CAREPATHrx™
Specialty Pharmacy & Infusion Solutions

INOTROPIC AGENT GUIDELINES

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I. POLICY

The following defines specific guidelines that will ensure the safe and effective use and administration of inotropic agents.

II. PROCEDURES

A. All patients referred for inotropic therapy shall meet the clinical admission criteria.

B. Nurses who have demonstrated competency in knowledge of inotropic agents may administer inotropic therapy

C. First dosing of inotropic agents in the home should be avoided due to the associated high risk and potential side effects. The decision to start a patient on inotropic therapy in the home will be determined on an individual basis and will be a joint determination between nursing and pharmacy management

D. Inotropic agents acceptable for home infusion include:

1. Milrinone (Primacor)
2. Dopamine (Intropin)
3. Dobutamine (Dobutrex)

E. Physician orders for inotropic agents will include:

1. Drug, dosage (including dosing weight), concentration.
2. Rate, and route of administration
3. Frequency of administration
4. Clinical monitoring and frequency, i.e., lab orders, weight etc.

5. Pre-defined parameters that require physician notification, i.e., blood pressure, pulse, weight fluctuations, noted changes in cardiopulmonary status, etc.; and
6. Overdose protocol and code status

F. The patient and caregiver should receive instructions regarding:

1. Management of potential side effects.
2. Care of central access device.
3. Use maintenance and troubleshooting of the infusion pump; and
4. Blood pressure and pulse monitoring

G. Documentation should include:

1. Clinical treatments and interventions.
2. Communications with other care team members; and
3. Patient response to therapy

III. PHARMACOLOGY

Dobutamine, Dopamine and Milrinone are positive inotropic agents used in the treatment of end-stage congestive heart failure when traditional regimes, (diet, medications such as digitalis, diuretics and/or vasodilators, and activity restrictions) have failed, resulting in cardiac decompensation. Dobutamine, Milrinone, and Dopamine are synthetic catecholamines which directly stimulate beta-1 receptors in the heart to increase myocardial contractility and stroke volume. Additionally, low dose infusions of dopamine have been used to increase urinary output. Dobutamine and Milrinone are inotropic agents most used for home infusion. The goal of therapy is to improve cardiac output without increasing the heart rate by more than 15 beats per minute, or the mean arterial pressure by more than 30%. Intermittent infusions of inotropic agents have also been used to stabilize patients awaiting cardiac transplantation.

A. Milrinone (Primacor) is a positive inotrope and vasodilator with phosphodiesterase inhibitor activity.

1. Pharmacology: Milrinone increases cellular calcium concentrations resulting in increased contractility. The drug's inotropic effect may cause vasodilation and reduced preload and afterload. Milrinone may also facilitate atrioventricular conduction.
   The drug is given by oral or intravenous routes.

2. Pharmacokinetics: Milrinone is rapidly absorbed following oral administration. The oral route has been associated with severe adverse reactions; therefore, the intravenous route is preferred.

   a. When given intravenously, the onset of action occurs within 2-5 minutes. Peak effects occur in 10 minutes. Duration of action is dose-related and is approximately 30 minutes to 2 hours.

   b. Milrinone is metabolized by the liver and primarily eliminated by the kidneys as metabolites and unchanged drug.

3. Indications: For short-term management of CHF for patients who have not responded adequately to digitalis, diuretics, or vasodilators. Duration of therapy depends on patient responsiveness.

4. Contraindications: Hypersensitivity to Milrinone, Amrinone or bisulfites.

5. Routes of Administration/Dosage:

    a. Adults:
        - Continuous intravenous infusion: 0.375-0.75 mcg/kg/min. based on response and side effects.
        - Intermittent maintenance infusion: 0.375-0.75 mcg/kg/min. infused 6-8 hours given 2-7 times per week. Slow or stop the infusion if extreme drops in blood pressure are noted.

    b. Pediatrics:
        - Safety and efficacy have not been established in children.
        - Some studies suggest improved cardiac function in children with severe CHF who received 0.75-1mcg/kg/min

6. Dosage adjustments may be required in patients with liver or kidney disease

7. Central venous access is recommended for Milrinone administration.

8. Incompatibilities:

    a. Furosemide: Do not inject Furosemide into IV lines containing Milrinone as immediate precipitate forms.

