Practical Aspects of Continuous Intravenous Treprostinil Therapy

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Patients with pulmonary arterial hypertension (PAH) are often admitted to the hospital electively for parenteral therapy or right-sided heart catheterization and urgently for worsening right ventricular failure, life-threatening illnesses such as pneumonia or sepsis, and a variety of other medical problems. Because of the novelty of intravenous (IV) treprostinil administration, in this review, we attempt to provide nurses with guidance and information about the overall requirements for safe administration of IV treprostinil. The information is based on our own experiences in administering this therapy to patients with PAH.

Epidemiology

PAH is a progressive disease characterized by an elevation in pulmonary artery pressure and pulmonary vascular resistance potentially leading to right ventricular failure and death.1,2 Idiopathic PAH (formerly termed primary pulmonary hypertension) occurs in the absence of known causes and is considered a heterogeneous group of abnormalities rather than a uniform clinical entity.2,3

Estimates of the incidence of idiopathic PAH range from 1 to 2 cases per million persons in the general population.1 Idiopathic PAH has been diagnosed in families worldwide and is termed familial idiopathic PAH. The prevalence of familial idiopathic PAH is uncertain; however, at least 6% of cases and probably a considerably higher number of cases (15%) of idiopathic PAH are familial.4
Although the incidence of PAH in patients with other illnesses is not known with certainty, PAH is reported in 2% to 4% of patients with portal hypertension and in 0.1% to 0.6% of patients infected with human immunodeficiency virus.\textsuperscript{5,6} The incidences of PAH in patients with connective tissue diseases are extremely variable. The prevalence ranges from 2% to 35% in patients with the scleroderma spectrum of disease and may be as high as 50% in patients with limited scleroderma (formerly termed the CREST [calcinosis cutis, Raynaud’s phenomenon, esophageal dysfunction, sclerodactyly, telangiectasia] variant of scleroderma).\textsuperscript{7} PAH has been reported to occur in 23% to 53% of patients with mixed connective tissue diseases and in 1% to 14% of patients with systemic lupus erythematosus.\textsuperscript{8}

**Pathophysiology**

PAH, regardless of the etiology or associated conditions, is characterized by abnormalities of the pulmonary arterioles.\textsuperscript{1} Despite the heterogenous nature of this disease, regardless of the etiology, the vascular lesions in each case are identical and consist of the following classic histopathological manifestations: medial hypertrophy, intimal proliferation, concentric laminar fibrosis, and plexiform and thrombotic lesions (Figure 1). These abnormalities are caused, in part, by an excess of endothelin-1 (responsible for vasoconstriction and smooth muscle proliferation), an overproduction of thromboxane (a potent vasoconstrictor), and a decrease in the production of endogenous prostacyclin and nitric oxide (a vasodilator and an antiproliferative). Under normal conditions, the endothelial and smooth muscle cells maintain a balance between the mediators that cause vasoconstriction and smooth muscle proliferation (thromboxane, endothelin-1) and the mediators that cause vasodilatation and inhibit proliferation (prostacyclin and nitric oxide). In PAH this balance is not preserved, and the classical histopathological features of the disease occur in the pulmonary arterioles.

**Medical Management**

Conventional nonspecific therapy for PAH includes anticoagulation, digoxin, diuretics, supplemental oxygen, and chronic high-dose oral calcium channel blockade in a small group of patients with acute vasoreactivity.\textsuperscript{12,13} Vasoreactivity is defined as a decrease in mean pulmonary artery pressure of more than 10 mm Hg to an absolute mean of less than 40 mm Hg with normal cardiac output during testing with IV adenosine, IV epoprostenol, or inhaled nitric oxide.\textsuperscript{14} Unfortunately, only a few patients are acutely vasoreactive, and even fewer remain responsive to chronic high-dose oral calcium channel blockade.\textsuperscript{12-14} Chronic IV epoprostenol (Flolan) therapy can improve exercise capacity, hemodynamic status, and survival in patients with idiopathic PAH.\textsuperscript{15-17}

