Complete resolution of chronic pericardial effusion with an intensive course of inhaled iloprost in an adult patient with unrepaired ventricular septal defect, and life-threatening severe pulmonary arterial hypertension

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ABSTRACT

شخص رجل يبلغ من العمر 38 عاما بارتفاع شديد في ضغط الشريان الرئوي المصاحب لعيب قلبي خلقي (عيب الحاجز البطيني)، وزراق مركزي وصعوبة الحركة. وقد أظهر مخطط صدى القلب اختلال البطين الأيمن وانصباب التامور المعتدل مع عدم وجود علامات دكاك القلب. و قد عولج المريض بدورة مكثفة من عقار الاليوبروست iloprost عن طريق الاستنشاق بالإضافة لعقار الفياغرا. و قد أظهر المريض استجابة سريرية دراماتيكية، و تحسن تشبع الدم بالأكسجين من 60% إلى 90% باستخدام مستويات منخفضة من الأكسجين، مع تحسن كبير في الأعراض الاكلينيكية وعلامات فشل القلب، وتحسن كامل للانصباب التاموري. وبعد 3 و 6 أسابيع، كانت حالة المريض مستقرة تماما ويمكنه المشي لمسافة 360 متر في 6 دقائق مع اختفاء الانصباب التاموري تماما. مع عدم توفر علاج البروستاسيكلين الوريدي، فقد أظهرنا في هذه الحالة أن العلاج المكثف من الاليوبروست iloprost المستنشق يمكن أن يستخدم كعلاج منقذ في حالات ارتفاع ضغط الشريان الرئوي الشديدة المصحوبة بانصباب تاموري واعتلال القلب مع نتيجة ممتازة.

A 38-year-old male was diagnosed with unrepaired ventricular septal defect associated with severe pulmonary arterial hypertension, cyanosis, and significant exercise intolerance. His echocardiogram showed right ventricular dysfunction and moderate pericardial effusion with no signs of cardiac tamponade. He was treated with an intensive course of inhaled iloprost and sildenafil. He showed a dramatic clinical response; his saturation went up from 60% on admission to 90% on minimal oxygen with significant improvement in his symptoms and signs of heart failure and total resolution of pericardial effusion. On follow up 3 and 6 weeks later, he was stable and could walk 360 meters in a 6 minutes walk test with disappearance of pericardial effusion. With unavailability of intravenous prostacyclin, we have shown in this case that intensive administration of inhaled iloprost could be used intensively as a rescue therapy in severe cases of pulmonary arterial hypertension with excellent results.

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Pulmonary arterial hypertension (PAH) is characterized by progressive elevation of the pulmonary arterial pressure, pulmonary vascular resistance, and right ventricular failure. Pulmonary arterial hypertension could be idiopathic or associated with underlying diseases.[1] The clinical picture depends on the severity of the disease. Symptoms such as progressive dyspnea, cyanosis, exercise intolerance, and right heart failure may eventually lead to death.[2] Current medical therapy provides a symptomatic benefit, increases exercise capacity, and delays the clinical progression of the disease, thus prolonging and improving the life expectancy. Treatment choices in PAH depend on the disease severity, the specific type of PAH, the presence of active vasoreactivity, and the patient's ability to response to medications with complex modes of administration. Inhaled iloprost has been approved for chronic treatment of PAH in adults. It is a stable prostacyclin analogue with vasodilatory, anti-inflammatory, and vascular remodeling properties. Similar to nitric oxide, when used by the inhaled route, it selectively dilates pulmonary vessels and improves oxygenation.[3] The presence of pericardial effusion (PE) in PAH usually represents advanced disease and carries a poor prognosis. The best treatment approach for those patients is still controversial. This report presents a successful trial of an intensive course of inhaled

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iloprost as a rescue measure in a patient presented in severe PAH and modified New York Heart Association (NYHA) functional class IV, with significant clinical, radiological, and echocardiographic improvement within a short period after initiation of the therapy.

Case Report. A 38-year-old Saudi male, a known case of ventricular septal defect (VSD) diagnosed at age 11 years, was admitted at the Prince Sultan Cardiac Center in Riyadh, Saudi Arabia. He underwent a diagnostic right heart catheterization to characterize his hemodynamics before surgical repair, which showed severe and non-reactive PAH. He was labeled inoperable and was kept on regular outpatient follow up. Five years prior to his current presentation, he became more cyanosed with a significant activity restriction and his serial echocardiographic assessment showed chronic PE.

