Canadian HCV management guidelines released

19 July 2012

About 1% of Canadians have hepatitis C virus (HCV). This germ damages the liver, and eventually, the overall health of HCV-positive people deteriorates as life-threatening complications, including liver cancer, can develop. Awareness of HCV itself, as well as the consequences of this infection and the effectiveness of treatment, needs to increase. New treatments for HCV infection have recently been licensed by Health Canada and this will increase cure rates. Moreover, research on the treatment of HCV has accelerated and many experimental therapies are now being tested.

To help physicians and nurses cope with the new data that have emerged in the past several years, the Canadian Association for the Study of the Liver (CASL) held a consensus conference in Toronto in late 2011. CASL subsequently produced guidelines for the care and treatment of HCV in Canada, which were published in the June 2012 issue of the *Canadian Journal of Gastroenterology*. The guidelines are a major step forward and will help healthcare providers deal with the complexity of care. The guidelines are rich in details and contain 48 recommendations that cover many important areas in HCV care. In this *CATIE News* bulletin, we summarize selected portions of the guidelines.

**HCV in Canada**

In Canada, most new cases of HCV infection occur through the sharing of contaminated equipment for substance use. Some new immigrants to Canada may have been inadvertently infected with HCV in their mother countries through exposure to unsterilized medical equipment or the receipt of unscreened blood or blood products. In Canada, researchers estimate that there are at least 245,000 people who are infected with HCV and 8,000 new infections occur every year.

Today the blood supply in Canada is screened for HCV, HIV and several other germs and is very safe. However, some Canadians who received blood or blood products (such as clotting factors) prior to the implementation of such screening may have become infected with HCV, HIV or both.

HCV can be divided into strains (called genotypes), such as genotypes 1 through 6. These can be sub-divided into sub-types, such as genotype 1a, 1b and so on. In Canada, genotype 1 is the most common strain of HCV.

**Therapy**

For the past decade, the standard of care for HCV infection was a combination of the following two drugs:

- a long-lasting form of interferon alpha called peginterferon, injected once weekly
- a broad-spectrum antiviral drug called ribavirin, taken orally twice daily

The duration of this therapy varied from 24 to 48 weeks.

Now two additional therapies have been approved by Health Canada—boceprevir (Victrelis) and telaprevir (Incivek). Each of these drugs is taken three times daily, together with peginterferon and ribavirin. These new regimens have complex schedules and their duration varies depending on each patient’s response to treatment.

**Multiple issues need to be tackled**
The CASL guidelines note that the “treatment of hepatitis C is complex and time consuming.” In part, this is due to the detailed algorithms for the use of triple therapy. Also, a relatively high degree of medical monitoring is required to judge the response to treatment and to monitor and manage potential side effects. Additionally, the guidelines note that co-morbidities, such as addiction to alcohol and drugs, are relatively common among people with HCV infection.

Therefore, to meet the complex health needs of patients, the guidelines encourage “a multidisciplinary approach that includes experienced physicians, nurses and allied health professionals (eg. psychologists, psychiatrists, addiction specialists and social workers).”

The guidelines state: “Currently in Canada, a relatively small number of physicians treat hepatitis C, leading in some cases to prolonged wait times for patients before being adequately evaluated and treated.”

If great strides against the burden of HCV are to be made, then, according to CASL, Canada needs to “expand treatment capacity via additional training and funding for experienced personnel [including physicians and nurses] and enhanced access to publicly funded antiviral therapies.”

Starting therapy

The guidelines state that “all patients with chronic hepatitis C who have compensated liver disease, are willing to undergo therapy and have no [conditions that preclude use of therapy], should be considered candidates for antiviral treatment.” Moreover, the guidelines note that “the decision regarding if and when to initiate therapy should be based on the balance between the perceived benefits and risks of treatment and the wishes of the individual patient.”

Factors that are considered in the initiation of HCV therapy include the following:

- probability of cure
- the likelihood of worsening liver disease without treatment
- the patient’s anticipated tolerance of treatment
- the life expectancy of the patient
- women of childbearing potential may choose to have therapy before becoming pregnant so as to reduce their future risk of mother-to-child transmission

Many experimental therapies for HCV are in development and in several years some of these therapies will hopefully become licensed. Such therapies are expected to have benefits (such as once-daily dosing, interferon-free regimens) over currently available therapy. The guidelines suggest that it is reasonable to consider the future availability of such therapies when making decisions about when to initiate HCV therapy.

Fibrosis

The degree of scar tissue (fibrosis) present in the liver should not be an absolute trigger for starting HCV therapy. However, the guidelines suggest that prompt initiation of therapy should be considered in patients with advanced fibrosis (graded as F3 to F4). Such patients are at greatest risk for the development of severe complications—including liver failure and liver cancer. The guidelines note that patients who have less severe liver damage (graded as F0 to F2) should also be considered for treatment before further liver damage occurs and reduces their chances of recovery from HCV infection.

