

Journal Club Block 3: Sep 8, 2015
Should We Apply Oxygen in Acute Coronary Syndrome?
Hosted by Dr. Leo Tanaka and Dr. Leslie Vojta

Scenario:

You are working a typical day shift and sign up for your first 3 patients simultaneously, who all have a chief complaint of chest pain. You look at all three ECGs and all have what appear to be ST elevation myocardial infarctions. They all happen to be of the same age, same gender, and have the same past medical histories (they are triplets!).

They all have the same vital signs (within normal limits) with one exception. Patient A has pulse-ox readings of 85% on room air, Patient B is 92% on room air, and Patient C is at 98%. The nurses gather and remark on the chances of three siblings appearing simultaneously with STEMIs (Lotto tickets, anyone?), but fortunately for these patients, three interventional cardiologists are on hand with three separate cath rooms ready.

Someone remembers the old adage of MONA and begins to put oxygen on each patient to get them to 100%. You remember a recent journal club and ask them to pause for a second as you try and recall what you heard...

Would you treat these patients differently? Think of your most recent shift; did you have an ACS rule-out patient and was the nasal cannula placed before you got there? Should you be treating these patients differently with regards to oxygen administration?

Introduction:

Since the early 20th century, oxygen has been used as a treatment for chest pain and has become medical dogma. MONA has been taught to all physicians of the modern era while studying in medical school yet there is very little evidence to back up our actions. It has been taken for granted and the discussion has moved on; until now.

On face value, it makes elementary sense that giving extra oxygen supports ischemic tissues, but our knowledge of physiology has since contradicted this assumption. Hyperoxia appears to lead to coronary artery vasoconstriction and decreased coronary artery blood flow. Moreover, reactive oxygen species are created which are postulated to cause tissue damage/death and dysfunction.

With these recently highlighted concerns, all major cardiology associations have deleted suggestions to supply oxygen administration to individuals with normal oxygen saturation, yet it occurs every day. Does it matter?

Articles:

- Controlled trial of oxygen in uncomplicated myocardial infarction. . Rawles JM, Kenmure AC. Br Med J. 1976 May 8;1(6018):1121-3

The goal of the articles was to access the latest scientific research regarding the question of the benefit or harm of oxygen in acute myocardial infarction. To date, there are truly only four studies that attempt to answer this question, but only one study is a double-blind randomized controlled trial. This RCT by Rawles is the first background article provided in the Journal Club packet and it is the latest and greatest from 1976. PCI did not exist back then and the marker for AMI was not troponin but rather AST. There was no mortality benefit found with using oxygen but there was statistically significant AST elevation in the oxygen group as well as incidence of sinus tachycardia. Despite all the advances in AMI care since then, such as PCI/beta blockers/thrombolytics/anticoagulation, no significant quality studies have since been performed. The remaining studies from 1997, 2005, and 2012 all were small in number and not gold-standard in terms of methodology with concern of significant bias.

- Oxygen therapy in myocardial infarction: an historical perspective. Beasley R, Aldington S, Weatherall M, Robinson G, McHaffie D. *J R Soc Med.* 2007 Mar; 100(3):130-3.

I included the Beasley article in the background papers because it was one of the first to openly question the use of oxygen in ACS, and recommendations from professional societies began to change.

- Oxygen therapy for acute myocardial infarction: a systematic review and meta-analysis. Burls A, Cabello JB, Empanaza JI, Bayliss S, Quinn T. *Emerg Med J.* 2011 Nov;28(11):917-23. doi: 10.1136/emj.2010.103564.

The 2011 Burls article was important to me because it shifted the discussion on oxygen use from saying, “There is not enough evidence not to use oxygen in AMI,” to, “There is not enough evidence to support using oxygen in AMI and it indeed may be harmful.” This article was identified by my British colleague as a reason for changing standard practice in the UK. The meta-analysis of the 1976/1997/2005 RCTs was persuasive enough to certainly cause pause, but not significant enough to give a definitive answer. The conclusion provided is that more quality studies are needed to further address this topic.

