Development of a Multidisciplinary Treatment Program for the Management of HIV/HCV Co-infected Patients

Suffolk County Department of Health Services (SCDHS)

Technical Assistance provided by HRSA
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HCV and HIV
HCV Characteristics

- Family Flaviviridae\(^1\)
- Enveloped\(^2\)
- Positive-sense single-stranded RNA (9.6 kb)\(^1,3\)
- 3000–amino acid polyprotein\(^3\)
- No RNA polymerase proofreading ability\(^4\) — Quasispecies\(^4\)
- Half-life: ≈2.7 hours\(^2\)
- Daily production: 10 trillion (10\(^{12}\)) virions\(^2\)

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Epidemiology of HCV
Genotype Distribution in the US*

- Genotype 1²: 74%
- Genotype 2,3¹: 22%
- Genotype 4,5,6¹: 4%

*In Hepatitis C Monoinfection

HCV Infection: Worldwide Genotype Distribution

Genotypes 1, 2, 3
Worldwide Distribution
Prevalent Genotype in US Infections

Genotype 4
Middle East, Africa

Genotype 5
South Africa

Genotype 6
Southeast Asia

Epidemiology: Quick Hits

- 5 million antibody positive
  - At least 4 Million have HCV RNA
  - CDC estimates may be as high as 7 million carriers

- 2.7 million are chronically infected with HCV

- Highest prevalence;
  - 30- to 54-year-olds
  - African American Males

- US disease burden and financial burden is steep
  - ~10,000 deaths per year attributed to CHC
Natural History of HCV Infection

Exposure (Acute Phase)
- 15% Resolved
- 85% Chronic

~20 year progression rate accelerated with HIV, HBV, alcohol

Resolved rate
20%

Chronic rate
accelerated

Cirrhosis
20%

6%/yr ESLD
4%/yr HCC

3–4%/yr Transplant/death

5-year survival in patients with HCC is < 5%²

HCC = hepatocellular carcinoma
ESLD = end-stage liver disease

# Financial Burden of HCV-Related Liver Transplant

## HCV-Related Liver Transplants Account for 40% of Total Transplants

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>~2000/year</td>
</tr>
<tr>
<td>Procurement, Hospital/Physician Charges</td>
<td>~$300,000</td>
</tr>
<tr>
<td>Evaluation, Follow Up</td>
<td>~$100,000</td>
</tr>
<tr>
<td>Total Transplant Cost</td>
<td>~$400,000</td>
</tr>
<tr>
<td>Immunosuppressant medication</td>
<td>~$30,000/year</td>
</tr>
<tr>
<td>Total cost (transplant + immunosuppressant tx)</td>
<td>~$430,000/ first year</td>
</tr>
</tbody>
</table>

HIV/HCV Co-infection
Overall Prevalence of HCV Among HIV-Infected Persons in the US

- HCV/HIV Coinfected: 30%
- HIV Monoinfected: 70%

Impact of HCV on HIV Disease Progression

- Prospective cohort study of 3111 patients on HAART between 6/96 to 5/99
- 37% were HCV+
- HIV-related progression and death higher in active IVDU with HCV infection
- HCV associated with blunted CD4 recovery
- Deaths from liver disease 3-fold higher

HCV/HIV Coinfection: An Area Of High Medical Need

- One third of HIV patients are coinfected with HCV\(^1\)
  - Among HIV-infected IVDU, this rises to 50% - 90%\(^2\)
- HCV viral load higher in HCV/HIV vs. HCV patients \(^3\)
- HIV accelerates clinical course of HCV-related liver disease
  - Time to cirrhosis is significantly reduced\(^4\)
  - Liver disease is now a leading cause of death in hospitalized AIDS patients\(^5\)
- HCV may also impact the course of HIV disease
  - Increases risk of ART-related hepatotoxicity\(^6\)
  - Apparent reduction in CD4 count responsiveness to ART\(^7\)

Barrier to HCV Treatment in an Urban HCV/HIV Clinic

149 HCV/HIV-Infected Patients

Eligible 30%

Ineligible 70%

ESLD 12%

AIDS 13%

Non-Adherence 23%

Drug Use 23%

Psychiatric 21%

Other 8%

ESLD, end stage liver disease

Conclusions

- HCV/HIV coinfected patients are less likely to be treated for HCV than those with HCV monoinfection

- Primary Barriers
  - Low physician referral rates
  - High no-show rates

- Additional reasons of ineligibility for HCV treatment
  - Non-adherence
  - Psychiatric illness
  - Relapsed drug or alcohol use

- Strategies to overcome these barriers are needed

Practice Guidelines Regarding HCV/HIV Coinfection

➢ 2004 AASLD Practice Guidelines, endorsed by the IDSA, recommend\textsuperscript{1}:
  ● All HIV-infected individuals should be screened for HCV antibodies in serum or plasma
  ● Including those previously diagnosed with HIV

