Comprehensive Treatment for Dyslipidemias

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Primary Prevention

41 y/o healthy male

• No Medications
• Normal BP, Glucose and BMI

Social History:
• Nonsmoker
• Rare alcohol

Family History:
• Father – MI at 52 y/o
• Mother & Siblings Healthy
Lipid Profile

Total Cholesterol – 235 mg/dl
LDL Cholesterol – 125 mg/dl
HDL Cholesterol – 35 mg/dl
Triglycerides – 375 mg/dl

Lipoprotein (a) – 10 mg/dl
Apolipoprotein B – 140 mg/dl
Evaluation – Risk Assessment

- Family History
  - Lipid Disorders
  - Atherosclerosis
- Cardiovascular Risk Factors
  - Hypertension
  - Tobacco Abuse
  - Diabetes
- Presence of Obesity
- Lipid Testing
HDL Cholesterol

- HDL levels are strong inverse predictors of CVD events
- High plasma triglyceride with low HDL is associated with premature CAD
- Independently raising HDL does not reduce CVD events
  - Torcetrepid
  - Niacin (Aim-High)
- Diet & Exercise can raise HDL
### LDL Cholesterol

**Table:**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Treatment (45 054)</th>
<th>Control (45 002)</th>
<th>RR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-fatal MI</td>
<td>2001 (4.4%)</td>
<td>2769 (6.2%)</td>
<td>0.74 (0.70–0.79)</td>
</tr>
<tr>
<td>CHD death</td>
<td>1548 (3.4%)</td>
<td>1960 (4.4%)</td>
<td>0.81 (0.75–0.87)</td>
</tr>
<tr>
<td>Any major coronary event</td>
<td>3337 (7.4%)</td>
<td>4420 (9.8%)</td>
<td>0.77 (0.74–0.80)</td>
</tr>
<tr>
<td>CABG</td>
<td>713 (1.6%)</td>
<td>1006 (2.2%)</td>
<td>0.75 (0.69–0.82)</td>
</tr>
<tr>
<td>PTCA</td>
<td>510 (1.1%)</td>
<td>658 (1.5%)</td>
<td>0.79 (0.69–0.90)</td>
</tr>
<tr>
<td>Unspecified</td>
<td>1397 (3.1%)</td>
<td>1770 (3.9%)</td>
<td>0.76 (0.69–0.84)</td>
</tr>
<tr>
<td>Any coronary revascularisation</td>
<td>2620 (5.8%)</td>
<td>3434 (7.6%)</td>
<td>0.76 (0.73–0.80)</td>
</tr>
<tr>
<td>Haemorrhagic stroke</td>
<td>105 (0.2%)</td>
<td>99 (0.2%)</td>
<td>1.05 (0.78–1.41)</td>
</tr>
<tr>
<td>Presumed ischaemic stroke</td>
<td>1235 (2.8%)</td>
<td>1518 (3.4%)</td>
<td>0.81 (0.74–0.89)</td>
</tr>
<tr>
<td>Any stroke</td>
<td>1340 (3.0%)</td>
<td>1617 (3.7%)</td>
<td>0.83 (0.78–0.88)</td>
</tr>
<tr>
<td>Any major vascular event</td>
<td>6354 (14.1%)</td>
<td>7994 (17.8%)</td>
<td>0.79 (0.77–0.81)</td>
</tr>
</tbody>
</table>

**Diagram:**

- Treatment better: Effect p < 0.0001

*Cholesterol Treatment Trialists’ Collaborators. Lancet 2005*
HDL and LDL - Risk for CHD

Triglycerides

- Marker for elevated small-dense LDL particles
- Correlates with a reduction in HDL
- Predicts CAD, but not after adjustment for HDL or LDL levels
- Little evidence triglycerides are a direct cause of CAD

Brunzell NEJM 2007; 357:1009
Disorders with Elevated Triglycerides and Low HDL

• Diabetes Mellitus (5%):
  – Residual dyslipidemia in well controlled DM

• Genetic Disorders:
  – Familial Combined Hyperlipidemia (<1%)
  – Familial Hypoalphalipoproteinemia (<1%)
  – Not Familial Benign Hypertriglyceridemia
Familial Combined Hyperlipidemia

- Most common inherited lipid disorder
  - 1:200
- Characterized by elevated triglycerides and LDL, often with low HDL
- Polymorphisms in molecules and enzymes
- Treatment usually involves combination therapy
Lp(a)

- Plasma lipoprotein consisting of a cholesterol-rich LDL particle
- Strongly associated with cardiovascular risk
- Thought to be pro-thrombotic due to structural homology with plasminogen and plasmin

Lp(a) Population Distribution

Shlipak et al. JAMA 2000;283(14):1845-1852
Lp(a) – Patient Selection

• Higher Risk Patients:
  – >10% 10-year risk
  – Familial Hypercholesterolemia
  – Family History of Premature CAD
  – Family History of elevated Lp(a)
  – Recurrent disease despite treatment

• Patients with Unclear Risk!!
Apolipoprotein B

Brunzell et al. NEJM 2001

B  Women

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>≥70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apolipoprotein B (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50th Percentile</td>
<td>94</td>
<td>93</td>
<td>99</td>
<td>116</td>
<td>119</td>
<td>118</td>
</tr>
<tr>
<td>90th Percentile</td>
<td>119</td>
<td>123</td>
<td>129</td>
<td>156</td>
<td>156</td>
<td>152</td>
</tr>
</tbody>
</table>
"I don’t think this is what your doctor meant by lowering your carbs, honey."

