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EARLY ADMINISTRATION OF IV VASOACTIVES IS ASSOCIATED WITH DECREASED TIME-TO-TREATMENT, LENGTH OF STAY, IN-HOSPITAL MORTALITY, AND RAPID HEMODYNAMIC IMPROVEMENT IN ACUTE HEART FAILURE

Nesiritide, an IV vasoactive, shows favorable effects vs. high-dose nitroglycerin

Episodes of acutely decompensated heart failure (ADHF) send millions of people to the emergency department (ED) and result in approximately 1 million hospital admissions each year. It is likely that each of the 5 million people with congestive heart failure in the United States will experience at least one episode of ADHF (*1*). Rapid, accurate diagnosis of ADHF and appropriate, early treatment have a critical impact on the patient's clinical course and outcome.

Nesiritide (Natrecor®), Scios Inc., (Fremont, CA) is a recombinant form of endogenous human B-type natriuretic peptide (hBNP), a naturally occurring protein secreted by the heart in response to acute heart failure. Nesiritide is indicated for treatment of patients with ADHF who have dyspnea at rest or with minimal activity. Nesiritide is a vasoactive agent with diuretic, natriuretic, vasoactive, lusitropic, and beneficial neurohormonal antagonistic properties in patients with ADHF (*2*). The onset of nesiritide is rapid; pulmonary capillary wedge pressure (PCWP) is significantly reduced after a 15-minute nesiritide infusion (*3*), a feature that makes it likely that patients would benefit from early initiation of therapy in the ED.

Emergency Department Vasoactive Treatment is Critical

In October 2001, **The Adhere® Registry** (*4*) was launched to collect data prospectively and track the medical management of acute heart failure patients in the United States. Approximately 250 hospitals are involved nationwide, and data on more than 130,000 patients have been collected. A recent report based on data from The Adhere Registry provides insight into the use of IV vasoactive therapy in the ED and its association with better patient outcomes (*2*). Only about 15% of ADHF patients received IV vasoactive treatments in the ED, which represented approximately half of the patients who received IV vasoactive treatment at some time during their hospitalization (*2*). Approximately two-thirds of ADHF patients treated in the ED received diuretic therapy, topical nitroglycerin, or morphine as their only treatment (*2*).

These data also show that if IV vasoactive therapy is not started until the patient is admitted to an inpatient unit, the time-to-treatment is over 22 hours (see Table 1); however, if the therapy is initiated in the ED, time-to-treatment is substantially decreased to only 1 hour (*2*). Administering IV vasoactive therapy in the ED is associated with hospital length of stay (LOS) about one-third shorter than when the same therapy is begun in an inpatient unit (*2*). In addition, early administration of IV vasoactive agents is associated with reduced in-hospital mortality, shorter LOS in the intensive care unit, and fewer invasive procedures (*2*).

Initiating IV Vasoactive Agents in the ED vs Inpatient Unit: Effects on Time-to-Treatment, LOS, and In-Hospital Mortality (*2*)

	ED	Inpatient Unit	p-value
Time-to-Treatment *(mean hours)*	1.0	22.2	NA
LOS *(median days)*	4.5	7.0	p<0.0001
In-Hospital Mortality *(percent)*	4.3	10.9	p<0.0001

Comparing IV Vasoactives: Nesiritide vs. High-Dose Nitroglycerin

Elkayam *et al*. (*5*) compared the effects of IV nesiritide and high-dose nitroglycerin on the left ventricular filling pressures in patients with ADHF. Nesiritide significantly reduced PCWP within 15 minutes of treatment initiation ($p \leq 0.01$), which continued for the 3-hour initial study period. High-dose nitroglycerin, however, did not produce a significant reduction in PCWP until 1 hour after treatment initiation. At 24 hours, continuous nesiritide infusion sustained the PCWP decrease (12.2 ± 7.5 mm Hg, $p = 0.02$ vs. baseline) without the need for up-titration. High-dose nitroglycerin was up-titrated according to the investigator's discretion, with a maximum reduction in PCWP seen at 2 hours. All 12 patients in the high-dose nitroglycerin group had their dose increased at some point during the study. In spite of the increased dose, high-dose nitroglycerin resulted in a 24-hour decrease in PCWP to only 3.2 ± 7.0 mm Hg ($p = 0.15$ vs. baseline). Only 3 patients in the nesiritide group required dose increases.

Conclusion

For patients presenting with ADHF, an early and effective treatment based upon a rapid and accurate diagnosis is essential. The use of IV vasoactives in the ED represents a potential treatment advance in ADHF, and is associated with decreases in time-to-treatment, length of stay, and in-hospital mortality. Nesiritide is an IV vasoactive that exhibits both early and sustained effects on PCWP, without the need for dose increases, in patients with ADHF. Nesiritide's diuretic, natriuretic, vasoactive, lusitropic, and beneficial neurohormonal antagonistic properties, along with its rapid onset of action, are likely to benefit patients when given early in the ED.

Scios Inc.

Scios Inc., a Johnson & Johnson company, is a biopharmaceutical company developing novel treatments for cardiovascular and inflammatory disease. The company's disease-based technology platform integrates expertise in protein biology with computational and medicinal chemistry to identify novel targets and rationally design small molecule compounds for large markets with unmet medical needs. Natrecor (nesiritide) was approved by the FDA in August 2001. To date, over 300,000 patients have been treated with Natrecor.

For more information concerning Natrecor, call Scios Inc. at 1-877-4-NATRECOR, or visit the Scios Web site at www.sciosinc.com.

References:

1. Scios Inc. sponsors mid-year national Adhere heart failure registry meeting. Available at: http://www.jnj.com/news/jnj_news/ 20030626_104525.htm. Accessed July 1, 2004.
2. Emerman CL. *Rev Cardiovasc Med*. 2003;4(suppl):S13-S20.
3. Publication Committee for the VMAC Investigators. *JAMA*. 2002;287(12):1531-40.
4. Acute Decompensated Heart Failure National Registry. at: http://www.adhereregistry.com. Accessed June 22, 2004.
5. Elkayam U, *et al*. *Am J Cardiol*. 2004;93:237-40.