➢ Recommendations endorsed by the CDC, NIH, HIVMA, and IDSA, based on safety and efficacy demonstrated in PEGASYS Trials\textsuperscript{2}:
  ● Antiviral treatment should be considered for all HIV patients coinfected with chronic hepatitis C infection


Guidelines may not necessarily reflect the approved labeling for Pegasys and Copegus
Hospital Admissions Among HIV-Infected Patients

5 Fold Increase in Liver Complications From 1995–2000

2007 Updated Recommendations From the HCV-HIV International Panel

- Optimal dosages of Peginterferon and RBV*
  - Current treatment of HCV in HIV+ should be pegylated interferon at standard doses plus weight-based RBV:
    - 1,000 mg/day if < 75 kg
    - 1,200 mg/day if > 75 kg

*Proposed RBV dosing is not reflective of current Copegus product labeling
Approved Copegus dosing is 800mg for HIV/HCV co-infected patients

Proposed Optimal Duration of Hepatitis C Therapy in HCV/HIV Coinfection Patients

Weight-based Ribavirin: 1,000 mg/day if < 75 kg and 1,200 mg/day if > 75 kg

*In patients with baseline low viral load and minimal liver fibrosis
W = week; neg = negative; pos = positive; G = genotype
# Definitions of Virologic Response to Antiviral Therapy for Hepatitis C

<table>
<thead>
<tr>
<th>Response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RVR</strong> Rapid Virologic Response</td>
<td>HCV-RNA negative at 4 weeks as defined by HCV-RNA &lt; 50 IU/mL</td>
</tr>
<tr>
<td><strong>EVR</strong> Early Virologic Response</td>
<td>HCV-RNA negative or &gt; 2 log$_{10}$ drop at week 12</td>
</tr>
<tr>
<td>Complete EVR (cEVR)</td>
<td>No RVR but HCV-RNA negative (&lt; 50 IU/mL) at week 12</td>
</tr>
<tr>
<td>Partial EVR (pEVR)</td>
<td>No RVR and detectable but ≥ 2 log$_{10}$ drop in HCV-RNA at week 12</td>
</tr>
<tr>
<td>Slow partial responder</td>
<td>≥ 2 log$_{10}$ drop in HCV-RNA at week 12 but not HCV RNA negative until week 24</td>
</tr>
<tr>
<td>Partial responder</td>
<td>≥ 2 log$_{10}$ drop in HCV-RNA at week 12 but HCV RNA positive at week 24</td>
</tr>
<tr>
<td><strong>SVR</strong> Sustained Virologic Response</td>
<td>HCV-RNA negative 24 weeks after end of treatment</td>
</tr>
<tr>
<td><strong>Relapse</strong></td>
<td>HCV-RNA negative at end of treatment but HCV-RNA positive after treatment stopped</td>
</tr>
</tbody>
</table>

RVR, cEVR, SVR in HIV/HCV Co-infection: Genotype 1 Virologic Responses

Pegasys 180 μg/week plus RBV 800 mg/day for 48 weeks

- **RVR**
  - 13% (22/176)
  - 82% (22/27)

- **cEVR**
  - 22% (38/176)
  - 63% (24/38)

- **pEVR**
  - 26% (46/176)

- **Non EVR**
  - 40% (70/176)

Community Health Center Network

- SCDOHS operates 9 community health centers
- Strategically located throughout Suffolk County
- Most patients do not have access to regular preventive care anywhere else
Health Center Patients

- **Patient Volume**
  - Approximately 60,000 unduplicated patients seen annually
  - Approximately 280,000 annual visits

- **Gender**
  - Male - 37.7%
  - Female - 62.3%

SUFFOLK COUNTY (NY)
Pop: 1,504,947 Area: 912 sq. miles
Health Center Locations

- **Amityville** – The Maxine S. Postal Tri-Community Health Center
- **Brentwood** – Brentwood Family Health Center
- **Coram** – Elsie Owens North Brookhaven County Health Center
- **East Hampton** – The Suffolk County Health Center at East Hampton
- **Patchogue** – South Brookhaven Family Health Center, West
- **Riverhead** – Riverhead Health Center
- **Shirley** – Marilyn Shellabarger South Brookhaven Family Health Center, East
- **Southampton** – Kraus Family Health Center at Southampton
- **Wyandanch** – Martin Luther King, Jr. Community Health Center
Approximately 500 HIV positive patients receive comprehensive primary care services at the health centers.

121 of these patients are HIV/HCV co-infected.

