## Angina Pectoris and Acute Coronary Syndromes

Robert J. Straka, Pharm.D. FCCP  
Associate Professor  
University of Minnesota  
College of Pharmacy  
Minneapolis, Minnesota, USA

### Learning Objectives

- Contrast and compare chronic stable angina, with acute coronary syndromes unstable angina with respect to presentation, pathophysiology and approach to treatment  
- Describe the role and clinical effects of agents used in the management of patients with chronic stable angina (ASA, anti-platelets, nitrates, beta-blockers, and CCBA’s, ACE inhibitors, lipid lowering agents)  
- Given a patient case, construct a treatment plan including selection of appropriate medication, sequencing of medications, dose, monitoring parameters and patient instructions.

### Angina: Introduction

- Ischemic heart disease accounts for a substantial portion of death, disability and economic loss in most industrialized nations  
- Coronary Artery Disease (CAD) is the leading cause of death in the U.S.  
- Estimated 6.6M Americans have Angina  
- 400,000 new cases diagnosed per year  
- 27% of men and 14% of women will develop angina within 6 years of AMI

### Angina Defined

- Angina pectoris is a clinical syndrome typically characterized by discomfort in the chest, jaw, shoulder, back or arm. Typically aggravated by exertion or emotional stress and relieved by nitroglycerine  
- Typically occurs in patients with CAD involving at least one large epicardial artery

### Angina General

- Angina pectoris is the development of chest pain due to myocardial ischemia  
  - coronary blood flow is inadequate to supply the heart with the needed oxygen and nutrients  
  - patients often have underlying coronary artery obstruction  
  - diagnosis of angina and its subclassification requires evaluation of the nature of the chest pain and circumstances surrounding its development

### Angina Types

- Chronic Stable Angina: a chronic and predictable development of chest pain upon exertion  
- Unstable Angina: a critical condition characterized by the unpredictable development of chest pain at rest or during minimal exertion. It is either accompanied by an increase in frequency and/or severity of pain within the recent (weeks to 1 or 2 months) past  
- Vasospastic Angina or Prinzmetal’s Angina: is characterized by the unprovoked coronary artery spasm resulting in chest pain.
Angina Types

Chronic Stable Angina: - a chronic and predictable development of chest pain upon exertion
- Patients rely on antianginal medication throughout the day to perform various degrees of activity however, may prophylax with sublingual nitrates based on anticipated exertions

Unstable Angina (UA): - a critical condition characterized by the unpredictable development of chest pain at rest or during minimal exertion. It is either accompanied by an increase in frequency and/or severity of pain within the recent (weeks to 1 or 2 months) past.
- Patients with unstable angina are admitted to an acute care setting and managed aggressively with nitrates, beta-blockers, CCBA's, antiplatelets and anticoagulants.
- UA is part of the spectrum of acute coronary syndromes (ACS, see ACS lectures)

Vasospastic Angina or Prinzmetal’s Angina: - is characterized by the unprovoked coronary artery spasm resulting in chest pain.
- Patients with this angina may be relatively young and have few or even no cardiac risk factors
- the chest pain is often unpredictable and cyclical in nature, sometimes reverting spontaneously into remission.

Other Forms of Ischemia

Silent Myocardial Ischemia: a phenomenon experienced by a large percentage of patients with ischemic heart disease who for various reasons do not perceive chest pain despite EKG changes consistent with ischemic heart disease.

