Management of the Patient With Pulmonary Arterial Hypertension Receiving Intravenous Prostacyclin

An Expert Nurse Practical Guide

ABSTRACT
Pulmonary arterial hypertension (PAH) is a severely disabling disorder characterized by elevated pulmonary artery pressure ultimately leading to right heart failure and death. Treatment options have significantly increased over the past decade. Intravenous prostacyclins remain the treatment of choice for advanced PAH, leading to long-term clinical benefits and improved survival. Their administration requires a high level of nursing competency and presents considerable challenges for patients and caregivers. This article reviews the characteristics of currently available intravenous prostacyclins and provides a practical guide for nurses who may have had limited exposure to intravenous prostacyclins and their unique dosing, side effects, and titration characteristics.

Key words: epoprostenol, intravenous prostacyclin, practical guide, pulmonary arterial hypertension, treprostinil

Pulmonary arterial hypertension (PAH), also known as World Health Organization (WHO) group 1 pulmonary hypertension (PH), is a rare but serious, life-threatening disease characterized by elevated pulmonary artery pressure and increased pulmonary vascular resistance, frequently resulting in right heart failure and premature death. Symptoms of PH include dyspnea on exertion, fatigue, syncope, and chest pain. These symptoms are also similar to PH seen in WHO groups 2 through 5, in which PH is the result of other pulmonary, cardiac, and extrathoracic conditions.1

Oral therapies such as phosphodiesterase type 5 inhibitors2-9 and endothelin receptor antagonists4-5 have been effective in patients with mild-to-moderate PAH, whereas intravenous (IV) prostacyclin therapy remains one of the most effective treatments for patients with advanced PAH who fail to respond to conventional therapy.6-9

PAH is a rare disease and few admitted patients are receiving IV prostacyclin therapy at any given time, even at PAH centers; therefore, many nurses have had limited exposure to IV prostacyclins and their unique dosing, side effects, and titration characteristics. In this article, we review the characteristics of the currently available

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IV prostacyclins and offer a practical guide for safe administration of IV prostacyclins to patients with PAH in emergency department and inpatient hospital settings.

## IV PROSTACYCLINS FOR PAH

Prostacyclins are potent vasodilators and possess antithrombotic and antiproliferative properties; by increasing cyclic adenosine monophosphate concentrations, they cause vasodilation in the pulmonary vasculature and inhibition of platelet aggregation.\(^{10,11}\) Vasodilation of the pulmonary arteries reduces the workload of the right ventricle, increases blood flow to the lungs, and reduces pulmonary artery pressure—all of which results in improvement of PAH symptoms and exercise capacity.\(^{12}\)

At present, there are 3 commercially available IV prostacyclins in the United States: epoprostenol sodium with glycine and mannitol excipients (epoprostenol GM; Flolan, GlaxoSmithKline); epoprostenol sodium with arginine and sucrose excipients (epoprostenol AS; Veletri [epoprostenol for injection], Actelion Pharmaceuticals US, Inc); and treprostinil (Remodulin, United Therapeutics Corp). These prostacyclins are administered via continuous IV infusion with a dedicated indwelling central venous catheter or via subcutaneous (SC) infusion with treprostinil.

Dosing of prostacyclins is highly patient-specific and is based on a balance between reducing PAH symptoms and limiting side effects; thus, dosing is often defined by the limits of tolerability.\(^{13}\) Adverse effects common to all prostacyclins include headache, jaw pain with the first bite of a meal, flushing, diarrhea, nausea, blotchy erythematous rash, musculoskeletal aches, and pain in the legs and feet. The type and severity of side effects vary among patients and generally worsen during dose escalation.\(^{14-16}\)

In addition, central line infections and bacteremia are well-documented risks of chronic IV therapy and may significantly contribute to morbidity and even mortality. Catheter failure due to dislodgment, occlusion, or infection is the leading complication of chronic IV therapy.\(^{17}\) The Scientific Leadership Council of the Pulmonary Hypertension Association provided guidelines for clinical practice regarding catheter care.\(^{17}\) Some of these recommendations include the use of a closed-hub system, preferably a split-septum device, and waterproofing catheter hub connections during showering, using a sealable wrap.\(^{17}\)

### IV PROSTACYCLINS

**Epoprostenol**

**Epoprostenol GM (Flolan)**

Since the early 1990s, IV epoprostenol GM (Flolan), a prostaglandin analogue, has been a mainstay of therapy for patients with advanced PAH. Epoprostenol GM is the treatment that has been most studied and is the only PH medication with proven survival benefit.