9. Adverse Effects/Complications:

    a. Hematologic
        - Thrombocytopenia is a drug-dependent reaction that occurs within 48-72 hours of initiating therapy. Nadir occurs within 1-4 weeks. This may be an idiosyncratic/ transient reaction since platelet levels return to baseline in some patients on long-term therapy.

    b. Cardiovascular:
        - Dose-related hypotension
        - Arrythmias: Usually occur with rapid infusion (1mg/min.) and typically resolve when the infusion rate is decreased.

    c. Gastrointestinal:
        - Nausea, vomiting, anorexia and abdominal pain may occur. Appears to be related to increased gastric acid secretion and intestinal motility. If severe GI effects occur, consider a dosage reduction.

    d. Hepatotoxicity:
        - Marked elevations in liver function tests may suggest an idiosyncratic hypersensitivity reaction (eosinophilia) and the therapy should be discontinued. If less marked elevations occur without any other symptoms, evaluate on a case-by-case basis.

    e. Hypersensitivity:

- These reactions may be caused by either the bisulfate content on the Milrinone preparation or by the Milrinone itself. Symptoms may include: pericarditis, pleuritis, ascites, vasculitis, hypoxemia, myositis and jaundice

10. Monitoring: (Refer to general inotropic monitoring recommendations in Section D.)

    a. Baseline:
    b. Serum creatinine
    c. Liver function tests
    d. CBC and electrolyte panel
    e. I/O's, including weight
    f. EKG
    g. Blood pressure, and apical heart rate and rhythm should be taken prior to and every 15 minutes for the first half hour, then every 30 minutes for the next 3 hours and hourly until the infusion is completed, unless otherwise ordered by the physician

11. Ongoing Monitoring:

    a. Platelets count daily or every other day during the first week of therapy and weekly for the first four weeks.
    b. Liver function tests every week for the first 2 weeks if on prolonged therapy or high dose therapy.
    c. Serum creatinine every 2 weeks or per MD
    d. I/O's
    e. Electrolytes, especially potassium; and
    f. Daily weights

B. Dopamine (Intropin, DuPont 40 mg/ml, 80 mg/ml, 160 mg/ml)

1. Classification: Positive inotrope and vasopressor

2. Pharmacology: Dopamine exerts a positive inotropic effect due to the direct action on the beta-1 cardiac receptors and indirectly by releasing norepinephrine from storage sites. The drug also acts on specific dopaminergic receptors resulting n renal and mesenteric vasodilation or vasoconstriction. Dopamine's effects are dose dependent. Additionally, dopamine may facilitate atrioventricular conduction.

3. Pharmacokinetics: Dopamine is administered intravenously, and its onset of action occurs within 5 minutes of administration. The duration of action is less than 10 minutes.

    a. Dopamine is metabolized in the liver, kidneys and plasma to largely inactive compounds. Approximately 80% of the dose is excreted in the urine within 24 hours, primarily as metabolites.

4. Indications: Correction of hemodynamic imbalances present in the shock syndrome due to myocardial infarction, trauma, open heart surgery, renal failure and in chronic cardiac decompensation as in refractory congestive failure.
5. Contraindications: Pheochromocytoma, uncorrected tachyarrhythmias or ventricular fibrillation.

6. Routes of Administration/Dosage:

NOTE: Dopamine is administered intravenously. The effects of dopamine are dose dependent. Low doses (0.5-2 mg/kg/min.) cause renal and mesenteric vasodilation. Low to moderate doses (2-10 mcg/kg/min.) produce an inotropic effect. Doses exceeding 10 mcg/kg/min. cause renal vasoconstriction, increased peripheral resistance and increased blood pressure.

a. Adults:
   - Continuous intravenous infusion for congestive heart failure (CHF): .5-2 mcg/kg/min. up to 10 mcg/kg/min. titrated according to desired patient response.
   - Intravenous infusion for increasing renal output: 1-5 mcg/kg/min. titrated according to urine output and used in conjunction with appropriate diuretics.

b. Pediatrics:
   - Safety and efficacy have not been established in children.
   - Some studies have shown improved cardiac functions in children who have low output state at doses of 1-10 mcg/kg/min.

7. Central venous access is recommended for dopamine administration. Monitor all sites closely for extravasation because of the potential risk of necrosis and gangrene.

8. Incompatibilities: Do not add Dopamine to alkaline solutions such as sodium bicarbonate, oxidizing agents or iron salts since the drug is inactivated in alkaline solutions and resultant admixtures will turn pink to violet in color.

