HCV infection should be managed in specialist centres

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Chronic hepatitis C virus (HCV) infection may cause slowly progressive chronic hepatitis, cirrhosis, advanced liver failure, and hepatocellular carcinoma. These varying outcomes of type C hepatitis pose a challenge and responsibility which requires firstly, that antiviral treatment is targeted as precisely as possible to those who have progressive disease, and secondly, that patients with advanced disease are managed by specialist centres with the capability of minimising the morbidity of the disease. Presently, most patients with community and hospital associated hepatitis C requiring treatment are referred to specialist liver centres.

The hepatologist has a pivotal role in the management of chronic hepatitis C. This includes the differential diagnosis, clinical management, and assessment of the stage of disease. Hepatology has become an increasingly specialised discipline and hepatologists are ideally placed to collate investigations and to ensure the appropriate management of coexisting liver disease. Specialist hepatologists also provide the continuity and follow up required for understanding the sometimes complex dynamic nature of the disease.

There is a unique requirement for the histopathological investigation of hepatitis C to inform and deliver the National Institute of Clinical Excellence (NICE) guidelines. Useful classifications for staging and grading of disease have been devised. There is a need for experienced clinical input to complement the interpretation of liver biopsies by histopathologists who should see sufficient numbers of patients with a full spectrum of disease. Liver biopsy moreover is an invasive technique and requires skilled and practised operators. If haemostasis is abnormal, transjugular biopsies may be required.

The hepatologist is required to ascertain the trajectory of the disease in chronically infected patients to make informed decisions regarding treatment. Alpha interferon and ribavirin are the current standard of care. NICE makes clear recommendations for the treatment of chronic disease, and the appropriate application of this treatment is an obvious example of specialist input to ensure that national guidelines are followed (www.nice.org.uk). The optimal timing of treatment necessary to minimise unnecessary treatment for those who would not progress to severe chronic disease, but avoiding treatment failure through delay, is being established. Generally, hepatologists are engaged in applying antiviral therapy for this disease and in monitoring patients for response or complications during treatment. They are also well placed to assess indications and contraindications for antiviral therapy and the management of resistance, relapse, or non-response. Hepatologists take a specialist research and clinical interest in therapeutic trials for HCV infection and are at the forefront of emerging technologies.

There is clearly a mandatory role for the hepatologist in the management of cirrhosis. This applies to the management of complications including the medical, endoscopic and portosystemic intrahepatic shunt management of variceal bleeding, and other complications of portal hypertension, including ascites, spontaneous bacterial peritonitis, hepatic encephalopathy, and the renal dysfunction associated with cirrhosis. Specialist transplant hepatologists together with pathologists, radiologists, and the surgeon provide the tools and full range of expertise for the seamless management of patients with decompenased cirrhosis. Appropriately timed referral for transplantation demands particular training and experience.

To date, hepatologists have played a pivotal role in the diagnosis and management of hepatocellular carcinoma (HCC). This includes aspects of surveillance for small HCC as well as the imaging and diagnosis of focal lesions. Hepatologists and interventional radiologists must be involved in decisions regarding the treatment of HCC, including liver biopsy, surgical resection, liver transplantation, or targeted treatment, which in some cases may be curative. The management of advanced HCC is aided by chemotherapy and specialist oncologists.

The hepatologist has also begun to play a unique role in coinfection clinics, assessing the clinical management of coinfection with human immunodeficiency virus (HIV) and HCV (or hepatitis B). Together with the retrovirologist, decisions must now be made regarding the prescription of complex multiple antiretroviral agents and their combination with other antiviral agents in this rapidly evolving field. Liver involvement in acquired immunodeficiency syndrome (AIDS) or antiretroviral therapy also requires the involvement of a hepatologist. A number of extrahepatic manifestations, including renal disease, mixed essential cryoglobulinaemia, and lymphoma are being encountered in association with hepatitis C, which may require assessment by the hepatologist and clinical interactions with appropriate specialists.

Hepatologists have overseen the generation of guidelines for the management of hepatitis C, including the NIH and EASL guidelines. Generally, the specialist with liver disease is likely to act as the “driver” in developing recommendations for implementing the requisite virological and other laboratory investigations, and for steering the migration of tests from the research laboratory to clinical practice. In this way a composite of clinical and laboratory results enable the development of suitable diagnostic algorithms. In turn,
Debate

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It has been estimated that between 200 000 and 400 000 people in England and Wales have hepatitis C virus (HCV) infection, with subgroup prevalences of 0.04% in healthy blood donors, 0.4% in antenatal clinic attendees (in London), 1% in genitourinary clinic attendees, and up to 50% in intravenous drug users.1 The population in England and Wales is close to 50 million,2 implying that approximately 0.5% are viraemic as 85% of acute infections lead to chronic disease.3 A district general hospital serving a population of 350 000 people may therefore have 1750 viraemic individuals in its catchment area. Although the fraction of this hypothetical iceberg that is visible to secondary care is currently small and varies according to local demographics, it is already of the order of 15% in rural Gloucestershire (personal data).

