DD Case # 03-21-13-01: TO MONA WITH LOVE

The classic teaching to treat acute coronary syndrome has been "MONA" --- morphine, oxygen, nitrates, and aspirin. Does the current literature indicate positive or negative outcomes with any of these interventions? Are there any "new" interventions that show greater promise for positive outcomes for acute cardiac chest pain?

Morphine --- Trend towards increased mortality

The CRUSADE initiative – a retrospective review of more than 57,000 patient encounters found that use of morphine alone or in conjunction with nitroglycerin for non-ST elevation ACS was associated with higher mortality, even after risk adjustments.
http://www.ahjonline.com/article/S0002-8703(05)00149-3/abstract
http://www.sciencedirect.com/science/article/pii/S0002870305001493

So does this mean we should never use morphine in Acute Coronary Syndrome? Not exactly. The best explanation for these findings is that while morphine will take the pain away, it does not change the underlying ischemic process. Getting the patient “pain free” should not allow for a false sense of security, or a sense that the underlying ischemia has been reversed. All other interventions --- close vitals monitoring, serial EKGs and enzymes, other medical therapies, and cardiac catheterization --- must still continue in parallel if narcotic analgesics are being used.
http://www.theheart.org/article/516527.do

Is there any data that morphine should be used over fentanyl? A literature search brings up one article from France that compares morphine and fentanyl and deems them equal in analgesic potency for pre-hospital care. But it was reviewing all sources of pain, and was not specific for acute coronary syndrome.
http://www.chu-poitiers.fr/docutheque/analgesie_pr_-hospitali_re.pdf

There are also articles published that suggest that morphine increases mortality for CHF patients as well. Primary line of treatment for CHF should be nitro, CPAP/BiPAP, and ACE inhibitors.
http://www.ncbi.nlm.nih.gov/pubmed/3115687
http://www.ncbi.nlm.nih.gov/pubmed/10530536

Oxygen --- No data supports use (but no evidence of harm)

There is one randomized double-blind controlled study that compares oxygen administration versus plain air administration for ACS. It was published in the British Medical Journal in 1976, and showed no positive or negative outcomes from oxygen use. There have not been any significant trials since then.
http://www.bmj.com/content/1/6018/1121?ijkey=a7a07fdf53dbcf02058ddb6c7efee3bf9771f831&keytype2=tf_ipsecsha

The 2010 AHA Guidelines do not suggest routine use of supplemental oxygen past 6 hours. That being said – if the patient is showing signs of hypoxemia, acute heart failure / pulmonary edema, dyspnea, shock, hypoperfusion, or other signs of distress oxygen is definitely indicated. Given that patients can decompensate, and in the acute phase of ACS there is no evidence of harm by EMS administration of oxygen, there is no reason to avoid the use of supplemental oxygen for cases of suspected acute coronary syndrome.

http://circ.ahajournals.org/content/122/18_suppl_3/S787.full

Nitrates --- No evidence of beneficial outcome (but can control symptoms)

There is no evidence that response to nitrates can be used as a diagnostic marker for an acute coronary syndrome. Many other causes of chest pain – chest wall muscle spasm, esophageal spasm, heartburn / PUD – can also respond to nitrate therapy due to its effect relaxing smooth and skeletal muscles.
http://www.ncbi.nlm.nih.gov/pubmed/14678917

There is an article from 1976 that shows that nitroglycerin improves regional blood flow to the ischemic heart and can decrease ST elevation. There is little research data since then. There are no studies that show a mortality or morbidity benefit. However, it is universally agreed that nitrates help with symptoms in ACS. It likely does not stop the ischemic process, so other interventions must be occurring in parallel. Caution must be used when patients are hypotensive, bradycardic, or when an inferior or right ventricular infarction is suspected based on the 12 lead EKG.
http://circ.ahajournals.org/content/54/5/766.short

Aspirin --- Definite benefit (always give if no contraindications)

There are numerous studies supporting reduction in both mortality and morbidity with aspirin use. The sooner aspirin is administered, the better the outcome, according to studies published in 2002 in the American Journal of Cardiology and Cardiology. This is confirmed by a meta-analysis published in the British Medical Journal that same year.

Aspirin reduces coronary reocclusion, and recurrent ischemic events after fibrinolytic or stent / reperfusion therapy. In the ISIS-2 study, aspirin alone reduced death from acute myocardial infarction, and it had an additive effect with reperfusion therapies. Aspirin reduces mortality, in both ST elevation and non-ST elevation patients. It can be given orally (preferably chewed), or rectally in the case of those that cannot swallow, are unresponsive, or are vomiting profusely.

http://www.ncbi.nlm.nih.gov/pubmed/11835915?dopt=Abstract
http://www.ncbi.nlm.nih.gov/pubmed/12417813?dopt=Abstract
http://www.bmj.com/content/324/7329/71.abstract?ijkey=67f57cfd810dbe0c1954f3671ea26eeb97fd4158&keytype2=tf_ipsecsha
http://www.ncbi.nlm.nih.gov/pubmed/2899772?dopt=Abstract
http://www.bmj.com/content/308/6921/81?ijkey=6c5a5bec22e3131bc9337398209d091444b353da&keytype2=tf_ipsecsha

The 2010 AHA guidelines can be seen here with more information…
http://circ.ahajournals.org/content/122/18_suppl_3/S787.full

Antiplatelet Agents --- May have benefit (but increased bleeding risk)

Clopidogrel (Plavix) has been shown to have a synergistic effect with ASA in patients with NSTEMI / ACS, however the risk of “major bleeding” is increased, so the risk/benefit ratio must be closely considered.
http://dare.uva.nl/document/36090

Prasugrel (Effient) has a similar effect and risk profile to Clopidogrel – decreased ischemia, but increased risk of bleeding.
http://www.nejm.org/doi/full/10.1056/NEJMoa0706482

Heparin --- Beneficial when used in conjunction with anti-platelet agents

For patients undergoing a NSTEMI, heparin halved the risk of death, when used in conjunction with aspirin (or other anti-platelet agents), according to this meta-analysis. There was no benefit in the long term use, it conferred a short term benefit. There was no significant difference between unfractionated heparin and low molecular weight heparin (LMWH).
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(00)02324-2/abstract

This systemic review gives a slight edge to LMWH (Enoxaparin or Lovenox) when it comes to progression to STEMI from NSTEMI, but there was no mortality difference between LMWH and unfractionated heparin.
http://jama.jamanetwork.com/article.aspx?articleid=199049

Heparin or LMWH also shows beneficial outcomes in STEMI when combined with anti-platelet therapies, with a slight edge given to LMWH in outcomes. LMWH does have an increased bleeding risk, however.

http://circ.ahajournals.org/content/112/25/3846.short
http://eurheartj.oxfordjournals.org/content/28/9/1066.short
http://eurheartj.oxfordjournals.org/content/28/17/2077.short

Other agents --- Mixed results

Apixaban – a direct Factor Xa inhibitor – increased the number of bleeding events without decreasing the number of ischemic events in ACS.
http://www.nejm.org/doi/full/10.1056/nejmoa1105819

Platelet Glycoprotein IIb/IIIa Inhibitors may show some reduction in mortality among ACS patients, but these patients have to undergo cardiac catheterization for these medications to reach their full efficacy potential. They have a somewhat protective effect in reducing complications post cardiac cath.
http://circ.ahajournals.org/content/104/23/2767.short
http://circ.ahajournals.org/content/100/20/2045.short