9. Adverse Effects/Complications:

a. Cardiovascular:
   - Ectopic heart beats (conduction abnormalities)
   - Tachycardia
   - Bradycardia (less frequently noted)
   - Anginal pain
   - Palpitation
   - Hypotension
   - Vasoconstriction
   - Ventricular Arrhythmias (at high doses); and
   - Hypertension

b. Respiratory:
   - Dyspnea

c. Gastrointestinal:
   - Nausea, vomiting

d. EENT:
   - Dilated pupils (at high doses)

e. CNS:
   - Headache
   - Anxiety

f. Genitourinary:
   - Decreased urinary output. Hypovolemia can occur and volume replacement may be needed during or post dopamine infusion due to the drug's effect on urine flow.

g. Other:
   - Gangrene due to vasoconstrictive properties. Gangrene can occur when high doses of dopamine are administered peripherally for extended periods of time or in patients receiving low doses of dopamine for occlusive vascular disease.
   - Less frequently noted side effects include azotemia, and piloerection.

NOTE: If extravasation of Dopamine occurs, the site should promptly be flushed (per physician's order) with 10-15 ml of normal saline containing 5-10 mg of phentolamine. Extravasation of dopamine is characterized by coldness, hardness and pallid appearance.

10. Drug Interactions:

a. Drugs that may increase the risk of developing arrhythmias are levodopa and digitalis glycosides.

b. MAO inhibitors: these agents may prolong and intensify the vasopressor and cardiac effects of dopamine, which may result in hypertensive crisis.

c. Drugs which can potentiate the cardiovascular effects of dopamine and thus can result in tachycardia, arrhythmias and severe hypertension are:
   - Ergotamine (and methylergonovine);
   - Guanadrel
   - Guanethidine
   - Maprotiline
   - Methyldopa
   - Methylphenidate
   - Tricyclic antidepressants

d. Concurrent use of intravenous phenytoin with dopamine can cause sudden hypotension and bradycardia. These interactions are dose and rate dependent.

e. Diuretics administered concurrently with low doses of dopamine increase the diuretic effect thus leading to electrolyte abnormalities.

f. Beta blocking agents may cause an inhibition of dopamine's cardiac effects.

g. Ergotamine may produce peripheral vascular ischemia and gangrene

C. Dobutamine (Dobutrex, Eli Lilly, 12.5 mg/ml. 20 ml vial)

1. Classification: Positive inotrope

2. Pharmacology: Dobutamine directly stimulates the heart's beta-1 receptors to increase myocardial contractility and stroke volume, resulting in increased cardiac output. Dobutamine exerts no effect on the dopaminergic receptors, thus, the drug does not cause renal or mesenteric

vasoconstriction. Usually, increases in heart rate do not occur, but excessive doses of Dobutamine will exert a positive chronotropic effect. Dobutamine can facilitate atrioventricular conduction.

3. Pharmacokinetics: Dobutamine is administered via the intravenous route with an onset of action within 2 minutes of administration. Peak drug effects occur within 10 minutes and the drug's duration of action is only a few minutes.

    a. Dobutamine is metabolized in the liver and eliminated primarily by the kidneys as various metabolites.

4. Indications: Inotropic support in the short-term management of adults with cardiac decompensation due to depressed contractility, resulting either from organic heart disease or from cardiac surgical procedures.

5. Contraindications: Idiopathic hypertrophic subaortic stenosis (IHSS). Patients hypersensitive to Dobutamine.

6. Routes of Administration/Dosage:

    a. Continuous infusion is not recommended because tolerance may develop to Dobutamine's hemodynamic effects within 48-72 hours of continuous drug infusion.

    b. Adults:
        - Intermittent infusion of 2.5-15 mcg/kg/min usually given over 48 hours once or twice a week, or less often. The rate of drug administration depends on individual patient response and side effects.

    c. Pediatrics:
        - Safety and efficacy have not been established in children
        - Dobutamine doses of 1-15 mcg/kg/min have been utilized to improve cardiac output post cardiac surgery as well as during cardiac catheterizations.

    d. Central venous access is recommended for Dobutamine administration.

