Therapy for Pulmonary Edema Often Misguided

Aggressively dosed nitroglycerin should be first-line therapy for cardiogenic pulmonary edema.

BY KATE JOHNSON
Montreal Bureau

MONTREAL — The most common emergency department treatments for cardiogenic pulmonary edema actually make the condition worse and should be abandoned in favor of aggressive, high-dose nitroglycerin combined with angiotensin-converting enzyme inhibitors, Amal Mattu, M.D., said at the International Interdisciplinary Conference on Emergencies.

Most emergency physicians combine low doses of nitroglycerin (NTG) with either morphine or a diuretic, or a combination of both—to the detriment of the patient, according to Dr. Mattu of the University of Maryland, Baltimore.

"For most physicians, nitroglycerin is first-line therapy, but it is still very underdosed. Most physicians are still not comfortable reaching doses like 50 mcg to 100 mcg to 200 mcg per minute—they are using very low doses, which don't really help that much," he said in an interview with this newspaper.

ACE inhibitor therapy produces an abrupt increase in diuresis and significant hemodynamic improvements in as little as 6-12 minutes.

Dr. Mattu recommends aggressive use of NTG sublingually as first-line therapy for rapid and effective treatment initiation, followed by topical NTG in those with moderate symptoms and intravenous NTG in those with the severe symptoms.

Caution should be exercised in hypotensive patients as well as those patients with acute mitral regurgitation, aortic stenosis, pulmonary hypertension, and those taking sildenafil, he said.

The goals in treating cardiogenic pulmonary edema (CPE) patients should be to decrease preload and afterload—both of which can be done with aggressive NTG therapy, Dr. Mattu said.

Although morphine is a common addition to the NTG regimen for preload reduction, there is very little evidence that it is effective in this regard, he said.

In fact, there is significant evidence that it can cause respiratory and myocardial depression at high doses, Dr. Mattu said, and its histamine-related side effects such as rash, urticaria, nausea, and vomiting can actually increase catecholamine release, which worsens the problem.

The basis for morphine's reputation for decreasing preload largely comes from studies in the 1970s in which morphine produced venodilation in the hands and forearms of pulmonary edema patients (Circulation 1976;54:335-7), but a handful of more recent studies actually show deterioration in patients receiving morphine, he said.

Furthermore, an abstract presented at this year's Society for Academic Emergency Medicine meeting demonstrated an almost fivefold increase in mortality among acute decompensated heart failure patients receiving morphine, compared with those who were not.

"Once this study is published, it may almost be malpractice to administer morphine to these patients," Dr. Mattu said.

The other common addition to NTG therapy is a diuretic such as furosemide to aid in preload reduction and act as a vasodilator.

But because many CPE patients have significantly impaired renal blood flow, this therapy takes between 30 minutes and 2 hours to reach the kidneys and initiate diuretic action, said Dr. Mattu.

It is important to remember that up to 50% of pulmonary edema patients may have general body euvolemia and are not actually fluid overloaded; they just have the wrong distribution of fluid in their lungs. "Diuretics drain the body, but not the lungs, so they will not necessarily produce the desired effect," he said.

Again, although studies showing hand and forearm venodilation with furosemide have formed the basis for this treatment approach (Circulation 1997;96:1847-52), many more studies demonstrate initial adverse hemodynamic effects, with only a delayed reduction in preload, Dr. Mattu said.

"This should be a third-line medication," he added.

For afterload and preload reduction, Dr. Mattu recommended angiotensin converting enzyme (ACE) inhibitors (enalapril or captopril), either intravenously or sublingually, as second-line therapy after NTG. This therapy produces an abrupt increase in diuresis even prior to the use of a diuretic, by improving renal blood flow, and significant hemodynamic and subjective improvements in as little as 6-12 minutes, he said.

"This is something I hope more people will catch on to. Almost everybody who I know who has tried this is a big fan of it," he said. "They are seeing a lot of patients who look like they are going to need intubation who will often turn around within 15 minutes and not need intubation, and often not even need to go to the intensive care unit."

The combination of ACE inhibitors with NTG therapy exceeds the benefit of either drug alone; however, ACE inhibitors are also an acceptable single agent for patients who cannot tolerate NTG therapy, he said.

