Meds Under Scrutiny

The Declining Roles of Furosemide, Morphine & Beta Blockers in Prehospital Care

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Like the rest of medical care, EMS continues to evolve and mature. In this article, we review the most recent medical information and care recommendations on: 1) the role of furosemide (Lasix) in heart failure and pulmonary edema, 2) the use of morphine for pulmonary edema and acute coronary syndromes (ACS), and 3) the role of beta blockers (BBs) for ACS, most specifically EMS use of IV beta blockers in acute ST elevation myocardial infarction (STEMI).

FUROSEMIDE

The diuretic furosemide (Lasix) has long been used in the prehospital care of patients who have shortness of breath and/or hypoxia believed to be secondary to acute pulmonary edema. Because patients with pulmonary edema have an in-hospital mortality of 15—20%, there’s an urgency to treat this condition aggressively and with the most effective medications.

Therapy usually begins with oxygen, often followed by nitroglycerin and/or furosemide, a loop diuretic that acts on the kidney to promote diuresis. Many paramedics are directed to administer furosemide by protocol or direct orders from medical control. It has long been believed that patients in pulmonary edema are “drowning” from fluid in their lungs, and administering a diuretic will improve respiratory status in these often critically ill appearing patients. However, during the past two decades, research into the usage of furosemide in the prehospital setting demonstrates it may not be indicated in the EMS management of acute cardiogenic pulmonary edema. Additionally, it’s possible that diuretics might actually be deleterious in the dyspneic patient believed to be suffering from pulmonary edema.

Acute pulmonary edema results from many different underlying conditions. The most common are cardiac ischemia, dietary and medication non-compliance, severe hypertension and cardiac arrhythmias. The syndrome represents a vicious cycle. The build-up of fluid in the alveoli leads to hypoxia. This lack of oxygen results in the release of catecholamines as a stress response. These hormones, such as epinephrine, result in constriction of blood vessels and an accompanying increase in blood pressure. As blood pressure increases, the heart is forced to pump against increasing resistance, leading to more edema in the lungs.

One of the mistakes in the use of furosemide in acute pulmonary edema is the assumption that the patient is “fluid overloaded.” Studies have shown that many patients with pulmonary edema are actually euvolemic, or even hypovolemic, in the acute setting and that furosemide can cause rapid deleterious fluid shifts. Despite these facts, many medical providers continue to believe that patients with acute heart failure syndromes are volume overloaded, thus necessitating a diuretic.

Studies have also shown that when patients in heart failure are acutely given furosemide, preload and blood pressure are paradoxically increased in the initial 15—20 minutes. Conversely, in 1987, Hoffman demonstrated that the administration of furosemide alone, or in combination with morphine, added no benefit in the acute management of pulmonary edema and led to deleterious side effects, such as hypotension, and worsened clinical outcomes.

In addition to the established fact that some patients with pulmonary edema are not volume overloaded and that furosemide may cause worsening hemodynamics in the acute setting, evidence also suggests that we may be doing harm to patients because of incorrectly identifying pulmonary edema. Patients may have other medical conditions that can lead to acute shortness of breath, such as congestive heart failure (CHF), pneumonia, chronic bronchitis and emphysema. Many patients also have co-existing medical conditions.

In 2006, Jaronik et al studied the appropriateness of prehospital furosemide. They retrospectively identified all patients given this medication in the prehospital environment. The results were substantial. Of the 144 patients included in the study, 60 patients (42%) did not have any evidence of CHF during their hospital stay and 33 patients (23%) needed IV fluid administration from the dehydrating effects of furosemide.

The most compelling statistic was that 17% of the patients who received furosemide ultimately received a diagnosis of sepsis, dehydration or pneumonia and were “potentially...
harmed by furosemide administration. The conclusion was that EMS personnel, faced with a sick patient with shortness of breath, don't have the time or resources to accurately diagnose a volume-overload patient in pulmonary edema. Moreover, almost half of the patients in this study received furosemide inappropriately.

