Nutrition and Metabolism in Hepatitis C Infection

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Understanding Nutrition and Metabolism in HCV Complicated by

• Genotype of HCV
• Degree of liver dysfunction
• Substance use
• HIV co-infection
  – Treatment of HIV infection
• Life style issues
  – Housing insecurity
  – Food insecurity
  – Dietary quality
  – Alcohol use

Insulin/Glucose Abnormalities in HCV

• Diabetes more common in HCV than in HBV
  – In young lean patient with no family history
• Glucose abnormalities in
  – 5.8 % of HCV-HIV coinfected patients
  – 2.8% of HIV mono-infection

• Kotler 2008
HCV and HIV

• HCV
  – Insulin Resistance
  – Low TC and LDL
  – Prothrombotic changes
    • P-selectin
    • Endothelial dysfunction
  – Low CRP
  – Fat atrophy

• HIV
  – Insulin resistance
  – Low HDL
  – Prothrombotic changes
    • D-dimer
    • Endothelial dysfunction
  – High CRP
  – Increased trunk fat
  – Fat atrophy

Kotler 2008, McGovern 2006

HCV, HIV and ART

– Insulin resistance
– Low HDL
– High or low CRP (depending on degree of liver dysfunction?)
– Prothrombotic changes
  • D-dimer, P-selectin
  • Endothelial dysfunction
– Increased trunk fat
– Fat atrophy
– Metabolic effects of ART (varies with agent)
  – Increased TG, TC, low HDL

HCV Genotype 3 & Steatosis

• Low TG
• Low TC
  – ? Mediated indirectly by more severe steatosis
  – Or directly by alterations in B lipoprotein production and secretion of VLDL
• HIV exacerbates abnormalities seen with GT 3
Prevalence of Overweight in HIV

<table>
<thead>
<tr>
<th>BMI</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20 kg/m²</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>20-25 kg/m²</td>
<td>30%</td>
<td>40%</td>
</tr>
<tr>
<td>25-30 kg/m²</td>
<td>30%</td>
<td>35%</td>
</tr>
<tr>
<td>&gt; 30 kg/m²</td>
<td>30%</td>
<td>20%</td>
</tr>
</tbody>
</table>

NFHL data, 2008

Overweight and Underweight in HIV-Infected Men

Source NFHL, n=276

Overweight and Underweight in HIV-Infected Women

Source NFHL, n=140
Nutritional Compromise may be Under-Nutrition or Over-Nutrition

**Under-nutrition**
- Access to food
- Physical barriers to intake
- Malabsorption
- Physical activity
- Alterations in metabolism
- Co-morbidities
- Effects of specific drugs

**Over-nutrition**
- Food insecurity
- Dietary quality
- Physical activity
- Alterations in metabolism
- Effects of specific drugs
Over-nutrition

Associated with:
- Food insecurity
- Dietary Quality
- Low level of education (surrogate of economic status)
- Decreased viral demands with suppression of viral load (in HIV and ? in HCV)
- Can we differentiate HIV-lipodystrophy from obesity with fat atrophy?

Hendricks, 2008

Predictors of Steatosis in HCV

- BMI > 30 kg/m²
- Increased viral load
- Increased glucose
- Lipohypertrophy (increased visceral fat)
- Age
- Alcohol use (? Direct or mediated through empty calories)
- Genotype 3
- HIV infection
- (Effective ART decreases steatosis)

Ryan 2001
Woreta 2011
Borgli 2008
Bani-Sadr 2006
Predictors of Fibrosis in HCV

- Age
- Low CD4
- Chronic HCV
- Alcohol use
- Increased ALT
- Increased TG
- Low TC
- Increased HOMA
- Use of D4t

• Bianco 2009

Treatment of HCV and Glucose

- Predictors of SVR (rapid VR)
  - Genotype 1 and 4
  - RNA < 400,000
  - HOMA > 3
- Diabetes (defined as FBS > 100 mg/dl)
  - Associated with relapse after HCV treatment

• Nasta 2008
  • Sulkowski 2009

Treatment of HCV Improves HOMA-IR

- Independent of
  - Age
  - Gender
  - Ethnicity
  - BMI
  - Duration of HCV
  - Fibrosis
- Adds credibility to the role of HCV in producing IR/ DM

• Delgado Borrego 2010
Lipids and HCV Treatment

- LDL and TC in normal range have positive predictive value for SVR in HCV mono-infection
- In HIV Co-Infected:
  - Significant association between pre-treatment lipids (TC, HDL, TG) and steatosis but not fibrosis and no association with SVR

  * Petit 2010; Clark

Treatment of HCV Alters Lipid Profile

- With treatment of HCV
  - Increased LDL
  - Increased TC
  - During treatment TC decreases further but increases after SVR
  - Post treatment levels may raise concern for CVD
- Response seen only in HCV treatment responders
  - Abnormalities persist in nonresponders

  * Corey 2009
  * Wagner 2010

Concerns about Nutritional/ Metabolic Status in HCV

- Bi-directional relationship:
  - HCV associated with abnormal lipids and glucose metabolism
  - Progression of HCV associated with presence of abnormal lipid and glucose metabolism
- As with HIV, treatment and longer survival permit development of co-morbidities of concern:
  - Diabetes
  - Metabolic Syndrome
  - Cardiovascular disease
Mortality associated with Metabolic Syndrome in HIV