Treatment with chronic IV epoprostenol also can improve exercise capacity and hemodynamic status in patients with PAH associated with the scleroderma spectrum of disease.\textsuperscript{18} Epoprostenol is approved by the Food and Drug Administration for New York Heart Association class III and class IV patients with idiopathic PAH or PAH associated with the scleroderma spectrum of diseases. Continuous IV epoprostenol has marked potential risks and drawbacks because of the drug’s short half-life (3-6 minutes), instability at neutral pH and ambient temperature, and cumbersome delivery system. Additional risks are associated with the long-term use of a central venous catheter (sepsis and thromboembolic events).\textsuperscript{19} Therapy with IV epoprostenol requires considerable time and emotional commitment by patients and their families; they must deal with the need for daily drug reconstitution.
care of a central venous catheter, and training to handle potential life-threatening situations if the delivery of the infusion is interrupted (eg, because of a pump malfunction or a clot in the catheter).

Treprostinil (Remodulin) was developed as a prostacyclin analog with antiplatelet and vasodilatory properties similar to those of epoprostenol and a more favorable safety profile.20,21 Treprostinil is approved by the Food and Drug Administration for PAH patients with New York Heart Association class II, III, or IV signs and symptoms. Continuous subcutaneous treprostinil can improve signs and symptoms of PAH associated with physical activity and prolong survival23-24; however, the treatment has marked limitations, including pain at the infusion site and localized skin reactions.22

Although treprostinil was originally developed to avoid the need for IV access, it has several characteristics that make it favorable for IV use, including stability at room temperature (alleviating the need for ice packs), a 4.5-hour half-life (imparting greater safety), and a 48-hour infusion interval (allowing for drug preparation every other day). On the basis of the bioequivalence of subcutaneous and IV treprostinil,25 the Food and Drug Administration approved IV treprostinil for continuous administration for PAH patients with New York Heart Association class II, III, and IV signs and symptoms in 2004 and further expanded the label in 2006 to include an indication for diminishing the rate of clinical deterioration in patients requiring transition from continuous IV epoprostenol to IV treprostinil.26

Pharmacology of Treprostinil

Treprostinil sodium is a tricyclic benzindene analog of prostacyclin. The major pharmacological actions of treprostinil are direct vasodilation of the pulmonary and systemic vascular beds and inhibition of platelet aggregation. The drug has no apparent inotropic effect, no intrinsic effect on the autonomic nervous system, and no marked effect on respiratory mechanics. A steady state occurs in approximately 10 hours. The elimination of treprostinil is biphasic; it has an elimination half-life of 4.5 hours and a distribution half-life of 40 minutes.

The majority of a treprostinil dose is metabolized in the liver before excretion; on average less than 5% of a treprostinil dose administered is excreted as unchanged drug in the urine. Treprostinil metabolites are predominantly excreted by the kidney. Therefore, in a patient with hepatic dysfunction, the initial treprostinil dose should be at least halved, and subsequent increments in treprostinil doses also should be reduced. Because renal excretion does not play an important role in the elimination of treprostinil, no adjustments in dose are recommended.

Treprostinil is supplied as a sterile solution in 20-mL multiuse vials in 4 strengths—1, 2.5, 5.0, and 10.0 mg/mL—and can be diluted with isotonic sodium chloride solution or sterile water. Treprostinil is chemically stable at room temperature and neutral pH. Once the seal is punctured, vials of treprostinil have a shelf life of approximately 30 days.26,27 Intravenous treprostinil is administered as a continuous infusion via a dedicated central venous catheter and a CADD-1 Legacy pump (SIMS Deltec, St Paul, Minn; Figure 2).28

The medication cassette should hold 100 mL of the reconstituted solution, which is typically 5 mL of treprostinil and 95 mL of sterile water or isotonic sodium chloride solution (depending on the weight of the patient and the desired dose). Ideally, the infusion rate should be 45 mL/d, ensuring a 48-hour infusion interval. The cost of treprostinil is comparable to that of epoprostenol.

