Chapter 29

Angina
Pathophysiology of Angina

- Clinical syndrome characterized by chest and/or arm discomfort
- Caused by an imbalance between myocardial oxygen supply and demand (ischemia)
- Associated with coronary artery disease
- Pain is reproducible with physical exertion or emotional stress
- Relieved by nitroglycerine
Goals of Drug Therapy for Angina

- Elimination of anginal pain
- Blood pressure (BP) less than 130/85 mm Hg and pulse greater than 70 beats per minute
- Reduce the risks of myocardial infarction (MI) and death
- Treatment is aimed at:
  - Increasing myocardial oxygen supply
  - Reducing myocardial oxygen demand
  - Minimizing or removing the occlusion
Treatment of Angina

- Lifestyle changes
- Surgical intervention
- Pharmacological management
  - Aspirin
  - Nitrates
  - Beta blockers (BBs)
  - Calcium channel blockers
  - Angiotensin-converting enzyme inhibitors (ACEs)
  - Statins
Coronary Vasodilators

- Agents that serve to increase myocardial oxygen supply
  - Nitrates (nitroglycerin, isosorbide)
    - Prototype: nitroglycerine (NTG)
  - Calcium channel blockers (CCBs)
Nitrates Action

- Low doses of NTG dilate the veins, decreasing venous return to the heart.
  - Decreases preload

- Higher doses dilate arterial vessels.
  - Decreased vascular resistance (afterload)

- Some dilation of coronary arteries occur.
  - Atherosclerotic vessels do not dilate.
NTG Precautions and Contraindications

- Contraindicated in hypersensitivity or idiosyncratic responses
- Transdermal patches: allergy to adhesive may limit their use
- Pregnancy category C
BBs for Angina

- BBs decrease the force of myocardial contractility and decrease heart rate and conduction velocity.
- BBs decrease systemic vascular resistance and BP (afterload).
- Decreased myocardial oxygen demand = decreased anginal pain.
CCBs for Angina

- CCBs cause arterial smooth muscle relaxation, which leads to peripheral vasodilation and decreased afterload.
- CCBs may cause coronary vasodilation.
  - Atherosclerotic vessels do not dilate.
ACEIs for Angina

- Act on the renin-angiotensin-aldosterone (RAS) system
- Decreased peripheral vascular resistance
  - Decreased afterload
- Indirectly reduce the secretion of aldosterone
  - Decreased sodium and water retention
  - Reducing extracellular fluid volume and preload
Aspirin and Statins for Angina

- **Aspirin**: decreases platelet aggregation to prevent cycle of vasoconstriction and platelet buildup

- **Statins**
  - Preventive
  - Reduce in low-density lipoprotein cholesterol levels, which plays a significant role in decreasing the formation of atherosclerotic plaque
Grading of Angina by the New York Heart Association and the Canadian Cardiovascular Society

All patients with angina should be on aspirin 81 to 325 mg/day

- If patient cannot tolerate aspirin, then clopidogrel (Plavix) 75 mg daily may be substituted.
• NTG for exertional angina
  • Sublingual tablet (0.3 to 0.4 mg) or translingual spray is used for immediate symptom relief.
## Grading of Angina

<table>
<thead>
<tr>
<th>Class</th>
<th>New York Heart Association</th>
<th>Canadian Cardiovascular Society</th>
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</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Proven coronary artery disease without symptoms</td>
<td>Ordinary physical activity, such as walking or climbing stairs, does not cause angina.</td>
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<tr>
<td>Class II</td>
<td>Mild symptoms: angina and slight limitation during ordinary activity</td>
<td>Slight limitation of ordinary activity. Angina occurs on walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, in cold wind, under emotional stress, or only during the few hours after awakening.</td>
</tr>
<tr>
<td>Class III</td>
<td>Marked limitations: angina during less-than-routine physical activity (walking short distances)</td>
<td>Marked limitations of ordinary activity.</td>
</tr>
<tr>
<td>Class IV</td>
<td>Severe limitations: angina during minimal activity or rest</td>
<td>Inability to carry on any physical activity without discomfort. Angina may occur at rest.</td>
</tr>
</tbody>
</table>
Drugs for Stable Angina

- **ACEIs**
  - Recommended for all symptomatic patients with chronic stable angina to prevent MI or death and to reduce symptoms

- **Angiotensin II receptor blocker**
  - For patients who are intolerant to ACEIs

- **BBs**
  - Recommended as initial therapy by all the guidelines for all patients
CCBs

- Initial drugs of choice for coronary artery vasospasm–associated angina
Long-Acting Nitrates

- Oral or transdermal (patch)
- Used for patients intolerant to BBs
- Isosorbide dinitrate (Isordil) given 2 or 3 times/day
  - With a 10 to 12 hour nitrate-free interval to prevent nitrate tolerance
  - Timing of the nitrate-free interval should coincide with the time of fewest episodes of angina
Ranolizine: a Non-nitrate

- Oral, extended-release capsule for chronic angina with continuous chest pain symptoms
  - Decreases use of NTG and frequency of events
- Unknown mechanism of action
- Not for emergency use
- QT interval prolongation issues at high doses
Multidrug Therapy

- Combinations of BBs and CCBs have been shown to be more effective than individual drugs used alone; can add ranolizine, too.
- Combinations of a long-acting nitrate and a BB are safe, effective, and low in cost.
- Combination of long-acting nitrates and CCBs is rarely used because of the high risk for hypotension and additive adverse reaction profiles.
Patient Variables

- Older adults
  - ACEIs and BBs if the patient has congestive heart failure (CHF)
  - CCBs will make CHF worse

- Women
  - No gender-based difference in therapy
  - Women undertreated
Cost of Treatment

- Nitrates cheapest
- BBs mid-range for cost
  - Older drugs cheaper
- CCBs and ACEIs the most expensive
  - Generics less expensive
Initial Assessment

- Electrocardiography (ECG)
- Fasting lipid levels
- Chest x-ray
- Complete blood count (CBC)
- Tests for diabetes, thyroid function, and renal function
Monitoring

- Angina episodes
  - Presence, characteristics, and timing
- Evaluation every 4 to 6 months during the first year of therapy
- Questions to ask:
  1. Has the patient’s level of physical activity decreased since the last visit?
  2. How well is the patient tolerating therapy?
Monitoring (continued)

3. How successful has the patient been in modifying risk factors and improving knowledge about ischemic heart disease?

4. Has the patient developed any new comorbid illnesses, or has the severity or treatment of known comorbid illnesses worsened the patient’s angina?
Patient Education

- Taking the drug exactly as prescribed
  - Eccentric dosing of some long-acting nitrates
  - Use of sublingual NTG
- If anginal symptoms occur at night, the nitrate-free time is during day
- Storage of NTG
  - Avoiding heat and moisture
- NTG expiration date