The efficacy and safety of epoprostenol GM have been evaluated in 3 pivotal, open-label, clinical trials.\(^{6-8}\) Although limited by the small number of patients enrolled, these studies showed significant improvements from baseline in cardiopulmonary hemodynamics and 6-minute walk distance (6MWD).\(^{6-8}\)

Epoprostenol GM has been shown to improve functional class, exercise tolerance, and hemodynamics compared with controls,\(^{7,18}\) as well as exercise capacity in patients with PAH associated with scleroderma.\(^{8}\) Improvements in quality of life (QOL) were also shown in 1 study, as well as short-term survival benefit with epoprostenol GM in the idiopathic PAH (IPAH)/heritable PAH (HPAH) population.\(^{19}\) Enhanced survival with epoprostenol GM has been confirmed in subsequent studies\(^{20-22}\); survival rates of 85%, 70%, and 63% have been reported after 1, 2, and 3 years, respectively, of epoprostenol GM therapy compared with historical data showing survival rates in untreated patients of 58.9%, 46.3%, and 35.4%.\(^{21}\)

Epoprostenol GM is provided as a powder that must be reconstituted and mixed daily with its specific diluent only. The drug is only stable for 8 hours at room temperature; therefore, if used longer than 8 hours, epoprostenol GM must be kept on ice during administration. Because epoprostenol GM has a very short half-life of 3 to 6 minutes, the infusion needs to be continuous (24/7) because interruption can be life threatening. Epoprostenol GM requires a minimal infusion rate of 1.2 mL/h. IV administration is initiated at 1 to 2 ng/kg/min and is gradually increased over weeks to months to a maximum of 12 to 24 ng/kg/min. Because the drug is highly temperature sensitive, the solution should only be used for a limited period (24 hours) and is therefore eliminated if used longer than 8 hours. Epoprostenol GM has been shown to improve functional class, exercise tolerance, and hemodynamics compared with controls,\(^{7,18}\) as well as exercise capacity in patients with PAH associated with scleroderma.\(^{8}\)

**Epoprostenol AS (Veletri)**

Epoprostenol AS (Veletri) is a version of epoprostenol that was formulated for greater drug stability to slow the rate of drug degradation at room temperature; it therefore eliminates the need for ice packs.\(^{23}\) Although clinical studies with the IV administration of epoprostenol AS are limited at present, direct biocompatibility has been shown with respect to pharmacokinetics, pharmacodynamics, safety, and tolerability between epoprostenol GM and epoprostenol AS\(^{23}\); in addition, both products have the same half-life because they contain the same active ingredient. Thus, the efficacy data gathered for epoprostenol GM were used for approval of epoprostenol AS by the US Food and Drug Administration.

Two prospective, open-label, randomized trials conducted with epoprostenol GM but used for the approval
of epoprostenol AS showed that chronic continuous administration in patients with IPAH/HPAH resulted in increased cardiac index, stroke volume, arterial oxygen saturation, decreased mean pulmonary artery pressure, mean right atrial pressure, and systemic vascular resistance after 8 to 12 weeks of treatment compared with patients who did not receive the treatment. These hemodynamic improvements appeared to persist when epoprostenol AS was administered for at least 36 months in an open-label, nonrandomized study. Acute IV infusion of epoprostenol AS for up to 15 minutes in patients with IPAH, HPAH, or PAH associated with scleroderma produced the same improvements in hemodynamic parameters as seen with epoprostenol GM. Survival was also improved in patients with New York Heart Association (NYHA) functional class (FC) III and IV IPAH who were treated with epoprostenol for 12 weeks in a multicenter, open-label, randomized, parallel-group study.

