Nesiritide (Natrecor®) Position Statement
12/2003

BACKGROUND

Traditionally, strategies to manage acute heart failure have focused on ways to improve symptoms and control hemodynamic parameters (i.e. ionotropes and diuretics). However, this approach does not necessarily address the neurohormonal factors that contribute to the development of the disease. Recently, the Food and Drug Administration approved Natrecor® (nesiritide) for the management of acute decompensated heart failure. Natrecor® (nesiritide) – a synthetic form of human brain natriuretic peptide (BNP) – is a novel intravenous vasodilator that opposes the deleterious effects of the renin-angiotensin-aldosterone and adrenergic systems.

Atrial natriuetic peptide (ANP) and brain natriuetic peptides are hormones secreted from the atria and ventricles of the heart in response to increased ventricular filling pressures and wall stress. At the cellular level, BNP increases levels of the second messenger cyclic guanosine 3'5'- monophosphate (cGMP), which leads to vasodilation (both arteries and veins), diuresis, natriuresis, and suppression of the renin-angiotensin-aldosterone and adrenergic systems.

DESCRIPTION

Natrecor® (nesiritide) is a synthetic analogue of brain natriuretic peptide produced in *E. Coli* by recombinant DNA technology. As expected, Natrecor® mimics the effects of naturally occurring BNP.

INDICATION

Natrecor® is indicated for the treatment of acutely decompensated heart failure in patients who have dyspnea at rest or with minimal activity.

CONTRAINDICATIONS / WARNINGS / ADVERSE EFFECTS

Natrecor® should not be used as therapy for cardiogenic shock or in patients with a systolic blood pressure (SBP) < 90mm Hg. Patients with low cardiac filling pressures or in whom vasodilators are contraindicated should not receive Natrecor®. This includes patients with pericardial tamponade, constrictive pericarditis, restrictive or obstructive cardiomyopathy, significant valvular stenosis or other conditions in which cardiac output depends on venous return.

The most common adverse event associated with Natrecor® therapy is hypotension. Approximately 11% of patients who receive Natrecor® will experience hypotension. Furthermore, hypotension is most often asymptomatic; therefore **Natrecor® should be limited to the intensive care and telemetry setting where 24-hour monitoring is possible.**

ROLE IN TREATMENT

Natrecor® therapy should be reserved for patients with decompensated heart failure who are not responding to intravenous diuretic therapy or those with baseline renal dysfunction (serum creatinine $\geq$ 2 mg/dL). An adequate response to intravenous diuretics is defined as urine output $\geq$ 400 mL and improvement in symptoms after 2 hours. Diuretic resistance should be suspected in patients on high-doses of furosemide (>160 mg orally/day) who fail to respond to therapy despite compliance. Those with renal dysfunction are also predisposed to diuretic resistance, and often require high doses of furosemide. Strategies to manage patients with diuretic resistance include high dose bolus therapy (max bolus dose 160 mg furosemide), initiation of a continuous infusion after a bolus loading dose, and addition of another diuretic. These strategies should be employed prior to the initiation of Natrecor®. Patients in whom diuretic resistance is not suspected should receive an initial bolus of furosemide, followed by a second bolus at least 2 hours later, before initiation of Natrecor®.

Conclusions: Natrecor® should be reserved for patients with decompensated heart failure who are diuretic resistant or those with baseline renal dysfunction.

References

1. Natrecor® (nesiritide) Package insert, Scios 2001.
2. Zineh I, Schofield RS, Johnson J. The evolving role of nesiritide in advanced or decompensated heart failure. Pharmacotherapy 2003; 23(10): 1266-80.
3. Noviasky JA, Kelberman M, Whalen KM, Guharoy R, Darko W. Science or fiction: use of nesiritide as a first-line agent? Pharmacotherapy 2003; 23(8): 1081-83.
4. UpToDate. Brain and atrial natriuretic peptides in left ventricular dysfunction. Available at: http://uptodateonline.com/application/topic.asp?file=hrt_fail/20422&type=A&selectedTitle=1~4 accessed December 9, 2003.