Nesiritide: Practical Guide to Its Safe and Effective Use

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The therapeutic goals for patients hospitalized with acute decompensated heart failure are to reverse acute hemodynamic abnormalities, relieve symptoms, and provide the ability to initiate early treatment, which will decrease disease progression and improve long-term survival. The use of nesiritide on top of standard care, such as diuretic therapy, has been proven to lead to meaningful clinical benefits in a broad range of 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 or dobutamine. The use of nesiritide represents an entirely new treatment approach to reverse acutely decompensated heart failure and to facilitate optimization of the heart failure medical regimen. [Rev Cardiovasc Med. *2(suppl 2):S32–S35*]

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Nesiritide possesses many of the characteristics of an ideal agent for treating acute decompensated heart failure (Table 1).[1,2] Nesiritide causes a balanced arterial and venous vasodilatation that has been shown to result in rapid reduction in ventricular filling pressure and reversal of heart failure symptoms, such as dyspnea.[2] Nesiritide also reduces levels of deleterious neurohormones (eg, aldosterone and endothelin-1). These beneficial effects are achieved with less adverse events than with such treatments as nitroglycerine or dobutamine. Nesiritide has been demonstrated to be safe and effective in the treatment of a broad range of patients with acute decompensated heart failure when added to standard care. This article will discuss the recom-

Table 1
Clinical Profile of Nesiritide

- Vasodilation (venous > arterial)
- Rapidly improves symptoms of congestion
- Does not increase heart rate (decreases myocardial oxygen demand)
- Is not proarrhythmic
- Neurohormonal suppression (decreases aldosterone, endothelin-1)
- Mild diuresis/natriuresis
- No evidence of tachyphylaxis
- Symptomatic hypotension as low as 4% in the VMAC study
- Dosing convenience (bolus plus standard-dose IV infusion)

mended use of nesiritide for acute decompensated heart failure, based on the key clinical trials.

Patient Profile

Potential nesiritide patients are those hospitalized with acute decompensated heart failure, including patients with systolic or diastolic dysfunction, renal insufficiency, arrhythmias, and those presenting with acute coronary syndromes. Based on the body of clinical work with nesiritide in heart failure, patients expected to derive clinical benefits would be those with signs and/or symptoms of congestion in the absence of cardiogenic shock or systemic hypotension (systolic blood pressure < 80–85 mm Hg). The Vasodilation in the Management of Acute Congestive Heart Failure (VMAC) study demonstrated that nesiritide added to standard care significantly reduced ventricular filling pressure to a greater extent than standard care plus placebo or standard care plus nitroglycerine in this board patient population. The VMAC study population is reflective of the types of patients commonly seen in clinical practice.[3]

Nesiritide may be initiated in patients who have not readily responded to an initial course of intravenous loop diuretics. Also, nesiritide may be started simultaneously with diuretic therapy at the time of initial presentation in patients unlikely to respond to diuretics alone. Nesiritide may be administered in conjunction with dopamine or inotropic agents, such as dobutamine, if the use of those agents is otherwise indicated. Nesiritide has been shown to be safely administered in monitored settings, such as telemetry or step down units, and does not require intensive care unit monitoring. Proarrhythmic effects were not seen, and there is evidence of a much lower rate of ventricular arrhythmias with nesiritide treatment as compared to treatment with inotropic agents, such as dobutamine.[4]

Dosing and Duration of Use

Table 2 summarizes the recommended use of nesiritide. It is recommended that nesiritide be administered as a bolus dose of 2 μg/kg followed by a continuous infusion at a dose of 0.01 μg/kg/min. Patients requiring a greater hemodynamic effect may receive an increased infusion rate at increments of 0.005 μg/kg/min up to 0.03 μg/kg/min; however, titration is recommended only after a 3-hour period of close clinical or hemodynamic monitoring at each infusion dose. Nesiritide has been shown to rapidly (within 15 minutes) lower ventricular filling pressures and reduce heart failure symptoms.[3] These beneficial hemodynamic effects may be maintained over the duration of active infusion. Tachyphylaxis to nesiritide has not been described. Dosing and duration of use may be guided by clinical assessment alone or clinical assessment along with right heart catheterization. The adverse effects seen with the recommended dosing of nesiritide are usually mild and readily reversible. Symptomatic hypotension, as evidenced in the comparative trial VMAC, was seen in only 4% of nesiritide-treated patients as compared to 5% treated with nitroglycerine.[3] The dose-limiting side effect of nesiritide is hypotension. With a half-life of 15 to 20 minutes, nesiritide should not be titrated at frequent intervals as is done with other intravenous agents that have a shorter half-life.