Epoprostenol AS can be reconstituted and diluted with sterile water for injection or sodium chloride 0.9% for injection. Epoprostenol AS can be prepared for immediate use, or up to 8 fully diluted cassettes can be prepared once weekly and refrigerated for up to 8 days. Epoprostenol AS is stable at all concentrations for 24 hours at room temperature, without ice packs. Patients can store a backup cassette for 24 hours at room temperature or up to 8 days refrigerated, then administer for 24 hours without ice packs. It is recommended that a single cassette not be administered by pump beyond 24 hours. Epoprostenol AS should not be exposed to direct sunlight. Patients may administer epoprostenol AS at 104°F (40°C) for short periods of time: 2 hours at concentrations below 15,000 ng/mL; 4 hours at concentrations between 15,000 and 60,000 ng/mL; and 8 hours at concentrations above 60,000 ng/mL. Even after these short periods at 104°F (40°C), patients may continue administration of epoprostenol AS without ice packs and remain on the same 24-hour cassette depending on the concentration. The most frequently reported adverse events include headache, flushing, jaw pain, bone pain, diarrhea, palpitations, and rashes. The number and severity of side effects vary among patients. The most common dose-limiting adverse events (occurring in ≥1% of patients) include flushing, headache, nausea, vomiting, and hypotension.

Treprostinil (Remodulin)

Treprostinil is a newer prostacyclin analogue that is similar to epoprostenol in its mechanism of action and relative efficacy. The same formulation of treprostinil is approved for IV use as well as SC use. A MiniMed portable infusion pump (CADD MS 3; Smiths Medical, St. Paul, MN) is used for all SC treprostinil infusions. The SC route eliminates the need for central venous access and the risk for central line sepsis.

The pivotal phase 3 study of treprostinil was conducted using the SC route of administration. Improvement from baseline in 6MWD was modest in this study because of the failure to reach the target dose of 22.5 ng/kg/min by week 12. However, patients who did receive higher doses had greater improvements in 6MWD. Significant improvements versus placebo were observed for Borg dyspnea score, cardiopulmonary hemodynamics, and aspects of QOL assessment. Treprostinil has been shown to improve hemodynamics and 6MWD in other studies. Improvements in exercise capacity and symptoms were maintained during long-term treatment with treprostinil, which may confer a survival benefit.

Treprostinil is available as a sterile solution that is compatible with normal saline, which is used as a diluent. Sterile water for injection or epoprostenol GM sterile diluent for injection may also be used. It has a half-life of 4.5 hours in human serum and a 48-hour infusion interval. Because treprostinil is stable at room temperature for 48 hours, it does not require refrigeration after dilution for IV administration. Treprostinil can be infused at lower flow rates than epoprostenol and thus allows for the use of smaller infusion pumps. The most common adverse events related to IV administration of treprostinil include line infections, sepsis, arm swelling, tingling sensations, bruising, and pain. General side effects (occurring >5% more than placebo) include diarrhea, jaw pain, vasodilation, and edema.

IV PROSTACYCLIN ADMINISTRATION

In most cases, patients with PAH will develop advanced disease and require treatment with a prostacyclin therapy. When the decision is made to start prostacyclin therapy, an application is submitted to a specialty pharmacy, which obtains approval for the medication through the patient's insurance plan and then provides training to the patient and family. IV prostacyclin therapy is initiated in the hospital, and patients are discharged only when they can demonstrate proficiency in sterile mixing techniques, aseptic catheter care, and pump management. IV prostacyclin therapy administration presents considerable challenges for both patients and caregivers, requiring advanced knowledge, skill, manual dexterity, and a high level of nursing competency to ensure patient safety.

Long-term administration of IV prostacyclins requires continuous infusion via a permanent central venous access catheter attached to an ambulatory battery-operated pump, which is to be carried at all times. All patients should have a backup pump in case of pump malfunction, and to use for priming the next cassette. Once the continuous infusion is started, it should never be interrupted except for brief episodes to change the
Continually monitoring patients’ clinical status and caregivers and managing side effects, in addition to failure, catheter-related infections and sepsis, catheter thrombosis, dislodgment, or perforation (Table 1). Nurses play a key role in educating patients and side effects, in addition to continually monitoring patients’ clinical status and adherence to the regimen, which is critical for treatment success and for optimizing patients’ QOL (Table 2).