The inability to correctly diagnose the cause of shortness of breath in the acute setting is not limited toprehospital care providers. In one study, initial clinical judgment by an emergency physician had a sensitivity of only 0.61 and a specificity of 0.86 in predicting CHF. Misdiagnosis was highest in those patients with a history of both heart and lung disease. Physicians now routinely rely on history, physical examination, chest X-ray and the blood test BNP to correctly diagnose CHF as the cause of shortness of breath.

In conclusion, it appears that the prehospital administration of a potent diuretic such as furosemide may no longer be indicated. Many patients with CHF are not volume-overloaded, furosemide may acutely worsen the status of a patient in pulmonary edema if given alone, and prehospital providers have difficulty identifying pulmonary edema as the underlying cause of hypoxia and shortness of breath.

A position statement published in Critical Care Medicine recommended against the use of furosemide as first-line monotherapy in patients with acute cardiogenic pulmonary edema. Treatment of hypoxia with supplemental oxygen, preload and afterload reduction with nitroglycerin, and possibly non-invasive positive pressure ventilation (PPV) appear to be the tools needed for the appropriate management of this patient population.

**MORPHINE**

For the past century, morphine has been widely used for the treatment of chest pain in the setting of acute coronary syndrome as well as in the treatment of patients with CHF exacerbations. However, morphine's role in both these conditions, most specifically pulmonary edema, is now changing. Ultimately, we must ask if morphine should continue to be used freely in prehospital treatment protocols for chest pain and pulmonary edema.

Although morphine has been used since the early 1900s, no large-scale studies have evaluated its benefits for the treatment of ACS, including acute myocardial infarction. Some studies, however, have demonstrated morphine's potential harm in ACS. A study in the American Heart Journal in 2005 reviewed the use of morphine in patients with non-ST elevation ACS enrolled in the CRUSADE initiative. The study demonstrated an increase in mortality among those patients who received morphine, either alone or in combination with nitroglycerin.

Although this wasn't a randomized placebo-controlled trial, it does put the use of morphine in this patient population into question. It's unclear why there was an increase in mortality, but it may have something to do with morphine's potential to mask ongoing pain, lower blood pressure and slow respirations. Given the lack of compelling evidence to support the routine use of morphine, this potent pain reliever should be used only after the use of nitroglycerin has been optimized, and then very carefully.

Morphine's role in patients presenting with pulmonary edema secondary to heart failure exacerbations has also come into question. Traditionally, morphine has been touted for its ability to reduce preload and relieve anxiety. However, similar to the use of morphine in ACS, we lack good evidence that supports the use of morphine in the setting of pulmonary edema.

However, multiple studies demonstrate morphine's potential dangers when used in patients with pulmonary edema. In 1987, Hoffman and Reynolds compared Lasix, nitroglycerin and morphine for the treatment of presumed pulmonary edema. Not only did this study demonstrate the potential for misdiagnosis of heart failure in the prehospital setting, as only 77% of patients received an emergency department (ED) or in-hospital diagnosis of CHF, it also demonstrated the potential for harm. They found adverse effects in the first hour of treatment only in patients who received morphine.Sacchetti et al also demonstrated a trend toward higher intubation rates and ICU admissions in patients receiving morphine.

In a recent study reported in the Critical Care Medicine in 2008, Peacock et al reviewed the ADHERE (Acute Decompensated Heart Failure National Registry) database in an attempt to compare the outcomes of patients who did and did not receive morphine during hospitalization for acute decompensated heart failure. This retrospective analysis demonstrated a higher rate of intropoe usage, longer hospitalization, higher need for mechanical ventilation, more ICU admissions and a greater mortality in the morphine group.

Although many studies evaluating morphine efficacy are often retrospective, there is no debate that the early aggressive treatment of patients presenting with acute decompensated heart failure can reduce morbidity and mortality; however, morphine does not appear to be the right medication.

