Review

Hepatitis ABC :
A Review of Viral Hepatitis

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Chronic viral Hepatitis is a major public health issue in Canada. Both Hepatitis B virus (HBV) or Hepatitis C virus (HCV) result in a slowly progressive liver disease, leading to cirrhosis, decompensation or hepatocellular carcinoma (HCC). Fortunately, effective therapy is now available for both Hepatitis B and Hepatitis C that should reduce the frequency of adverse outcomes.

Hepatitis C

Epidemiology

Hepatitis C remains a significant medical and economic burden to Canadians. The estimated prevalence is about 0.8% to 1% of the Canadian population. Injection drug use accounts for > 65% of cases, 20% of cases are accounted by the immigrant community and transfusion of blood products accounts for 13% of cases.

Natural history

The majority of acute Hepatitis C patients are asymptomatic with a high rate of spontaneous clearance between 20% to 30%, though in some cases this is up to 50%. In patients with chronic Hepatitis C, there is a variable progression of fibrosis. In 30% of persons, there is a slowly progressive course, 40% have variable progression and 30% develop cirrhosis at a faster rate. Once patients develop cirrhosis, the rate of decompensated liver disease is 4% to 5% per annum and a further HCC risk at a rate of 1% to 3% per annum.

Table 1
Testing for Hepatitis C virus (HCV)

Who should be tested?
- Those with common risk factors for contracting Hepatitis C, including:
  - Past or active injection drug use
  - Blood product transfusion prior to 1991
  - Immigrants from countries of high prevalence
- Persons with abnormal aminotransferase levels

How should we test for Hepatitis C?
- The primary screening test is an antibody test against HCV
- In persons who are positive for the antibody, a HCV RNA assay can be used for confirmation

Additional tests
- HIV and Hepatitis B virus (HBV) serology
- Baseline abdominal ultrasound—to detect obvious signs of cirrhosis/portal-hypertension, or presence of hepatocellular carcinoma (HCC)
- Useful secondary tests:
  - HCV genotype
  - Viral load

Therapy

Treatment decision is made on an individual basis and should consider the patient's wishes, risk of disease progression, the probability of a favourable response to therapy, the risks of adverse effects and particularly, presence of co-morbid conditions. Patients with advanced liver disease are most in need for therapy, though usually have lower response rates.

Treatment regimens

Combination pegylated interferon and ribavirin are standard of care regimens.

Treatment duration and efficacy rates are primarily based on HCV genotype:

- Genotype 1: Duration of therapy is for 48 weeks. Sustained virological response (SVR) rates for genotype 1 infection range from 42% to 46%
- Genotype 2 or 3: Duration of therapy is for 24 weeks. SVR rates range from 72% to 80%
- Genotypes other than 4, 5, or 6 are less common and SVR rates are better than genotype 1 but not as good as with genotypes 2 and 3, with duration of therapy for 48 weeks

Adverse effects of these regimens are multiple and include:

- Myalgias and fatigue (45% to 50%)
- Nausea (30%)
- Arthalgias (30%)
- Irritability and depression (25% to 30%)
- Pruritis (20%)

There is often hemolysis and pancytopenia which is usually dose-related.

Hepatitis B

Epidemiology

Prevalence of chronic Hepatitis B in Canada is unknown, but it is estimated at 600,000 people being infected. Overall, the highest prevalence is in the immigrant population at 6%.

Natural history

Hepatitis B is a slowly progressive disease which may be asymptomatic, until complications of cirrhosis and HCC develop. The risks for cirrhosis and HCC development are multifactorial and associated with the degree and severity of liver disease, male gender, older age, level of Hepatitis B (HBV DNA) and presence of other liver diseases. The progression to cirrhosis is variable at an estimated rate of 2% to 10% per year. The risk of decompensation in patients with cirrhosis is 4% to 5% per annum.

Treatment regimens

Therapeutic modalities can be divided into interferon-based or nucleoside/nucleotide base regimens. For the purposes of this text only a brief description of these agents are provided. Efficacy and resistance profiles of nucleoside/nucleotide are quite variable.

Interferons

Interferons induce a Hepatitis B 'e' antigen (HBeAg) seroconversion at a rate of 25% to 40% (most studies at 25% to 30%). Potential advantages include the absence of resistance mutations and a shorter fixed duration of therapy. However, disadvantages include adverse effects and the route of administration (subcutaneous injection). Pegylated interferon is available but not universally accessible for use.

Table 2

Testing for Hepatitis B virus (HBV)

Specific HBV testing should include:
- Hepatitis B surface antigen (HBsAg) (to screen and confirm HBV infection)
- hepatitis B e antigen (HBeAg)/anti-HBe
- Serum HBV DNA quantitation

Additional tests:
- HIV and HCV serology
- Baseline abdominal ultrasound should be done to detect obvious signs of cirrhosis and/or portal-hypertension and presence of HCC

Nucleoside analogues

Although a number of agents discussed below are available in Canada, they are not universally accessible through provincial paying agencies, though are generally covered through third-party extended medical coverage. An important consideration with these agents is development of resistance which generally increases over time and varies for each agent:

- Lamivudine is a pyrimidine nucleoside analogue that inhibits binding of nucleosides to the HBV polymerase. It was the first oral agent approved in the treatment of HBV in Canada. HBeAg seroconversion can be expected in about 20% at one year and rises slowly thereafter to 40% at three years. However, the durability of seroconversion is not as good as for interferon. High rates of resistance are noted
- Adefovir dipivoxil is a purine nucleotide analogue which has a moderate potency of viral suppression. The majority of patients do not have viral suppression within the first year, but rates of HBeAg seroconversion are similar to other agents of 40% at three years of use. Adefovir has a relatively high genetic barrier to resistance and is the drug of choice for patients with lamivudine resistance
- Entecavir is a selective guanosine analogue and is the most potent inhibitor of HBV DNA replication currently available. At three years, its seroconversion rate is also similar to the above agents. Overall rates of resistance are low
- Telbivudine is a pyrimidine nucleoside analogue with more potent antiviral efficacy against HBV than lamivudine
- Tenofovir is a purine analogue with potent efficacy. However, it is presently only licensed for treatment of HIV

Due to the difficulty in predicting sustained durability, these agents are initiated for long-term use, often up to a few years, if not indefinitely in some cases. Dx

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Resources
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