**PRACTICAL GUIDE FOR PATIENTS REQUIRING INITIATION OF THERAPY**

The following is based on our extensive experience and protocols that are in place at some PH treatment centers, such as that of the University of California San Diego, for care of the patient requiring IV prostacyclin therapy.

**Medication Orders**

IV prostacyclins are high-risk medications that should only be prescribed and managed by expert PH clinicians. When patients are admitted to the hospital, the hospital pharmacist should contact the patient’s specialty pharmacy to verify current dose, dosing weight, concentration, and pump rate. IV prostacyclin orders must include the following: patient identifiers, drug, dose in nanograms per kilogram per minute, dosing weight (the first weight used for calculating the prostacyclin dose),

### TABLE 1

**General Safety Measures**

<table>
<thead>
<tr>
<th>General guidelines</th>
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<tbody>
<tr>
<td>• Develop clear order sets for each type of IV prostacyclin.</td>
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<tr>
<td>• At each shift, verify the dose, reservoir volume, and that the pump is in “Run” mode.</td>
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<tr>
<td>• Attempt to match the concentration the patient uses at home.</td>
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<tr>
<td>• Confirm with a second nurse the patient’s name, dose, and pump rate at each cassette change.</td>
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<tr>
<td>• Ensure that cassettes are clearly labeled with the patient’s name, medical record number, and dosing regimen.</td>
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<td>• Never mix any other medications in the same line in which IV prostacyclin is infusing, and never flush the line.</td>
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<tr>
<td>• Ensure that the dedicated central line is not interrupted at any time.</td>
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<tr>
<td>• Use a closed-hub system, preferably a split-septum device.</td>
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<tr>
<td>• Waterproof catheter hub connections during showering, using a sealable wrap.</td>
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<tr>
<td>• Avoid multiple cassette storage on nursing units to minimize the possibility of a cassette mix-up.</td>
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**What to do in the ambulance**

- Assess patient’s blood pressure, heart rate and rhythm, and oxygen saturation.
- Verify that pump is in “Run” mode and that there is medication left in the cassette.
- Verify the patient’s prostacyclin dose and rate of infusion either with the patient or, if the patient is unable to verify, call the specialty pharmacy number on the infusion pump.
- Never stop the infusion or flush the line.
- If the central catheter is nonfunctioning, immediately start a short peripheral catheter until a central venous catheter can be placed.
- Avoid additional IV fluid as this can cause right ventricular failure; for hypotension, contact the medical director to receive an order for a vasopressor such as dopamine.
- Do NOT use the dedicated central line to administer other medications UNDER ANY CIRCUMSTANCES.

**TABLE 2**

**Practical Guide for Hospital Nurses**

1. Upon arrival at the nursing unit, verify that the pump is in “Run” mode, and document reserve volume, dosing, continuous rate, and when the next cassette will be needed.
2. Have the pharmacist contact the patient’s specialty pharmacy to verify current dose, dosing weight, concentration, and pump rate; document this in the patient’s record.
3. Ensure the patient receiving epoprostenol GM has ice packs in his or her pump carrying case.
4. If hospital policy requires changing from an ambulatory pump to a hospital pump, double-check the calculations, as ambulatory pumps provide medication in milliliters per 24 hours while hospital pumps infuse in milliliters per hour.
5. Keep a spare pump with the patient at all times, and change the batteries in each pump every Monday.
6. Ensure that a PAH-trained pharmacist or nurse double checks the dose, concentration, and pump rate whenever a rate change is made or whenever a new cassette is placed into the pump.
7. If prostacyclin concentration needs to be changed, carefully prime the catheter (should be done by a nurse trained in this process).
8. Follow guidelines for sterile technique with tubing and dressing changes, and evaluate the site for any signs of infection.
9. When a cassette change is needed, the pharmacy will bring a newly prepared cassette to the nursing unit, properly labeled with all of the patient’s information and dosing.

