Hepatitis C: Elimination in the East?

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Disclosures

• Industry:
  • Abbvie
  • Gilead
  • Merck
  • BMS
  • ViiV

• Academic:
  • Affiliation with Dalhousie University and Nova Scotia Health Authority
  • HCV virology / immunology lover

• Advocacy:
  • HCV and HIV advocacy groups
Objectives

• Review the basics of Hepatitis C virus (HCV) infection

• Know about new Hepatitis C treatments

• Be aware of global and local HCV elimination efforts
Key facts about hepatitis C

• Hepatitis C virus (HCV) is major public health threat

• Hepatitis C is the FIRST and only chronic viral infection that we can reliably cure

• HCV elimination is the global goal

• People engaged with the justice system and who are otherwise vulnerable are at much higher risk for having, acquiring or transmitting HCV
The Hepatitis C virus

- RNA virus
- In vivo replication: hepatocytes and lymphocytes (?)
- Highly error prone, up to 85% of virions have unique RNA sequence, trillions of virions/day
- 7 genotypes (1,2,3,4,5,6,7)

Most new HCV infections are within actively using populations.

BUT

Most referrals are in the non-actively using population.
HCV transmission
HCV: chronic infection in the liver

Liver failure
Liver transplant

Hepatitis C viral infection
Chronic hepatitis
Normal liver
Cirrhosis
HCC

1-2 DECADES (unless HIV or other liver infection, alcohol)
Acute HCV infection

• Acute infection
  • Usually asymptomatic (rarely diagnosed)

• High rate of spontaneous clearance within 14 weeks

• Higher cure rates (SVR12) with treatment (than for chronic HCV)
Chronic HCV infection

• Develops in 70 - 85%, usually asymptomatic

• Most will have elevated ALT (but not all)
  • 20% with normal ALT may have fibrosis on biopsy

• All eventually develop cirrhosis
  • 3% / yr risk of hepatocellular carcinoma

• Extrahepatic manifestations:
  • arthritis, PCT, leukocytoclastic vasculitis, cryoglobulinemia, monoclonal gammopathy, ITP, MGN, etc.
Impact
HCV infection

• Leading indication for liver transplantation
  • > 50% incident hepatocellular carcinoma

• Fastest growing cause of cancer-related death

• HCV-related mortality increased by >50% from 1999-2007

• HCV-related deaths > HIV-related deaths

• 1945-1975 birth cohort: 1.8% in Canada
  • Versus (<1% in non-1945-1965 adult birth cohort)
HCV testing

Test more people than less people

Currently still a blood test (order an HCV screen)

If the screen is positive in Nova Scotia: Lab will automatically do an HCV viral load and a genotype

IF 2 gold top tubes of blood are drawn!!
Goal of HCV treatment

Virologic cure

=sustained virologic response (SVR)

Global elimination
Ideal treatment

✓ Highly efficacious
  ✓ All oral
  ✓ (Interferon free)
  ✓ Ribavirin free
✓ No/low side effects
  ✓ Short course
  ✓ Once daily
✓ Pangenotypic
What treatments are available
Resources

Canadian HCV care guidelines
http://www.cmaj.ca/content/cmaj/190/22/E677.full.pdf

Comprehensive drug listing
http://www.hepatitisc.uw.edu/page/treatment/drugs

American Infectious Diseases and Liver guidelines (updated regularly)
http://www.hcvguidelines.org/

Case based learning designed specifically for Canada and primary practice
http://inhsu.org/education-program/canada-2/
HCV treatment primer

• Revolution in viral therapy
• Curative therapy for >95%
• Drugs that treat all genotypes
• Short treatment
• Very very few side effects
• >95% people do NOT require on-treatment medical visits for follow up
<table>
<thead>
<tr>
<th>NS3/4A Protease Inhibitors</th>
<th>NS5A Inhibitors</th>
<th>NS5B Polymerase Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boceprevir</td>
<td>Daclatasvir</td>
<td>Dasabuvir</td>
</tr>
<tr>
<td>Glecaprevir</td>
<td>Elbasvir</td>
<td>Sofosbuvir</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>Ledipasvir</td>
<td></td>
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<tr>
<td>Paritaprevir</td>
<td>Ombitasvir</td>
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<tr>
<td>Simeprevir</td>
<td>Pibrentasvir</td>
<td></td>
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<tr>
<td>Telaprevir</td>
<td>Velpatasvir</td>
<td></td>
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<tr>
<td>Voxilaprevir</td>
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</tbody>
</table>

https://www.hepatitisc.uw.edu/go/treatment-infection/treatment-genotype-1/core-concept/all
HCV treatment: It works

Sofosbuvir and velpatasvir

One pill once a day
All genotypes
12 weeks
Sofosbuvir and velpatasvir

Table 10. Recommended Treatment Regimen for HCV Mono-infected and HCV/HIV-1 Co-infected Patients (All HCV Genotypes)

