Angina Pectoris

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Angina Pectoris

- Chronic disease
- Intermittent attacks of chest pain that radiates through the left shoulder and arm
- 3 million in USA (approx. 1% population)

A. Typical (Effort) angina:
- \( \uparrow O_2 \) demand - fixed supply

B. Variant (Unstable, Prinzmetal's) angina:
- \( \downarrow O_2 \) supply - unchanged demand
- i.e. at rest, coronary spasm (PGs?)

Leading Causes of Death

- Diseases of Heart: 34.3%
- Cancer: 21.0%
- Diabetes: 6.0%
- Accidents: 4.7%
- Pneumonia & Influenza: 3.8%

Determinants of Oxygen Demand

- Need to improve ratio
- Coronary blood flow / cardiac work
- \( O_2 \) Supply / \( O_2 \) Requirement

Coronary Circulation vs Other Circulation

- most tissues can increase \( O_2 \) extraction with demand
- heart extracts near maximal amount of \( O_2 \) at rest
- therefore can only increase \( O_2 \) delivery by increasing coronary blood flow
Angina – Coronary Occlusion

Angina – Surgical Treatment

Angina Risk Factors

- Obesity
- Na+ intake
- Physical inactivity
- Smoking
- Hypertension
- Stress
- High blood cholesterol
- Age
- Gender
- Family history

Cholesterol Levels

- Total cholesterol less than 200 mg/dl – desirable
- 200 – 239 mg/dl – borderline high
- 240 mg/dl and over – high

- HDL cholesterol greater than 35 mg/dl is desirable, the higher the better
- LDL cholesterol less than 130 mg/dl – desirable
- 130-159 mg/dl – borderline
- 160 mg/dl or higher – high

- Ratio LDL:HDL < 3 is desirable

Improving supply/demand ratio

- Relaxation of resistance vessels (small arteries and arterioles)
  \[
  \Delta \text{TPR} \rightarrow \Delta \text{BP} \rightarrow \Delta \text{Afterload} \\
  \text{(Nitrates and calcium channel blockers)}
  \]

- Relaxation of capacitance vessels (veins and venules)
  \[
  \Delta \text{Venous return, } \Delta \text{heart size, } \Delta \text{Preload} \\
  \text{(Nitrates and calcium channel blockers)}
  \]

- Blockade or attenuation of sympathetic influence on the heart
  \[
  \Delta \text{Contractility, } \Delta \text{HR, } \Delta \text{O}_2 \text{ demand} \\
  \text{(Beta blockers)}
  \]

- Coronary Dilation
  \[
  \Delta \text{O}_2 \text{ supply} \\
  \text{(Nitrates)}
  \]

Nitrate and Nitrite

- Formation of Nitric oxide (NO) → activation of guanylate cyclase
- ↑ Ca2+ uptake SR

Tolerance: frequency / dose dependence (absence periods)

Absorption and disposition: well absorbed, first-pass metabolism with oral administration

Toxicity: headache, flushing, hypotension, possible circulatory collapse

- Nitroglycerin
  - Sublingual (duration 30min), buccal (4hr), oral tablets (6hr)
  - Oral spray (30min)
  - Transdermal patch (4hr), transdermal patches (8hr)
  - Intravenous (instant)

- Isosorbide dinitrate: sublingual (2hr), oral (4hr)
- Isosorbide mononitrate: oral (8hr)
- Amyl nitrite, butyl nitrite: volatile, “recreational use”
Nitrates – Mechanism of Action

![Nitrates Mechanism of Action Diagram]