Abbreviation: IV, intravenous.

Abbreviation: PAH, peripheral arterial hypertension.
concentration, pump rate in milliliters per 24 hours, and whether ice packs are required (Table 3). To lessen the risk of a calculation error, the same medication concentration that is used at home should be used in the hospital. Changes in dose should only be made by, or in consultation with, the expert PH clinician.

**IV Access**

If time allows, patients should have a tunneled central venous catheter placed before starting the prostacyclin infusion. In emergent cases, a peripherally inserted central catheter may be used until a more permanent central venous catheter can be placed. Prostacyclin through a dedicated central venous catheter must not be interrupted at any time, even for blood draws. No other medications can be mixed in the same line as the prostacyclin infusion, even in a code situation. Epoprostenol tubing should be changed every Monday, Wednesday, and Friday, and treprostinil tubing should be changed every 48 hours or every time the cassette is changed. Central line dressings are changed per hospital policy.

**Initiation of Therapy**

Initiation of therapy should only occur in an area where nurses have been trained in the administration of prostacyclin and expert pharmacy assistance is available. This unit may be a telemetry unit or intensive care unit setting depending on hospital policy and PH clinician preference.

**Safety Measures**

A double-check should be completed and documented by 2 prostacyclin-trained pharmacists or 2 prostacyclin-trained nurses at initiation of therapy, at each dose change, and whenever a new cassette or bag is placed.

The double-check includes the 5 rights of medication administration (the right patient, the right drug, the right dose, the right route, and the right time) and that the pump is in “Run” mode at the accurate rate.

**Catheter Priming for Concentration Changes or Line Changes**

In general, the concentration used in the hospital should match the concentration the patient is using at home in order to avoid calculation errors. In the event the concentration must be changed in the hospital, the catheter must carefully be primed by a nurse trained in this process to prevent prostacyclin side effects that will occur if the patient receives a bolus. Each hospital should determine whether prostacyclin cassettes will be kept on the nursing unit or in the pharmacy. Because of the short half-life of epoprostenol, there may be a safety advantage to keeping the next cassette on the nursing unit. Consider keeping treprostinil in the pharmacy because it has a longer half-life, which allows enough time to obtain another cassette in the event of an emergency. As epoprostenol and treprostinil are similar in appearance, efforts should be made to distinguish them from one another in order to prevent cassette mix-ups.37

**Pump Management and Maintenance**

Epoprostenol is only administered outside the hospital with a CADD-Legacy pump (Smiths Medical, St. Paul, MN), and most patients receiving treprostinil will be using this pump (Figure 1). A spare pump must be kept with the patient at all times, which is used to prime the tubing for the next cassette. The batteries must be changed in both pumps every Monday.

Because of the stability of treprostinil at room temperature and its pharmacologic properties, smaller infusion pumps such as the CADD-MS 3 (Smiths Medical) or the Crono-5 PCA pump (Cané S.r.l.; Rivoli, Italy) at lower flow rates (as low as 0.1 mL/h) can be used for its administration; however, these should only be used in select patients because they are much more concentrated, and any error in administration can result in significant side effects. These smaller pumps can be more challenging to operate, making technical skill and dexterity important requirements in patient selection. Similar to the CADD-Legacy pump, the CADD-MS 3 has many safety features including alarms for occlusion or low reservoir volume.

**Care of the Central Line and Patient Education**

Central line infections and bacteremia are well-documented risks of chronic IV therapy; therefore, it is critical that patients and caregivers be educated regarding

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**TABLE 3**

**What the Intravenous Prostacyclin Order Should Contain**

- Patient’s identifiers
- Drug name (for epoprostenol, consider using brand names of Veletri and Flolan in order to avoid errors)
- Dose in nanograms per kilogram per minute
- Dosing weight
- Drug concentration
- Specification of milliliters per 24 hours for ambulatory pumps or milliliters per hour for hospital pumps
- Requirement for ice packs
given a 24-hour emergency number to call if they see signs of infection or have a fever, or if the catheter is dislodged, becomes cracked, or leaks. Patients should be trained to call the specialty pharmacy for nonemergent questions regarding pump operation, mixing, or dressing changes. In addition to shipping the medication, the specialty pharmacy will train patients on how to mix their medication, prime their tubing, operate their infusion pump, and care for their central line.