Liver enzymes—ALT

ALT (alanine aminotransferase) is one of several enzymes produced by the liver. Levels of this enzyme can be measured in blood samples. Levels of ALT often rise when the liver is inflamed and damaged. The guidelines state that “in some regions within Canada, public reimbursement for [HCV] therapy is restricted to patients with elevated ALT concentrations.” However, research has found that about 25% of HCV-infected patients can have normal ALT levels yet still have a significant degree of liver damage. Therefore, the guidelines state that having normal ALT levels should not be a reason to deny patients HCV treatment.

Evaluation issues
The guidelines have an extensive list of proteins, enzymes and other markers physicians find useful when assessing the health of HCV-positive people. Several assessments are noteworthy, as follows:

**Viral load**

The guidelines state that HCV RNA (viral load) testing should be done using a sensitive assay, with a lower limit of detection ranging between 10 and 15 IU/ml. The results of this testing “should be available within a maximum of seven days to facilitate management decisions,” state the guidelines.

**IL-28B**

Studies have found that some people have certain genetic markers (or genotype) that are linked to different rates of response (good, intermediate or poor) when treated with peginterferon and ribavirin. Specialized laboratory tests focus on the gene for interleukin-28B (IL-28B, also known as interferon lambda). There are several different tests that look for genetic markers associated with IL-28B; such tests are not standardized, are costly and not widely available for routine care across Canada. According to the guidelines, despite having an unfavourable IL-28B assessment, some people can still respond well to treatment. The guidelines state that in people who have previously been exposed to interferon and ribavirin and whose treatment failed, the IL-28B test “is of limited value.” Although the IL-28B test “may provide information regarding the likelihood of treatment response,” the guidelines state that it “should not be used to determine the need or eligibility for therapy, or to determine the type of therapy used.”

**The liver**

In past decades the main means for assessing the degree of liver damage was a biopsy—the removal of a small amount of tissue for examination under a microscope. However, not all of the liver can be biopsied, so doctors may not see damaged tissue in parts of the liver that were not biopsied. In about 1 in every 1,000 cases, biopsy can lead to serious bleeding, and in about 1 in every 10,000 cases, people can die as a result of complications arising from a liver biopsy. Ways of assessing liver damage that are not invasive have been developed. The guidelines state that “acceptable methods” of assessing liver damage include liver biopsy, specialized ultrasound scans called FibroScan, blood tests such as APRI: the AST to platelet ratio index, FibroTest and FibroMeter “either alone or in combination.” Severe liver damage (cirrhosis) may alternatively be diagnosed, note the guidelines, by “clear clinical or radiographic evidence.”

**Barriers to treatment**

The only “absolute contraindication” in the guidelines to treatment is pregnancy. Previously, conditions that were once considered absolute barriers to treatment are now only considered to be relative barriers. Conditions such as “major depression” or “major psychosis” can be assessed on an individual basis, treated and stabilized with appropriate therapy and referral, and when the patient is ready and psychiatrists consider it safe, antiviral therapy can be offered.

The guidelines note that people who inject drugs may be co-infected with other viruses such as HIV and/or hepatitis B virus and “face significant social challenges.” However, research has found that, when given help for managing (and recovering) from addiction and mental health issues and under the supervision of experienced health professionals, people who inject drugs can achieve recovery rates similar to those seen in HCV-positive people who do not inject drugs.

The guidelines state that prisoners tend to have greater rates of HCV infection than non-prisoners. The document notes that research has found that “in appropriately selected inmates” the response to therapy is similar to that of HCV-positive people outside of prisons. Therefore, the guidelines state that people in prison “should be considered for antiviral therapy” just like anyone else.

**Special populations**

According to the guidelines, boceprevir and telaprevir (and experimental anti-HCV drugs) have not yet been extensively tested in certain groups who have “the greatest need for treatment,” such as the following:

- people with severe HCV-related complications
people who have had a liver transplant
people who are co-infected with HCV and HIV

Studies are underway to assess the effect of treatment in these populations. The guidelines caution that “particular attention will be necessary to avoid drug-drug interactions, especially between boceprevir, telaprevir and similar drugs and transplant drugs and those used for the treatment of HIV.” Also, the guidelines warn doctors and nurses that side effects may be more common among these groups of patients. The guidelines noted some good news: Preliminary reports suggest that people co-infected with HCV and HIV can achieve cure rates from HCV similar to those seen in people infected with HCV alone.

Treatment of HCV infection is entering a new and exciting phase. The 2012 CASL guidelines pave the way for better care for people with this infection. Currently a subscription to the Canadian Journal of Gastroenterology is required to access the guidelines but perhaps in the future this will not be the case, as this very important document needs to be widely disseminated.

Resources

CATIE’s hepatitis C site (www.hepCinfo.ca)
CATIE’s Living with HIV and Hepatitis C Co-infection
Canadian HIV Trials Network

REFERENCE:

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Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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