



## Short Term Sildenafil Treatment and Successful Percutaneous Closure in a Patient with a Large Secundum - Type Atrial Septal Defect and Pulmonary Arterial Hypertension

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### Abstract

Secundum Atrial Septal Defect (ASD) is the most common form of congenital heart disease in adults. Transcatheter closure of ASD is commonly accepted as a treatment option. There are some disagreements about closing of defects in patients with Pulmonary Arterial Hypertension (PAH). We report a case of a 68-year-old male with large ASD and severe PAH who undergone successful percutaneous closure of ASD and following short-term use of oral sildenafil.

**Keywords:** Atrial septal defect; Pulmonary hypertension; ASD closure; Sildenafil treatment

### Introduction

Secundum Atrial Septal Defect (ASD) is the most encountered type of Congenital Heart Disease (CHD) in adults. Patients with ASD and left-to-right shunt are at risk for developing Pulmonary Arterial Hypertension [1]. PAH is often associated with high Pulmonary Vascular Resistance (PVR) and long-lasting left-to-right shunt [2]. In addition to this, a minority of patients (<1%) have early developed, severe pulmonary hypertension with shunt reversal [3]. Interventional and surgical closures of ASD are widely performed treatments. Closure of ASD in patients with severe PAH carries high risk for provoking right ventricular failure and pulmonary hypertensive attack [4]. In patients with severe PAH, however, closure presents the risk of provoking right ventricular failure and pulmonary hypertensive crisis [4]. According to the last ESC guidelines of pulmonary hypertension [5] patients with PVR between "2,3-4,6" should be evaluated individually in tertiary centers. In selected patients with severe PAH after advanced therapy with pulmonary vasodilators (i.e. oral bosentan, intravenous epoprostenol, and oral sildenafil) [6-9].

### Case Presentation

A 68-year-old male was admitted to our hospital on account of exertional shortness of breath. He had suffered from exertional dyspnea for about two years. The New York Heart Association (NYHA) functional class of the case was II-III on admission. He reported no symptoms of chest pain, syncope or palpitations. Chest X-ray showed increasement of cardio-thoracic ratio (Figure 1). The physical examination revealed a short systolic murmur consistent with high pulmonary flow in the left sternal border. The electrocardiogram showed an atrial fibrillation with a right-axis deviation and an incomplete right bundle branch block, and the initial Transthoracic Echocardiogram (TTE) revealed right ventricular dilatation and hypertrophy with secundum ASD (diameter measuring 36-38 mm in the apical four-chamber view) with left-to-right blood shunt. Using tricuspid valve velocity pulmonary artery systolic pressure of 65 mm Hg was estimated.

Initial Transesophageal Echocardiography (TEE) showed an ASD diameter of 38 mm. The posterior rim of the defect was found to be insufficient. Nevertheless we decided to try closing the defect percutaneously.

Right heart catheterization showed elevated PAP and PVR of 82/33 mm Hg (mean 49 mmHg) and 4,3 wood units, respectively. Cardiac output was 3.14 l/min calculated by the Fick method. The pulmonary-to-systemic flow ratio (Qp/Qs) was 2,0.

After fully informed consent, and under the guidance of TEE, we occluded the defect with 40 mm Amplatzer Septal Occluder (ASO; AGA Medical Corporation, Plymouth, MN, USA), In the

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Received Date: 30 Jul 2018

Accepted Date: 21 Aug 2018

Published Date: 23 Aug 2018

#### Citation:

Abusharkh M, Gocer H, Gunday M. Short Term Sildenafil Treatment and Successful Percutaneous Closure in a Patient with a Large Secundum - Type Atrial Septal Defect and Pulmonary Arterial Hypertension. *World J Surg Surgical Res.* 2018; 1: 1044.

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Figure 1: Preprocedure chest X-ray.

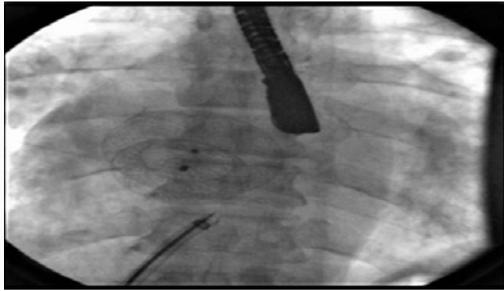


Figure 2: Implantation of the Amplatzer Atrial Septal Occluder (ASO) under the guidance of Transesophageal Echocardiography (TEE).



