

Paramedic CAT (Critically Appraised Topic)

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

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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:

Author, Date	Population: Sample Characteristics	Design	Outcomes	Results	Strengths/Weaknesses
Zhou, 2010	-Individuals with acute coronary syndromes given nitrates	Systematic review	-Platelet adherence/activation -Thrombus formation -Mortality	-Stimulate endogenous endothelial NO release -Inhibit platelet aggregation by increasing cGMP levels in platelets (p < 0.01) therefore have anti-thrombotic effects -Lower mortality in those given nitrate infusions >9 hours after the onset of chest pain -Occurrence of tolerance/beneficial effects may be outweighed by oxidative stress associated with nitrate use	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

Kline, 2015	-Individuals classified as having one of five types of myocardial infarctions	Systematic review	-Evidence for the individual components of “MONA” therapy -Mortality benefit of nitro	-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	Strengths: review of multiple studies, comparison to other treatment options and suggested a new mnemonic (THROMBINS2) Weaknesses: validity depends on quality and biases of studies included, conflict of interest (Dr. Winchester on the advisory board for Roche Diagnostics), nitrate use is a Class I recommendation with LOE C (limited data)
El-Kadri, 2012	-Individuals with ACS divided into ST elevation, non-ST elevation, or unstable angina and given various antiischemic agents	Meta-analysis	-Anti-inflammatory and antithrombotic effects of nitro -Prognostic benefit	-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	Strengths: pooled data from multiple large scale studies, no conflicts of interest Weaknesses: dependant on validity of studies used, no comparison to mortality rates with other antiischemic agents
Collins, 1995	-58 050 patients hospitalized <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	Randomized 2 x 2 factorial trial	-Mortality -Effects on in hospital clinical events	-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-	Strengths: strict patient inclusion criteria, randomization of treatment and control groups Weaknesses: lack of control over pre-trial characteristics (74% male, 17% had a previous MI, 47%

				infarction angina during hospital stay -Increase in severe hypotension; 8.1% in experiment vs 6.7% in control group (p< 0.0001)	had previous non-study nitrate use)
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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:

Zhou, R. H., & Frishman, W. H. (2010). The antiplatelet effects of nitrates: is it of clinical Significance in patients with cardiovascular disease? *Cardiology in review*, 18(4), 198-203.

Kline, K. P., Conti, C. R., & Winchester, D. E. (2015). Historical perspective and contemporary management of acute coronary syndromes: from MONA to THROMBINS2. *Postgraduate medicine*, 127(8), 855-862.

El- Kadri, M., Sharaf- Dabbagh, H., & Ramsdale, D. (2012). Role of Antiischemic Agents in the Management of Non- ST Elevation Acute Coronary Syndrome (NSTE- ACS). *Cardiovascular therapeutics*, 30(1), e16-e22.

Collins, R., Peto, R., Flather, M., Parish, S., Sleight, P., Conway, M., ... & Budaj, A. (1995). ISIS-4-A randomised factorial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patient with suspected acute myocardial infarction. *Lancet*, 345(8951), 669-685.

Morrow, D. A., Scirica, B. M., Karwatowska-Prokopczuk, E., Murphy, S. A., Budaj, A., Varshavsky, S., ... & MERLIN-TIMI 36 Trial Investigators. (2007). Effects of ranolazine on recurrent cardiovascular events in patients with non-ST-elevation acute coronary syndromes: the MERLIN-TIMI 36 randomized trial. *Jama*, 297(16), 1775-1783.

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)

Search ID#	Search Terms	Search Options	Actions
S8	S1 AND S7	Limiters - Date of Publication: 20070101-20171231; English Language Expanders - Apply related words Search modes - Find all my search terms	View Results (170) View Details Edit
S7	S2 OR S3 OR S4 OR S5 OR S6	Expanders - Apply related words Search modes - Find all my search terms	View Results (80,214) View Details Edit
S6	glyceryl trinitrate	Expanders - Apply related words Search modes - Find all my search terms	View Results (2,347) View Details Edit
S5	GTN	Expanders - Apply related words Search modes - Find all my search terms	View Results (1,851) View Details Edit
S4	NTG	Expanders - Apply related words Search modes - Find all my search terms	View Results (2,742) View Details Edit
S3	nitroglycerin	Expanders - Apply related words Search modes - Find all my search terms	View Results (15,155) View Details Edit
S2	nitrate	Expanders - Apply related words Search modes - Find all my search terms	View Results (64,334) View Details Edit
S1	acute coronary syndrome	Expanders - Apply related words Search modes - Find all my search terms	View Results (31,935) View Details Edit