PRACTICAL GUIDE FOR CARE OF THE PATIENT RECEIVING IV PROSTACYCLIN WHO REQUIRES EMERGENCY MEDICAL SERVICES

Patients receiving IV prostacyclin therapy may require emergent hospital admissions for infection, inpatient procedures, or management of other medical conditions such as volume overload from right ventricular failure.

Care of the Patient in the Ambulance

When a patient on IV prostacyclin requires emergency medical services, management begins in the ambulance (see Table 1). First, emergency medical services should assess the patient’s vital signs and oxygen saturation. Next, they should verify that the pump is in “Run” mode and that there is medication in the cassette. Verify the patient’s prostacyclin dose, rate of infusion, and concentration with the patient or a family member. If the patient or family is unable to communicate this information, the specialty pharmacy should be contacted; the pharmacy number is listed on the infusion pump. If there is a catheter complication, request immediate assistance from the hospital’s PAH team or pharmacist.

If the central IV access is lost, the emergency provider should immediately place a peripheral IV until a central line can be placed at the hospital to avoid interruption of the infusion. In most cases, additional IV fluids should be avoided as many patients will develop right ventricular failure if given large amounts of IV fluid. Under no circumstances can the patient’s dedicated central line be used to administer other medications; therefore, a peripheral IV catheter should be initiated in the event that emergency medications are needed in the ambulance or upon arrival at the emergency department.

Care of the Patient on Arrival at the Emergency Department

The status of the pump should be verified: it should be in “Run” mode. Reserve volume, dosing, continuous rate, and volume given should be documented. (with the CADD Legacy pump, this information can be accessed by pressing the “Next” button on the pump.) If the patient was receiving epoprostenol GM, fresh ice should be placed in the carrying case around the pump. The
pharmacy should confirm dosing weight, dose, and concentration with the patient’s specialty pharmacy.

Patients may present to the emergency department for a variety of reasons. If the patient’s permanent central venous catheter has been disrupted, the patient should immediately have a short peripheral catheter placed so that the prostacyclin can be restarted as quickly as possible. A peripheral line should only be used for the shortest time possible until a central venous line can be placed. Occasionally, a patient may present to the emergency department with a cracked or leaking central line. The emergency department should have repair kits available and receive training for repairing these lines. Any pump issues can be addressed by calling the number of the specialty pharmacy located on the pump. Upon arrival at the emergency department, the PH treatment team should be made aware of the patient’s status.

### Care of the Patient on Admission to the Hospital

It has been suggested that hospitals consider standardized prostacyclin administration policies and ongoing training of staff to decrease the likelihood of a serious adverse event. It is strongly recommended that each facility develop clear, concise, standardized order sets for each of the prostacyclin infusions used in the inpatient setting. If the patient is admitted to the hospital, the preparation, administration, and programming of the ambulatory infusion pump become the responsibility of the pharmacy and nursing staff. Patient placement will be determined by the clinical indication for admission and where nurses have been trained in the administration of IV prostacyclin. Each hospital will need to determine whether patients will remain on their own CADD pump or transition to a hospital pump. The pump type, concentration, dose, location of the catheter, reserve volume, continuous rate, and last dressing change should all be documented.

Before the next cassette change, the pharmacy will bring the next cassette labeled with the patient’s name, medical record number, and dosing regimen. It is recommended that patients be involved in the medication administration process, especially if they are kept on their home infusion pump, because they have been highly trained and will be able to confirm the concentration, dose, and pump rate. At the beginning of each shift, the proper operation of the pump at a rate that matches the order on the medication administration record should be documented.

