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■ Case report ■

The effect of perioperative inhaled iloprost on congenital heart disease with severe pulmonary arterial hypertension

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= Abstract =

A 47-year-old male patient in whom atrial septal defect (ASD) had been diagnosed 15 years previously was admitted for cardiac catheterization. He had definite cyanotic lips and nail beds and severe pulmonary arterial hypertension (PAH). He had received medical treatment only for the last few years after being diagnosed with Eisenmenger syndrome. After cardiac catheterization, he received iloprost inhalation therapy pre and postoperation and was discharged after successful surgical closure of the ASD. (Korean J Pediatr 2010;53:93-96)

Key Words : Atrial septal defect, Pulmonary arterial hypertension, Iloprost

Introduction

Congenital Heart Disease (CHD) with pulmonary arterial hypertension (PAH) has high risk of postoperative morbidity and mortality. Iloprost (Ventavis® inhalant, Bayer Schering Pharma AG, German) is a chemically stable prostacyclin analogue with has potent pulmonary vasodilatation, anti-thrombotic, anti-inflammatory, and anti fibrotic effects[1, 2]. The inhaled iloprost has been approved to be effective in the treatment of PAH. We report a case of successful closure of ASD with severe PAH who was considered inoperable after using of inhaled iloprost.

Case report

A 47-year-old male patient was referred to the Pediatric Cardiology Department by Internal Medicine Department. The patient was diagnosed as ASD 15 years ago, but he did not visit the hospital regularly. Six years ago, he visited the adult Cardiology Department because of dyspnea on exertion and systemic edema. At that time, the size of ASD was about 40mm with grade 3 tricuspid regurgitation (TR) and enlarged right atrium and ventricle. Also, the shunt ratio (Qp/Qs) was about 5.8. He was recommended to undergo cardiac operation, but he strongly refused because he was afraid of the procedure. Afterwards, he visited our institute intermittently and received conservative management from several cardiologists. During the follow-up, he was not recommended to have cardiac operation because he was diagnosed Eisenmenger syndrome.

The patient was referred to the Department of Pediatric Cardiology by pulmonary hypertension clinic to have evaluated his heart condition with cardiac catheterization. A physical examination upon admission revealed that he had definite cyanosis shown on his lips and nail beds. Regular heartbeat with grade 1-2 systolic murmur was heard on the left upper sternal border. The chest X-ray revealed cardiomegaly, but the cardiac size decreased compared to that of 6 years ago (Fig. 1). Systemic O_2 saturation measured by pulse oximeter was 79 to 86 percent. The laboratory results were as follows: hemoglobin 20.2 g/dL, hematocrit 56.8%, platelet count 184,000/mm^3, total bilirubin 2.5 mg/dL, GOT/GPT 81/23 U/L, uric acid 7.4 mg/dL. BUN/Cr 16.2/1.1 mg/dL. The blood gas in room air was as follows: PH 7.43, pCO_2 29 mmHg, pO_2 33 mmHg, HCO_3 19.5 mmol/L, BE -2.7 mmol/L, SaO_2% 67.7. The echocardiography revealed large type II ASD with bidirectional shunt and severe PAH with estimated right ventricular systolic

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pressure of 115 mmHg. The defect size was 39 mm. Grade 3 TR and severely enlarged right side heart were being observed. Cardiac catheterization confirmed the diagnosis of severe PAH with mean pulmonary arterial pressure of 62 mmHg and pulmonary vascular resistance over 17 Wood unit.

After oxygen inhalation (10 L for 10 minute) the systemic and pulmonary arterial pressure was not changed significantly, but systemic O_2 saturation increased up to 93%, Qp/Qs and Rp was also changed to 1.3 and 12.1 Wood unit, respectively, which indicates that the patients pulmonary bed had reversibility.