In September 2012, he visited the outpatient clinic complaining of severe shortness of breath with activity limitation. On examination, he was tachypneic and tachycardiac at rest, deeply cyanosed with oxygen saturation of 65 -70% and showing signs of congestive heart failure. Electrocardiogram showed sinus rhythm with right axis deviation and P pulmonale. The initial chest x-ray (CXR) showed cardiomegaly, oligemic lung fields with chronic hypoxic changes. Echocardiogram revealed large unrestrictive peri-membranous VSD with biventricular hypertrophy, mild tricuspid regurgitation with supra-systemic right ventricular pressure and a moderate PE with no signs of tamponade. The overall picture was compatible with Eisenmenger's syndrome. Left ventricular systolic function was normal. A baseline 6 minutes walk test (6MWT) was carried out and the patient could only walk for 2 minutes with a maximum distance of 120 meters and Borg dyspnea scale of 4. He was on oral furosemide, captopril, and sildenafil (50 mg TID) as a chronic treatment. He was hospitalized for the management of his hypoxia, PE, and right-sided congestive heart failure. He was started on oxygen, inotropes and aggressive diuresis with fluid restriction, aside from his previous medication. He stayed for 24 hours in the adult congenital heart disease ward, but he did not show any improvement despite the aggressive management. On the discussion of patient's case with the pulmonary hypertension team, it was suggested to start a course of intensive inhaled iloprost therapy (intravenous prostacyclin was not available) at a dose of 5 micrograms every 2 hours along with intravenous furosemide and oral sildenafil. There was also a careful follow up of patient's daily CXR, echocardiography, and laboratory work. He showed a dramatic response to this regimen and at the end of the first week, his oxygen saturation was above 90% on 1L oxygen, and the signs and symptoms of heart failure were controlled. The heart shadow on the CXR became smaller, and echocardiogram showed improvement of right ventricular contractility with minimal residual PE. Inhaled iloprost was reduced gradually to the final dose of 5 micrograms every 4 hours with no documented side effects. He was discharged from the hospital after 3 weeks in excellent condition on inhaled Iloprost 5 micrograms every 4 hours, aside from his usual medications. He was still in good condition with oxygen saturation ranging from 85-90% in room air and no symptoms or signs of heart failure during the follow up visits at week 3 and 6. His daily activities improved, and he could manage to walk 360 meters on 6MWT. His echocardiogram showed a complete resolution of PE. At 3-months, he was asymptomatic [modified NYHA functional class I] and could walk 408 meters on 6MWT. **Figure 1** illustrates the improvement in clinical and physiological parameters. He was advised to continue the same treatment with regular follow up at the clinic.

Discussion. Management of PAH is complex. The presence of PE in PAH usually represents severe right heart failure and is associated with poor prognosis.[4] Small or moderate PE may be present in up to 54% of patients.[5] Patients with severe PAH and circumferential PE may develop cardiac tamponade with isolated left heart compression, as the elevated pressure in the right heart chambers prevent right atrial and ventricular compression. As the pericardial pressure continues to

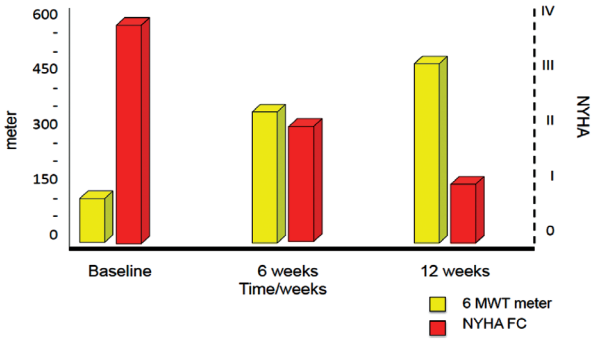

Figure 1 - Improvement in 6 minutes walk test (6MWT) and New York Heart Association functional (NYHA FC) class I with 3 months of treatment.