Patients in pulmonary edema should be aggressively treated with high flow O2, nitroglycerin (unless hypotensive), beta agonists (only if the patient is wheezing), and positive pressure ventilation (PPV), such as CPAP. In critically ill patients who fail to respond, PPV has been shown beneficial in patients with acute decompensated heart failure. (See the previous section for our views on furosemide in pulmonary edema.)

Given the lack of good data showing a significant benefit of the use of morphine in ACS, we recommend it not be first line for pain relief presumably caused by ischemia. We believe the current evidence clearly shows morphine should be reserved for patients who continue to have ischemic pain after aggressive nitroglycerin administration. The lack of any evidence that morphine helps patients in pulmonary edema, coupled with evidence of its deleterious effects in multiple studies, mandates that all EMS systems strongly consider removing morphine from their protocols (and allowed drugs) for presumed pulmonary edema.

**BETA BLOCKERS**

The early and aggressive use of BBs to treat patients with presumed myocardial ischemia or infarction has dramatically changed due to the recent release of the new 2007—2008 ACC-AHA STEMI and non-STEMI guidelines.

It had previously been thought that BBs had numerous beneficial effects, including decreasing ischemia, decreasing infarct size, preventing arrhythmias, beneficially lowering BP and providing long-term mortality benefits by decreasing both reinfarction rates and the incidence of sudden death.

These presumed benefits were based on the pharmacologic actions of BBs, which have negative inotropic and negative chronotropic actions.

This mandate to provide early IV BB therapy has led a number of EMS systems to make N BB administration a standard part of their early rule-out (R/O) AMI care. EMS protocols for this patient group often included aspirin, nitroglycerin and the IV beta blocker metoprolol (Lopressor).

Unfortunately, much of what we previously knew about the many beneficial effects of BBs come from smaller, not well-controlled studies. Almost all studies “proving” the benefits of BBs were done before the routine use of aspirin, heparin or lytic therapy and well before...
clopidogrel (Plavix), lib-lla inhibitors and PCI were even invented or readily available. More recent studies that involve modern AMI care have brought us important information about the current role of BBs in ACS and STEMI.

The COMMIT Trial of more than 45,000 patients was performed in China and randomized patients to BB or placebo. The results seemed to support previous views on the benefits of BB use. However, when the data was more closely evaluated, two key facts emerged. First, BB use increased the risk of cardiogenic shock, heart failure, heart block and symptomatic bradycardia. Almost all of these highly deleterious effects occurred on day one of the patient's infarct. The major hemodynamic, antiarrhythmic and mortality benefits of BBs almost all emerged from day one onward.

Thus, although long-term BBs confer many benefits, overly aggressive use of BBs on day one—especially in the ED or by EMS—could result in higher morbidity and mortality. The new 2007-2008 AHA-ACC guidelines now recommend that immediate BB administration be reserved for patients with either refractory hypertension or refractory tachycardia after maximal medical therapy who have no increased risk for cardiogenic shock, are under age 70, have no evidence of heart failure, no heart block, no prolonged condition intervals on bradycardia and no reactive airway disease.

For most AMI and ACS patients, this means they should receive oral beta blockers once they’re deemed stable by their cardiologist in the CCU and not by an ED physician or a paramedic in the field. IV beta blockade for patients with chest pain, unstable anagia or STEMI before the patient has been carefully evaluated and had a chest X-ray performed, is no longer within the accepted standard of care. Thus, the role of beta blockers, just like morphine and Lasix, has changed.

**SUMMARY**

Now more than ever, it is essential for EMS providers to stay current with the evolution of prehospital care. There’s no convincing evidence that early aggressive use of furosemide benefits patients with heart failure or pulmonary edema. Its use should, therefore, be either minimized or eliminated in the prehospital setting.

Morphine has no role in pulmonary edema, and its use in AMI should be in conjunction with maximal use of nitroglycerin and rapid transport to a PCI center. When used, morphine should be administered in a titrated manner, with paramedics understanding that its use does not appear to improve mortality.

Finally, early IV beta blocker use by EMS, or in the ED, for ACS and STEMI patients is no longer recommended and may be both dangerous and contraindicated for many patients.

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