7. Incompatibilities:

    a. Dobutamine is incompatible with alkaline solutions. Do not mix with sodium bicarbonate. Do not use Dobutamine in conjunction with other agents/diluents containing Sodium Bisulfite and Ethanol. Dobutamine is also physically incompatible with Hydrocortisone Sodium Succinate, Cefazolin, Cefamandole, Neutral Cephalothin, Penicillin, Sodium Ethacrynate, Sodium Heparin.

8. Adverse Effects/Complications:

    a. Cardiovascular:
        - Increased systolic blood pressure of 10-20 mm Hg occurs in most patients and is dose related. Some patients may have an increase of 50 mm Hg or more. If this occurs, reduce dosage and/or stop the infusion.

- Increased heart rate of 5-15 beats per minute (bpm) occurs in most patients. Some patients may experience increases of 30 or more bpm. If this occurs, reduce dosage and/or stop the infusion.
- Chest pain; and
- Increased number of premature ventricular beats

b. Respiratory:
- Dyspnea

c. Gastrointestinal
- Nausea, vomiting

d. CNS:
- Headache
- Tingling sensations
- Paresthesia

e. Other:
- Phlebitis
- Local inflammation after infiltration
- Leg cramps

9. Drug Interactions:

a. Beta blocking agents: Recent or concomitant use of beta blocking agents may antagonize the inotropic effects of dobutamine.

b. Furazolidone, methyldopa, rauwolfia alkaloids: May prolong the pharmacologic action of Dobutamine. Hypertension may result

c. Guanethide: May increase pressor response.

d. Halogenated hydrocarbon anesthetics: May increase risk of arrhythmias be sensitizing cardiac tissue to sympathomimetic agents.

e. Tricyclic antidepressants: May potentiate effect of Dobutamine; use combination with caution.

IV. NURSING CONSIDERATIONS

Once accepted for home care, the patient should be visited and assessed twice weekly for the first 1-2 weeks; weekly for the next 4 weeks; and then every 2 weeks thereafter. More frequent visits may be required and scheduled at the discretion of the home care nurse or the physician. In addition, arrangements should be made with the patient to call daily, at a specified time to report blood pressure, pulse, weight, intake and output, and any shortness of breath.

Each visit and pre and post infusion assessment should include, at a minimum:

1. Cardiopulmonary status:

a. Blood pressure: Notify physician of systolic BP decreases more than 10 mm Hg from baseline.

b. Apical pulse: Notify physician of pulse increases more than 10-15 beats per minute or if different in rhythm and/or quality from baseline.

c. Respiratory rate: Notify physician of an increase of more than 10 breaths/minute or if shortness of breath increases from baseline or if rales are present.

d. Weight: Notify physician of weight gain of more than 2 lbs. In 24 hours, or 4 lbs. In a week from baseline.

e. Intake and Output: Notify physician of any deviation from normal urinary output.

f. Edema and/or jugular vein dilation: Notify physician of changes.

g. Level of Consciousness: Notify physician of any changes in sensory.

2. Review of systems per company protocol.

3. Status of venous access site.

4. Patient understanding and compliance with treatment plan of care.

IV. DRUG ADMINISTRATION

A. Follow company protocols for specific venous access device care.

B. Dobutamine is not compatible with heparin. Flush with normal saline before initiating infusion to clear the access device of heparin.

C. To prevent administering a bolus injection of Dobutamine when discontinuing the infusion, aspirate a minimum of 5 cc of blood from the venous access device prior to flushing with normal saline and heparin.

D. Draw lab specimens per physician's order. Include potassium, sodium, BUN and Creatinine, or Chem Profile 20

E. A back up infusion pump will be dispensed for all patients on continuous inotrope infusion.

V. PATIENT TEACHING

A. Signs and symptoms of pulmonary congestion secondary to decreased cardiac output that require notification of the physician:

1. Increasing shortness of breath
2. Edema
3. Productive cough

4. Decreased urinary output
5. Fluttering of palpitations of the heart.
6. Cold extremities
7. Diaphoresis

B. Signs and symptoms of Dobutamine overdose requiring immediate notification of the physician. (If unable to reach physician, call 911).

1. Tachycardia
2. Increased dryness of skin and mucous membranes
3. Dizziness or faintness
4. Decreased blood pressure

C. Patients should observe for bruising and bleeding, thrombocytopenia and notify the physician if this occurs.

D. Central venous access device care per company protocol.

E. Operation, maintenance, and troubleshooting of infusion pump.