Treatment of pulmonary hypertension in three patients with β-thalassemia intermedia using pulmonary arterial hypertension-specific medications

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Introduction

Pulmonary hypertension (PH) is frequent among patients with β-thalassemia intermedia (TI) and β-thalassemia major (TM) (1). Almost 60% of all TI patients develop PH (2). However, no randomized controlled trials have evaluated this condition-specific treatment options. Recent guidelines for the treatment of PH offer no specific recommendations for these patients; moreover, the classification of chronic hemolytic anemia was changed from group I PH to group V PH, in which group pulmonary arterial hypertension (PAH)-specific therapy is not recommended (3). We report three patients with β-TI who developed severe PH and were successfully treated with PAH-specific therapies.

Case Reports

Case 1

A 39-year-old man with β-TI was admitted with new-onset dyspnea and fatigue. On further examination, systolic pulmonary arterial pressure (sPAP) was measured as 115 mm Hg on trans-

thoracic echocardiography (TTE). The right heart catheterization (RHC) was performed to confirm the diagnosis of PH. It showed sPAP, pulmonary artery diastolic pressure (dPAP), and mean pulmonary artery pressure (sPAP) of 70, 38, and 49 mm Hg, respectively. The pulmonary capillary wedge pressure (PCWP) was 11 mm Hg. Treatment with bosentan (62.5 mg bid) and sildenafil (25 mg tid) was initiated. He has been followed-up in our outpatient clinic during the past 2 years and his sPAP decreased to 45 mm Hg after the first year of therapy.

Case 2

A 52-year-old man with β-TI and PH was admitted because of progressive dyspnea under sildenafil. His sPAP was measured as 80 mm Hg on TTE. The RHC showed sPAP, dPAP, and sPAP of 79, 29, and 45 mm Hg, respectively. The PCWP was 13 mm Hg. Inhaled iloprost (20 mcg q4h) was added, and the dosage of sildenafil was increased (25 mg qid). Two years after discharge, he was drecompensated, and a control TTE showed a sPAP of 95 mm Hg. The dosage of iloprost was increased to 20 mcg q3h, while the dosage of sildenafil was raised to 80 mg tid. After 1 year of this therapy, PH (sPAP: 80 mm Hg) and functional limitations were persistent. Therefore, bosentan (125 mg bid) was initiated, and sPAP decreased to 65 mm Hg; after 3 months, symptomatic relief was observed.

Case 3

A 51-year-old woman with β-TI presented with dyspnea and palpitations. During the further investigation, TTE revealed PH (sPAP: 80 mm Hg). After excluding other possible etiologies, the patient was assumed to have thalassemia-related PH. Because of her poor health condition and thrombocytopenia, she was unable to undergo RHC. After 3 months of therapy with sildenafil (20 mg tid) and an iloprost inhaler (20 mcg q3h), her symptoms and 6-min walk distance (6MWD) improved. Also, the sPAP decreased to 60 mm Hg after 1 year of dual PAH-specific therapy. After 5 years of this treatment, which provided a favorable functional capacity for her, she died following pneumonia.

Discussion

The pathophysiology of PH in thalassemia is multifactorial, and treatment may be based upon these factors. Chronic hemolysis causes PH by inducing nitric oxide (NO) and arginine deficiency (4). Low NO bioavailability causes endothelial dysfunction, which leads to inflammation, vasoconstriction, and hypercoagulopathy (5). Published data indicate that transfusion therapy decreases chronic hemolysis and also chronic tissue hypoxia, which is a risk factor for PH (6). Unlike patients with TM, those with TI do not require regular transfusions. Our three patients only received transfusions intermittently as needed. Therefore, the protective effect of regular transfusion was not probable.

Case reports have shown that PAH-specific drugs might be useful in patients with thalassemia. A 12-week prospective study of sildenafil that enrolled 10 patients with β-thalassemia and PH revealed an improvement in New York Heart Association (NYHA) class and a 13% reduction in tricuspid regurgitation velocity (7). A case report described an improvement in pulmonary hemodynamics after 1 year of bosentan therapy in a patient with TI-related PH (8). Tam et al. (9) showed that intravenous epoprostenol improved symptoms and reduced mPAP in a TM patient with PH. In addition, an increase in 6MWD, a decrease in PAP, and an improvement in the NYHA class and function of right ventricle were shown following the continuous infusion of epoprostenol in a patient of β-TI and PH (10).

We recorded symptomatic relief, a decrease in sPAP, and an increase in 6MWD in all three patients with a combination of PAH-specific medications. However, these improvements cannot be attributed to a single agent due to the concomitant use of these drugs.

Conclusion

This case reports support the use of PAH-specific medications in this group. To the best of our knowledge, this is the first case report to show a possibrle benefit of treatment with inhaled prostaglandin. However, further studies will be needed to determine the best treatment for PH in patients with β-thalassemia.

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Accepted Date: 20.08.2015

DOI:10.14744/AnatolJCardiol.2015.6624