Antianginal Drugs

Gary Collins, MD, FACC
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Definition of Terms

**Angina Pectoris** – is the principal symptoms of patient with ischemic heart disease.

- Manifested by sudden, severe, pressing substernal pain that often radiates to the left shoulder and along the flexor surface of the left arm.

- Usually precipitated by exercise, excitement, or a heavy meal.
Types of Angina

Typical Angina (Classical Angina)

- Pain is commonly induced by exercise, excitement or a heavy meal
- Secondary to advanced atherosclerosis of the coronary vessels
- Associated with ST-segment depression on ECG
Types of Angina (cont.)

Variant Angina (Prinzmetal Angina)
- Pain is induced while at rest
- Associated with ST-segment elevation on ECG
- Secondary to vasospasm of the coronary vessels

Unstable Angina
- May involve coronary spasm and may also have the component of atherosclerosis
- The duration of manifestation is longer than the first two and may have the manifestation of progression to Myocardial Infarction
Myocardial ischemia which produces angina results from imbalances in myocardial oxygen supply & demand relationship such as decreased oxygen supply and/or increased oxygen demand.

Etiology

1. Decrease oxygen supply
2. Increase demand for oxygen
Determinant of Myocardial Oxygen Demand

Major Determinants

- Wall stress
  - Intraventricular pressure
  - Ventricular volume
  - Wall thickness
- Heart rate
- Contractility
Treatment Plan

- Decrease the risk factor like atherosclerosis, hypertension, smoking
- Increase oxygen supply
- Decrease oxygen demand
Treatment

- Coronary intervention
  - Angioplasty – Stents
  - CABG
- Medical therapy
  - Unsuitable anatomy for intervention
  - Not a surgical candidate
  - Small vessel disease
  - Micro vascular issues
Antianginal Drugs

Agents which ↓ O2 demand & ↑ O2 supply
- Nitrates
- Calcium Channel Blockers

Agents which ↓ O2 demand
- Beta Blockers
Nitrates and Nitrites

Classification of nitrates:

- **Rapidly acting nitrates**
  - Used to terminate acute attack of angina
  - e.g. – Nitroglycerin
  - Usually administered sublingually

- **Long acting nitrates**
  - Used to prevent an attack of angina
  - e.g. – Isosorbide dinitrate, Isosorbide mononitrate
  - Administered orally or topically
Nitrates

Coronary artery dilatation

↓

Decrease coronary bed resistance

(Relieved coronary vasospasm)

↓

Increase coronary blood flow

↓

Increase oxygen supply
Nitrates

Reduction on peripheral resistance
(Secondary to dilatation of aorta)

↓

Decrease blood pressure

↓

Decrease after load

↓

Decrease workload

↓

Decrease oxygen consumption
Nitrates

- Reduced venous return
  (Due to dilatation of the veins)
  - Decrease left ventricular volume
    - Decrease preload
      - Decrease workload
        - Decrease oxygen consumption
Effects

- Coronary artery dilatation
- Reduction of peripheral arterial resistance – decrease after load
- Reduce venous return – decrease preload
# Potential Deleterious Effects

<table>
<thead>
<tr>
<th>Deleterious Effects</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reflex tachycardia</td>
<td>Increase myocardial oxygen requirement</td>
</tr>
<tr>
<td>Reflex increase in contractility</td>
<td>Decrease microvascular perfusion</td>
</tr>
<tr>
<td>Decrease diastolic perfusion</td>
<td>Decrease myocardial perfusion</td>
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</tbody>
</table>
Adverse Effects

- Throbbing headache
- Flushing of the face
- Dizziness – especially at the beginning of treatment
- Postural Hypotension – due to pooling of blood in the dependent portion of the body.
B-Blockers

Hemodynamic Effects

- Decrease heart rate
- Reduced blood pressure and cardiac contractility without appreciable decrease in cardiac output
B-Blockers