We provided iloprost inhalation therapy (20 μg divide 6 time per day) before operation for 18 days. Patient's general condition improved, and dyspnea on exertion decreased. Systemic O_2 saturation measured by pulse oximeter was 90 to 95 percent. The follow up echocardiography revealed decreased TR jet velocity (Fig. 2). We performed surgical closure of ASD with fenestration (5 mm) and tricuspid annuloplasty. After operation we used NO gas continuously with mechanical ventilation. We experienced transient pulmonary hypertensive crisis, but it was not fatal. Four days after operation the patient weaned from mechanical ventilation and extubated. After extubation, we started inhaled iloprost therapy again. Five days after operation the patient transferred to general ward. Cardiac inotropic drug was discontinued and chest tube was removed on the 6th day after the operation. Two weeks after operation echocardiography revealed as follows: grade 1−2/4 TR, decreased TR jet velocity, decreased pulmonary hypertension (estimated RVsP=73 mmHg), still enlarged right side heart and diastolic D−shaped LV. The patient was discharged under good health, and he is currently being followed−up as an outpatient in our clinic.

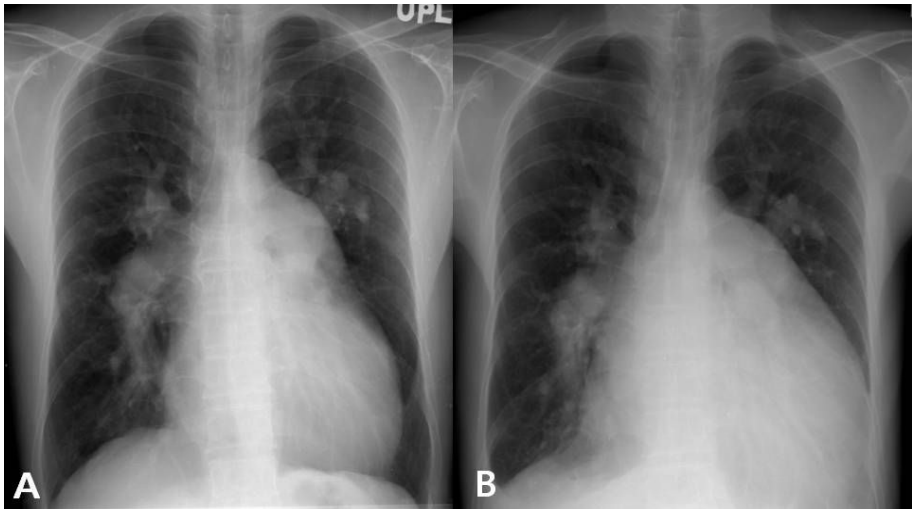

Fig. 1. (A) Chest posterior−anterior (PA) at admission. (B) Chest PA 6 years prior to admission.

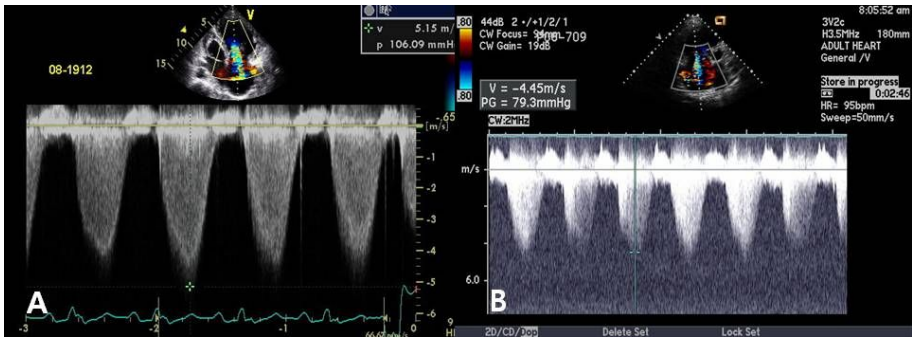

Fig. 2. (A) Echocardiography at admission shows 5.15 m/s tricuspid regurgitant (TR) jet velocity. (B) After the use of iloprost, TR jet velocity decreased to 4.45 m/s.

