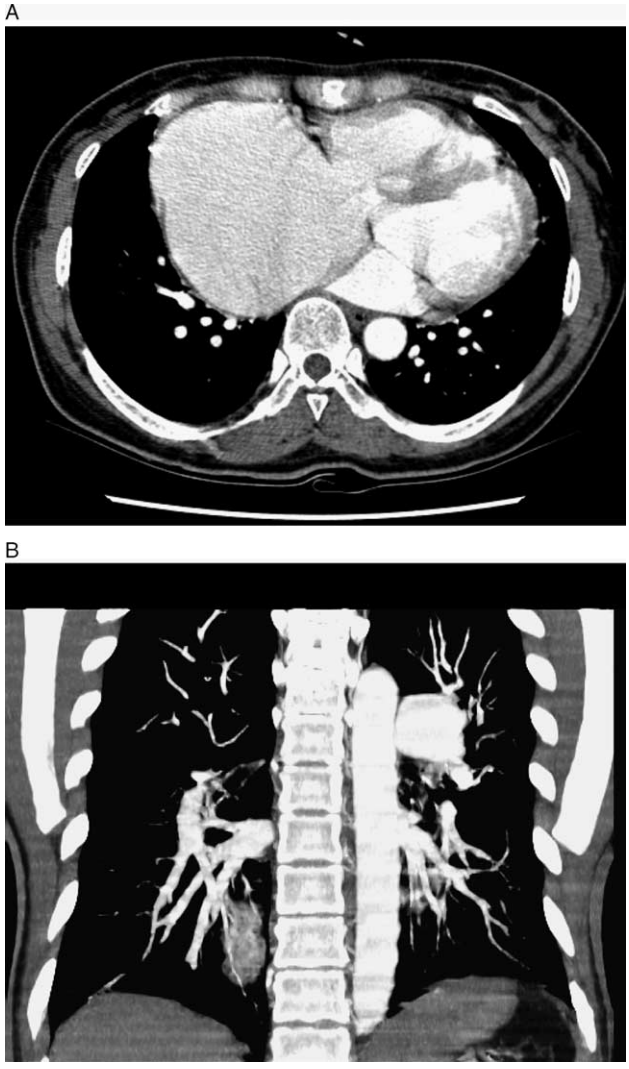

Fig. 1. (A) Transaxial CT scan obtained at lower lung level shows markedly dilated right atrium and right ventricle. Also noted is the thickening of right ventricular wall. No clots are noted in the peripheral pulmonary arteries. (B) Coronal reformatted image shows marked dilatation of central pulmonary artery and tortuous and narrow peripheral branches without any clots.