
Pulmonary Artery Hypertension: The Link Between Prostanoids and Bloodstream Infections

Because of their vasodilatory and antiproliferative effects, the administration of prostanoids has become an important part of treatment for patients with pulmonary arterial hypertension (PAH). The intravenous infusion of the 2 prostanoids, epoprostenol (epoprostenol sodium [brand name Flolan, Glaxo SmithKline, Research Triangle Park, North Carolina]) and treprostinil (treprostinil sodium [brand name Remodulin, United Therapeutics, Silver Spring, Maryland]) are approved by the U.S. Food and Drug Administration for use in patients with PAH and are commonly used in many centers today. These drugs are discussed by Chin and Rubin (1) in their review on the topic in a recent issue of the Journal. However, there is no mention of the caution raised by a study performed at 7 PAH centers during 2003 to 2006 by the Centers for Disease Control and Prevention (CDC) on the possible link between treprostinil and greater rates of bloodstream infections (BSIs); (primarily gram-negative infections) when compared with the use of intravenous epoprostenol (2). The overall BSI pooled mean rate (per 1,000 medicine days) was 1.11 for patients receiving treprostinil compared with 0.43 in those receiving epoprostenol (pooled incidence rate ratio: 2.57; 95% confidence interval: 1.81 to 3.64). The rate of gram-negative infections was also much greater with treprostinil, with gram-negative infections actually more common than gram-positive infections. This finding suggests that, when line infection is suspected in patients receiving intravenous treprostinil, the empiric use of antibiotics with both gram-positive and -negative coverage should be considered until blood culture results are available.

However, these findings do not rise to the level of robust scientific proof: First, just before the initiation of the study, an alert letter from United Therapeutics (Silver Spring, Maryland), the manufacturer of treprostinil, was distributed requesting that physicians report any gram-negative bacteremia cases for further evaluation. Shortly after this concern was raised, the CDC asked centers where treprostinil was used frequently to participate in a more formal study. It is possible that centers with increased rates of gram-negative infections were more likely to participate, particularly given the increased awareness prompted by the alert letter. Second, there appeared to be significant heterogeneity within the results, with incidence rate ratios for infections with treprostinil compared with epoprostenol ranging from 0.59 to 3.90 across the 5 centers from which data were available for both medications. Finally, data were collected retrospectively and over different years at each site, the CDC was not directly involved in the data collection at most sites, and the information was only presented as a 2-page brief rather than a full, peer-reviewed research paper. Thus, although the CDC report raises awareness to the risk and provides guidance for the current treatment of suspected line infections, additional formal study is required.

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