**Paramedic CAT (Critically Appraised Topic)**

**Title:** Outcomes of acute coronary syndrome patients administered nitro vs. traditional therapy

**Reported by:** Brittany D’Angelo

**2nd Party Appraiser:** Alan Batt and Christopher Slabon

**Clinical Scenario:**
Paramedics are on scene with a 68-year-old male complaining of chest pain. Further assessment suggests he is suffering from a myocardial infarction, so they administer 160mg of ASA. Should the paramedics also consider giving the patient nitro to increase his chance of survival?

**PICO (Population- Intervention- Comparison- Outcome) Question:**
In acute coronary syndrome patients (ACS), does the administration of nitroglycerin decrease the chance of mortality compared to traditional therapy?

**Search Strategy:**
Acute coronary syndrome AND (nitrate OR nitroglycerin OR NTG OR GTN OR glyceryl trinitrate)
Limits: last 10 years, English
*See Appendix A

**Search Outcome:** 170 results from Medline and 55 from CINAHL

**Relevant Papers:**

<table>
<thead>
<tr>
<th>Author, Date</th>
<th>Population: Sample Characteristics</th>
<th>Design</th>
<th>Outcomes</th>
<th>Results</th>
<th>Strengths/Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhou, 2010</td>
<td>-Individuals with acute coronary syndromes given nitrates</td>
<td>Systematic review</td>
<td>-Platelet adherence/activation -Thrombus formation -Mortality</td>
<td>-Stimulate endogenous endothelial NO release -Inhibit platelet aggregation by increasing cGMP levels in platelets (p &lt; 0.01) therefore have anti-thrombotic effects -Lower mortality in those given nitrate infusions &gt;9 hours after the onset of chest pain -Occurrence of tolerance/beneficial effects may be outweighed by oxidative stress associated with nitrate use</td>
<td>Strengths: review of multiple studies, compared acute and long-term nitrate use as well as various administration routes (IV, SL, PO) Weaknesses: validity depends on quality and biases of studies included, need for large scale clinical trials and research on long-term clinical benefits</td>
</tr>
<tr>
<td>Author, Year</td>
<td>Study Details</td>
<td>Study Design</td>
<td>Findings</td>
<td>Strengths</td>
<td>Weaknesses</td>
</tr>
<tr>
<td>-------------</td>
<td>---------------</td>
<td>--------------</td>
<td>----------</td>
<td>-----------</td>
<td>------------</td>
</tr>
<tr>
<td>Kline, 2015</td>
<td>Individuals classified as having one of five types of myocardial infarctions</td>
<td>Systematic review</td>
<td>Evidence for the individual components of “MONA” therapy - Mortality benefit of nitro</td>
<td>Coronary dilator properties help redistribute blood flow to ischemic tissue - Decrease BP in peripheral vessels due to dilation - Beneficial effects on chest pain symptoms - No significant effect on mortality</td>
<td>Strengths: review of multiple studies, comparison to other treatment options and suggested a new mnemonic (THROMBINS2)</td>
</tr>
<tr>
<td>El-Kadri, 2012</td>
<td>Individuals with ACS divided into ST elevation, non-ST elevation, or unstable angina and given various antiischemic agents</td>
<td>Meta-analysis</td>
<td>Anti-inflammatory and antithrombotic effects of nitro - Prognostic benefit</td>
<td>Nitrates improve the oxygen/supply demand mismatch - Effective for symptom relief - No statistically significant reduction in mortality, but also no increase in mortality - Should be used when other antiischemic agents are ineffective or contraindicated</td>
<td>Strengths: pooled data from multiple large scale studies, no conflicts of interest</td>
</tr>
<tr>
<td>Collins, 1995</td>
<td>58,050 patients hospitalized &lt;24 hours (median 8) after acute MI, given either one month of oral captopril or mononitrate (30mg initial titrated up to 60mg once per day) vs placebo</td>
<td>Randomized 2 x 2 factorial trial</td>
<td>Mortality - Effects on in hospital clinical events</td>
<td>No significant reduction in 5 week or 1 year mortality; death rate of 7.34% among experiment group vs 7.54% in control group during the first 35 days (p= 0.3) - Benefit during days 0-1 supports the safety of early nitrate use but does not demonstrate efficacy - No association or reduction in reinfarction rates or post-</td>
<td>Strengths: strict patient inclusion criteria, randomization of treatment and control groups</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Weaknesses: lack of control over pre-trial characteristics (74% male, 17% had a previous MI, 47%)</td>
</tr>
</tbody>
</table>
Comments:
Large scale randomized trials are lacking on the benefits of nitrates on mortality rates, therefore it was difficult to find studies with a focus on nitrate use alone. Many of the systematic reviews found focused on all pharmacological treatments for acute coronary syndromes. In addition, there is a need for further research on the efficacy of different routes of administration for nitroglycerin use; such as sublingual (used by paramedics) vs intravenous (in-hospital).

Consider: Why would we not use an alternative medication for pain relief?
As outlined in the research findings, there is little to no evidence suggesting that sublingual nitroglycerin use has any benefit on the outcomes of acute coronary syndrome patients. However, there is evidence of detrimental side effects of nitroglycerin use, such as severe hypotension (Collins, 1995). As mentioned by El-Kadri (2012), ranolazine can be used as an alternative to nitroglycerin for symptom relief. In a randomized double blind control trial by the name of MERLIN-TIMI 36, patients were treated with ranolazine or a placebo within 48 hours of ischemia onset. Although it had no statistically significant effect on mortality, ranolazine did have a significant effect on the reoccurrence of ischemia (p= 0.03). In addition to the safety of ranolazine as an alternative to nitro, it has been proven to have antianginal properties for symptom relief (Morrow, 2007).

Clinical Bottom Line:
Further research is needed to determine which pharmacological options can not only relieve chest pain but also reduce mortality rates in acute coronary syndrome patients. Until then, nitroglycerin guidelines should continue to be followed as it has been proven to provide symptom relief and have no adverse effects on mortality if blood pressure is monitored properly.

References:


**Appendix**

Medline: 170 results (49 after a title scan and 8 after an abstract scan, 4 were reviewed)
*Back chaining was performed for one article
CINAHL: 55 results (12 after a title scan and 4 after an abstract scan, 1 was reviewed that was a repeat from the Medline search)