- Cabello JB, Burls A, Empanaza JI, Bayliss S, Quinn T. Oxygen therapy for acute myocardial infarction. *Cochrane Database Syst Rev.* 2013 Aug 21;8:CD007160. doi: 10.1002/14651858.CD007160.

The Cochrane Review of 2013 was included since it deftly presents a systematic synopsis of our current studies, analyzing the quality of each of the four studies and providing an analysis of bias. Interestingly, it suggests that the sheer age of the 1976 study is enough to suspect scientific integrity (purportedly, the scientific method has advanced light-years from the 1970s) and the era of pre-PCI renders the results obsolete, which I completely disagree with. My understanding is that we should attempt to limit confounders (beta-blockers, PCI/thrombolytics, anticoagulation) as much as possible to look at the intervention in question (oxygen), thus the 1976 study is an ideal evaluation of oxygen use in AMI. I suppose you could argue that the benefit of PCI renders any deleterious effects of oxygen moot, thus it does not matter, but the question of whether oxygen is harmful is still relevant in my mind. Ultimately, Cochrane

strongly urged more quality studies to be performed on this topic before coming to a definitive conclusion, but also advocated no O₂ use in AMI if not hypoxemic.

- Oxygen therapy in acute coronary syndrome: are the benefits worth the risk? Shuvy M Atar D, Gabriel Steg P, Halvorsen S, Jolly S, Yusuf S, Lotan C. *Eur Heart J*. 2013 Jun;34(22):1630-5. doi: 10.1093/eurheartj/eh110.

The Shuvy article provides a literature review of the current research and is not a meta-analysis. It specifically reviewed all relevant studies like Cochrane and Burls, but instead of crunching numbers, simply provided a synopsis and interpretation of results. From a scientific standpoint, it does not necessarily contribute much to the debate other than giving a novice researcher an introduction to the studies at hand. This was included to provide a visual display of the proposed manner in which hyperoxia could cause harm in AMI plus gave a brief intro to other concepts related to our question but beyond the scope of our Journal Club, such as hyperbaric oxygen and hyperoxemic reperfusion therapy.

We concluded Journal Club with a brief review of the AVOID study presented by Stub at the AHA 2014 Scientific Session. The main points brought up were evidence that oxygen use may lead to greater infarct size as determined by the surrogate marker of CK. They also reported statistically significant Cardiac MRI (gold standard) data that demonstrated greater ischemic injury in the oxygen group at six months, but found that after adjusting for LV mass, the significance was lost. Now we did note that AVOID used 8 L oxygen therapy, which is not usually seen in clinical practice, and this may certainly play a role in the results. I alluded to multiple recent articles in both *Emergency Medicine News* and *ACEP Now* which indicated this study being enough proof to change clinical practice, despite its lack of significant mortality risk.

Discussion and Topic Revisited:

Not everyone was convinced that the evidence exists to necessarily mandate a change in practice, and I agree, but the writing appears to be on the wall. Change is coming. The AHA in their recommendations of management of ACS and STEMI currently do not support routine oxygen use and other international organizations have similar statements. There was discussion about how to change such a fundamentally ingrained practice as giving oxygen but this is where EM excels. As EMS Medical Directors or as the first to see these patients prior to handing over to the cardiologist, we affect change. If a patient were to inadvertently get oxygen prior to us seeing them, would it be worth it to take them off of oxygen, even for 5 minutes? If indeed reactive oxygen species are being created by hyperoxia, the question would be akin to asking if a patient should be kept in an enclosed garage with car running for an extra 5 minutes because they have already been exposed to carbon monoxide.

I'm being facetious and there are a number of "ifs" that I have thrown out, but ultimately, at the end of the day, we do what we believe is right by our patients. You can continue giving oxygen but know that multiple studies and physiology cited (reactive oxygen species) indicates possible harm. More importantly, there should be further data coming out; keep on the lookout for the DETO2X study, which is a Swedish RCT involving 6,600 patients with multiple endpoints (M&M, ischemia, cost, heart failure) scheduled to end this December!