5 year follow up of treatment of chronic hepatitis C virus infection in IVDU in correctional institutions and community settings: Implications for a successful Hepatitis C Virus (HCV) treatment program

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Epidemiology and Natural History of HCV Infection

• World wide prevalence of HCV: 170 Million
• Canada HCV prevalence: 300 000 (~1% of population)
• Prevalence in Canadian correctional institutions: 20- 40% (2008)

<table>
<thead>
<tr>
<th>HCV prevalence by exposure category in Canada, 2002</th>
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<tbody>
<tr>
<td>IVDU</td>
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<tr>
<td>Blood transfusion</td>
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<tr>
<td>Hemophilia</td>
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<tr>
<td>Other (piercings, tattoos, unprotected sex, blood splashes from fights, etc.)</td>
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</table>
Rate of Incarceration:
Canada
118/100,000 population
(1999/00)
OBJECTIVE

• To share our experience treating Hepatitis C Virus infections in (I) DUs in real life: settings (prison/ community)

• Review the data of at least five years of follow up of those “successfully” treated: achieved SVR.

• Highlight Reinfection as an important consideration in the management of HCV in IDUs & propose that the conventional measurement of SVR as the primary endpoint/indicator of successfully treating HCV in the non-IDU population is inadequate for the IDU population
• THE CORRECTIONAL SERVICE OF CANADA
  Corrections and Conditional Release Act
  Section 86 – Inmate Health

• The Service shall provide every inmate with (a) essential health care; and (b) reasonable access to non-essential mental health care that will contribute to the inmate's rehabilitation and successful reintegration into the community.

• The provision of health care under subsection (1) shall conform to professionally accepted standards.

• Services provided by CSC Health Services Branch
Infectious Diseases Program

• Activities of CSC HSB to prevent/control infections:
  – Voluntary testing (at admission, any time) for HIV, HBV, HCV, STDs
  – Education
  – Harm reduction programs
    • Condoms
    • Dental dams
    • Lubricants
    • bleach
  – Immunization for Hep A, Hep B
  – Methadone maintenance program (expanded 2002)
  – Surveillance system: non-nominal, aggregate – based on voluntary testing or disclosure of status

(CSC, 2003)
CSC contract physician-coordinated Infectious Diseases services Pacific Region Institutions (8); ~2,500 Inmates
Figure 1. Regions administered by the Correctional Service of Canada.
Clinical evaluation, testing and treatment of HCV

• Detailed medical history including determining of possible high risk activities, physical exam and relevant laboratory tests (liver transaminases, liver function studies, HCV RNA, ultrasound and liver biopsy if necessary) were done for each patient entering the study.

• **Follow up**: lab tests (liver transaminases, HCV RNA PCR) done at the start of treatment and at weeks 4, 8, 12, 24, 36, 48 and 6 months post treatment.

• **Treatment regimen**: Treatment was implemented according to current protocols & guidelines.
  - Interferon alpha: 65 patients
  - Pegylated interferon alpha 2 a + Ribavirin: 115 patients
  - Pegylated interferon alpha 2b + Ribavirin: 199 patients
Evaluation and Clinical assessment by Infectious Diseases Consultant
Inmate Community Health Reintegration Services (INCOHRS)

- Advised by CSC Nursing Staff
- Appointments made by my office staff
  - Seen at my office, or referred to other physician if going out of the Vancouver area
- Mechanisms set up for getting medications, social services assistance as necessary
- If do not show up call (or try to)
Treatment regimen

- **Treatment duration:**
  - 24 weeks for Genotypes 2, 3.
  - 48 weeks for Genotypes 1, 4, 5.
  - Some were treated longer if they were a “slow responders” (HCV still detected at 12 weeks or if there’s not 2 log drop in viral load).

- Some patients discontinued treatment prematurely due to various reasons: unable to tolerate adverse side effects, discharged from institutions and did not have treatment coverage once in community, not responsive to treatment.
Summary: Method & Study Population

- Method: retrospective chart review
- Study population: 588 - including inmates, former inmates discharged to community and individuals in the community who were treated between 1999-2010 and with relevant data.
- Of those, 379 likely acquired HCV through IVDU.
  - 352 Males (92.9%)
  - 27 Females (7.1%)
  - Age range: 25-69 years. Mean Age: 45.18 ± 9.86
  - On MMT program: 117 (30.9%)
  - HIV co-infection: 34 (9.0%)
  - Tattoos: 183 (48.3%)
Results

Place of IVDU initiation

- Community (27.5%) (N=106)
- Prison (4.4%) (N=17)
- Unanswered (68.1%) (N=262)
Genotypes Distribution