### Care of the Patient During Outpatient Procedures

Nurses working in outpatient areas such as the cardiac catheterization laboratory and interventional radiology should undergo training in the administration of IV prostacyclin. They should verify the dose and reservoir volume and ensure that the pump is in “Run” mode. If the patient is undergoing a line change, the nurse in these settings should be trained in the process for careful line priming. In addition, a procedure must be in place for magnetic resonance imaging (MRI) procedures because the infusion will either need to be changed to an MRI-compatible pump or extra tubing will need to be added so that the CADD-Legacy pump can be placed outside the door of the MRI suite. Nursing staff will need to know how to properly attach the tubing, and extra tubing should be available in the MRI suite.

#### TRANSITIONING PATIENTS FROM ONE IV PROSTACYCLIN TO ANOTHER

Occasionally, clinical circumstances may lead patients to be switched to IV treprostinil after receiving IV epoprostenol therapy for some time, or vice versa (Figure 2). Transitioning patients with stable PAH from IV epoprostenol GM to IV treprostinil has been shown to be effective with maintenance of exercise capacity and functional class at week 12 in a prospective, open-label study (N = 31) in the hospital setting by increasing the dose of treprostinil while simultaneously decreasing the dose of epoprostenol, with vital sign monitoring over a 24- to 48-hour period. The 12-week dose of IV treprostinil was greater than twice the dose of IV epoprostenol before the transition (83 ± 38 vs 40 ± 4 ng/kg/min). In general, the dose between both types of epoprostenol would be the same. Hemodynamic differences associated with IV treprostinil were observed at week 12. Mean pulmonary artery pressure increased 4 ± 1 mm Hg (P < .01), cardiac index decreased 0.4 ± 0.1 L/min/m² (< P = .01), and pulmonary vascular resistance increased 3 ± 1 Wood units per meter squared (P < .01). Although there were no deaths, and no serious adverse events were attributed to treprostinil, the platelet count was higher at week 12 versus the baseline (P = .0001), and 4 patients were transitioned back to IV epoprostenol (3 because of leg pain and 1 because of worsening PAH symptoms with pneumonia). One patient had syncope, and 4 patients reported worsening dyspnea during the up titration of treprostinil. Other common adverse events included extremity pain (such as leg, arm, foot, and toe pain); headache; diarrhea; and jaw pain—all of which are typical of prostacyclin-related side effects.

A more recent study described a rapid switch protocol for transitioning patients with stable PAH from IV epoprostenol GM to IV treprostinil. This protocol, also performed in the hospital, involved a direct switch of the medication reservoir from epoprostenol GM to treprostinil. Patients were initially transitioned to IV treprostinil at the same dose they used for IV epoprostenol GM (1:1 ng/kg/min basis), then discharged after a
significantly increased within 1 hour after discontinuation of treprostinil in all patients,42 which is a shorter time frame than what is known to be the pharmacokinetic terminal half-life (4.4 hours) of treprostinil.43 Mean pulmonary arterial pressure immediately before discontinuation of treprostinil (53.4 ± 7.5 mm Hg) was significantly lower than the values 1 hour after discontinuation (63.6 ± 9.6 mm Hg, P = .026), but it was significantly higher than the values after transition to epoprostenol (45.4 ± 5.5, P = .049).42 In the 4 patients who had clinical follow-up data available, all improved functional class. No drug-related adverse events occurred during the transition, and no patient experienced increased prostacyclin-related adverse events.42 The authors have not experienced any difference in PAH symptoms or prostacyclin side effects when patients were changed rapidly from one form of epoprostenol to the other.

CONCLUSIONS

Poor prognosis coupled with severe functional impairment means that it is vital for patients with NYHA FC III and IV PAH to receive the most effective treatment options. IV prostacyclin therapy is a treatment for advanced PAH that can improve symptoms, exercise capacity, hemodynamics, and survival. IV prostacyclin therapy remains arguably the most effective treatment for advanced PAH. However, administration of the 3 currently available IV prostacyclins presents considerable challenges for emergency nurses, PAH nurse specialists, and staff nurses caring for this patient population, and for the patients who use these therapies. It is our recommendation that hospitals conduct regular training sessions on prostacyclin infusion and ambulatory infusion pumps and differences in the prostacyclin therapies for all nurses and specialty pharmacies on units where patients with PAH are likely to be admitted.

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