Pharmacological Management for PAD

Clifford J. Buckley, MD, FACS
Professor of Surgery

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Central Texas Veterans Health Care System
Disclosure

I have no relevant financial relationships with proprietary entities producing health care goods or services related to the content of this presentation. I am a consultant for Endologix and participate in research for Endologix, Medtronic and Gore. Content may not reflect position of US Government.
Risk Factor Modifications

- Tobacco avoidance
  - Essential for patients with hyperlipidemia or diabetes
  - Support groups
  - Medically supervised nicotine withdrawal or weaning
Risk Factor Modifications

- Exercise and conditioning
  - Increases collateral vessel formation/function
  - Improves hypertension and reduces heart rate
- Types
  - Graduated/supervised walking program
  - Exercise - stationary bicycle/similar conditioning machine
  - Supervised aquatic exercise program
  - Buerger’s exercise
Risk Factor Modification

• Weight reduction
  • Supervised calorie restricted diet
  • Modify/change eating habits
    • Eat three meals per day
    • Binge avoidance
    • Avoid fad diets
    • Easy off/Easy on
  • Reduce saturated fat intake
Risk Factor Modification

- Lipid assessment and management
  - Determine lipid profile
    - Primary hyperlipidemia
      - Predominant hypercholesterolemia
      - Predominant hypertriglyceridemia
    - Mixed
  - Secondary hyperlipidemia
    - Hypothyroidism
    - Diabetes mellitus
    - Nephrotic syndrome
Risk Factor Modification

• Lipid assessment and management
  • Type specific treatment
    • Diet
    • Cholesterol and triglyceride lowering agents
      • Nicotinic acid - 1.5 gm/day
      • Exogenous cholesterol absorption inhibitors
        • Bile acid resins - 4-8 gm/day
        • Zetia – 10mg/day
      • Gemfibrozil - 600 mg bid
Risk Factor Modification

- Hydroxymethylglutaryl coenzyme A reductase inhibitor
  - Mevacor - 20-40 mg/day
  - Zocor - 5-80 mg/day
  - Lipitor - 5-80 mg/day
  - Probucol – 250-500 mg bid
  - Crestor – 10-20mg/day
    - Contraindicated with Digoxin use
- Combination therapy
  - Vytorin – Zetia 10mg + simvastatin dose/day
    - Multiple drug interactions
Risk Factor Modification

- Diagnose & control diabetes mellitus
  - Undiagnosed diabetes mellitus
    - Associated with increased lipids, especially triglycerides
  - Rigorous blood glucose control
    - May NOT prevent vascular complications
    - Important in overall patient management
Pharmacologic Interventions

- Antiplatelet agents
  - Aspirin - 81 mg/day or bid
    - Irreversibly blocks formation Thromboxane A2
    - Inhibits platelet aggregation
  - Clopidogrel bisulfate (Plavix) - 75 mg/day
    - Inhibits binding of ADP
    - Metabolized in liver
    - Will prolong bleeding time - usually gone 5-7 days
Pharmacologic Interventions (cont.)

- **Antiplatelet agents**
  - **Sulfinpyrazone (Anturane)**
    - Blocks formation Thromboxane A2
    - Weaker than ASA
  - **Dipyridamole - 75mg/bid**
    - Increases cAMP
    - Inhibits platelet adhesion to damaged endothelium or abnormal vascular surfaces
Pharmacologic Interventions (cont.)

- Anticoagulant agents
  - Warfarin (Coumadin)
    - Oral systemic anticoagulant blocks formation of Vitamin K-dependent clotting factors
  - Useful
    - Diffuse non-reconstructable vascular disease
    - Improve patency duration for endovascular & direct surgery revascularization procedures
Pharmacologic Interventions (cont.)

- Anticoagulant agents
  - Warfarin (Coumadin)
    - Disadvantages
      - Potential for hemorrhagic complications
      - Cost – lab monitoring surveillance
      - Reversal requires FFP or Vitamin K – may produce hypercoagulable rebound
    - ? Adjunctive heparin window / bridge
Pharmacologic Interventions (cont.)

- **Anticoagulant agents**
  - **Pradaxa**
    - Direct thrombin inhibitor – inhibits both free & clot bound thrombin as well as thrombin-induced platelet aggregation
    - Oral anticoagulant used to prevent blood clots due to non-valvular A-fib
    - Not shown to be helpful in treatment of PVD or maintain patency in arterial reconstruction procedures
    - Single daily dose – no monitoring
    - Contraindicated in patients with mechanical heart valves
Pharmacologic Interventions (cont.)

- Anticoagulant agents
  - Xarelto (Rivaroxaban)
    - Direct factor Xa inhibitor
    - Approved in US for DVT & PE prevention in hip & knee replacement
    - Used for stroke prophylaxis in non-valvular A-fib
    - Effective as warfarin in preventing non-hemorrhagic stroke & embolic events
    - Single daily dose – no monitoring – no antidote
Pharmacologic Interventions (cont.)

- Vasodilator Agents - includes calcium channel blockers
  - Ischemia from anaerobic glycolysis is the MOST potent stimulus for vasodilatation
  - Ischemic tissue usually maximally vasodilated
  - May cause “steal” phenomenon
  - Not useful except in vasospastic disorders
Pharmacologic Interventions (cont.)

- Vasodilator Agents – Topical Nitroglycerin
  - Effect primarily on pre-capillary arterioles and post-capillary venous channels
  - Numerous reports substantiate local adjunctive effect on wound healing
  - No significant systemic effects
Pharmacologic Interventions (cont.)

- Combination Agents - Cilostazol (Pletal) - 50-100 mg/bid
  - Quinolinone - inhibits platelet aggregation and induces blood vessel dilatation
  - Nonhomogeneous vasodilatation effect - femoral outflow beds
  - Metabolized in liver
  - CONTRAINDICATED IN Class III & IV CHF patients
Pharmacologic Interventions (cont.)

• Other agents - Trental - 400 mg/tid
  • Hemorheologic agent which decreases blood viscosity
  • Inhibits neutrophil adhesion and response to injured endothelium
  • Use for treatment of PVD controversial.
  • Useful in treating arterio-spastic disorders - Raynaud's, etc.
• Metabolized in the liver and excreted in urine
• Anorexia & nausea most common side effect
Pharmacologic Interventions (cont.)

- Two European agents
  - Naftidrofuryl
  - Buflomedil
    - Efficacy reported similar to pentoxifylline
- Policosanol
  - Mixture of fatty alcohols derived from honeybee wax
  - Reduces symptoms of claudication – limited data
- Angiogenesis mediated by growth factors currently under investigation
Thank You