Discussion

The ASD is one of the most common congenital heart diseases. Patients with long-standing ASD, clinical deterioration, such as PAH and arrhythmic complications tend to worsen over time[3, 4]. The survival depends on whether pulmonary hypertension develops during adulthood or not. The most cause of death in ASD patients is right ventricular heart failure and arrhythmia[5].

Pulmonary arterial hypertension frequently complicates the postoperative management of patients after congenital cardiac surgery[6, 7]. Especially, post-operative pulmonary hypertensive crisis is especially life threatening, which makes vasodilators, NO gas, muscle relaxant and Extracorporeal Membrane Oxygenation are treatment options[8, 9].

The iloprost- a potent pulmonary vasodilator-directly act to lungs, so it is very effective in improvement of ventilation-perfusion mismatching and shunting flow[10], pulmonary circulation, and gas exchange. In addition, it stabilizes the stretch induced surfactant production of type II alveolar cells and has potent anti-inflammatory effects [1, 2]. Therefore, inhaled iloprost has been approved to be effective in the treatment of PAH.

Recently, several authors reported operation after vasodilative therapy in CHD with PAH, who were considered inoperable[11-13]. They used the oral bosentan or intravenous prostacyclin for several months preoperatively.

Our patient is a similar case, but we used inhaled Iloprost instead. Iloprost shows superiority to the other products in that it is worth acting and a potent pulmonary vasodilator. The treatment period is relatively short and there is no need for intravenous delivery system and side effects of oral bosentan, such as elevated liver enzyme, can be avoided. Our patient showed transient hypotension and decreased O_2 saturation during mechanical ventilation, but he recovered rapidly after infusion of inotropic agents and sedatives. In general, CHD with irreversibly obstructed pulmonary vasculature (Eisenmenger syndrome) is contraindicated for operation, but if there is some reversibility of the pulmonary vasculature, the use of inhaled iloprost may be very effective. Kim DK et al[14] reported liver transplantation of a patient with portopulmonary hypertension after "conditioning" therapy with iloprost and sildenafil. Winterhalther M et al[15] reported that inhaled iloprost was effective in reducing PAH during cardiac surgery, immediately after weaning from cardiopulmonary bypass.

It is not easy to decide whether a patient, who has had a long-standing left to right shunt lesion and pulmonary hypertension, retains reversibility of pulmonary vasculature or not. Even though a thorough review of clinical manifestations, echocardiography, and cardiac catheterization is suggested as standard evaluation[16, 17], a definite boundary is still obscure. In our case, it was reasonable for the patient to receive only medical treatment for few years, considering how he showed cyanosis and clubbing of fingers, and showing only scanty change of shunt ratio and pulmonary resistance during cardiac catheterization, leading the medical staff to believe he had Eisengmenger syndrome.

We take notice of the fact that pulmonary vascular disease may continue to progress even after the abolishment of left to right shunt, and that prolonged pulmonary vasodilator therapy may be required in patient with significant residual PAH, but we believe that elimination of hemodynamic substrate to the detrimental cascade caused by underlying disease would be beneficial in terms of improving patient's quality of life as well as increasing the chance of recovery from Eisenmenger-like physiology.

When pulmonary vasodilator is employed properly with aggressive therapeutics purpose, more successful surgical repair will be accomplished in patients who have CHD with severe PAH.

한 글 요 약

심한 폐동맥 고혈압을 동반한 선천성 심장병 환자에서 수술 전후 Iloprost 효과

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15년전 심방중격 결손증 진단을 받은 47세 남자 환자가 심도자 검사를 위해 입원하였다. 환자는 입술과 손톱에서 명확한 청색증을 보이고 있었으며 심한 폐동맥 고혈압을 나타내고 있었다. 본 환자는 지난 수년간 아이젠멩거 증후군으로 진단되어 대증적 치료만을 받아오고 있었다. 심도자 검사 후 환자는 흡입형 Iloprost 치료를 시작 하였으며 성공적으로 심방중격결손증 수술을 받을 수 있었다. 환자는 수술 후에도 치료를 지속하였다.

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