Each health center has an HIV Care Team (HIV specialist, HIV Nurse Coordinator, Case Manager/Social Worker) to take care of the HIV positive patients.
Issues and Barriers to Treatment of HIV /HCV Co-Infected Patients

- Shortage of specialists in the area
- Co-infected patients could not obtain appointments in timely fashion and treatment for HCV was delayed
- Lack of adequate transportation
Solution

- January 2009, HRSA consultant provided in-depth training on treatment of co-infected patients to the SCDHS HIV Care Teams
- Patient assessment and audit tools developed
- All HIV + patients screened for HCV and placed into one of five categories
## Patient Assessment at Baseline

<table>
<thead>
<tr>
<th>Liver Evaluation if Needed</th>
<th>Clinical Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV Genotype</td>
<td>PHQ9 Depression Screen</td>
</tr>
<tr>
<td>HCV RNA</td>
<td>Weight Evaluation</td>
</tr>
<tr>
<td>Liver Biopsy</td>
<td>Adverse Events</td>
</tr>
<tr>
<td>Liver Sono</td>
<td>ETOH counseling</td>
</tr>
<tr>
<td>AFP</td>
<td>Cardiac Eval/EKG</td>
</tr>
<tr>
<td><strong>Lab Tests</strong></td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>Hep A serology</td>
</tr>
<tr>
<td>PLT</td>
<td>Hep B serology</td>
</tr>
<tr>
<td>ANC</td>
<td>Hep A vaccination</td>
</tr>
<tr>
<td>Hgb/Hct</td>
<td>Hep B vaccination</td>
</tr>
<tr>
<td>ALT</td>
<td>Pneumococcal vaccine</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Flu Vaccine</td>
</tr>
<tr>
<td>Pregnancy test</td>
<td>HIV Markers</td>
</tr>
<tr>
<td>Cr</td>
<td>HIV RNA</td>
</tr>
<tr>
<td>Glu</td>
<td>CD₄</td>
</tr>
<tr>
<td>TSH</td>
<td></td>
</tr>
<tr>
<td>ANA</td>
<td></td>
</tr>
</tbody>
</table>
Assessment:

- Patient is a candidate for HCV treatment or not; if not, what is the reason
- Treatment deferred at this time with the reason
# Hepatitis C Treatment Audit Tool

**Health Center**

**Patient**

**MR#**

<table>
<thead>
<tr>
<th>Test</th>
<th>DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD₄</td>
<td></td>
</tr>
<tr>
<td>HEP C VL</td>
<td></td>
</tr>
<tr>
<td>HEP GENOTYPE</td>
<td></td>
</tr>
<tr>
<td>DEPRESSION SCREEN (PHQ9)</td>
<td></td>
</tr>
<tr>
<td>ETOH EVALUATION</td>
<td></td>
</tr>
<tr>
<td>HEP A SEROLOGY</td>
<td></td>
</tr>
<tr>
<td>HEP B SEROLOGY</td>
<td></td>
</tr>
<tr>
<td>HEP A VACCINE (if indicated)</td>
<td></td>
</tr>
<tr>
<td>HEP B VACCINE (if indicated)</td>
<td></td>
</tr>
<tr>
<td>PNEUMOCOCCAL VACCINE</td>
<td></td>
</tr>
<tr>
<td>FLU VACCINE</td>
<td></td>
</tr>
<tr>
<td>EKG</td>
<td></td>
</tr>
<tr>
<td>Sonogram</td>
<td></td>
</tr>
<tr>
<td>AFP</td>
<td></td>
</tr>
<tr>
<td>PREGNANCY TEST</td>
<td></td>
</tr>
</tbody>
</table>

**Patient is a candidate for treatment**  Yes _____  No _____

**Treatment Success**  ______________  **Treatment Failure**  ______________
**Client Categories**

### Hepatitis C - Co-infected HIV Client Categories

1. **Category 1:** Patient is Hep C+, yet has cleared virus, previous exposure - no active infection (self cured, +HepC AB no virus detected)
2. **Category 2:** Patient with previous treatment, treatment failure in the past.
3. **Category 3:** Patient with previous treatment and cure.
4. **Category 4:** Patient who has active current barriers to treatment (low CD4, ETOH abuse, thrombocytopenia, etc.).
5. **Category 5:** Patient in the process of pre-treatment, target date for treatment initiation is to be determined, or in current active Hepatitis C treatment.

![Graph showing categories and number of patients]
Results

- Candidates for treatment (Category 5) underwent screening, education and counseling on treatment options and side effects.

- HRSA consultant remained available by telephone for questions.

- Follow up visit by HRSA consultant in May 2009 to review and discuss cases of screened patients.
Where We Are Now

- A total of 9 patients began treatment
- The first patient began treatment in July 2009
- Treatment takes extended time and patients need support of entire team
- HRSA consultant made a return visit in July 2010 to meet with the HIV Care Team to discuss patient management issues
- In the process of analyzing additional data
Lessons Learned

- Primary care providers can be effectively trained to become self-sufficient in providing the prevention education and treatment to HIV/HCV co-infected patients, with technical assistance from agencies like HRSA.

- Appropriate leadership is essential for the success of the program.

- In future, mono-infected patients may be treated using the same model.