Nitroglycerin and Nitrates

| Nitroglycerin and Nitrates for Chronic Stable Angina |
|---|---|---|
| **Compound** | **Route** | **Dose** | **Duration** |
| Nitroglycerin | Sublingual tablet | 0.3-0.6 mg epa or 1.1 mg | 5-7 min |
| Nitroglycerin | Spray | 3.4 mg | 5-6 min |
| Nitroglycerin | Patches | 13.5-37.5 mg | 1-2 h |
| Nitroglycerin | Transdermal | 2.4-2.8 mg/hr, every 3 h | 6-12 h |
| Nitroglycerin | Chewable tablet | 5-15 mg | 60 s |
| Nitroglycerin | Oral | 5-10 mg TID | 5-7 h |

Beta-Blockers

Propranolol, Atenolol, Nadolol

- ↓ myocardial O₂ consumption by ↓ HR and ↓ force contraction
- ↓ BP, after-load, pre-load

Mechanism of Action

![Mechanism of Action Diagram]

Angina – Beta Blockers

| Table 5. Beta Blockers for Chronic Stable Angina |
|---|---|---|
| **Drug** | **Partial Selectivity** | **Usual Dose** |
| Propranolol | None | 20-80 mg twice daily |
| Metoprolol | β₁ | 50-200 mg twice daily |
| Atenolol | β₁ | 50-200 mg/day |
| Nadolol | None | 40-80 mg/day |
| Timolol | None | 10-50 mg twice daily |
| Acebutolol | β₁ | 200-400 mg twice daily |
| Bucindolol | β₁ | 50-100 mg/day |
| Bisoprolol | β₁ | 10 mg/day |
| Enalapril (intravenous) | β₁ | 50-300 mg/hour |
| Labetalol* | None | 200-300 mg twice daily |
| Pindolol | None | 25-50 mg 3 times daily |

Ca++ Channel Blockers

- Main: Verapamil, Diltiazem, Nifedipine
- Others: Nicardipine, Bepridil

↓ Ca++ influx → ↓ TPR → ↓ afterload (also ↑ coronary flow)

**Toxicity**

- a. Hypotension
- b. Effects related to vasodilation (dizziness, flushing, headache)
- c. Gingival hyperplasia
- d. Constipation, especially with verapamil
- e. Cardiac depression with verapamil and diltiazem
- f. Tachycardia with nifedipine and nicardipine
- g. Arrhythmias and agranulocytosis with bepridil
Intracellular Action of Calcium

Drug Choices in Angina
A. Effort: nitrates, calcium blockers, beta blockers
B. Variant: nitrates, calcium blockers, beta blockers, aspirin, anticoagulants, thrombolytics

Aims in the use of antianginal drugs:
- Treatment of acute attack - nitroglycerin very effective
- Short term prophylaxis - taking nitroglycerin prior to anticipated physical or emotional stress may prevent attack
- Long term prophylaxis - objective is to reduce frequency of anginal attacks. Many options are now available ie. long-acting nitrates, Ca²⁺-blockers, β-blockers, aspirin, anticoagulants, thrombolytics

Angina Drug Treatment

Agents used in the treatment of HT, CHF, Arrhythmia and Angina

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Hypertension</th>
<th>CHF</th>
<th>Arrhythmia</th>
<th>Angina</th>
<th>Contraindications/Cautions/Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-Blockers</td>
<td>***</td>
<td>**</td>
<td>***</td>
<td>***</td>
<td>Caution: CHF, arrhythmia, CHF, bronchospasm, significant bradycardia, asthma, heart block 3 or 4, sick sinus syndrome</td>
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<tr>
<td>ACEI</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>Low GFR, renal stones, preeclampsia</td>
</tr>
<tr>
<td>Diuretics</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>Low GFR, hypokalaemia, hypokalaemia, diabetes</td>
</tr>
<tr>
<td>Cardiac glycosides</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>Many Rx interactions, (K⁺) important, low K⁺ - toxicity</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>Flushing, dizziness, headache, rash, haematuria</td>
</tr>
<tr>
<td>Slow-Channel Blockers</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>Flushing, dizziness, headache, rash, haematuria</td>
</tr>
<tr>
<td>Nitrates</td>
<td>***</td>
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