Concomitant Use of Other Medications

Heart failure patients should continue to receive diuretic therapy (intravenous or oral) in conjunction with nesiritide until the symptoms and signs of congestion have resolved. Patient's concomitant heart failure medications, including diuretics, angiotensin-converting enzyme (ACE) inhibitors, β-blockers, spironolactone, or digoxin may be continued and dose adjusted as clinically indicated. Once the patient is compensated and free of congestion, nesiritide can be discontinued (no taper is usually necessary). With the addition of nesiritide, the reversal

Table 2
Recommended Use of Nesiritide

- Use in patients with acute decompesated heart failure without cardiogenic shock or systemic hypoperfusion.
- Nesiritide should be administered with an initial bolus dose (2 μg/kg) followed by a continuous infusion at a dose of 0.01 μg/kg/min.
- Patients requiring a greater hemodynamic effect after 3 hours of monitoring may receive an increased infusion rate of nesiritide at 0.005 μg/kg/min increments up to 0.03 μg/kg/min.
- Use nesiritide in conjunction with intravenous diuretics. May continue ACE inhibitor and/or β-blocker therapy. May use dopamine or inotropic agent if indicated.
- Once the patient is compensated and free of congestion, discontinue nesiritide.
- Optimize survival enhancing oral medications (ACE inhibitors, β-blockers, spironolactone).
- Optimize patient education and heart failure disease management.

of an acutely decompensated state can usually be achieved over 1 to 3 days of hospitalization. After reversal of decompensation, comprehensive neurohumoral blockade with ACE inhibitors, β-blockers, and aldosterone antagonists can then be initiated or the dose adjusted to further reduce disability, hospitalizations, and death from heart failure. Nonpharmacologic therapy should also be optimized and patient education provided prior to hospital discharge. By facilitating the rapid reversal of decompensation through the use of nesiritide in the initial management of the hospitalized patient, earlier administration of other beneficial heart failure therapies, such as β-blockers, may occur, whereas typically contraindicated in a decompensated state.

Impact on Length of Critical Care and Rehospitalization

Rapid reversal of the decompensated state may also allow for shorter duration of intravenous therapy and potentially impact length of intensive care unit stay. In a study of 262 patients with decompensated heart failure, comparing patients treated with one of two doses of nesiritide (0.015 μg/kg/min and 0.03 μg/kg/min) or dobutamine added to standard care, the duration required for continued infusion of nesiritide therapy was significantly shorter.[5] The duration of study drug averaged 88 hours in the dobutamine group versus 51 hours ($P < .05$) in the nesiritide 0.015 μg/kg/min group and 44 hours ($P < .05$) in the nesiritide 0.030 μg/kg/min group. Similar differences occurred in the groups when measuring duration of treatment with all intravenous vasoactive drugs. The duration of treatment for the dobutamine group was 90 hours compared to 65 hours ($P < .05$) for the two nesiritide dose groups. With such results, it may be anticipated that treatment with nesiritide would lead to a reduced length of stay in the critical care unit.

More rapid and complete reduction in elevated filling pressures may reduce the risk of recurrent decompensation and rehospitalization. In the same study above, fewer nesiritide patients were readmitted for all causes, as well as for heart failure. During the 21-day follow-up period, there was a 20% rate for all readmissions in the dobutamine group versus 8% ($P < .05$) and 11% in the nesiritide 0.015 μg/kg/min

Main Points

- Potential nesiritide patients are those hospitalized with acute decompensated heart failure, including patients with systolic or diastolic dysfunction, renal insufficiency, arrhythmias, and those presenting with acute coronary syndromes.
- It is recommended that nesiritide be administered as a bolus dose of 2 μg/kg followed by a continuous infusion at a dose of 0.01 μg/kg/min.
- Patient's concomitant heart failure medications, including diuretics, angiotensin-converting enzyme (ACE) inhibitors, β-blockers, spironolactone, or digoxin may be continued in conjunction with nesiritide and dose adjusted as clinically indicated.
- Study results indicate that treatment with nesiritide could lead to a reduced length of stay in the critical care unit, decreased recurrence of decompensation, and less likelihood of rehospitalization.

and 0.030 μg/kg/min groups, respectively.[5] When combined with a comprehensive heart failure disease management program, the strategy of using intravenous vasodilators to normalize ventricular filling pressure and oral heart failure medications to maintain these effects has been associated with an 85% reduction in hospitalization and has been proven to improve functional capacity as compared to conventional heart failure management.[6]

The favorable hemodynamic effects and rapid onset of action make nesiritide an attractive agent to consider for use in varied settings. The use of nesiritide in the urgent care setting is being actively investigated in the Prospective Randomized Outcomes Study of Acutely Decompensated CHF Treated Initially in Outpatients with Natrecor (PROACTION) trial. This trial will evaluate the whether a 12-hour infusion of nesiritide versus placebo infusion added to standard care in the urgent care observation unit can reduce the rate of hospitalization and rehospitalization for heart failure. Other uses such as outpatient infusions are likely to be the subject of prospective clinical trials.

Summary

In conclusion, nesiritide has been demonstrated to lead to sustained clinical benefits in a broad range of acute decompensated heart failure patients when added to standard treatment regimens. Nesiritide offers the clinical benefits of a more rapid and sustained hemodynamic effect with less adverse effects than alternative heart failure treatments, such as nitroglycerine or dobutamine. The use of nesiritide represents an entirely new treatment approach to reversing acutely decompensated heart failure and to facilitating optimization of the heart failure medical regimen. ■

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