Pregnancy outcomes in patients with severe pulmonary hypertension and Eisenmenger syndrome treated with sildenafil monotherapy

Reinalyn S Cartago¹, Pichy Ann Alan² and Jubert Benedicto³

Abstract

Pregnancy outcomes in patients with pulmonary arterial hypertension have not been documented in our local setting. In our institution, access to therapies like nitric oxide, inhaled prostacyclin and iloprost is limited. We describe two such women given sildenafil monotherapy between April and May 2011. Both had an atrial septal defect complicated by Eisenmenger syndrome. Both survived – one after elective Caesarean section for malpresentation (breech) under general anaesthesia, the other after an assisted vaginal delivery. In addition to oral sildenafil, both received oxygen supplementation. To date, there have been three reported cases of pulmonary arterial hypertension in pregnancy treated with sildenafil in combination with another drug. Our two cases demonstrate that treatment for pulmonary arterial hypertension using sildenafil as monotherapy may allow stabilization of the maternal condition and improve clinical outcomes for both mother and baby. However, pregnancy is still discouraged in women with pulmonary arterial hypertension.

Keywords

High-risk pregnancy, complications

Case reports

Case 1

I.D., a 33-year-old woman with known atrial septal defect (ASD) was admitted to our institution at 34 weeks' gestation in her second pregnancy following the onset of uterine contractions. She gave a history of cyanosis when crying during childhood. During her first pregnancy six years prior, she developed exertional dyspnoea and although she delivered at term, there was a neonatal death on day seven, allegedly due to congenital heart disease (CHD).

In this second pregnancy she again described exertional dyspnoea from 16 weeks but the patient had not sought medical advice until the admission.

On examination, there was digital clubbing, a grade 3/6 systolic murmur audible in the second to fourth intercostal space at the right parasternal border, a split second heart sound, with a palpable pulmonary component, a right ventricular heave and clear breath sounds. Oxygen saturation on room air ranged from 78% to 81%.

Echocardiography confirmed a 1.3 cm ASD, with pulmonary artery pressure (PAP) 122 mmHg (Figure 1). Oxygen support via face mask at 10 l/min improved the saturation to between 81% and 89%. She was commenced on sildenafil 50 mg 8 hourly, together with nifedipine 10 mg every 4 h to inhibit the premature labour. The nifedipine was reduced after 48 h to 10 mg every 6 h and discontinued after 72 h upon cessation of uterine contractions. Four doses of dexamethasone 6 mg IM were administered to improve foetal lung maturity. She underwent elective lower segment Caesarean section under general anaesthesia for malpresentation (breech) as on the fourth hospital day delivering a live baby (1.6 kg) APGAR 9, 9, by elective. At that time bilateral tubal ligation was performed at operation. The patient was extubated after delivery. Oxygen saturations improved to between 89% and 92% on oxygen support 2–4 l/min via nasal cannulae. She was discharged on the 15th hospital day – although tolerating room air, she was advised to continue oxygen support at home as well as to maintain sildenafil 50 mg 8 hourly. Unfortunately, she did not return for follow up.

Case 2

M.V., a 28-year-old woman in her first pregnancy presented at 29 weeks' gestation, describing progressive easy fatigability and exertional dyspnoea from 16 weeks' gestation.

On examination, she had peripheral cyanosis and digital clubbing. Respiratory rate was 24 breaths per minute; she had clear breath sounds, a split second heart sound and a grade 3/6 systolic ejection murmur at left parasternal border. Oxygen saturation on room air ranged from 76% to 85%.

Echocardiography showed 3 cm ASD; PAP 125 mmHg (Figures 2 and 3). Oxygen support given through a face mask at 6 l/min slightly improved saturations to 88%. Sildenafil was initially given at 25 mg 8 hourly, and then increased to 50 mg 8 hourly. Isoxsuprine and dexamethasone were given following the onset of irregular uterine contractions. Her oxygen saturation improved to 95% with oxygen support through nasal cannulae at 4 l/min on her seventh hospital day. At 35 weeks' gestation, she went into spontaneous premature labour, and had an assisted vaginal delivery of a live male infant, APGAR 9, 9, birth weight 2550 g, under epidural anaesthesia with bilateral tubal ligation. She was discharged on the 11th day post-partum with oxygen saturation 94% on room air. She remains under regular review as an outpatient and is maintained on sildenafil 25 mg three times daily.

Discussion

Pulmonary arterial hypertension (PAH) is a known complication of uncorrected increased pulmonary blood flow associated with CHD, such as ASD. Secundum type ASD occurs in 10% of pregnant patients with CHD.¹ Approximately 10% of patients with uncorrected ASD develop PAH.

¹Department of Internal Medicine, Las Pinas Doctors Hospital, Manila, Philippines

²Department of Internal Medicine Section Of Adult Cardiology, Philippine General Hospital, Manila, Philippines

³Department of Internal Medicine Adult Pulmonary Medicine, Philippine General Hospital, Manila, Philippines

Corresponding author:

Reinalyn S Cartago, #1302 Barletta Street, Cittadella Executive Village, Pulang Lupa Dos Las Pinas 1740, Philippines.

Email: rencartago@gmail.com

Figure 1. Four-chamber bubble contrast study showing atrial septal defect.

Figure 2. Doppler view showing atrial defect measuring 3 cm.

Figure 3. Spectral Doppler across the pulmonary valve showing severe pulmonary hypertension.

The most appropriate study for patients suspected to have PAH is echocardiogram, with complete right heart catheterization for confirmation.² In both these cases, only echocardiogram was done, with the limited resources at our institution.

Pregnancy complicated by PAH and Eisenmenger syndrome is associated with significant maternal and fetal risk. Management of such women will depend on several factors, including disease severity, gestation at diagnosis and foetal viability. Termination of pregnancy is usually recommended; however, if pregnancy continues, hospitalization is necessary with continuous oxygen administration and pulmonary vasodilator treatment. Since hypoxaemia is a potent pulmonary vasoconstrictor, oxygen supplementation is recommended to maintain oxygen saturation greater than 90%.³

According to the ACCP, the only disease-specific targeted PAH therapy effective in patients with PAH associated with CHD is bosentan.² In our literature reviews, PAH during pregnancy has been treated with anti-pulmonary hypertensive medication with sildenafil as adjunct. Oral sildenafil at a dose of up to 50 mg four times per day⁴ has been shown to improve both hemodynamics and oxygenation in patients with PAH. To our knowledge, there are three reported cases of PAH in pregnancy treated with sildenafil, but in all these reports, there has been another drug used in the treatment – one with L-arginine,⁴ one with bosentan⁵ and one with epoprostenol.⁶ Currently, efficacy of sildenafil monotherapy in patients with PAH/CHD requires further studies.¹

Conclusion

Our cases demonstrate that sildenafil monotherapy may allow stabilization of the maternal condition and thereby improve clinical outcomes of both mother and baby in women with PAH and Eisenmenger syndrome. The authors acknowledge that recommendations of treatment to be offered to affected women during pregnancy are based on case report data. Due to the rarity of this condition and the high mortality of untreated PAH, future recommendations are most likely to be based on individual case reports and/or series rather than trial data.

Declaration of conflicting interests

None declared.

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Ethical approval

The authors confirm that verbal patient consent was obtained. Written consent was also obtained from patient for publication.

Guarantor

Dr. Jubert Benedicto.

Contributorship

Dr. Reinalyn Cartago – primary author, literature reviewer; Dr. Pichy Ann Alan – co-author, literature reviewer, provided echocardiography interpretation for the cases; Dr. Jubert Benedicto – consultant and adviser for the case report.

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