Pharmacokinetics

In 51 subjects who received at least 24 hours of treprostinil administered subcutaneously and intravenously, the steady-state ratios of the geometric means (IV/subcutaneous) and 90% CIs for the area under the curve and maximal concentration were 93% (90%-96%) and 106% (99%-113%), respectively.27 Secondary pharmacokinetic assessments confirmed the comparability of the 2 routes of administration at
steady state and also indicated that the elimination half-life of treprostinil was 4.4 hours after IV administration and 4.6 hours after subcutaneous administration. On the basis of these findings, it was concluded that intravenously and subcutaneously administered treprostinil are bioequivalent at steady state.25

Clinical Findings

In a 12-week, prospective, uncontrolled, open-label multicenter trial,26,30 47 PAH patients with World Health Organization/New York Heart Association class II to class IV signs and symptoms were treated with IV treprostinil either as initial therapy for PAH (de novo) or as a transition therapy from IV epoprostenol to IV treprostinil (transition). The goal of therapy was improvement in de novo patients and maintenance of efficacy (functional capacity and signs and symptoms) in the transition patients.

Patients were assessed by using a 6-minute walk test, a modified Naughton-Balke treadmill test, and a right-sided heart catheterization at baseline and at 12 weeks after the start of therapy. Intravenous treprostinil appeared to improve exercise capacity, Borg dyspnea score, functional capacity, and hemodynamic status in de novo patients.29 In transition patients, exercise capacity, functional capacity, and the Borg dyspnea score remained stable after 12 weeks of therapy.30 The side effects were similar to those associated with other prostacyclins (eg, headache, jaw pain, leg pain, and diarrhea).29,30 Intravenous treprostinil appears to have an efficacy similar to that of IV epoprostenol and the distinct advantages of ease of use, convenience for patients, stability at room temperature, and potentially greater safety.

Nursing Considerations

As with any therapy for PAH, effective nursing management is critical for optimizing patients’ quality of life and outcome. Intravenous treprostinil therapy involves advanced clinical skills in evaluating the signs and symptoms of pulmonary hypertension, managing side effects, and caring for central venous catheters.

A team approach involving nurses, allied health professionals, case managers, physicians, the patient being treated, and the patient’s family members will lead to the best outcome. Patients are encouraged to seek care from a pulmonary hypertension center for the treatment of PAH and for the appropriate and safe use of specialized medications such as IV treprostinil.

When a patient receiving IV treprostinil arrives in the critical care unit, the bedside nurse has several priorities. First, the patient is assessed for vital signs, the overall stability of his or her condition, blood pressure, heart rate and rhythm, and oxygen saturation. Next, the patient’s infusion and central venous catheter should be evaluated for dose, rate of infusion, and concentration; any catheter complications should be resolved with the assistance of the pulmonary hypertension team or a pharmacist as soon as possible.

Intravenous infusion of treprostinil via a peripheral IV catheter is appropriate until a new central venous catheter can be placed. A back-up second peripheral IV catheter should be maintained at all times because treprostinil is incompatible with other medications, and the infusion should not be interrupted because of the potential risk of rebound pulmonary hypertension. Finally, the nurse should thoroughly assess the patient’s signs and symptoms of PAH and the level of the side effects.

Clinical Assessment

Any PAH patient beginning a new therapy should have a thorough baseline evaluation of the signs and symptoms of pulmonary hypertension.

The most common symptom is dyspnea on exertion. Patients should be asked about what daily activities elicit breathlessness, including questions about bathing and dressing, climbing inclines and stairs, and walking a specific distance on level ground. The clinician can determine if dyspnea occurs with mild exertion (minimal household chores), moderate exertion (climbing stairs), or at rest and the recovery time after dyspnea occurs. Determining the patient’s overall level of fatigue is also important. A patient who fatigues easily may have impaired cardiac output.

Palpitations may occur; patients often describe them as pounding, fluttering, racing, or skipping a beat. Assessment of frequency, duration, and exacerbating factors of palpitations at baseline is also important for future comparisons.

Chest discomfort should also be thoroughly evaluated. Patients may have intermittent episodes of substernal chest heaviness, pressure, tightness or even sharp pain, with or without exertion. Patients should be asked about the duration, frequency, exacerbating factors, and alleviating factors of such episodes. Chest pain in PAH patients is often attributable to right ventricular ischemia.
Dizziness or lightheadedness with or after exertion, known as presyncope, and actual syncope, or fainting, can be an indication of more advanced PAH and should be assessed by a physician urgently. Syncope occurs in PAH patients when the increase in pulmonary artery pressure impairs cardiac output. Similarly, the frequency, intensity, duration, and exacerbating factors of presyncope or syncope should be ascertained.

