Introduction: Optimizing Heart Failure Management

J. Thomas Heywood, MD, FACC

Department of Cardiology, Loma Linda University Medical Center, Loma Linda, CA

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In 1956, Kisch[1] described granules in guinea pig atria seen on electron micrographs that were similar to secretory granules seen in the pancreas. Similar findings were seen in human atrial tissue by Jamieson and Palade[2] in 1964. The granules responded to changes in salt and water balance in experimental animals.[3] In 1981, de Bold and colleagues[4] found that a crude extract of rat atrial tissue, when injected into another animal, produced a brisk diuresis. Deth and colleagues[5] found that similar extracts had a vasorelaxing effect on an aortic ring preparation, demonstrating the vascular as well as renal effects of the natriuretic peptides (NPs). A peptide originally found in the porcine brain and thus initially described as "brain" NP (BNP) was discovered by Sudoh and colleagues[6] in 1988.

For the next 2 decades, the NPs were the focus of intense scientific and clinical interest. These peptides form a family of compounds that exist not only in the atria but also in the ventricles, brain, and vascular tissue. They react with cellular receptors in the kidney, adrenal gland, vascular smooth muscle, and brain, resulting in elevated levels of cyclic guanosine monophosphate. Unlike the many neurohormones present in mammals to maintain stable blood pressure levels and prevent loss of sodium, the NPs lower blood pressure and filling pressures and promote loss of salt and water. They form part of the delicate hormonal balance that results in homeostatic control of blood pressure and adequate total body sodium level.

In the last 4 years, both the diagnostic and therapeutic importance of BNP (or B-type NP) has been recognized. For the first time, a clinically available blood test to help diagnosis of heart failure (HF) by measuring BNP levels has been developed, with widespread clinical acceptance. The test was approved in November 2000 and is currently available in almost 50% of hospitals in the United States. As with any new test, the significance of BNP level measurement is still being evaluated. For example, the level of BNP is significantly higher in patients with renal disease and significantly lower in obese patients. In this supplement to *Reviews in Cardiovascular Medicine*, Dr. Berkowitz reviews the role of BNP in the diagnosis and management of HF.

In August 2001, the US Food and Drug Administration approved exogenous BNP (nesiritide) for treating patients with acute decompensated HF. BNP infusion increases BNP levels to 3 to 5 times higher than levels typically seen in HF. Filling pressures fall significantly while symptoms improve more rapidly when nesiritide is added to standard therapy for HF.[7]

Who is the ideal patient for nesiritide therapy, and how should it be incorporated into the treatment of the patient admitted for decompensated HF? These questions about the use of nesiritide have spurred a reexamination of what optimal management of patients hospitalized with HF should be. Although HF is the most common diagnosis in patients over 65 years old,[8] protocols for inpatient care of HF have not been well defined, especially when compared with treatment of myocardial infarction. Dr. Saltzberg reviews inpatient management of HF and provides a treatment algorithm developed at the Midwest Heart Research Foundation, Downers Grove, IL.[9]

Nesiritide provides significant hemodynamic and symptomatic benefits to hospitalized patients with HF. Outpatient nesiritide infusions are now being administered throughout the United States; however, its use in the outpatient setting needs to be better defined. The Follow-Up Serial Infusions of Natrecor (FUSION)-I trial provided evidence that regular outpatient nesiritide infusions provide benefit in very ill patients with HF.[10] These and other data, including the ongoing FUSION-II trial of outpatient nesiritide therapy, are reviewed by Dr. Marc A. Silver.

Management of patients with preserved systolic function (PSF) has been one of the most neglected areas in HF treatment. The Acute Decompensated Heart Failure National Registry (ADHERE) database comprises over 140,000 admissions for HF from 270 hospitals over the past 3 years. HF with PSF in this real-world dataset is even more common than low ejection fraction HF. Despite the frequency of this syndrome, very little is known about optimal therapy for these patients. Even its name seems to shift every few years, a sure sign that a syndrome is not very well defined. Still, it is clear from elegant work by Zile and colleagues[11] that diastolic HF does exist. In this issue, Dr. le Jemtel presents data from ADHERE on patients who were admitted with decompensated HF yet who had PSF.

As we approach the 50th anniversary of the discovery of NPs, it is staggering to reflect on the journey the scientific world has taken: from an electron micrograph in 1956 to genetically engineered, *Escherichia coli*–produced peptides used daily in clinical practice. The articles presented in this supplement provide a glimpse into the clinical use of BNP, an area that is progressing very rapidly. ■

References

1. Kisch B. Electron microscopy of the atrium of the heart. I. Guinea pig. *Exp Med Surg.* 1956;14:99–112.
2. Jamieson JD, Palade GE. Specific granules in atrial muscle cells. *J Cell Biol.* 1964;23: 151–172.
3. Marie JP, Guillemot H, Hatt PY. [Degree of granularity of the atrial cardiocytes. Morphometric study in rats subjected to different types of water and sodium load (in French, author's transl)]. *Pathol Biol (Paris).* 1976;24:549–554.
4. de Bold AJ, Borenstein HB, Veress AT, Sonnenberg H. A rapid and potent natriuretic response to intravenous injection of atrial myocardial extract in rats. *Life Sci.* 1981;28: 89–94.
5. Deth RC, Wong K, Fuzokawa S, et al. Inhibition of rat aorta contractile response by naturesis-inducing extract of rat atrium [abstract]. *Fed Proc.* 1982;41:983.
6. Sudoh T, Kangawa K, Minamino N, Matsuo H. A new natriuretic peptide in porcine brain. *Nature.* 1988;332:78–81.
7. Publication Committee for the VMAC Investigators. Intravenous nesiritide vs nitroglycerin for treatment of decompensated congestive heart failure: a randomized controlled trial [Erratum appears in *JAMA*. 2002;288:577]. *JAMA*. 2002;287:1531–1540.
8. Kozak LJ, Owings MF, Hall MJ. National Hospital Discharge Survey: 2001 annual summary with detailed diagnosis and procedure data. *Vital Health Stat 13*. 2004;1–198.
9. Costanzo MR, Saltzberg MT, Gupta V. Early goal-directed therapy in the management of acute heart failure. Available at: *http://medicalmedia.net/pdf/241.pdf*. Accessed October 30, 2004.
10. Yancy CW, Saltzberg MT, Berkowitz RL, et al. Safety and feasibility of using serial infusions of nesiritide for heart failure in an outpatient setting (from the FUSION I Trial). *Am J Cardiol.* 2004;94:595–601.
11. Zile MR, Baicu CF, Gaasch WH. Diastolic heart failure—abnormalities in active relaxation and passive stiffness of the left ventricle. *N Engl J Med.* 2004;350:1953–1959.