

Nesiritide Use for Decompensated Heart Failure

Background

B-type natriuretic peptide (BNP) is a naturally occurring cardiac neurohormone secreted from membrane granules in the cardiac ventricles as a response to ventricular volume expansion and pressure overload. The natriuretic peptide system allows the heart to participate in the regulation of vascular tone and extracellular volume status. The natriuretic peptide system and the renin angiotensin system counteract each other in arterial pressure regulation. Levels of BNP are elevated in heart failure.

Nesiritide is human BNP produced by recombinant DNA technology. Nesiritide produces dose-dependent balanced arterial and venous vasodilatation and has been shown to result in rapid reduction in ventricular filling pressures and reversal of heart failure symptoms such as dyspnea. Nesiritide also reduces levels of deleterious neurohormones such as aldosterone and endothelin. The use of nesiritide in addition to standard decompensated heart failure care, such as diuretic therapy, has been demonstrated to lead to meaningful clinical benefits in acutely decompensated heart failure patients. Nesiritide is an attractive therapeutic option because of its more rapid and sustained hemodynamic profile with less adverse effects than alternative heart failure treatments such as nitroglycerine, dobutamine, or milrinone.

Indications

Nesiritide is indicated for the intravenous treatment of patients with acutely decompensated congestive heart failure who have dyspnea at rest or with minimal exertion. In these patients, the use of nesiritide is expected to reduce pulmonary capillary wedge pressure and improve dyspnea with fewer side effects than other intravenous agents (i.e. dobutamine, milrinone, nitroglycerine, nitroprusside).

Patient Selection

Nesiritide should be considered for the volume overloaded acutely decompensated CHF patient with adequate blood pressures. It should be used in addition to IV diuretics and before initiating other intravenous therapies. Patient specifics include:

Dyspnea at rest or minimal exertion due to congestive heart failure
Systolic blood pressure ≥ 90 mmHg or ≥ 80 mmHg with SVR ≥ 1500 dyne-sec-cm⁻⁵
Patient hospitalized for acute decompensated congestive heart failure
Patient requires intravenous therapy
Elevated ventricular filling pressure (≥ 20 mmHg if pulmonary artery catheter in place or by clinical estimate)

Patient Exclusions

Patients in cardiogenic or other forms of shock
Patients with systolic blood pressure < 90 mmHg without PAC or < 80 mmHg with PAC.
Patients with low cardiac index ≤ 2.0 L-min-m² with normal or low SVR ≤ 1200 dyne-sec-cm⁻⁵
Patients with low ventricular filling pressures (PCW ≤ 12 mmHg)

Dosage/Administration

Reconstitution

1. Add 5 mL diluent from pre-filled 250 mL plastic IV bag to 1.5 mg vial of nesiritide. (Recommended preservative-free diluent 5% Dextrose Injection [D5W], USP.)

2. **Do not shake the vial.** Rock vial gently so that all surfaces, including the stopper, contact the diluent. Use only clear, essentially colorless solution. The constitution concentration achieved is 1.5 mg/5mL = 0.3 mg/mL or 300 mcg/mL.

Preparation for Infusion

Take the reconstituted 5 mL and add to a 250 mL bag of the recommended diluent to yield a final concentration of 6 mcg/mL. Invert the bag several times to ensure complete mixing of the solution.

Nesiritide should be administered through either a peripheral IV or centrally placed non-heparin coated catheter. Prime the IV tubing with an infusion of 25mL prior to connecting to the patient's vascular access port.

Initiation

The recommended bolus dose for nesiritide is 2 mcg/kg. The bolus dose should be administered over 60 seconds. NOTE: The bolus should be drawn from the diluted 250 mL bag and **NEVER** from the reconstituted vial.

Maintenance Infusion

After completion of bolus infusion begin maintenance infusion of 0.01 mcg/kg/min immediately.

Titration

Nesiritide infusion should be continued until the patient is compensated, usually within 24 to 48 hours. Those patients who worsen or are not symptomatically improved at 48 hours should be considered for invasive hemodynamic monitoring.

Up titration of nesiritide is generally not required. If the patient has a pulmonary artery catheter in place and titration is hemodynamically indicated, this should be done at increments of 0.005 mcg/kg/min up to a maximum dose of 0.03 mcg/kg/min. Titration of the maintenance infusion should be preceded by a re-bolus of 1 mcg/kg/min. Each dose increment should be made only after at least one hour of observation at the prior dose. For patients without a PAC titration is generally not required, but should be made only after at least three hours of observations at the prior dose.

Monitoring

Blood Pressure

Baseline systolic blood pressure ≥ 90 mmHg or ≥ 80 mmHg if PAC in place and SVR ≥ 1500

Check blood pressure after initiating infusion or for change in dose:

- Every 30 minutes for first hour
- Every hour for the next 3 hours
- Every 4 hours thereafter

Notify physician if patient develops symptomatic hypotension or SBP ≤ 80 mmHg.

Urine Output

Strict input and output should be documented. If urine output is < 50 cc/hr in the first four hours after the initiation of nesiritide, notify physician.

Weight

Daily weights should be obtained and recorded.

Symptoms

Improvement of dyspnea is expected. If respiratory rate or dyspnea do not change or worsen during the course of nesiritide therapy, notify physician.

BNP levels

In patients where it is not clear what the ventricular filling pressure status is, consider obtaining a BNP level. BNP levels measured during Nesiritide infusion are not clinically meaningful as exogenous BNP and endogenous BNP are indistinguishable. It is recommended that BNP levels be obtained prior to hospital discharge.

Concomitant Drug Therapy

Nesiritide should be administered while maximizing standard heart failure medical therapy. ACE inhibitors and/or beta blockers can be initiated, continued, or dose adjusted during nesiritide infusions. Nesiritide is not a substitute for intravenous diuretics and diuretic therapy should continue to be administered and adjusted while patients are receiving nesiritide. However, reduced doses of diuretics are expected once nesiritide infusion is initiated. Nesiritide, in general, should not be administered with concomitant intravenous nitroglycerine or nitroprusside, but can be given in addition to dopamine, dobutamine, or milrinone. BP should be monitored closely if co-infusing with Nesiritide

Restrictions

Units:

Intensive Care Units

Cardiac Observation Unit

Emergency Medical Center (Room 10)

Physicians:

Cardiologists

Pulmonary and Critical Care Medicine

Emergency Medicine Physicians

Cost Comparison of IV Agents Used for Acutely Decompensated Heart Failure

Drug	Average Dose	ADULT Dose/Day (based on 70kg)	Drug Cost per Day
Nitroprusside (50mg/vial)	1 mcg/kg/min	100 mg/day	\$ 2
Nitroglycerin premix (100mg/250ml)	75 mcg/min	108 mg/day	\$ 8
Dobutamine (premix 500mg/250ml bag)	10 mcg/kg/min	1008 mg/day	\$ 13
Milrinone (20mg/vial)	50 mcg/kg bolus; 0.5 mcg/kg/min	53,900 mcg/day (=53.9 mg)	\$ 335
Nesiritide (1.5mg/vial)	2 mcg/kg bolus; 0.01 mcg/kg/min	1200 mcg/day (=1.2mg)	\$ 370

Total medical costs are significantly impacted by location of care and length of stay. For example, administration of nitroprusside in the CCU which requires PAC guidance would be expected to cost at least \$1500 more than administration of nesiritide on the COU without a PAC. Reductions in length of stay by ≥ 0.5 days and/or avoidance of serious adverse events with nesiritide would be expected to offset increased medication costs.

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