Peripheral edema should be evaluated for frequency and intensity. Patients may characterize the edema as mild, moderate, or severe and as pitting or nonpitting and should indicate the specific location (feet to ankles vs feet to knees vs feet to thighs). Weight gain associated with edema, meals, sodium and fluid intake, compliance with diuretic regimen, and increased activity level should be documented. Finally, abdominal distention or ascites should be assessed in terms of daily abdominal girth and associated and alleviating factors.

All these signs and symptoms together can be summarized as a World Health Organization classification of the functional status of patients with pulmonary hypertension (Table 1) modified from the New York Heart Association functional classification. Although this classification might be considered somewhat subjective, it clearly gives the PAH team a baseline for future dosing strategies and treatment decisions.

**Dosing Guidelines**

**De Novo Patients**

De novo patients should be admitted to the hospital and monitored via central telemetry. Two peripheral IV catheters should be placed, and treprostinil should be started at a rate of 2 to 4 ng/kg per minute. Vital signs should be recorded often (every 4-6 hours with dose escalation), with special attention given to blood pressure and heart rate. Patients should be taught to notify staff if they experience any increase in the signs or symptoms of pulmonary hypertension or have any side effects of the medication (Table 2). If tolerated, the dose of treprostinil is increased each day by 2 to 4 ng/kg per min; with these increases, patients should be receiving an approximate dose of 10 to 12 ng/kg per minute when they are discharged from the hospital.29

Patients are typically in the hospital 2 to 3 days for teaching, placement of a central venous catheter, and dose optimization. All dosing is individualized and is based on disease severity, signs and symptoms of pulmonary hypertension, and adverse experiences or side effects of the drug (Table 3).

**Transition Patients**

Transition patients should be admitted to the hospital, monitored via telemetry, and have 2 peripheral IV catheters placed. The transition from IV epoprostenol to IV treprostinil can be carried out in several different ways and is ultimately at the

<table>
<thead>
<tr>
<th>Class</th>
<th>Characteristics</th>
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<tbody>
<tr>
<td>I</td>
<td>No limitations of physical activity&lt;br&gt;No undue dyspnea or fatigue, chest pain, or near syncope with ordinary physical activity</td>
</tr>
<tr>
<td>II</td>
<td>Slight limitation of physical activity&lt;br&gt;Comfortable at rest&lt;br&gt;Undue dyspnea or fatigue, chest pain, or near syncope with ordinary physical activity</td>
</tr>
<tr>
<td>III</td>
<td>Marked limitation of physical activity&lt;br&gt;Comfortable at rest&lt;br&gt;Undue dyspnea or fatigue, chest pain, or near syncope with less than ordinary activity</td>
</tr>
<tr>
<td>IV</td>
<td>Inability to carry out any physical activity without signs or symptoms of pulmonary hypertension&lt;br&gt;Signs and symptoms of right ventricular failure&lt;br&gt;Dyspnea and/or fatigue even at rest&lt;br&gt;Increase in discomfort with any physical activity</td>
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</tbody>
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*Modified from the New York Heart Association functional classification.

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Remedies</th>
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<tbody>
<tr>
<td>Headache</td>
<td>Acetaminophen, ibuprofen</td>
</tr>
<tr>
<td>Jaw pain</td>
<td>Behavioral techniques</td>
</tr>
<tr>
<td>Nausea</td>
<td>Ondansetron</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Loperamide</td>
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<tr>
<td>Cutaneous flushing</td>
<td>Dose adjustment</td>
</tr>
<tr>
<td>Extremity pain</td>
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<tr>
<td>Systemic hypotension</td>
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discretion of the treating physician. For example, the IV dose of epoprostenol could be decreased by 10% each hour with simultaneous increases of 5% to 10% in the dose of treprostinil. The amount of IV treprostinil given is increased hourly to give a final dose equal to or greater than the original dose of epoprostenol. Alternatively, each hour the epoprostenol dose could be decreased by 2 ng/kg per minute and the treprostinil dose increased by 2 to 4 ng/kg per minute until the epoprostenol is discontinued and an optimal dose of IV treprostinil has been achieved.

