Primary pulmonary hypertension (PPH) is a rare but intractable disease entity of unknown etiology (1, 2). It is seen mainly in young females with symptoms due to markedly elevated pulmonary arterial impedance, commonly associated with severe pulmonary hypertension and low output. The life expectancy after the definite diagnosis is usually within a couple of years (3–5). Recently several agents, such as aminorex, fenfluramine, and toxic rapeseed oil have been reported to develop pulmonary hypertension. The pulmonary hypertension due to these agents has been excluded from PPH, though etiologies still are not specified and remain unknown in the most of the patients with PPH (4).

As the cause is unknown, the causative treatment for the patients is not possible so far. The major target for the treatment is to manage the pathophysiology, mainly to decrease the pulmonary vascular impedance with various vasodilators (6). These vasodilators, including calcium channel blockers (6), nitric oxide (7), and prostaglandins (4, 8, 9), have shown some beneficial effects on the pathophysiology and the quality of life as well as the survival rate of the patients.

Prostaglandin derivatives, such as prostacyclin (PGI2) within these agents with vasodilatating action, have the most attractive effect on PPH. There are several representative papers published in the last few years (4, 10, 11). Clinical data suggests that it lowers the pulmonary artery pressure, raises the cardiac output, improves systemic oxygen transport, and possibly reverses pulmonary vascular remodeling (4). The lack of an acute response to prostacyclin does not preclude a chronic beneficial effect.

Hoeper et al (12) reported that the long-term treatment of PPH with aerosolized iloprost, a PGI2 analogue, showed sustained effects on exercise capacity and pulmonary hemodynamics. Twenty-four patients with PPH recieved the therapy for at least one year. The mean distance covered in the six-minute walk test improved with the decrease in the mean pulmonary arterial pressure and the increase in the cardiac output. The pulmonary vascular resistance declined. Stewart et al (11) reported, in a patient with PPH and pregnancy, a successful maternal-fetal outcome with epoprostenol (PGI2) therapy. Friedman et al (10) demonstrated that continuous infusion of PGI2 normalized plasma markers of endothelial cell injury and platelet aggregation in PPH. They measured endothelium-derived clotting factors and assayed platelet aggregation in 64 patients with PPH before long-term PGI2 therapy, and repeat studies were performed in 42 patients after one year of the therapy. At baseline, platelet aggregation, factor VIII, von Willebrand antigen and ristocetin cofactor levels were abnormal in most of the adult patients. With long-term PGI2, these factors were normalized or decreased. In conclusion, alteration in the coagulation system may contribute to the pathogenesis of PPH. Long-term PGI2 remodels the pulmonary vascular bed with subsequent decreases in endothelial cell injury and hypercoagulability.

Nagaya et al (13) reported that plasma brain natriuretic peptide was useful as a prognostic indicator in patients with PPH. Takahashi et al in the Journal (14) demonstrated the effects and problems of continuous infusion of epoprostenol for the 11 adult Japanese patients with PPH.

Acute challenge test in 6 patients revealed that PGI2 reduced both systemic and pulmonary vascular resistance and increased cardiac output. Interestingly however, in the chronic study in 9 patients PGI2 decreased pulmonary artery pressure without a change in systemic blood pressure and increased cardiac output. The level of brain natriuretic peptide, as well as atrial natriuretic peptide decreased with improved NYHA functional class with the therapy.

Systematized research for PPH in Japan was started in 1975 as the Research Committe for Primary Pulmonary Hypertension, a research group of specific diseases of the Ministry of Health and Welfare (3). The head of the committee was Sasamoto. Since then, a vast amount of knowledge on the clinical diagnosis, pathophysiology, pathology, genetics and the measure of treatment has been accumulated. Prostaglandin derivatives have high expectations in the treatment of PPH patients. However, we still have not gained satisfactory progress to overcome the disease. By the effort to clarify the etiologies of the disease, we should change the name of the disease from “primary” to “secondary” pulmonary hypertension in future.

See also p 784.

Internal Medicine Vol. 41, No. 10 (October 2002) 757