Events Associated with Ischemia

Exercise Provokes Ischemia
Typical ECG Complex and ST segment

Unstable Angina: Prognosis
- Risk of death or ischemic complications is lower than with MI but higher than with stable angina.
- Prolonged episodes of severe chest pain are important markers of high-risk unstable angina

Angina Therapy: General
- Ranges from intensive medical management (unstable angina) to conservative medical management with the goal of preventing progression to MI or death to death.
- Drug therapy may include:
  - Antiplatelets: ASA, GPIIb/IIIa and ADP inhibitors
  - beta-blockers
  - calcium channel blockers
  - nitrates
  - Anticoagulants: (UFH/LMWH)heparin
  - Lipid lowering agents
  - ACE inhibitors
  - analgesics (morphine)

Angina Therapy: General
- Therapy may require cardiac catheterization and myocardial revascularization: (usually unstable angina or advanced stable angina)
  - Goal: to risk stratify and place in context the need for CABG or PTCA or stenting

Pharmacologic Therapy Angina
- ASA in absence of contraindications
- B-blockers in pts. With prior MI or without prior MI
- ACE Inhibitors to pts with CAD who have diabetes an/dor LV systolic dysfunction
- LDL-C lowering therapy
- SI or nitroglycerin spray for immediate relieve of angina
- CCBA or long-acting Nitrates for reduction in symptoms (if b-blockers contraindicated)
- CCBA and long-acting Nitrates for reduction in symptoms (if b-blockers not successful)
- CCBA and long-acting Nitrates for reduction in symptoms (if b-blockers tolerated)
**Beta-Blockers for Angina**
- Beta-Blockers should be started in the absence of contraindications (IV for high-risk patients) or oral for intermediate and low-risk patients for pts with prior MI.
- Consider pt. intolerance due to pulmonary disease, especially asthma, LV dysfunction, risk of hypotension or severe bradycardia, diabetes, lipid disorders.

**Nitrates for Angina**
- Mechanism: reduce cardiac work afterload and preload reduction as well as coronary dilation and possibly antiplatelet effects.
- Pharmacologic Issues: Variable bioavailability, short half-life, tolerance.
- Monitor: SE's are extension of pharmacologic effects, hypotension, headache, especially post withdrawal.
- Other Issues: multiple dosage forms, durations of action, cost, compliance.

**Nitrates for Angina**
- If symptoms not relieved with 3 sl NTG tablets and initiation of B-Blocker therapy (when possible), IV NTG is recommended.
- Inpatient only- IV NTG should start at 5-10 mcg/min continuous infusion and titrated up by 10 mcg/min q 5-10 minutes until relief of symptoms or limiting side effects (headache/hypotension SBP <90) or dose exceeds 200 mcg/min.
  - Switch to oral nitrates within 24 hours when possible.

**Nitrate Tolerance**
- Main limitation of long-term prophylactic nitrate therapy is the development of tolerance (both to hemodynamic effects on exercise capacity).
- Definition: decrease in response to a given amount of nitrate or the need of increased amounts of nitrate to maintain a continuous effect.
- Numerous trials, using exercise testing to assess the efficacy of nitrate therapy, have shown an attenuation of antianginal effect with chronic therapy.

**Nitrate Tolerance**
- Tolerance can develop with all forms of nitrate therapy that maintain continuous blood levels of the drug.
- Tolerance can develop after only a few doses.

**Nitrates**
- Issues of Metabolism:
  - ISDN has a high first pass effect -> low blood levels of ISDN
  - Approx. 26% (F = 26%) enters systemic circ. from po dose
  - Majority of effect from ISDN is IS-5-MN
  - ISMN (F=100%, t1/2 approx. 5 hrs, duration of effect 12 hrs, elimination- hepatic)

<table>
<thead>
<tr>
<th>GI Tract ISDN 100%</th>
<th>Circulation ISDN (26%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) gut wall</td>
<td>IS-5-MN (84%) [47(a) + 17(b)%]</td>
</tr>
<tr>
<td>(b) hepatic</td>
<td>IS-2-MN (19%) [14(a) + 5(b)%]</td>
</tr>
</tbody>
</table>
Patient Information: Nitrates

- Discuss issue of tolerance (rational ISDN-ISMN, importance of following instructions)
- Do not crush or chew IMDUR tablets
- Potential for hypotension and headache with all nitrates
- ISMO or ISDN are not choice for immediate anti-anginal effect
- Eccentric dosing (7 hour separation)
- SL NTG - storage, dating, dosing,