During the transition period, any increase in the signs and symptoms of PAH should be treated with an increase in the dose of IV treprostinil. Any increase in side effects (headache, nausea, vomiting, flushing, leg or foot pain) that might be due to prostacyclin should be managed by reducing the dose of IV epoprostenol. The overall goal is for the dose of treprostinil at the time of discharge from the hospital to be 10% to 50% higher than the epoprostenol dose was at the time of admission; the target dose is the maximum tolerated dose of treprostinil

<table>
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*Dosing is individualized and is based on disease severity, signs and symptoms, adverse experiences or side effects, and the treating physician’s clinical expertise.

Each sign or symptom should be evaluated for frequency, duration, intensity, location, exacerbating and alleviating factors, and correlation with the increase in the dose of treprostinil. Patients should be instructed to characterize each sign and symptom as mild, moderate, or severe and as tolerable or intolerable. Most side effects can be managed. Patients should be encouraged to keep a diary or journal of treprostinil dose adjustments as well as side effects and signs and symptoms of PAH.

Each patient’s nursing plan of care should be individualized because of the marked variations between patients. Whereas some patients seem to experience a greater number of side effects early in the course of therapy and fewer later, other patients have minimal side effects at lower doses and more adverse effects later when the dose has been increased. No general rules apply to all patients. Each patient should be assessed at a determined interval (in our experience, weekly for new patients and monthly for existing patients), and the dosing plan should be revised with each assessment. Patients with no side effects or mild side effects can have their dose of treprostinil increased cautiously, and those with severe side effects (systemic hypotension or intractable pain) should be observed and possibly have their

Table 3 Dosing guidelines for intravenous treprostinil*

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Side Effects Assessment

In addition to monitoring for signs and symptoms of PAH, patients should have monitoring for side effects of treprostinil; each patient’s dosing schedule is based partly on the side effects he or she experiences. As in the management of any prostacyclin therapy, the dose of IV treprostinil should be increased to a tolerable, mild level of side effects to ensure maximum effect on pulmonary vasculature and optimization of the overall quality of life. Patients with advanced disease are an exception. They may require aggressive dosing with treatment of treprostinil-related side effects.

Table 2 lists the most common side effects associated with IV treprostinil. The cause of these side effects is unknown and therefore makes treatment challenging. Systemic hypotension may occur as well and can be treated by reducing the dose of treprostinil and/or administering a fluid bolus. Nurses should be assessing patients for potential systemic hypotension and be prepared to treat it accordingly.

A thorough medication history may reveal a concomitant medication that may be contributing to the hypotension and that could be adjusted accordingly.

Each sign or symptom should be evaluated for frequency, duration, intensity, location, exacerbating and alleviating factors, and correlation with the increase in the dose of treprostinil. Patients should be instructed to characterize each sign and symptom as mild, moderate, or severe and as tolerable or intolerable. Most side effects can be managed. Patients should be encouraged to keep a diary or journal of treprostinil dose adjustments as well as side effects and signs and symptoms of PAH.

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All Patients

After discharge, for both groups of patients, de novo and transition, the dose of treprostinil is increased each day an average of 1 ng/kg per minute as tolerated by the patient. These increases in dose can be accomplished with daily, biweekly, or less frequent increases so long as the increases are well tolerated. Again, the changes in dose are individualized and are based on the signs and symptoms of pulmonary hypertension and adverse experiences or side effects of the medication.
dose reduced until tolerability or resolution of the side effects occurs.

Management

Headaches are associated with the use of treprostinil. Some patients experience mild or moderate headaches with each increase in dose. Headaches can be managed with the usual remedies such as acetaminophen, ibuprofen, or, rarely, narcotic medications as the treating physician deems appropriate. Ibuprofen is generally avoided in patients taking oral anticoagulants.

Intermittent jaw discomfort, known as “first bite jaw pain” can occur with IV treprostinil and is less intense and less frequent than with IV epoprostenol. The usual remedies such as beginning a meal by chewing slowly, sipping something hot, or rubbing the cheeks during the first bite can lessen the severity. In general, jaw pain is not an indication for reducing the dose of treprostinil, and patients rarely require analgesia.