Adjusted Cox proportional hazards of mortality for high triglycerides and metabolic syndrome before and after 36 months follow-up

<table>
<thead>
<tr>
<th></th>
<th>Adjusted Hazard Ratio (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High triglycerides ≤36 months</td>
<td>1.03 (.55, 1.94)</td>
<td>.924</td>
</tr>
<tr>
<td>High triglycerides &gt;36 months</td>
<td>2.96 (1.44, 6.08)</td>
<td>.003</td>
</tr>
<tr>
<td>Metabolic syndrome ≤36 months</td>
<td>.96 (.51, 1.82)</td>
<td>.900</td>
</tr>
<tr>
<td>Metabolic syndrome &gt;36 months</td>
<td>2.64 (1.33, 5.22)</td>
<td>.006</td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, albumin, current smoker and CD4<200

45% of this cohort acquired HIV through injection drug use

Kaplan Meier Survival Curve for cIMT (as a CVD surrogate marker) in HIV-associated deaths (16% drug users at the time of death)

Nutrition in HCV/DU/HIV

- Issues are:
  - Assessment of nutritional status
  - Access to nutrition
  - Appetite
  - Symptoms which may decrease intake
  - Dietary quality
  - Metabolism (what are nutrient requirements in setting of inflammatory infections?)
  - Malabsorption
Predictors of Food Security

\( (n=592) \)

<table>
<thead>
<tr>
<th></th>
<th>Food secure</th>
<th>Food insecure</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>42 years</td>
<td>40 years</td>
<td>0.01</td>
</tr>
<tr>
<td>Female</td>
<td>23%</td>
<td>77%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-white</td>
<td>19%</td>
<td>81%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IDU</td>
<td>16%</td>
<td>84%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No ART</td>
<td>34%</td>
<td>66%</td>
<td>0.08</td>
</tr>
<tr>
<td>BMI</td>
<td>25.0 kg/m(^2)</td>
<td>26.4 kg/m(^2)</td>
<td>0.01</td>
</tr>
<tr>
<td>CD4</td>
<td>311</td>
<td>342</td>
<td>0.08</td>
</tr>
<tr>
<td>Viral load (log)</td>
<td>3.4</td>
<td>3.5</td>
<td>0.38</td>
</tr>
</tbody>
</table>

McMahan 2011

NFHL Cluster Analysis Results

- **Fruits/ Vegetables:**
  - Lowest risk of poverty or food insecurity
  - Highest intakes of protein, fiber, and micronutrients
  - Highest levels of LBM and CD4 count

- **Fast Food:**
  - More likely to live in poverty, be food insecure or IDU
  - Diets of lower nutrient density
  - Highest levels of viral load, lowest mean CD4, most likely to have AIDS diagnosis

- **Juice and Soda:**
  - Lowest BMI and highest reported mean calorie intake


Top 3 vegetables by study site:

<table>
<thead>
<tr>
<th>Location</th>
<th>Vegetable</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baltimore</td>
<td>Onion, cooked</td>
<td>(18%)</td>
</tr>
<tr>
<td></td>
<td>Potato Chips</td>
<td>(14%)</td>
</tr>
<tr>
<td></td>
<td>French Fries</td>
<td>(10%)</td>
</tr>
<tr>
<td>Providence</td>
<td>Potato Chips</td>
<td>(20%)</td>
</tr>
<tr>
<td></td>
<td>Onion</td>
<td>(9%)</td>
</tr>
<tr>
<td></td>
<td>Iceburg Lettuce</td>
<td>(7%)</td>
</tr>
<tr>
<td>Boston</td>
<td>Vegetable mix, corn and lima beans</td>
<td>(7.5%)</td>
</tr>
<tr>
<td></td>
<td>French Fries</td>
<td>(7.5%)</td>
</tr>
<tr>
<td></td>
<td>Tossed salad</td>
<td>(6%)</td>
</tr>
</tbody>
</table>
Potential for Nutrition Interventions

• To attempt to slow steatosis:
  – Weight reduction (decrease BMI)
  – Improve glucose tolerance/ decrease HOMA
• To attempt to slow fibrosis
  – Improve glucose tolerance
  – Reduce alcohol consumption
• To improve treatment response:
  – Treat glucose intolerance/ decrease HOMA

Recommendations

• Monitor weight (with height) in HCV infection
• Monitor glucose and insulin
  – \( \text{HOMA} = \frac{\text{fasting insulin} \times \text{fasting glucose}}{22.5} \)
• ? Monitor Hgb A1c
• Monitor lipid profile (TG, TC, LDL, HDL)

Recommendations

• Consider
  – Treatment for elevated HOMA prior to HCV treatment
  – Insulin sensitizing agents
  – No evidence to support success
• Treat lipids if response to treatment increases TC/ LDL to level of CVD risk
Summary

• Nutritional/ Metabolic parameters
  – occur with HCV infection
  – appear to contribute to HCV progression
  – may play a role in response to HCV treatment

Summary

• Lipid abnormalities occur in HCV
• Weight/BMI contribute to outcomes in HCV
• More research is needed on impact of intervention in these abnormalities
• Nutritional or metabolic interventions may offer additional means to effect improvements in quality of care in HCV