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Curing hepatitis C

Up to 75% of those infected with hepatitis C might not be aware of their status, only finding out when they have already progressed to liver failure or liver cancer.

THERE is hope yet for patients suffering from chronic hepatitis C. This disease is a major public health problem, and an important cause of preventable death and morbidity from chronic liver disease.

Interestingly, 2014 marks the 25th anniversary of the identification of the hepatitis C virus (HCV).

Globally, an estimated 185 million people have been infected with the HCV, with 350,000 dying each year from complications of the disease.

In Malaysia, the incidence rate of chronic hepatitis C was 6.8 per 100,000 population in 2013. In the United States, chronic hepatitis C is the commonest cause of death from liver disease and the leading indication for liver transplantation.

There is a high probability that more and more people will continue to die from HCV-related liver disease (liver failure or liver cancer) over the next two decades.

The concern is that most people are unaware of their infection.

There is therefore, an urgent need to address this public health problem, which includes hepatitis B. Hepatitis B is actually a bigger problem in this region, but has a lesser chance of complete cure, compared with hepatitis C.

This article focuses on chronic hepatitis C, as the cure rate for this disease has improved tremendously over the years with the introduction of new oral medicines that can now cure more than 90% of persons with HCV infection.

Unaware of infected state

The Malaysian Liver Foundation (MLF) has been screening individuals for hepatitis A, B and C throughout Malaysia, via their Hepatitis Days campaigns since 1997.

The foundation's objective is to detect patients early, so that more will be aware of the disease and seek advice from their doctors as to whether they are eligible for treatment. Those found to be free of hepatitis A or B will be offered vaccination at subsidised rates.

HCV screening is recommended for patients who received blood transfusions, transfusion of blood products or organ

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transplants before 1995, intravenous drug users, patients with HIV infection, those on haemodialysis, those with unexplained fatigue or abnormal liver enzymes, healthcare workers and current sexual partners of HCV-infected persons.

According to a report by the prestigious American Institute of Medicine (IOM) in 2010, the main reason why many individuals remain undetected is because of the lack of knowledge and awareness of chronic viral hepatitis amongst healthcare providers and the public.

In the US, only a quarter of those infected are aware that they have the virus, and only 21% have been referred for care and treatment.

The situation could be worse in Malaysia as there may be a large number of unsuspecting individuals walking around with undetected hepatitis B and C. MLF has written to major corporations in Malaysia to help screen their staff.

Most patients with chronic hepatitis C do not have symptoms apart from fatigue.

Around 60-80% of patients with chronic hepatitis C will progress to chronic liver disease. Some 20-30% of these patients will develop cirrhosis, and a proportion will end up with liver cancer. Sadly, many of these patients are unaware of their infection and are shocked to learn for the first time from their doctors that they have liver cirrhosis or liver cancer at an advanced stage during their first consultation.

By that time, treatment options for them are limited.

Improving cure rates

HCV has at least six major genotypes (1-6).

In Malaysia, the common genotypes are genotype 3 and 1, based on tests conducted at MLF's Molecular Research Laboratory.

HCV genotyping should be done in all HCV-infected persons prior to treatment to establish the dose and duration of therapy, and estimate the likelihood of response.

The goal of treatment is to eradicate HCV by achieving a sustained viral response (SVR), defined as the absence of HCV RNA by polymerase chain reaction six months after stopping treatment.

SVR is associated with a 99% chance of being HCV RNA-negative during long-term follow-up; therefore, patients who achieve SVR can be considered cured of HVC infection.

The current treatment for patients with chronic hepatitis C is a combination of pegylated interferon and ribavirin.

Patients with genotype 2 or 3 will be treated for 24 weeks, while those with genotype 1 will need a longer duration of 48 weeks.

The former is expected to achieve higher SVRs (80%) compared with the latter (40-50%).