- Number of patients: 219 (57.8%)
- Percent of genotypes:
  - 45 (11.9%)
  - 113 (29.8%)
  - 2 (0.5%)
Outcome: SVR By Treatment Regimens

- Total number of patients; Interferon alpha; 65
- Total number of patients; Pegylated interferon alpha 2a & 2b + Ribavirin; 310
- Total SVR; Interferon alpha; 32
- Total SVR; Pegylated interferon alpha 2a & 2b + Ribavirin; 152

% SVR = 49.2%
% SVR = 49.0%
Outcome: SVR, By Treatment Regimens

- **Number of patients**: SVR = 49.2% (32/65)
- **Total # of patients**: SVR = 54.1% (60/111)
- **% SVR**: 46.2% (92/199)
Outcome: SVR, By Genotype

- % SVR = 41.6
- %SVR = 57.8%
- % SVR = 62.8%

Total number
Number with SVR
Effect of Methadone Maintenance Treatment (MMT) on SVR

- Percent SVR: 50.4% (N=59/117)
- Percent SVR: 40.0% (N=104/262)
SVR of patients on MMT by genotype

<table>
<thead>
<tr>
<th>Genotypes</th>
<th>Number of patients with SVR</th>
<th>% SVR</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>66.7% (8/12)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>63.2% (24/38)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50.7% (34/67)</td>
</tr>
</tbody>
</table>
**SVR: MMT & non-MMT**

<table>
<thead>
<tr>
<th>Genotype</th>
<th>MMT (% of SVR)</th>
<th>Not on MMT (% of SVR)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1 (total: 218)</td>
<td>67 (50.7%)</td>
<td>151 (41.6%)</td>
<td>0.95</td>
</tr>
<tr>
<td>Genotype 2 (total: 45)</td>
<td>12 (66.7%)</td>
<td>33 (57.8%)</td>
<td>0.52</td>
</tr>
<tr>
<td>Genotype 3 (total: 116)</td>
<td>38 (63.2%)</td>
<td>78 (62.8%)</td>
<td>0.60</td>
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</tbody>
</table>

Patient on MMT achieved higher SVR rates among the different genotypes than those not on MMT.
Outcome: SVR, BY Fibrosis stage

119/379 patients had core liver biopsies
Criteria to establish re-infections

- Initially infected with HCV
- Completion of recommended treatment regimen
- Clearance of HCV RNA as evidenced by PCR 6 months post therapy (SVR)
- Subsequently tested positive for HCV RNA PCR (re-genotyped)
Outcome: Follow up post-treatment

- 243 with available data followed up for the range of six months to eleven years.
Frequency of distribution to re-infection

Average time to re-infection: 2 years

Number of patients

Time interval (years)
Outcome: Reinfection

Number of patients followed up:
- 1 year: 80
- 2 years: 44
- 3 years: 21
- 4 years: 18
- 5 years: 8
- > 5 years: 11

Number of patients re-infected:
- 6 months: 19
- 1 year: 6
- 2 years: 6
- 3 years: 11
- 4 years: 9
- 5 years: 2
- > 5 years: 1

Time interval (years)
Reinfection Incidence

Rate of Re-infection **18.5 per 100PY**
Re-infection: Characteristics

- Likely etiology of 44 re-infection patients
  - 41 by IVDU
  - 2 by tattooing with shared needles in prison
  - 1 by blood splash due to fist fight

- Males: 43
- Females: 1
- Mean age: 44.1 ± 7.6
- HIV co-infection: 5 (11.4%)
- Continued IVDU after SVR of HCV treatment: 10 (22.7%)
- On Methadone program: 17 (38.6%)
- Tattoos: 26 (59.1%)
- 2 re-infected but had spontaneous clearance
Re-infection in individuals on MMT

Percent SVR

- 59% (10/17)
- 41% (7/17)
- 29% (5/17)
Estimation of time to re-infection

- The probable date of the re-infection was assumed to be the halfway-point between the date of the last negative HCV test and the date of the first subsequent positive HCV test.
- There was a cumulative total of 44 re-infections with a range of 2 weeks to 338.6 weeks and median time to re-infection of 106.7 weeks after SVR (SD 83.1 weeks)
Implications for a successful HCV treatment program

• Treatment of HCV Feasible and effective >>go where the action is
Treating HCV in Correctional Institutions

- **PURPOSE:** To assess sustained viral response rate and adherence to standard interferon alpha-2b and ribavirin therapy in inmates with chronic hepatitis C (HCV) in Canadian penitentiaries in the Pacific region.

- **METHODS:** A retrospective chart review of all inmates with chronic HCV who were treated with standard interferon alpha-2b and ribavirin therapy between March 2001 and October 2002.

