COMMENTARY

OPEN

Epoprostenol Exposure During Pregnancy

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ABSTRACT: Institutional policies restricting pregnant providers from caring for patients receiving inhaled epoprostenol exist across the nation based on little to no data to substantiate this practice. Over the last 2 decades, the use of inhaled pulmonary vasodilators has expanded in patients with cardiac and respiratory disease providing more evidence for the safety of these medications in obstetrical patients. We propose a thoughtful consideration and review of the literature to remove this restriction to reduce the need to reveal early pregnancy status to employers, to alleviate undue stress for pregnant caregivers who are exposed to patients receiving epoprostenol, and to ensure safe, equal employment, and learning opportunities for pregnant providers.

KEY WORDS: acute respiratory distress syndrome; cardiac critical care; critical care; maternal critical care; obstetric critical care; pulmonary vasodilators

An institutional policy restricting pregnant providers from caring for patients receiving inhaled epoprostenol prompted a multidisciplinary group to evaluate this practice locally, regionally, and nationally. We engaged members from the Society of Critical Care Medicine (SCCM) in a closed forum query of the clinical pharmacy and pharmacology as well as the women in critical care sections discussion forums that revealed variability in institutional practice across the country with several major centers maintaining restrictions for pregnant providers. We also made direct inquiries to five academic institutions with professional connections to the group of authors. Responses were completely voluntary and a total of 10 institutions comprised of a mix of academic and community hospitals responded over a 30-day period to the SCCM forum query. Only one of the 15 institutions listed that they had restrictions for administration of inhaled epoprostenol for pregnant providers. Respondents did not include specifics on the policies, simply whether they had restrictions or not. Inhaled epoprostenol is used primarily in critical care and we felt that this was an important topic to address in our ICUs at Massachusetts General Hospital (MGH) to provide safe recommendations for providers and other caregivers when this medication is being delivered.

Over the last 3 decades, the prevalence of cardiovascular disease in obstetrical patients has risen to become the leading cause of death in pregnant women in the United States (1). Between this rise in cardiac conditions and the COVID-19 pandemic, the use of IV and inhaled pulmonary vasodilators as well as the published literature has expanded substantially in the pregnant population with pulmonary hypertension and acute respiratory distress syndrome (2). Early in vitro studies of the IV prostacyclin/prostaglandin, epoprostenol, demonstrated muscular contraction when applied to nonpregnant human uterus and fallopian tubes as well as inhibition of human fetal and maternal platelet aggregation (3, 4). This may have led to the initial consideration of safety with exposure to epoprostenol during pregnancy and the historical origin of policies restricting pregnant providers from caring for patients receiving inhaled epoprostenol. Since those initial findings, animal studies at

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significantly higher than standard doses have showed no evidence of harm and the drug is considered nonteratogenic (5). Starting in the late 1980s, the use of IV epoprostenol was described in cases of hypertension and preeclampsia and considered to be safe for mother and the fetus (6–8).

Importantly, in the last 2 decades, there have been multiple modern case reports and case series that have reaffirmed the safety and efficacy with the use of epoprostenol in parturients with pulmonary hypertension without evidence of preterm labor, bleeding complications, and/or detrimental fetal effects (5, 9–14). The clinical efficacy, evidence for safety, and lack of demonstrated harm with exposure to IV or aerosolized epoprostenol in human studies has led to the recommendation for its use as first line in pregnant women with pulmonary hypertension (15). During the COVID-19 pandemic, the medical community had the unfortunate responsibility to care for millions of patients with viral pneumonia and this expanded the clinical experience of critical care providers in managing refractory acute respiratory distress with adjuncts including inhaled prostaglandins. Experts who cared for severely ill pregnant women with refractory disease used pulmonary vasodilators including epoprostenol without evidence of harm and, in fact, inhaled pulmonary vasodilators are recommended as a rescue therapy in obstetrical patients by the Society for Maternal-Fetal Medicine (16–20).

Given that the majority of nurses and respiratory therapists in the United States are women and these providers spend the highest percentage of time in the room, this policy may have a huge impact on coverage and staffing models nationally. Inhaled epoprostenol is often preferred over nitric oxide as a pulmonary vasodilator given the cost difference in use and comparable efficacy and safety (21, 22). The National Institute for Occupational Safety and Health is a U.S. Federal agency responsible for conducting research and making recommendations for the prevention of work-related injury and does not list epoprostenol as a risk to women who are actively trying to conceive, pregnant, or breastfeeding. Furthermore, the technical administration of aerosolized epoprostenol using high-efficiency particular filters in the expiratory limb results in little to no aerosol particles outside of the respiratory circuit and environmental exposure is negligible (23).

Policies that specifically restrict patient care access for pregnant providers has the potential for discrimination and harm. Studies of medical residents who have been pregnant during training suggest that negative attitudes and the perceived inconvenience may prompt trainees to desire some control in when to reveal pregnancy status (24). The American College of Obstetricians and Gynecologists' advocates that pregnant women be treated the same as nonpregnant employees with the same work abilities and explicitly states that employers may not force a woman to take medical leave because of pregnancy if she is capable of performing

Prior Policy:

Aerosolized Drug	Administration Requirements	PPE Required
▪ Inhaled pulmonary vasodilators [e.g., epoprostenol (Veletri®)]	Administered by: ▪ RRT Patient Room Requirements: ▪ Private, single room (door can remain open) ▪ A sign should be placed on the door to alert others that inhaled epoprostenol is being administered	Applicable to: ▪ Healthcare workers Required PPE: Masks are not required when entering the room or when involved in usual caregiver activities in the room, but N95 masks will be available for those who choose to use them. **Women who are pregnant should not enter the room during treatment.**

New Policy:

PPE Required
Applicable to: ▪ Healthcare workers ‡Required PPE: ▪ N-95 respirator mask ‡**Exception**: Healthcare providers MUST follow current patient-specific infection-control precautions for PPE requirements

Figure 1. Prior and updated policies. RRT = Registered Respiratory Therapist, PPE = Personal Protective Equipment.

in her job role (25). Medically necessary work accommodations for pregnant women are imperative, and we are firmly against forcing pregnant healthcare providers into environmentally unsafe conditions. This is important to highlight as the proposed policy change does not assert sending pregnant providers into an unsafe working environment but rather lifting restrictions that, when present, make the pregnant provider feel at risk.

Our critical care clinical operations committee at MGH consisting of a multidisciplinary and cross-specialty providers and caregivers at MGH including nurses, pharmacists, physicians, and respiratory therapists updated our own policy after thoughtful consideration and review of the data. The pharmacy executive committee, critical care division, maternal-fetal medicine division, and respiratory therapy department had independent meeting and review of this proposal and each group provided their approval based on the data. **Figure 1** demonstrates the prior as well as updated policy. Given the history of this policy and the sensitive nature of pregnancy safety, we conducted dedicated, in-person education with the respiratory therapists, ICU nurses, advanced practice providers, and physicians across our critical care units where inhaled epoprostenol is used. Strong, direct communication with the opportunity to ask questions of the team that researched and proposed this change was instrumental to acceptance of this revision in policy. We advocate to remove this restriction wherever it may remain in order to reduce the need to reveal early pregnancy status to employers, to alleviate undue stress for pregnant caregivers who are exposed to patients receiving epoprostenol, and to ensure safe, equal employment, and learning opportunities for pregnant providers.

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