Decrease heart rate & Contractility

- Increase duration of diastole
- Increase coronary blood flow
- Decrease workload
- Decrease O₂ consumption
- Increase oxygen supply
Ca Channel Blockers

Effects

- Coronary artery dilatation
- Reduction on peripheral arterial resistance – decrease after load
Ca Channel Blockers

- Coronary artery dilatation
- Decrease coronary bed resistance
  (Relieved coronary vasospasm)
- Increase coronary blood flow
- Increase oxygen supply
Most Commonly Used Ca Channel Blockers

- Nifedipine
- Verapamil
- Diltiazem
Unwanted effect
- Nausea and vomiting
- Dizzyness
- Flushing of the face
- Tachycardia – due to hypotension

Contraindications
- Cardiogenic shock
- Recent myocardial infarction
- Heart failure
- Atrio-ventricular block
Combination Therapy

Nitrates and B-Blockers

- The additive efficacy is primarily a result of one drug blocking the adverse effect of the other agent on net myocardial oxygen consumption.
- B-Blockers – blocks the reflex tachycardia associated with nitrates.
- Nitrates – attenuate the increase in the left ventricular end diastolic volume associated with B-Blockers by increasing venous capacitance.
Combination Therapy (cont.)

Ca Channel Blockers and Nitrates

- Useful in severe vasospastic or exertional angina (particularly in patients with exertional angina with congestive heart failure and sick sinus syndrome).
- Nitrates reduce preload and after load.
- Ca channels reduce the after load.
- Net effect is on reduction of oxygen demand.
Combination Therapy (cont.)

Triple drugs – Nitrate + Ca Channel Blockers + B-Blockers

- Useful in patients with exertional angina not controlled by the administration of two types of anti-anginal agents
- Nifedipine – decrease after load
- Nitrates – decrease preload
- B-Blockers – decrease heart rate & myocardial contractility
Ranolazine - Ranexa

- Represents a new class of anti-anginal drugs
- Partial inhibitor of fatty acid oxidation [pFOX]
Ranolazine – Benefits

- Blocks late inward Na currents in cardiomyocytes
- Reduction in calcium overload
  - Thus reduces diastolic stiffness and improves myocardial perfusion
  - Along with pFOX, contributes to anti-anginal efficacy
Diastolic Stiffness

- Impaires coronary flow during diastole
- Increases wall stress and end diastolic pressure
- Mechanical compression of microcirculation
- Ischemia in sub-endocardial regions
Benefits of pFOX

**What?**
- Shift in ATP production from fatty acid to more oxygen efficient carbohydrate oxidation

**How?**
- By stimulating glucose oxidation reducing fatty acid levels thus improving myocardial ischemia
Drug Interactions

Reduce doses of the following drugs

- Simvastatin
- Digoxin (1.5)

Prolongs QT hence contraindicated in patients with prolonged QT-intervals
Insurance Issues

- For approval will most likely need to already be failing on standard medical therapy.

- Or can’t take standard meds due to side effects.

- Only continue if symptoms improve.
To stent or not to stent!

- Courage Trial
- Fame 1
- Fame 2
<table>
<thead>
<tr>
<th>Type of Angina</th>
<th>Other Names</th>
<th>Description</th>
<th>Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>STABLE</td>
<td>Classic</td>
<td>Obstruction coronary artery</td>
<td>Nitrates</td>
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<td></td>
<td>Exertional</td>
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<td>CCB</td>
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<td></td>
<td>Fixed</td>
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<td>B-blockers</td>
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<td>Atherosclerotic</td>
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<tr>
<td>VARIANT</td>
<td>Prinzmetal’s</td>
<td>Vasospasm at any time</td>
<td>Nitrates</td>
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<tr>
<td></td>
<td>Vasospastic</td>
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<td>CCB</td>
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<tr>
<td>UNSTABLE</td>
<td>Crescendo</td>
<td>Combined effect Pre= MI</td>
<td>Nitrates</td>
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Questions?