- **RESULTS:** A total of 90 male inmates were treated. The mean age at time of treatment was 40 years. There were 49 inmates with HCV genotype 1, 11 with HCV genotype 2 and 30 with HCV genotype 3. Eight inmates discontinued treatment because of intolerance to side effects. Nine inmates were stopped by the physician because of nonresponse at an average of 27 weeks. All inmates achieved at least 80% adherence of interferon and ribavirin therapy. The overall sustained virological response (SVR) was 55.9%. SVR was 31.6% for genotype 1, 100% for genotype 2 and 71.4% for genotype 3.

- **CONCLUSION:** There was excellent SVR and adherence to treatment with interferon and ribavirin. This experience highlights an important opportunity to treat a population with a high prevalence of HCV-positive persons who may otherwise not seek treatment.

- **Key Words:** Hepatitis C; Incarcerated; Inmates; Interferon; Prison; Ribavirin; Therapy; Treatment of chronic hepatitis C in Canadian prison inmates; John D Farley MB BS FRCP C 1 2; Victor K Wong MD 3; Henry V Chung MD 3; Elizabeth Lim MD 4; Gavin Walters BSc 2; Theresa A Farley BA 2; Eric M Yoshida MD MHS FRCP C
Treating HCV in Correctional Institutions

• Hepatitis C treatment in a Canadian federal correctional population: Preliminary feasibility and outcomes

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Treating HCV in Correctional Institutions

- Feasibility and Outcome of HCV Treatment in a Canadian Federal Prison Population
- John Farley, MD, Shawn Vasdev, MEd, Benedikt Fischer, PhD, Emma Haydon, BSc, Jürgen Rehm, PhD and Theresa A. Farley, BA
- John Farley is with the University of British Columbia and John Farley, Inc, Vancouver, British Columbia. Shawn Vasdev is with University of Ottawa, Ottawa, Ontario. Benedikt Fischer, Emma Haydon, and Jürgen Rehm are with Centre for Addiction and Mental Health and University of Toronto, Toronto, Ontario. Jürgen Rehm is also with Addiction Research Institute, Zurich, Switzerland. Theresa A. Farley is with John Farley, Inc, Vancouver.
- Correspondence: Requests for reprints should be sent to Benedikt Fischer, PhD, Centre for Addiction and Mental Health, 33 Russell St, Room 2035, Toronto, Ontario, Canada M5S 2S1 (e-mail: benedikt_fischer@camh.net).
- We assessed feasibility and outcome of hepatitis C virus (HCV) treatment in male correctional inmates in British Columbia, Canada. We reviewed the medical charts of 114 treated inmates; 80 had complete data for treatment outcome. Approximately 4 of 5 inmates completed treatment (78.8%); 66.3% achieved sustained virological response. Those who completed treatment, those with injection drug use as a risk factor, and those with genotypes 2 and 3 were significantly more likely to achieve sustained virological response. HCV treatment in correctional inmates is feasible and effective.
Implications for a successful HCV treatment program

- Treatment requires a coordinated, multidisciplinary health professional team/approach and a committed patient willing to adhere to treatment regimen and protocol. Not one strategy for all settings.

- Educate patient regarding adherence, treatment-associated side effects: fatigue, N/V, weight loss, irritability, anemia, depression, etc.

- Establishing trusting relationship
Implications for a successful HCV treatment program: Beyond the SVR

- A continuum of care necessary. Treatment does not stop with the test for SVR...Continue engagement with those affected. The Combination Peg-IFN Ribavirin attacks the virus. We omit the dealing with the environment at our own peril.

- Clinical Registration Trials—done in Contrived settings with little regard for the “real world” setting or for the delivery of the treatment. Concerned with getting the drug funded

- Academic bias of funders...more concerned about publications
  - Need more avenues for real life demonstration efforts.
Implications for a successful HCV treatment program

• “Dangerous to get this information out”
• Costly - Risk cutting already fragile funding

• Contrary view:
  – WE need to take the lead in advocating for management beyond the SVR

• Re enforce harm reduction

• Advocate for Housing…Stability of prison positive impact for prison-INCoHRS experience

• One strategy not for all
Implications for a successful HCV treatment program

• Treat concurrent co-morbidities such as HIV, alcohol addictions, diabetes, depression or other psychiatric disorders.

• Prior to discharge, inmates should be linked to other services in the community such as parole officers, outreach, advocacy and support groups to aid in stabilizing life in the community.
Acknowledgements
CSC Staff & IDN Nurses
THANK YOU FOR YOUR INTEREST AND ATTENTION