Hepatitis C and obesity
A weighty issue

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Hepatitis C virus is directly implicated in the development of insulin resistance which, along with obesity, is associated with a worse prognosis in chronic hepatitis C and poorer response to interferon–ribavirin therapy.

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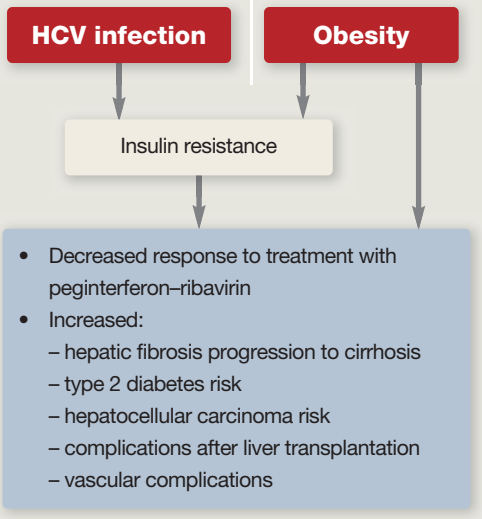
REMEMBER

- Obesity (body mass index, [BMI] of 30 kg/m^2 or more) is common in patients with chronic hepatitis C; it has been found in up to 28.8% of patients.[1] Obesity is associated with the metabolic complications of insulin resistance and type 2 diabetes.
- Hepatitis C virus (HCV) has been directly implicated in the development of virus-mediated insulin resistance and therefore, in itself, increases the risk of type 2 diabetes.[2]
- HCV infection and obesity occurring concurrently thus compound the risk of developing insulin resistance and type 2 diabetes.
- The metabolic syndrome, which comprises obesity and insulin resistance along with the cardiovascular and metabolic risk factors of high blood pressure and dyslipidaemia, is also more prevalent in people with chronic hepatitis C than in the general population.[3]
- Obesity, insulin resistance and type 2 diabetes significantly reduce the rate of sustained virological response to peginterferon–ribavirin therapy.[4,5] However, these metabolic factors appear not to influence the response to regimens containing the recently approved direct-acting antivirals, telaprevir and boceprevir, in combination with peginterferon–ribavirin. Of note, telaprevir and boceprevir-based treatments are used only in patients with genotype 1 HCV infection, and peginterferon–ribavirin therapy remains the standard of care for all other HCV genotypes.

RELATION BETWEEN HEPATITIS C, OBESITY, INSULIN RESISTANCE AND SEQUELAE



ABBREVIATION: HCV = hepatitis C virus.

- Obesity, insulin resistance and type 2 diabetes are independently associated with adverse hepatic outcomes in chronic hepatitis C, including more rapid progression of hepatic fibrosis towards cirrhosis, increased incidence of hepatocellular carcinoma and higher complication rates after liver transplantation.[6-11] The relation between hepatitis C virus, obesity and insulin resistance and their adverse clinical sequelae is shown in the flowchart on this page.
- Interventions targeted at reversing obesity and/or insulin resistance have the potential to reduce morbidity and mortality in chronic hepatitis C.

ASSESSMENT

- Measure body weight (kg) and height (m) to calculate BMI.
- Examine for features of the metabolic syndrome in addition to obesity: measure waist circumference and blood pressure.
- Measure fasting plasma glucose (FPG) level to check for overt type 2 diabetes (FPG of 7 mmol/L or more) or impaired fasting glucose (FPG between 6.1 and 6.9 mmol/L). Also measure fasting plasma insulin (FPI) level, which should be interpreted in conjunction with FPG. For example, in the liver clinic setting, the homeostasis model assessment of insulin resistance (HOMA-IR) may be calculated by the equation: HOMA-IR = FPI (mU/L) x FPG (mmol/L)/22.5. A HOMA-IR value over 2.0 suggests insulin resistance.[12]
- Measure serum cholesterol and triglyceride levels to check for dyslipidaemia (low HDL cholesterol and elevated triglycerides).
- Have a low threshold for performing an oral glucose tolerance test, as this may uncover a pattern of impaired glucose tolerance or overt type 2 diabetes, even in the presence of a normal FPG.[13] Current guideline recommend performing a 2-hour oral glucose tolerance test when FPG is between 5.5 and 6.9 mmol/L.

MANAGEMENT

- It is appropriate to counsel patients with chronic hepatitis C who are overweight or obese (BMI of 25 kg/m^2 or more) to try to lose weight because of the potential benefits for their liver disease as well as for the metabolic and vascular complications of overweight and obesity.
- Management of overweight or obesity may be recommended across all stages of chronic hepatitis C, from mild or early stage disease through to hepatic cirrhosis.
- Weight loss can potentially increase the chance of a response to peginterferon–ribavirin therapy. Although excess body weight and insulin resistance appear not to influence outcomes of treatment with the recently approved direct-acting antiviral regimens (telaprevir or boceprevir in combination with peginterferon–ribavirin), measures to reduce obesity and insulin resistance should still be recommended in candidates for this treatment. This is to reduce the risks of progression of hepatic fibrosis to cirrhosis, hepatocellular carcinoma, and type 2 diabetes and its sequelae.
- Obesity (and concomitant insulin resistance) should be managed with lifestyle interventions, including diet and physical activity. Lifestyle interventions have been shown to reduce body weight and markers of insulin resistance as well as to improve liver histology.[14,15]
- Patients with chronic hepatitis C should gradually increase their physical activity through incidental and intentional exercise. Simple recommendations include using a pedometer to encourage and monitor walking (aiming for a daily step count of more than 10,000 steps) and undertaking 30 minutes of aerobic exercise per day.[14,15]
- Patients should be referred to a dietitian for specific advice on dietary adjustments which, combined with increased physical activity, should aim for a weight loss of 0.5 kg per week.[14,15] Dietary modifications should also aim to manage dyslipidaemia, insulin resistance or overt type 2 diabetes, if present.
- Insulin-sensitising medications (e.g. metformin, pioglitazone) have a limited role in management of chronic hepatitis C. Pioglitazone and metformin co-administered with peginterferon–ribavirin failed to improve rates of viral clearance in patients with chronic hepatitis C caused by HCV genotype 1 (the most common HCV genotype in Australia). However, pioglitazone enhanced the rate of response to

peginterferon–ribavirin in patients with insulin resistance and genotype 4 chronic hepatitis C.[16]

- The influence of insulin sensitisers on hepatic outcomes in chronic hepatitis C is yet to be evaluated. Insulin-sensitising medications should therefore be prescribed in patients with chronic hepatitis C for the indication of managing pre-diabetes or diabetes, in accordance with national guidelines.
- Bariatric surgery and pharmacotherapies targeting obesity have not been studied in the setting of chronic hepatitis C but are therapeutic options in individuals who otherwise meet the criteria. MT

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COMPETING INTERESTS: None.