Intravenous Morphine and Chest Pain

By C. Richard Conti, MD, MACC, Editor Emeritus

Introduction

During my medical school and housestaff training, morphine sulfate was used to treat pulmonary edema and acute myocardial infarction.

Many older physicians will remember that therapy for acute pulmonary edema consisted of the combinations of morphine to calm the patient, oxygen that treated hypoxia, and circulating tourniquets that decreased venous return to the heart. This was before the time of intravenous loop diuretics and drugs such as nitroprusside and intravenous nitroglycerine. However, this therapy seemed to work quite well in many patients. The other indication for morphine was to relieve pain and anxiety in patients with acute ST elevation myocardial infarction (STEMI). Morphine was often combined with phenobarbital and 3 weeks of semicomatose bed rest, followed by another 3 weeks of easy ambulation (my, how times have changed), and then finally discharge. Sublingual nitroglycerin and nitroglycerin paste, but not intravenous nitroglycerine, were available. Herrick, in his classic paper published in 1912, commented that in one of his patients “nitroglycerine (Sublingual) combined with digitalen (Digitalis) seemed to improve the quality of the pulse.”¹ The patient he described had 3 years of typical exertional angina and developed symptoms of heart failure, which temporarily responded to his therapy. In another patient, who probably was in cardiogenic shock, he recommended digitalis rather than the “routine practice of giving nitroglycerin or allied drugs.” I suspect his concern was related to the hypotension produced by sublingual nitroglycerine that could not be reversed promptly, as it is now with the intravenous formulation. For many reasons, including the above, nitroglycerine was not recommended for patients with STEMI until recent times.

Current Use of Morphine in Patients With Acute Coronary Syndromes

In 2011, intravenous nitrates are one of the major drugs used to manage patients with an acute coronary syndrome (ACS), whether it be STEMI, non-STEMI, or unstable angina pectoris. Intravenous morphine sulfate is used appropriately for many patients presenting with an ACS, who continue to have symptoms related to myocardial ischemia (usually chest pain) despite aggressive therapy with nitrates, β -blockers, and angiotensin-converting enzyme inhibitors (ACEI). Unfortunately, many patients with an ACS who have not been treated aggressively, or who just complain of chest pain of uncertain etiology and oftentimes of noncardiac etiology, are given intravenous morphine to relieve their pain. In my opinion, the use of morphine to treat chest pain

in patients with chest pain of uncertain etiology or chest pain of noncardiac etiology may foster the repetitive demand for this drug by patients who think this drug is the appropriate one for use.

I have no problem with the use of intravenous morphine in patients who are resistant to therapy that has been directed at the pathophysiologic root cause of symptoms (ie, nitrates, β -blockers, ACEI). I do have a problem when patients are given morphine without attention to the details of the other therapies, such as increasing the dose of intravenous nitroglycerin, lowering blood pressure with β -blockers, and ACEI. Morphine sulfate masks rather than treats the etiology of ischemic cardiac pain. I doubt that any physician would treat a patient with morphine whose pain (other than chest pain) is of uncertain etiology.

Admittedly, morphine does reduce blood pressure, slows heart rate, and relieves anxiety, which makes the patient feel better and may decrease myocardial oxygen demand. However, it also depresses respiration, which may decrease oxygenation, and in my opinion should not be used unless the patient is refractory to guideline-based therapy for ACS.

Guideline-Based Therapy With Morphine for ACS

Guideline-based therapy is directed at decreasing myocardial oxygen demand and increasing myocardial oxygen supply.

According to current guidelines, morphine sulfate (2–4 mg intravenously [IV] with increments of 2–8 mg IV repeated at 5–15-minute intervals) has a class 1 indication for STEMI and is the analgesic of choice for management of pain associated with STEMI (level of evidence C). Level of evidence C means “by consensus opinion of experts.” For patients with unstable angina, morphine sulfate (1–5 mg IV) is a class 2A recommendation (level of evidence C) and is thought to be reasonable for patients whose symptoms are not relieved despite nitroglycerine therapy, or recur despite adequate anti-ischemic therapy. I fail to understand why morphine is a class 1 indication for STEMI, yet only a class 2A for unstable angina patients, because the etiology of the continuing pain experienced by either patient groups presumably is related to myocardial ischemia.

When using morphine to relieve pain in these ACS patients, physicians must be aware that hypotension, nausea, and respiratory depression are potential unwanted side effects of the drug.

Clinical Study of Morphine in NSTEMI Patients

Meine et al² reported on the association of intravenous morphine use and outcomes in ACS patients. Their study

population consisted of 57 039 non-ST elevation acute coronary syndromes (NSTEMI-ACS) patients entered into the CRUSADE initiative (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines), a nonrandomized, retrospective, observational registry. Outcomes were evaluated in 17 003 (29.8%) patients receiving morphine vs intravenous nitroglycerin, and morphine plus intravenous nitroglycerin vs nitroglycerin. The bottom line findings were that use of morphine either alone or in combination with nitroglycerin for these patients was associated with higher mortality than when nitroglycerin was used alone. According to the investigators, those patients who received morphine did not have substandard care (with other drugs) and did not demonstrate more heart failure than those who did not receive morphine. They also commented that “rather than simply masking the pain associated with myocardial ischemia, perhaps morphine actually exacerbates the crisis.” According to the investigators, their analysis “raises concerns regarding the safety of using morphine in patients with NSTEMI-ACS.” Because this was not a randomized trial the investigators recommended a prospective randomized trial to resolve the issues.

Conclusion

No one would argue that morphine relieves pain, whether it be due to myocardial ischemia, trauma, or other causes.

Masking myocardial ischemic symptoms makes the patient (and the doctor) feel better, but some of the deleterious effects of morphine can result in diminution of myocardial oxygen delivery.

Any ACS should be treated with drugs known to decrease myocardial oxygen demand and potentially increase myocardial oxygen supply. Nitroglycerin intravenously may be the drug that satisfies those criteria, because it decreases venous return, decreases left ventricular filling pressure, and allows better perfusion of ischemic subendocardium. However, it also decreases systolic pressure, which may decrease perfusion of the ischemic myocardium. Thus, it is an ideal drug to use in patients who are not symptomatic from hypotension.

The use of morphine should be reserved for patients with myocardial ischemia who are refractory to drugs that favorably alter myocardial oxygen supply and demand. Morphine should not be used in patients whose chest pain syndrome has not been treated with nitrates and β -blockers.

References

1. Herrick JB. Clinical features of sudden obstruction of the coronary arteries. *JAMA*. 1912;59:2015–2022.
2. Meinel TG, Roe MT, Chen AY, et al; for the CRUSADE Investigators, Durham and Chapel Hill NC, Cleveland and Cincinnati Ohio, and Philadelphia PA. Association of Intravenous Morphine Use and Outcomes in Acute Coronary Syndromes: results from the CRUSADE Quality Improvement Initiative. *Am Heart J*. 2005;149: 1043–1049.