Diltiazem versus verapamil for the prevention of arterial spasm during transradial access for coronary procedures: a non-inferiority trial

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Disclosures

- IRB Status: Approved
- Funding: None
- Co-investigators:
  - Stacy Emmett, B.S.Pharm, BCCCP
  - William Knopf, MD
  - JoEllen Maurer, B.S.Pharm, MHA
- I have no relevant financial relationships with the manufacturers of any commercial products and/or provider of commercial services discussed in this CME activity
- This program **DOES** include a discussion of off-label treatment options not approved by the FDA for use in the United States
  - Neither diltiazem or verapamil are approved by the FDA to prevent or treat radial artery spasm during coronary procedures

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Learning Objectives

- Describe the reasons for using non-dihydropyridine calcium channel blockers for the prevention of arterial spasm during coronary angioplasty
- Identify the stakeholders and processes involved in performing a non-inferiority study in a rural hospital

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St. Vincent Healthcare

- 286-licenced bed hospital (204 staffed beds)
- Level II trauma center
- Cardiothoracic and vascular medicine center
- 30 primary care and specialty clinics

St. Vincent Healthcare. Available at: http://lastbestnews.com/site/wp-content/uploads/St.-Vincent-Healthcare-1.jpg. Last accessed April 11, 2017.

Cardiac Cath Lab

Cardiac Catheterization Lab. Available athttp://cathlabs.net/wp-content/uploads/2015/10/IMG_2599.jpg Last accessed April 11, 2017.

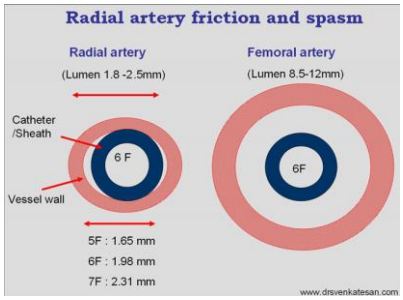
Background

- Radial artery becoming preferred access site versus femoral
- Major complication of radial access is radial artery spasm (RAS)
- RAS prevented by intra-arterial heparin, nitroglycerin, and verapamil
- Diltiazem another non-dihydropyridine calcium channel blocker studied for this use

Montalvenne filho JR, Assad JA, Zago Ado C, et al. Comparative study of the use of diltiazem as an antispasmodic drug in coronary angiography via the transradial approach. Arq Bras Cardiol. 2003;81(1):59-63, 54-58.

Rao SV, Cohen MG, Kandzari DE, et al. The transradial approach to percutaneous coronary intervention: historical perspective, current concepts, and future directions. J Am Coll Cardiol. 2010;55(20):2187-2195.

Vessel Size Affecting Outcomes



Radial artery spasm and friction. Available at: https://drsvenkatesan.com/2009/04/16/is-radial-artery-size-more-important-than-allen-test-in-planning-radial-coronary-angiogram/. Last accessed, March 28, 2017.

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Objectives

- Investigate the non-inferiority of diltiazem compared to verapamil in the prevention of radial artery spasm during percutaneous coronary interventions
- Examine the impact that each medication has on blood pressure and heart rate 10 minutes after administration
- Observe the incidence of procedural success of radial artery access when each medication is used

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Methods

- Design was a single site, randomized, non-inferiority study of 12.5 mg diltiazem versus 2.5 mg verapamil in percutaneous coronary interventions (PCI)
- Primary outcome: Incidence of radial artery spasm
- Secondary outcomes:
  - Change in vital signs 5-10 minutes after injection
  - Burning sensation at injection site
  - Successful procedure using radial artery

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Methods (cont.)

- Inclusion criteria:
  - Inpatient subjects age ≥ 18
  - Planned radial PCI
  - Positive Barbeau test
- Exclusion criteria:
  - Prior calcium channel blocker therapy
  - Emergency procedures
  - Pregnant females
  - Severe systolic dysfunction (LVEF ≤ 20%)
  - Systolic blood pressure ≤ 90 mmHg

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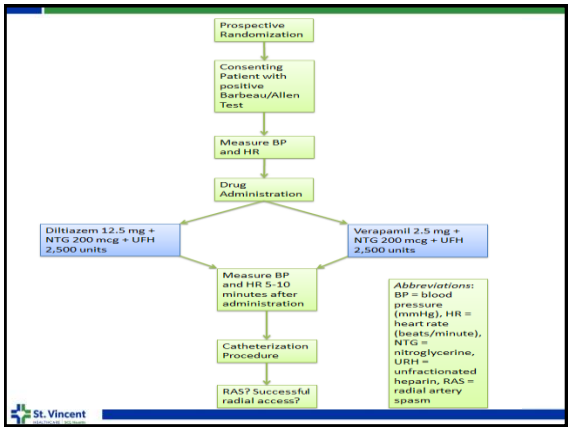

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Power Calculator for Binary Outcomes

Significance level (alpha)	5%
Power (1-beta)	80%
Percentage 'success' in control group	96 %
Percentage 'success' in experimental group	96 %
Non-inferiority limit, d	10 %
Calculate sample size	
Sample size required per group	48
Total sample size required	96

You could say:

> If there is truly no difference between the standard and experimental treatment, then 96 patients are required to be 80% sure that the upper limit of a one-sided 95% confidence interval (or equivalently a 90% two-sided confidence interval) will exclude a difference in favour of the standard group of more than 10%

Sealed Envelope Ltd. 2012. Power calculator for binary outcome non-inferiority trial. [Online] Available from: https://www.sealedenvelope.com/power/binary-noninferior/ [Accessed Tue Sep 27 2016].

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Randomization and Blinding

- Randomized list of diltiazem/verapamil created for 120 patients
- Diltiazem is refrigerated; verapamil stored at room temperature
  - Pharmacy technicians used for input on blinding
- Cath lab staff would receive 5 mL vial of clear IV solution
- Primary investigator would review charts for primary and secondary outcomes
- 340B coordinator consulted for not charging items

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Stakeholders

- Primary author and pharmacy department
- Investigational review board (consent form requirements)
- Chief cardiologist
- Interventional cardiologists
- Nurse practitioners charged with gathering consent
- Cath lab nursing staff

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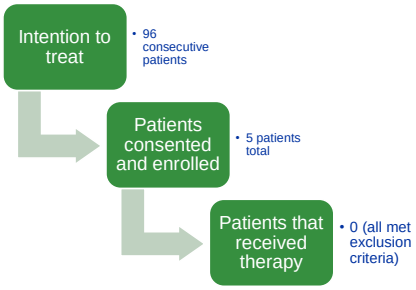
Results



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Discussion: Lessons Learned

- Know your stakeholders and what they think of the study
  - Get all cardiologists on board early
- Ensure your exclusion criteria will allow for enough patients
  - Verify that previous studies easily met power
- Understand where the majority of subjects come from
  - Standardization of workflow
- Communicate with each member of the team!
  - Regular emails on where we were with patient enrollment

Conclusions

- There were no patients that completed the trial and formal evaluation was incomplete
- Future trials bolstered by provider involvement are needed to validate diltiazem non-inferiority to verapamil

Future Opportunities for Residency Projects

- Attempt a retrospective analysis of medication interventions
- Utilize strategic planning to optimize workflow
- Pursue input from outside of the department
- Investigate areas where medications are used and pharmacy is not involved

Questions and Contact Information

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