Primary Pulmonary Hypertension and Its Life Prognosis

Primary pulmonary hypertension (PPH) is a life-threatening and progressive fatal disease, mostly affecting young women around the age of 30-year-old, and patients with PPH have been reported to die within 2 to 10 years from the onset of clinical symptoms (1) such as exertional dyspnea, syncopal attack, and appearance of leg edema. Especially the survival after the established diagnosis is extremely limited. Most patients die within 5 years from diagnostic catheterization (2). Classical treatment using various pulmonary vasodilators is ineffective. Despite many positive endeavor devoted to patients suffering from PPH, the life prognosis of PPH has remained unchanged for the last several decades. Several studies, however, have been reported to be effective to improve the life prognosis of PPH: Long-term anticoagulant therapy is fundamentally effective to suppress clot genesis of pulmonary vasculature in situ and prevents pulmonary vascular resistance from further increase (3). Oral use of high doses of calcium-channel blockers for only the responder patient group has been reported to improve the 5-year survival (4). This is not widely accepted as the typical dosing regimen for the long follow-up period, because approximately doses of calcium-channel blockers of 5-fold the usual dose are too excessive to administer to patients with PPH, even though the patients responded to the initial dose due to sufficiently defined decrease in pulmonary artery pressure and the decrease in pulmonary vascular resistance.

The prognostic indicator of PPH essentially depends on a highly elevated pulmonary vascular pressure and resistance associated with low cardiac output, because sustained vasoconstrictive changes of pulmonary vasculature of unknown origin have been regarded as a causative factor. Recent advances in the knowledge of PPH concerning the etiology, pathophysiology, prognosis, epidemiology and treatment have accumulated world-wide. Appetite suppressants such as fenfluramine and dexfenfluramine induce PPH (5) and human immunodeficiency virus infection also induces PPH (6). Despite these accumulated data, little is known about prognostic determinants. Prediction of the life expectancy in PPH is difficult to assess (7). It has been reported that the length of survival in patients with PPH awaiting heart lung transplantation was longer than expected (8). The retrospective nation-wide survey of 1980-90 reported by Okada et al (9) considers the life prognosis of PPH in Japan.

Date were accumulated from various institutions, however, there were certain unresolved problems concerning multiple interinstitutional differences in the technical experience of diagnosis, the medical therapy introduced, and the purpose of cardiac catheterization and the period of diagnosis. In particular, the one-year life expectancy in the survival of PPH after cardiac catheterization may be influenced to some extent by these multi-institutional differences.

Discovery of prostacyclin (PGI₂) (10) and knowledge of its continued intravenous infusion have made it possible to treat PPH medically and non-invasively (11). Pulmonary vasodilator effects combined with platelet anti-aggregation decrease pulmonary vascular resistance and thereby increase cardiac output and improve oxygen delivery to peripheral tissues and organs. It has been reported that long-term continuous intravenous PGI₂ administration by portable infusion pump to the patients with PPH improves not only the survival rate but also the quality of life (QOL) by increasing exercise capacity (12). It has been gradually apparent to improve individual activity even enough to return to the usual social work activity (13). In Japan the brain death has been defined by the government’s newly established rule as of October 16, 1997. There is, however, no lung nor heart-lung transplantation from the donor of brain death to date, due to lack of an appropriate donor, although partial lung transplantation for a 24 year-old female patient with severe bronchiectasis from familial two living donors of her mother and a her younger sister was performed successful on October 28, 1998 in Japan. Clinical use of epoprostenol sodium (PGI₂ in intravenous use supplied by Glaxo Wellcome company) has not been approved yet by our government. A clinical multi-center trial has finished, showing a remarkable clinical usefulness in patients with PPH (14), but final governmental approval is pending. Portable infusion pump therapy using PGI₂ is currently being carried out in Japan as of October 31, 1998 in 11 patients with PPH including patients with approved continuation of epoprostenol sodium after our clinical multi-center trial; also there are patients starting initial portable infusion pump therapy of PGI₂ in USA. Moreover the long-term use of an oral prostacyclin derivative (beraprost sodium) developed in our country (15) has been effective for patients with PPH (16) and has also improved the prognosis of PPH (17). The predictive indicator of lung and heart-lung transplantation for patients with PPH is now changing following the introduction of prostacyclin and its oral analogue to treat PPH. Bilateral sequential lung transplantation is the ultimate therapy for PPH with the most poor life expectancy of probably within one year (18). However, this prognosis must be reconsidered after this epoch-making intravenous prostacyclin therapy has been introduced. Based on clinical findings, the additional criteria concerning the one-year life expectancy will be necessary.
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References