© 2005 Diabetes Health
Treatment Approach

• Treat Secondary Causes

• Discontinue Offending Medications
  – Beta-blockers, Thiazides, Estrogens

• Lifestyle – Diet, Exercise, Weight Loss

• Cardiovascular Risk Factor Modification
Pharmacologic Treatment

• Statins First Line Therapy for Most Dyslipidemias
• Statin Intolerance is Problematic
• Combination Therapy Often Necessary
  – Zetia
  – Niacin
  – Fibrates
  – Welchol
Patient Evaluation

Total Cholesterol – 235 mg/dl
LDL Cholesterol – 125 mg/dl → Normal
HDL Cholesterol – 35 mg/dl → Low
Triglycerides – 375 mg/dl → Markedly Elevated

Lipoprotein (a) – 10 mg/dl → Normal
Apolipoprotein B – 140 mg/dl → Markedly Elevated

** Risk Factors: Family History
Hypertriglycerideridemia

• Secondary Causes
  – Uncontrolled Diabetes
  – Medications
  – Etoh Consumption

• Obesity

• Genetic Disorders
  – Familial Combined Hyperlipididemia
  – Familial Hypertriglycerideridemia
  – Familial Hypoalphalipoproteinemia
Management

• Initial
  – Secondary Causes
  – Discontinue Offending Medications
  – Lifestyle Modification

• Pharmacologic Therapy – Consider RISK!!
  – Fibrates
  – Niacin
  – Statins
  – Fish Oil
Vascepa

- Omega-3 Fatty Acid → Prescription
- Synthetic Ethyl Eicosapentaenoic Acid (EPA)
- Patients with TG > 500 mg/dl
- Take 2 capsules BID
- Evidence there is no increase in LDL like Lovaza
  - Vascepa: EPA
  - Lovaza/OTC Omega-3: EPA/DHA
YOU BE THE GOOD CHOLESTEROL AND I’LL BE THE BAD CHOLESTEROL.
Secondary Prevention

45 y/o female

- CAD requiring CABG at 28 y/o
- Normal BP, Glucose, and BMI
- Presents with Progressive Disease
  - Currently on Simvastatin/Zetia

Social History:
- Negative

Family History:
- Father – treated for HLP
Lipid Profile

Total Cholesterol: 236
Triglycerides: 175
LDL Cholesterol: 150
HDL Cholesterol: 51

Lipoprotein (a): 77 mg/dl (>95 percentile)
Premature CAD

• Identified Risk Factors:
  – BMI, DM, Hypertension, Dyslipidemia, & Tobacco
    • DM and Tobacco Most Potent Factors
  – Family History of Premature CAD
  – Lipoprotein (a)

• Rapidly Expanding Population due to the Obesity Epidemic
Approach in Secondary Prevention

• Risk Factor Modification

• Aggressively Treat Premature CAD

• Recurrent Events
  – Marker for Inadequate Treatment

• Consider Combination Therapy
Combination Drug Therapy in Hypercholesterolemia

• Statin plus:
  – Niacin
  – Bile acid resin
  – Zetia

• Triple Therapy
  – Used in high risk patients, particularly those with recurrent events
Patient Evaluation

Total Cholesterol: 236
Triglycerides: 175
LDL Cholesterol: 150
HDL Cholesterol: 51

Lipoprotein (a): 77 mg/dl (>95 percentile)

– On Simvastatin 80 mg and Zetia 10 mg
Familial Hypercholesterolemia

- Genetic disorder characterized by very high LDL
- Mutations in LDLR gene or ApoB
- Heterozygotes develop premature CAD <50 y/o
  - Occurs in 1:500 people
- Mainstay of treatment: Statins
  - Also use Bile acid binders, Niacin, & Zetia
Conclusions

• Properly assessing risk is crucial
• Lipoprotein (a) should be considered in patients with intermediate to high risk
• Consideration of combination therapy in select patients
• Premature CAD is a distinct disease and will likely increase given the obesity epidemic
“If a vegetarian diet is good for losing weight, how come they use grain to fatten pigs and cows?”
Triglyceride level 250–1000 mg/dl, without increased LDL cholesterol

Rule out secondary causes

With premature CAD?

No

Reliable family history of premature CAD?

Negative

FHTG?

Yes

Lifestyle modification alone

No

Decreased apolipoprotein A-I?

Yes

FHA?

Yes

Lifestyle modification, consider drug therapy

No

Increased apolipoprotein B?

Yes

FCHL?

Yes

Lifestyle modification, consider drug therapy

Unknown

Positive

Probable FCHL or FHA

Yes

No

Lifestyle modification and combination drug therapy

Yes

FHA?

Yes

Lifestyle modification, consider drug therapy

No

FCHL?
# Niacin Therapy - 1500 mg/day

<table>
<thead>
<tr>
<th>Meals Per day</th>
<th>Type</th>
<th>Dosage</th>
<th>$/year</th>
<th>Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Niacin</td>
<td>500 mg TID</td>
<td>$24**</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Slo-Niacin</td>
<td>750 mg BID</td>
<td>$101</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Niaspan</td>
<td>1500 mg QHS</td>
<td>$2936</td>
<td>&gt;95%</td>
</tr>
</tbody>
</table>

** Costco Feb 2011: 500mg pills

Meyers et al. Ann Int Med 2003; 139:996
Niacin Pearls

• Tailor niacin type to eating pattern
  – QHS vs. BID vs. TID
• Always take after a meal
• If needed, precede meal with ASA 81mg
  – Non-coated: chewable or 1/4 of ASA 325mg
• Never miss a dose: compliance
• “ASA is appetizer & niacin is dessert”
• Start at a low dose & titrate slowly (every 4 weeks)
Fibrates

A. Subgroups with Dyslipidemia

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<th>Odds Ratio (95% CI)</th>
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<tr>
<td>VA-HIT</td>
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Summary: 0.65 (0.54–0.78)

B. Complementary Subgroups

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Summary: 0.94 (0.84–1.05)