The use of the recombinant natriuretic peptide nesiritide has come under fire recently, Dr. Mattu said, after publication of two metaanalyses associating it with increases in mortality and worsening of renal function in acute decompensated heart failure patients (Circulation 2005;111:1487-91; JAMA 2005;293:1900-5).

"This therapy is unproven as an additional therapy in patients who are already receiving optimal treatment," he said. ■

LV Dysfunction Portends Poor Heart Transplant Outcomes

BY MITCHEL L. ZOLER
Philadelphia Bureau

PHILADELPHIA — Left ventricular dysfunction is a powerful predictor of poor outcome in patients who have received a heart transplant.

During 13 years of follow-up of almost 19,000 patients with transplanted hearts, the cumulative rate of left ventricular dysfunction was 23%, Katherine Lietz, M.D., reported at the annual meeting of the International Society for Heart and Lung Transplantation. Left ventricular dysfunction was defined as ejection fractions of 40% or less.

Among heart transplant patients with a left ventricular ejection fraction of 40% or less, the relative risk of cardiac death was 2.65-fold higher than the risk faced by heart transplant patients without left ventricular dysfunction. The risk of noncardiac death in patients with impaired left ventricular function was almost twice that of control patients, due mostly to renal dysfunction that was secondary to heart failure, said Dr. Lietz, a cardiologist at the University of Minnesota in Minneapolis.

The study used data from the U.S. Scientific Registry of Transplant Recipients for heart transplants done during 1990-2003. This registry includes all heart transplant recipients in the United States during this period, a total of 25,719. Exclusion of patients who were lost to follow-up and those who did not survive for at least 1 year left a study group of 18,854 patients, who were followed until they died, until their transplanted hearts failed, or through the end of May 2004.

Aside from the patients who developed heart failure, left ventricular function stayed fairly constant through follow-up that lasted as long as 13 years. The average left ventricular ejection fraction for the entire group was about 59% after 1 year of follow-up and 57% after 13 years. Development of heart failure occurred at a fairly constant rate, in about 2% of patients per year.

The two most powerful risk factors for the development of left ventricular dysfunction were coronary vasculopathy and renal dysfunction, both of which boosted the risk more than twofold.

Other significant risk factors were African American race, which raised the risk by 89%; need for retransplantation, which raised risk by 67%; and acute rejection, which increased the risk by 65%.

The prevalence of vasculopathy was 34% in patients with an ejection fraction of more than 40%. Among those with lower ejection fractions, the prevalence of vasculopathy was much higher, 57%.

The increased risk of death associated with left ventricular dysfunction was proportional to the severity of the dysfunction. Patients with an ejection fraction of 45%-55% had a 25% increased risk of death, compared with patients with ejection fractions of more than 65%. The mortality risk was 57% higher in patients with an ejection fraction of 35%-45%, and was 2.6-fold higher in those with an ejection fraction of less than 35%.

Morbidity and mortality increased dramatically as ejection fraction fell to 35% and less. Among patients with an ejection fraction of 40% or less, the mortality rate was 24%, and an additional 2% of patients needed a repeat transplantation. But among those with ejection fractions of 35% or less, the cumulative mortality was 46%, and 5% of these patients needed repeat transplantation. ■

Long-Term Survival With LVAD Decreases With Age, Study Says

WASHINGTON — Receipt of a left ventricular assist device at an older age may adversely affect long-term, but not short-term survival with the device, Evgenij V. Potapov, M.D., reported at the annual conference of the American Society for Artificial Internal Organs.

In a review of 403 patients who have received left ventricular assist devices (LVADs) at the German Heart Institute in Berlin since 1987, the 116 patients who were older than 60 years were 2.5 times more likely to have a negative long-term outcome after LVAD implantation than were the younger patients.

Negative long-term outcomes included no heart transplantation, an inability to wean off the LVAD within 6 months, support for less than 6 months in patients with permanent implants, and failure to continue support for more than 6 months in other patients, said Dr. Potapov, a cardiothoracic surgeon at the institute.

No risk factor significantly predicted a negative long-term outcome in patients older than age 60.

"Postcardiotomy support in older patients should be performed in really selective cases," he said.

All age groups (younger than 18 years, 18-40 years, 41-60 years, and older than 60 years) had similar short-term outcomes for 30-day survival, heart transplantation, and weaning from LVAD during the first 30 days.

—Jeff Evans