Comprehensive consensus guidelines for the management of HCV infection have been published by both the NIH4 and EASL5 and one of the major factors in delay of implementation in the UK has been lack of resources in terms of clinicians’ time, nursing supervision, counsellors, and the drug budget. Nevertheless, in order to help British clinicians meet the ever increasing demand for the management of HCV, the Royal College of Physicians (RCP) of London and the British Society of Gastroenterology (BSG) have recently compiled Clinical guidelines on the management of hepatitis C6 in order “to improve the patient’s management from first diagnosis to completion of a course of antiviral therapy and during follow-up” (section 1.2.3). These national guidelines were drawn up by specialists and the editorial board of this journal, at the request of the BSG, took the

REFERENCES

progressive view that they should be available on the Gut website before appearing in print. It would appear therefore that the BSG and RCP have already concluded that hepatitis C is unlikely to be managed exclusively in centres of tertiary referral (which only exist to provide foci of expertise and resource for rare conditions or complex treatments) as there would be no requirement to take such unprecedented action unless they were intended for gastroenterologists working in general hospitals. Indeed, the first author of the document, which provides “a framework for local groups to develop according to local needs” (section 1.2.4) is a consultant working in a district general hospital. The summary states, “Patients infected with HCV should be referred to a clinician with a particular interest in the infection. Patients must have access to adequate counselling from a doctor with knowledge and experience of chronic HCV infection. All patients must have access to the appropriate diagnostic and therapeutic options available in the management of HCV infection”. Is this achievable in a district general hospital?

The answer is “yes” if there is a clinician with an interest and a counsellor with knowledge that is keen to gain experience. The British Liver Trust has a national support group network and can provide high quality patient information leaflets, as do the major suppliers of antiviral therapies. Industry is only too keen to assist in the training of counsellors, as they are usually nurse practitioners with concurrent responsibility for the supervision of antiviral therapy. Although the current recommendations for duration of treatment are related to viral load and genotype there is no “house” requirement for these advanced molecular virological techniques as cost and quality assurance considerations dictate centralisation within the PHLS.

The guidelines state “All liver biopsies should be examined by a histopathologist with experience in liver pathology and who can apply the recently reformed grading and staging scores” (section 4.6) but there is no evidence that such a sophisticated scoring system is required in clinical practice. The section concludes “In patients with mild, slowly progressive disease it may be best to withhold treatment until more efficacious treatments are available. Others would regard this as the best time to treat, perhaps resulting in higher numbers of responders, and others would argue that the virus rather than the disease process needs to be treated and so all infected patients need to be considered for treatment”. This would suggest that simple reproducible schemes for the interpretation of liver biopsies by general pathologists are just as good for the stratification of patients for treatment as this still remains a matter of opinion (category of evidence—level C).

One of the major difficulties in establishing a local service for patients with HCV infection is meeting the cost. Although the National Institute of Clinical Excellence (NICE) guidelines give advice on clinical audit and implementation, it is the Commission for Health Improvement (CHI) that will eventually monitor adherence in NHS trusts and primary care. The cost of drugs, molecular virological tests, and nursing salaries remain beyond our control and there are insufficient gastroenterologists nationally to satisfy all the other requirements of the service. Nevertheless, there is such a local abundance of patients that most interested clinicians would accumulate a case load sufficient to consolidate expertise, and NHS trusts would do well to nurture such individuals before CHI impose a less palatable implementation.

At first sight, section 3.2 of the national guidelines appears to be inconsistent with the philosophy of developing a local management framework—“Following a positive antibody test, patients should be referred to the nearest specialist service for further clinical assessment. Specialist clinicians will be responsible for the care of these patients and will ensure some uniformity of approach, whilst facilitating data collection, audit and research”—unless it is envisaged that successful implementation creates specialist clinicians within a specialist service. Those gastroenterologists who are not selected to work in a specialist centre for HCV should take heart. They are probably already working in a specialist centre for inflammatory bowel disease or peptic ulceration.

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