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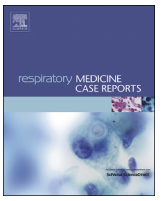

Case Report

The use of selexipag, a prostacyclin receptor analog, for treatment of severe pulmonary artery hypertension during pregnancy, a case report

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ABSTRACT

Pregnancy in patients with pulmonary artery hypertension (PAH) is associated with high mortality and morbidity. Despite the risks, more patients with PAH are becoming pregnant. Case reports and case series have described the use of IV epoprostenol in these patients with some success. However, there are no published reports regarding the use of oral prostacyclins and prostacyclin receptor agonists in pregnancy.

We describe the use of selexipag, an oral prostacyclin receptor agonist, for treating severe PAH during pregnancy in a patient who refused IV prostacyclin therapy. She remained stable throughout pregnancy and delivered a healthy baby girl; however, she died 13 days after her delivery by cesarean section due to developing worsening heart failure.

While there is data and support for IV prostacyclins in pregnancy, patients may opt for oral formulations, like in our case. Registry data on the use of oral prostacyclins and prostacyclin receptor agonists in pregnancy may help improve patient outcomes.

1. Introduction

Pulmonary artery hypertension (PAH) is a debilitating disease with increased morbidity and mortality [1]. Pregnancy in patients with PAH is associated with a high risk of maternal death, with mortality ranging from 17 to 37%. [2–5] PAH-specific treatment options for pregnant patients with PAH are limited. However, the number of women with PAH who become pregnant continues to increase [6,7]. We present a case in which we used selexipag, a prostacyclin receptor analog, to treat severe PAH during pregnancy.

2. Case report

Our patient was diagnosed with idiopathic PAH at age 12. An initial right heart catheterization revealed a mean pulmonary artery pressure of 92 mmHg, cardiac index of 2.1 L/min/m^2, and pulmonary vascular resistance of 40 Woods units. She was started on tadalafil and intravenous (IV) treprostinil. She stopped treprostinil due to repeated line infections and could not use ambrisentan as she declined contraception. At age 17, she became pregnant against medical advice. Termination was recommended multiple times,

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Table 1
Serial echocardiograms before, during, and after pregnancy showing worsening hemodynamics, evidence of worsening right heart function, and rising NT pro-BNP levels. Weeks denote week of gestation; POD denotes post-operative day from her scheduled C-section.
LVEF: Left Ventricular Ejection Fraction
RVSP: Right Ventricular Systolic Pressure
RVSF: Right Ventricular Systolic Function
TAPSE: Tricuspid Annular Plane Systolic Excursion
TR: Tricuspid Regurgitation
NT proBNP: N-terminal pro b-type natriuretic peptide.

	Before Pregnancy	8 weeks	16 weeks	20 weeks	24 weeks	28 weeks	34 weeks	POD #1	POD #4	POD #11
LVEF	Normal	Normal	Normal to High	Normal	Hyperdynamic	Normal	Normal	Normal	Normal	Normal
RVSP (mmHg)	65	114	130	145	138	132	140	181	153	173
TAPSE (cm)	2.13	1.6	1.2	1.56	1.45	1.8	1.7		1.5	1.4
RVSF	Normal	Mildly reduced	Mildly reduced	Mildly reduced	Moderately reduced	Mildly reduced	Low normal	Severely reduced	Moderately Reduced	Moderately Reduced
TR	Mild	Mild-moderate	Mild-moderate	Moderate to severe	Moderate	Severe	Severe	Severe	Severe	Severe
Pericardial effusion?	No	No	Yes, small	No	No	Yes, small	No	No	No	Yes, small
NT proBNP (pg/mL)	372	655	316	–	–	316	–	1330	1712	7288

but she declined and was considered competent to make decisions. The patient declined IV prostacyclin therapy during pregnancy. She was admitted with worsening heart failure at eight weeks pregnant. She was started on inhaled iloprost, then transitioned to oral selexipag, started at 200 μg twice daily and increased by 200 μg weekly. She had improvement in her exercise capacity and her symptoms of heart failure. She was titrated up to 1600 μg twice daily of oral selexipag and followed as an outpatient with serial echocardiograms and fetal ultrasounds.

She was admitted for a scheduled cesarean section at 34 + 1 weeks and again declined to transition to IV prostacyclin. She had an epidural and arterial line for perioperative monitoring but refused central line or pulmonary artery catheter placement. She delivered a healthy 4lb baby girl. Perioperatively, she required dobutamine and vasopressin, but both were titrated off within 24 hours. Her postpartum echocardiogram revealed extremely high right-sided pressures (Table 1). She was started on bosentan, and her selexipag was increased to 1800 μg twice daily. She was aggressively diuresis and her weight decreased by more than 8kg. She was discharged on selexipag, bosentan, tadalafil, furosemide, and subcutaneous enoxaparin with a scheduled follow-up in the PAH clinic three days later. She missed her appointment and presented to the emergency room that evening with two episodes of syncope, elevated NT-proBNP to the 7000s, and a 7kg weight gain. PE-CT was negative for pulmonary embolism. She reported medication compliance. She was admitted for diuresis with inotropic support. She refused aggressive care including IV prostacyclins despite multiple discussions with a multidisciplinary team. She had a cardiac arrest on post-operative day 13 without return of spontaneous circulation and was pronounced dead.

3. Discussion

Multiple studies and case reports have demonstrated the safe use of prostacyclin analogs epoprostenol, parenteral treprostinil, and inhaled iloprost in pregnant patients [6–10]. Selexipag is a new oral medication approved for PAH. [11] Unlike the other IV or inhaled prostacyclin analogs, selexipag is an oral prostacyclin receptor agonist. [12] Currently, there is no data on the use of selexipag in pregnant PAH patients. It is a pregnancy category B medication, and animal studies have not demonstrated teratogenicity. In trials with selexipag compared to placebo, patients on the drug had a lower risk of a composite end point of death or a complication related to PAH. [11] Selexipag has not been compared to intravenous or oral prostacyclin analogs but is oral and relatively well-tolerated. [13,14]

In this case, we felt an oral prostacyclin analog was the best choice, given the challenges of caring for this patient. Our patient had symptomatic improvement with the initiation of selexipag and remained stable enough to deliver a healthy baby in the third trimester of pregnancy. The etiology of her postpartum decline is unclear and has been described in another case series. [4] Differential diagnosis includes postpartum fluid shifts, noncompliance, or that her oral regimen was insufficient to support her postpartum.

4. Conclusion

To our knowledge, this is the first case report describing the use of selexipag in a pregnant patient with severe PAH. Despite severe PAH, our patient survived delivery and gave birth to a healthy baby girl on oral medications. While IV epoprostenol is still the only treatment to demonstrate a mortality benefit and the regimen we used in this patient was not ideal, given the ease of oral administration, more patients may opt for this therapy. Registry data may help with a better understanding of the role of these agents in pregnant patients.

Data availability

HIPPA identifiers retracted patient it is available on request.

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Author contributions

All authors participated in the patient's care and contributed significantly to the manuscript. All authors reviewed the manuscript and figure and approved the final edits.

Declaration of competing interest

The authors report no conflict of interest related to the current work.

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