The current treatment for chronic hepatitis C is not ideal as interferon has to be injected, and may cause troublesome side effects that include depression, fatigue, flu-like illness, low blood counts, hair loss and thyroid abnormalities.

Patients with psychiatric illnesses or autoimmune disease are contraindicated for interferon. Better alternatives are therefore being sought. There was a breakthrough in 2011 with the approval of two direct-acting antiviral drugs (DAAs).

Boceprevir and telaprevir improve SVR specifically for patients with genoytpe 1 when used in combination with pegylated interferon and ribavirin, achieving SVR of 40-44% to 68-75% in those who have not been previously treated.

However, their use was associated with frequent side effects and drug interactions. And now, both drugs can be replaced with better-tolerated oral drugs such as simeprevir and sofosbuvir, which was approved in the US last year and in Europe this year.

Newer DAAs and host-targeted agents (HTAs) are now in clinical development.

The ideal drug or combination of drugs must be one that can be given orally once daily, with few side effects, minimal drug interactions and resistance, short treatment duration, and effective against all major genotypes.

Hepatologists all over the world are waiting eagerly for the day we can achieve cure rates of over 95% with the new oral drugs – something that was inconceivable as recent as three years ago.

Affording the latest drugs

While we rejoice at the discovery of more effective therapies in the future, we must be cognisant of several issues, including access to care and the high costs of these new drugs. Such high costs may be beyond the reach of those who need the drugs the most.

It is for this reason that the Drugs for Neglected Diseases Initiative (DNDi) convened a one-day expert meeting in March in Geneva to explore the feasibility of expanding its portfolio to include hepatitis C, in order to make new highly-effective combination regimens available to the world's poorest patients.

I was invited to be part of the expert panel on chronic hepatitis C, representing the Asia Pacific region.

DNDi is a not-for-profit research and development organisation founded in 2003 to develop safe, effective and affordable medicines for neglected diseases that afflict millions of the world's poorest.

Malaysia is one of the seven founding members of DNDi, together with Medecins San Frontieres (Doctors Without Borders), Brazil's Oswaldo Cruz Foundation, the Kenya Medical Research Institute, Indian Institute for Medical Research, Institute Pasteur and the World Health Organisation.

Malaysia will have access to some of the

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new oral drugs soon, but the costs may prevent many from receiving the drugs, unless subsidised by the Government or some special arrangement is made with the pharmaceutical companies.

It would be even better if we can manufacture the drugs locally – something that is being considered by DNDi.

Curing is cheaper

Treatment for both chronic hepatitis B and C is cost effective. A study in the US revealed that the annual direct medical care costs of treating patients with hepatitis C were US$1.1bil (RM3.6bil), while the annual indirect medical care costs related to premature mortality and disability of hepatitis C patients less than 65 years of age were estimated at US$7.5bil (RM24.2bil).

The MLF will continue to enhance its efforts to create awareness amongst healthcare providers and the population, conduct nationwide screening and identify infected subjects, and link them to trained clinicians.

We hope that the Health Ministry will join us in this initiative and facilitate access to care by putting in more resources and making treatment more affordable to patients.

We hope general practitioners and primary care physicians, who are expected to see the bulk of the cases for the first time, will do the necessary tests to detect patients who would require more definitive care.

Let us all do our part in keeping Malaysians healthy and productive for as long as possible.

■ *Tan Sri Dr Mohd Ismail Merican is the MLF president and a consultant hepatologist. For more information, e-mail starhealth@thestar.com.my. The information provided is for educational purposes only and should not be considered as medical advice. The Star does not give any warranty on accuracy, completeness, functionality, usefulness or other assurances as to the content appearing in this column. The Star disclaims all responsibility for any losses, damage to property or personal injury suffered directly or indirectly from reliance on such information.*

A woman grimaces as a volunteer takes her blood for screening during the recent Penang Hepatitis Day event organised by the Malaysian Liver Foundation at Gurney Plaza, Penang. - JEREMY TAN/ The Star