Nausea and overall anorexia may occur, although perhaps less frequently with IV treprostinil than with IV epoprostenol. Nausea markedly hinders quality of life, and adequate caloric intake is imperative in patients with pulmonary hypertension. Furthermore, vomiting can induce a vagally mediated pulmonary hypertensive event. Therefore, nausea or vomiting is often a rationale for decreasing the dose of treprostinil. If a patient seems prone to nausea with increases in dose, a gentler adjustment schedule should be considered and/or use of around-the-clock antiemetics when the dose is increased. Nonpharmacological methods to prevent nausea include avoiding large meals or large amounts of liquid intake, avoiding excessive intake of carbonated beverages, avoiding greasy and fatty foods, snacking on food high in carbohydrates such as crackers or dry toast, and sitting upright when eating.

Diarrhea or loose stools are common with IV treprostinil, just as with IV epoprostenol. Patients who have 4 or more loose stools per day are instructed to take over-the-counter loperamide (maximal daily dose 16 mg) as needed. If the diarrhea is significant, the dose of treprostinil may need to be temporarily reduced.

Leg and foot pain can occur, although the exact location and character may be somewhat different than that experienced by patients receiving IV epoprostenol. Some patients have this side effect when treatment with IV treprostinil is started, and others have foot pain withstanding when they are receiving higher doses later on. Dose reduction may be necessary to decrease the severity of the pain. The pain is similar to that associated with IV epoprostenol, and seems to respond inconsistently to analgesics and/or medication (eg, gabapentin) for neuropathic pain.

Cutaneous flushing can occur with IV treprostinil and is considered a mild tolerable side effect.

Nursing Guidelines

All nurses treating patients with IV treprostinil therapy should have access to an infection protocol for central venous catheters, for the prompt and appropriate treatment of site and tunnel infections. If there is any indication of a localized or systemic infection, samples from the central venous catheter and the catheter exit site should be cultured. Additionally, samples of peripheral blood should be cultured. Patients are taught standard central venous catheter care, as well as signs of infection. If a catheter is dislodged, becomes cracked or leaks, or is occluded, an emergency plan must be in place. Patients should be given a 24-hour emergency telephone number to call with questions and/or concerns and should be instructed to seek emergency care for further treatment as needed.

If a catheter becomes occluded or is dislodged, the IV treprostinil infusion can be administered through a peripheral IV catheter until a more permanent solution (new central venous catheter or a peripherally inserted central venous catheter) can be placed. An infusion of IV treprostinil should never be abruptly discontinued for any reason. Rebound signs and symptoms of PAH may occur and have been fatal in some patients receiving IV epoprostenol. Additionally, a central venous catheter with treprostinil in it should never be flushed until the medication has been removed with a syringe and discarded.

All PAH patients should be counseled on healthy life behaviors and risk factors that may be within their control. Behaviors include maintaining a balanced overall diet; maintaining an ideal body weight; maintaining a sodium-restricted diet; maintaining daily prescribed fluid intake; smoking cessation; maintaining a modest exercise and activity level; maintaining adequate sleep patterns; and managing any anxiety, stress or depression. Patients should be counseled that the use of any over-the-counter or herbal
medications should be discussed with a physician before the medications are used.

Throughout a PAH patient’s hospitalization, nursing education is a critical aspect of the patient’s medical regimen. The education should include a discussion of the disease state and the medications prescribed (including mechanism of action, dose, risks, potential side effects, benefits, alternatives). Education about treprostinil reconstitution, pump manipulation, and care of the central venous catheter should involve both the patient and the patient’s home caregivers (eg, significant other, spouse, or child). After discharge from the hospital, home nursing visits should be scheduled to assess the home environment for safety, cleanliness, and proximity to local medical care to avoid potential preventable complications of treatment.

Conclusion

Despite the complex nature of continuous IV treprostinil therapy and its delivery system, the therapy is safe and effective for the treatment of PAH. With the care and attention of an expert pulmonary hypertension nurse and team, patients with PAH can maintain a meaningful and productive life.