Figure 3: Post-procedure echocardiogram shows the defect occlusion with Amplatzer septal occluder (ASO).

TEE no residual shunt was found. Device stability was controlled by means of the Minnesota maneuver (Figure 2). Follow-up TTE showed no residual shunt (Figure 3).

After the closure, Oral sildenafil (100 mg/day) had been given to the patient for one month then 50 mg daily for second and third month, respectively.

Third months after closure of ASD, the patient's complaints and exercise capacity improved from NYHA class III/II to I. There was no residual leakage on the follow-up TTE. The mPAP declined from 65 to 45 mmHg and additional 10 mmHg fall after vasodilator test had been observed. At the same time, PVR went down from 4.3 to 3.6 Wood units. Sildenafil treatment had been successfully weaned off after third month of closure.

## Discussion

The non selective vasodilators, which especially targets pulmonary vasodilatation, have beneficial effect in patients with secondary PAH related to intra cardiac shunts [12,13]. Schwerzmann et al. [10] and Jung et al. [11]. Used one-year parenteral prostacyclin and oral bosentan treatment, respectively, to treat ASD patients with moderate PAH. These patients showed significant improvement after ASD closure following long-term vasodilator treatment. But there is no evidence for short-period treatment. Our patient shows that a similar result might be achieved in patients with severe PAH if patient is treated with sildenafil for only 3 months. Sildenafil is a selective inhibitor of phosphodiesterase enzyme (type 5) that degrades cyclic guanosine monophosphate in the pulmonary artery, which then acts to mediate smooth muscle relaxation of the vessel. Three randomized controlled trials showed the safety and efficacy of sildenafil in ameliorating mPAP, PVR, the cardiac index, and exercise capacity in patients with PAH [13]. On the other hand, in our case, sildenafil was used for a short period after closure.

American and European practice guidelines [14,15] report that

an ASD can be closed if the PVR is lower than two thirds of the Systemic Vascular Resistance (SVR) and at the same time, there is a proof of pulmonary-to-systemic flow ratio ( $Q_p: Q_s$ ) bigger than 1.5. According to the last ESC guidelines for the management of grown-up congenital heart disease patients with significant shunt and PVR <5 WU should undergo ASD closure regardless of symptoms. On the other hand the last ESC guidelines of pulmonary hypertension [5] suggested different criteria for shunt closure based on baseline PVR. Accordingly, correction of congenital heart disease with prevalent systemic-to-pulmonary shunts is recommended if the PVR is lower than 2,3 WU and should be evaluated individually in tertiary centres if the PVR is between 2,3 and 4,6.

The irreversible PAH in patients with cardiac defect is still thought to be obstacle for shunt closure. Closure of such shunts is related to deterioration of cardiac output and enhancement of right sided heart failure and death. Therefore, shunt closure in these kinds of patients ought to be performed in case the benefits of closing the shunt overcome outweigh the risks of surgical or transcatheter closure [16].

Previously, in order to establish whether adult patients with severe PAH and left-to-right shunt were compatible with closure, pulmonary biopsy was performed to determine the histological changes were reversible or not. Currently, vasodilator agents are used to evaluate the degree of reversibility. However, there is a lack of evidence about their usefulness in anticipating the response of PAH to shunt closure. With the recommendation of the latest American and European practice guidelines temporarily occlusion of the defect (Temporary balloon test occlusion) and evaluating pulmonary response during occlusion is recommended to assess the response of PAH following definitive closure. Because of the absence of balloons at the appropriate size for the defect the temporary balloon test occlusion couldn't be performed in our patient.

The benefits of the transcatheter procedure over standard cardiac surgery are avoidance of thoracotomy and cardiopulmonary bypass, and reduced requirement for blood products [17]. Transcatheter ASD closure using the Amplatzer septal occluder in adults is reported as safe and effective for patients with PAH [18-20]. Balint et al [19] informed about the results of transcatheter closure of ASD in patients with PAH. They reported that percutaneous closure of ASD in patients with PAH can be successfully performed in selected patients with good results.

The long-term impact of defect closure in the presence of PAH with increased PVR is largely unknown. There is a lack of data in this controversial area, and caution must be exercised.

As a result, short-term sildenafil treatment after closure of ASD with severe PAH may offer the possibility for shunt closure in situations where it was not formerly considered possible. This result also suggests that short-term vasodilator therapy with sildenafil can be effective in the treatment of patients with ASD-related PAH.

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