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rises to the point exceeding the left chambers pressure, left atrial, followed by left ventricular, diastolic collapse occurs leading to impaired filling of the left ventricle causing a drop in cardiac output.[6] Subsequently, a high index of suspicion is required to detect the development of the atypical form of cardiac tamponade in this group of patients. Many studies have reported the detrimental effect of pericardiocentesis in this particular indication, including mortality.[4,7] The exact mechanism of this clinical deterioration is unclear, but may be related to the sudden loss of RV muscle tone with inter-ventricular septal bowing secondary to the removal of large amounts of pericardial fluid that lead to decreased left heart filling pressures and death.[8] Intravenous epoprostenol is the drug of choice for patients presented in modified NYHA functional class IV and pericardial effusion, unfortunately, it was not available to treat this patient. However, acute administration of inhaled iloprost has been shown to lower mean pulmonary artery pressure and improved the right ventricular function, and subsequently decreases the PE.[9] This has been proven to be well tolerated as a long-term therapy with no substantial risk. In an uncontrolled trial of 19 patients[10] with progressive right heart failure despite receiving maximum conventional therapy, inhaled iloprost given 6-12 times per day was shown to improve the right ventricular function in 8 patients. Furthermore, when combined with oral sildenafil, inhaled iloprost may produce a much greater beneficial response than each agent alone. This combined vasodilatory effect can lead to significant improvement of the patient's condition, including exercise capacity, and pulmonary hemodynamics. In our patient, and because of the risk associated with pericardiocentesis, we choose to use inhaled iloprost as a rescue intensive therapy to unload the failed right ventricle and improve cardiac output. The subjective improvement was noticed very shortly after commencing the iloprost rescue therapy, and the objective improvement was detected in as early as 3 weeks with a significant increment in walking distance and other prognostic clinical parameters.

In conclusion, this report shows that the intensive use of inhaled iloprost may have an important role in the management of patients with severe PAH and chronic pericardial effusion who remain symptomatic despite the conventional treatment. We believe that using this therapeutic approach as early as possible in those patients might shorten their need for oxygen, improve exercise capacity, and decrease the complications. This might further reduce the need for intensive care, shorten hospital stay, and possibly prevent further deterioration in their condition. This observation should be further tested in randomized clinical trials.

References

1. Simonneau G, Galiè N, Rubin LJ, Langleben D, Seeger W, Domenighetti G, et al. Clinical classification of pulmonary hypertension. ***J Am Coll Cardiol*** 2004; 43: S5-S12.
2. D'Alonzo GE, Barst RJ, Ayres SM, Bergofsky EH, Brundage BH, Detre KM, et al. Survival in patients with primary pulmonary hypertension. Results from a national prospective registry. ***Ann Intern Med*** 1991; 115: 343-349.
3. Wilkens H, Guth A, König J, Forestier N, Cremers B, Hennen B, et al. Effect of inhaled iloprost plus sildenafil in patients with primary pulmonary hypertension. ***Circulation*** 2001; 104: 1218-1222.
4. Hemnes AR, Gaine SP, Wiener CM. Poor outcomes associated with drainage of pericardial effusions in patients with pulmonary arterial hypertension. ***South Med J*** 2008; 101: 490-493.
5. Akinci SB, Gaine SP, Post W, Merrit WT, Tan HP, Winters B. Cardiac tamponade in an orthotopic liver recipient with pulmonary hypertension. ***Crit Care Med*** 2002; 30: 699-701.
6. Aqel RA, Aljaroudi W, Hage FG, Tallaj J, Rayburn B, Nanda NC. Left ventricular collapse secondary to pericardial effusion treated with pericardicentesis and percutaneous pericardiotomy in severe pulmonary hypertension. ***Echocardiography*** 2008; 25: 658-661.
7. Nafsi T, Bopanna S, Vedavalli A, Al-Nassir K, Tandon R. Pericardial effusion in pulmonary arterial hypertension. to drain or not? ***Chest*** 2011; 140: 178A.
8. Ivy DD, Doran AK, Smith KJ, Mallory GB Jr, Beghetti M, Barst RJ, et al. Short- and long-term effects of inhaled iloprost therapy in children with pulmonary arterial hypertension. ***J Am Coll Cardiol*** 2008; 51: 161-169.
9. Olschewski H, Hoeper MM, Behr J, Ewert R, Meyer A, Borst MM, et al. Long-term therapy with inhaled iloprost in patients with pulmonary hypertension. ***Respir Med*** 2010; 104: 731-740.
10. Olschewski H, Ghofrani HA, Schmehl T, Winkler J, Wilkens H, Höper MM, et al. Inhaled iloprost to treat severe pulmonary hypertension: an uncontrolled trial. ***Ann Intern Med*** 2000; 132: 435-443.