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Recommended Dose and Duration of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients without cirrhosis and patients with compensated cirrhosis</td>
<td>EPCLUSA one tablet daily for 12 weeks</td>
</tr>
<tr>
<td>Patients with decompensated cirrhosis</td>
<td>EPCLUSA one tablet daily + ribavirin for 12 weeks</td>
</tr>
</tbody>
</table>

Caution: Proton pump inhibitors
Glecaprevir and pibrentasvir

Three pills once a day
All genotypes
8 weeks
Glecaprevir and pibrentasvir

Caution:
Some hormonal contraceptives (ethinyl estradiol)

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without Cirrhosis</td>
</tr>
<tr>
<td>GT-1, -2, -3, -4, -5 or -6</td>
<td>8 Weeks</td>
</tr>
</tbody>
</table>

GT= genotype
Elbasvir and grazoprevir

One pill once a day
GT1, GT4
12 – 24 weeks
Elbasvir and grazoprevir

Table 11 - Recommended Dosage Regimens and Durations for ZEPATIER® for Treatment of Chronic Hepatitis C Infection in Patients with or without Cirrhosis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1 or 4 TNα or PR-TEα Relapsers; Genotype 1 PI/PR-TEα Relapsers</td>
<td>12 weeks&lt;br&gt;&lt;span&gt;(8 weeks may be considered in treatment-naïve genotype 1b† patients without significant fibrosis or cirrhosis*)&lt;/span&gt;</td>
</tr>
</tbody>
</table>

Caution:
GT1a with advancing liver disease

Okay with all OCP and PPI
The only real rule in HCV

Thou shalt never (ever) prescribe interferon
(for HCV)
Key features to deciding on drug and duration

• Previous treatment (HCV specialist supervises treatment)

• Advanced liver disease (HCV specialist supervises treatment)

• Drug drug interactions (proton pump inhibitors, ethinyl estradiol, some seizure medications)

• Kidney disease (advanced kidney disease HCV specialist supervises treatment)

• Pregnancy

80% of HCV patients in the community DO NOT require an HCV specialist to supervise treatment
HCV: it’s an infection

Infectious diseases can be eliminated
HCV elimination strategies

• Treat HCV infection with highly efficacious therapy
  TREATMENT IS CURE

• Treat all individuals with chronic HCV infection
  – Prevent progression to more expensive advanced liver disease
  – Increase work productivity
  – Increase quality of life
  – ? Decrease stigma

• Treat everyone, early or late disease; high or low risk
ELIMINATE HEPATITIS
28 countries accounting for 70% of the burden take action

Planning
- 89% Establishing high level national committees

Targets
- 86% Setting national elimination targets

Plan
- 75% Developing national hepatitis plans

Funding
- 67% Of national plans have dedicated funding

Universal treatment access
- 43% Aiming for elimination through universal access to treatment
Iceland and Hepatitis C

- Population of 330,000
- Universal health insurance
- Mandatory reporting - HCV Registry since 1991
- Estimated viremic prevalence of HCV 0.3%
- 800-1000 cases total, >80% already diagnosed

TraP HepC: Treatment as Prevention for Hepatitis C in Iceland 2016-2018

- The concept: To reduce incidence and prevalence by targeting the ones most likely to transmit the disease
- Nationwide effort using combination of DAAs, addiction treatment and harm reduction
- Mathematical modelling for Iceland: the WHO target of HCV elimination by 2030 could possibly be achieved in Iceland in 2020

Scott N et al, J Hepatol 2018
How are we similar to Iceland?

Iceland and Hepatitis C

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The Nova Scotia hepatitis C situation

• Excellent work within **public health** to identify and contact trace individuals newly positive for HCV

• Lab facilitating one-time blood draw for diagnosis

• Expert providers in multiple disciplines who want to work together
  • Good: expert treatment capacity exists

• Highly invested in:
  • HCV elimination and public health (prevention)
  • Excellent patient care
  • Equitable access to care
  • Judicious, evidence based use of new therapies
  • Assessing outcomes to guide future program decisions
HARM REDUCTION

Identification of HCV positive

Automatic referral to provincial HCV program

Centralized triage and workup

Referral to appropriate provider

Treatment timing

Education and Evaluation

HCV elimination

Correctional system

Education and Evaluation
TREATMENT SUPPORT, EVALUATION AND EDUCATION

Science of cure research

- On-treatment adherence support, advice to patient
- Liver health and blood borne pathogen education
- Informed consent and enrollment in a provincial de-identified clinical database
- Health systems outcome measurement and cost effectiveness analysis

Implementation science of elimination
The Nova Scotia current plan

• Offer testing to all your patients who:
  • Were born 1945-1975, one time HCV screen
  • Have other identified risk factors, including new to Canada from endemic countries
  • Ask!

• If the person is positive, tell them (public health will also be in contact)

• Send a referral to the HCV program:
  • **FAX 902 473 7394**
  • People can self refer
  • We will contact the patient, do baseline bloodwork, assess drug drug interactions, get medication approved, and allow you to focus on the supervision of treatment IN PLACE in the community

• After treatment: ongoing education and support to prevent reinfection and liver disease in general
Real life situations
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ELIMINATE HEPATITIS