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References

Test ID: C0723  Form expires: April 1, 2009  Contact hours: 1.5  Fee: $11  Passing score: 11 correct (73%)  Category: A  Test writer: Ann S. Lystrup, RN, BSN, CEN, CCRN, CFRN

1. Pulmonary arterial hypertension (PAH) is characterized by what abnormality?
   a. Increased pulmonary capillary wedge pressure
   b. Hyperplasia of lung capillaries
   c. Vascular lesions in pulmonary arterioles
   d. Right ventricular hypertrophy

2. Conventional nonspecific therapy for PAH includes which of the following?
   a. Supplemental oxygen and adenosine
   b. Diuretics and digoxin
   c. Prostacyclin and oral calcium channel blockade
   d. Anticoagulation and nitric oxide

3. What is the half-life of treprostinil (Remodulin)?
   a. 3 to 6 minutes
   b. 30 to 60 minutes
   c. 4.5 hours
   d. 2.5 hours

4. The incidence of PAH is highest among patients with which other diagnosis?
   a. Mixed connective tissue disease
   b. Systemic lupus erythematosus
   c. Portal hypertension
   d. 2.5 hours

5. Treprostinil causes which of the following?
   a. Positive inotropic effect
   b. Decreased platelet count
   c. Depression of the autonomic nervous system
   d. Decreased systemic vascular resistance

6. Treprostinil is an analog of which of the following?
   a. Prostacyclin
   b. Endothelin-1
   c. Epoprostenol
   d. Thromboxane

7. The initial dose of treprostinil should be halved for a patient with which diagnosis?
   a. Renal failure
   b. Acute vaso-reactivity
   c. Thrombocytopenia
   d. Hepatic dysfunction

8. Side effects of prostacyclins include which of the following?
   a. Constipation
   b. Chest pain
   c. Dizziness
   d. Leg pain

9. Which of the following statements is true?
   a. Treprostinil has a 24-hour infusion interval and is administered every other day.
   b. Treprostinil may be administered via a peripheral intravenous (IV) catheter until a central catheter can be placed.
   c. Two significant drawbacks of treprostinil are its instability at neutral pH and ambient temperature and its short half-life.
   d. The majority of a treprostinil dose is excreted as unchanged drug in the urine.

10. The IV infusion of treprostinil should not be interrupted because of the risk of what complication?
    a. Pulmonary edema
    b. Rebound pulmonary hypertension
    c. Pulmonary embolus
    d. Clot formation in the catheter line

11. A patient with PAH who fatigues easily should be assessed for which of the following?
    a. Acute hemorrhage
    b. Pulmonary edema
    c. Impaired cardiac output
    d. Decrease in the dose of IV epoprostenol

12. What is the recommended treatment when increased signs and symptoms of PAH occur during the transition from IV epoprostenol to IV treprostinil?
    a. Increase in the dose of IV treprostinil
    b. Decrease in the dose of IV treprostinil
    c. Increase in the dose of IV epoprostenol
    d. Decrease in the dose of IV epoprostenol

13. Dosing of IV treprostinil will likely be aggressive and combined with treatment of treprostinil-related side effects for which group of patients?
    a. De novo patients
    b. Transition patients
    c. Patients with advanced PAH disease
    d. All patients

14. Management of which of the following side effects of IV treprostinil will most likely include a reduction in dose?
    a. Jaw pain
    b. Systemic hypotension
    c. Headache
    d. Nausea associated with anorexia

15. A central venous catheter with treprostinil should have the medication removed with a syringe and discarded before which of the following?
    a. Flushing of the catheter
    b. Catheter removal
    c. Collection of samples for culture
    d. Initiating each successive infusion of newly reconstituted medication

Test answers: Mark only one box for your answer to each question. You may photocopy this form.

1. 
   a. 1  b. 1  c. 1  d. 1

2. 
   a. 1  b. 1  c. 1  d. 1

3. 
   a. 1  b. 1  c. 1  d. 1

4. 
   a. 1  b. 1  c. 1  d. 1

5. 
   a. 1  b. 1  c. 1  d. 1

6. 
   a. 1  b. 1  c. 1  d. 1

7. 
   a. 1  b. 1  c. 1  d. 1

8. 
   a. 1  b. 1  c. 1  d. 1

9. 
   a. 1  b. 1  c. 1  d. 1

10. 
   a. 1  b. 1  c. 1  d. 1

11. 
   a. 1  b. 1  c. 1  d. 1

12. 
   a. 1  b. 1  c. 1  d. 1

13. 
   a. 1  b. 1  c. 1  d. 1

14. 
   a. 1  b. 1  c. 1  d. 1

15. 
   a. 1  b. 1  c. 1  d. 1

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Practical Aspects of Continuous Intravenous Treprostinil Therapy
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