BVHG

• BRITISH VIRAL HEPATITIS GROUP •

Provision of antiviral services for patients with chronic viral hepatitis

BVHG RECOMMENDATIONS

FOREWORD

Chronic viral hepatitis is common in the UK affecting many hundreds of thousands of patients. Many of those who are infected are from minority and disadvantaged groups whose health care needs are often overlooked. Without effective management many of those with chronic viral hepatitis will develop end stage liver disease and die and there is clear evidence of an increase in mortality from chronic viral hepatitis in the UK. Effective therapies are available and, if used appropriately, can reduce mortality and morbidity. However, therapies for viral hepatitis are complex and sub-optimal therapy has the potential to cause significant harm, specifically viral resistance, that may compromise future care. These guidelines represent a consensus statement that aims to improve the quality of care for all those suffering from viral hepatitis. Children and young people with viral hepatitis should be managed differently to adults and there is a limited role for the non-specialist. Paediatric care guidelines are provided separately to the guidelines for the adults (Appendix 1). It is our intention in publishing and distributing these guidelines to influence commissioning for positive change affecting improvements in the quality of patient-focused care. Specifically, it is our goal is to set baseline standards for the management of both Hepatitis B (HBV) and Hepatitis C (HCV) that will benefit all patients.

Process

Members of the British Viral Hepatitis Group and other invited stakeholders met at the King’s Fund, 26 February 2010, to discuss the provision of services for patients with chronic viral hepatitis.

The aim of the day was to produce a set of recommendations for the management of patients with chronic viral hepatitis. The meeting led to the production of a set of draft guidelines that was reviewed by the attendees and then circulated widely for further consultation. Following a period of consultation (March to June 2010) the final guidelines contained in this document were developed.

SUMMARY OF KEY RECOMMENDATIONS

All patients with viral hepatitis should have access to high quality care provided by an experienced team led by a specialist with appropriate training and experience.

Robust policies to ensure that all those diagnosed with viral hepatitis have multiple opportunities to access services must be put in place.

All the required investigations needed to confirm the diagnosis should be performed prior to specialist review and therapy should be initiated within 18 weeks of referral.

A variety of different monitoring schemes should be in place to meet the differing needs of different patient groups.

Support services including radiology, histopathology, virology and psychiatry should be readily available, appropriately funded and must conform to national standards. All imaging procedures (including ultrasounds) must be performed by appropriately trained, registered, monitored personnel and there is no role for ultrasound examinations by untrained clinicians.

All those treating patients with viral hepatitis must have ready access to liver transplantation and services for the management of liver cancer. Clear referral pathways must be in operation.

Service provision in the community is a welcome innovation that may increase access to care. Provision of anti-viral therapy in the community should be safe, clinically and cost effective and must provide care of equal quality to that delivered in tertiary centres. Out-reach services must be managed by an appropriate specialist and patients treated in the community must have equal access to support services. Since it is not possible to predict in advance of therapy which patients will require additional support it is not appropriate to stratify patients and provide reduced support for patients being managed in the community.

Local networks play a key role in developing local services and ensuring that high quality care is available to all. Networks should be multidisciplinary and should inform commissioning and monitor outcomes.

All those involved in managing patients with viral hepatitis must commit to a program of regular audit and should actively contribute to on-going research programs.

1. The patient pathway

Recommendations on access to care, timelines and provision of therapy

Access to therapy:

Overview

All patients with chronic viral hepatitis should have ready access to high quality care. Expertise is needed to safely supervise and support therapy and to ensure that the patient experience is satisfactory and care must therefore be provided by an experienced treatment provider. Care should be provided in a setting that is appropriate for the patient's needs and a variety of services in different settings should be developed to ensure that appropriate services are available for different patient groups. In each setting the same standard of specialist delivered care should be provided. BVHG does not believe that provision of different levels of care by health care providers with varying levels of expertise is appropriate and models of care should be developed where every patient is provided with specialist led care, wherever therapy is provided. Models of care where 'easy to treat' patients are managed in peripheral centres by inexperienced practitioners is not appropriate for patients with viral hepatitis as stratification by disease complexity is often not possible prior to therapy and the rapidly changing therapeutic repertoire precludes high quality information dissemination by those without specialist interest in this disease area. In all cases care should be supervised and monitored by experienced health care workers with appropriate training and expertise with supervision from a knowlegeable clinician who will be able to demonstrate appropriate experience and training.

The patient pathway to care should be initiated by the health care worker who makes the diagnosis and appropriate pre-referral investigations should be performed to minimise diagnostic and treatment delay. Following referral and specialist review a rapid decision on the required therapy should be completed and, where appropriate, treatment should be initiated within 18 weeks of referral, but ideally within 8 weeks. Therapy should be monitored in a manner that is best suited to the patient's needs and appropriate support services should be available to assist in the management of the complications and side effects of antiviral treatment. Regular review and audit of the numbers of patients who test positive for viral hepatitis, the numbers who access care, the numbers entering treatment and their outcomes are essential for monitoring of the patient pathway and this activity should be supervised by the local network (see later).

Guidelines:-

a) Pre-specialist consultation:

- Patients should be referred for specialist care with a comprehensive set of diagnostic investigations that should be readily available to the specialist. These investigations should include the results of molecular diagnostic tests including HCV PCR status and HBV DNA levels.
- Viral Hepatitis networks should establish local funding to facilitate access to appropriate diagnostic tests and should audit the proportion of patients who attend with inadequate, or unavailable, investigations.

Specialist care – definition:

- High quality care for patients with viral hepatitis requires a team of individuals with appropriate training and skills. Each specialist team must contain:-

- A designated clinical lead in viral hepatitis with specific training in the management of both viral hepatitis and end stage liver disease (including liver cancer). In most cases this will be provided by either a consultant in Hepatology, a consultant in Infectious Diseases with specific training in the management of cirrhosis or a consultant Gastroenterologist with specific training in the management of viral hepatitis. In rare cases other clinicians may take the lead in managing patients but all those who initiate therapy for patients with viral hepatitis must have received significant post-graduate training in both viral hepatitis and in the management of end-stage liver disease and should have completed a competency based review to demonstrate an appropriate level of proficiency. Current certificates of specialist training in hepatology, gastroenterology and infectious diseases provide such a competency based review and some clinical virology training programs provide appropriate training.

- A Specialist Nurse – In the absence of national guidelines and competency standards for specialist nurses in viral hepatitis the BVHG recommends that all those providing nursing support for patients with viral hepatitis should have completed a minimum of 6 months supervision with an experienced viral hepatitis nurse. Once national competencies and standards are developed (by the BASLNF) these should be adhered to.

- A Pharmacist with specific interest and knowledge of the medications required must be available.

Access to other support services should be available via the hepatitis network and in smaller units with single practitioners appropriate ‘cross cover’ arrangements must be in place to ensure continuous provision of care by appropriate personnel.

It is envisaged that each specialist team will manage a minimum of 20 patients per year, although developing teams with close links to networks providing support services may initially treat fewer cases.

b) Post specialist referral

- From referral decision to treatment decision the 18-week pathway rules must apply
- The timeline from referral decision to first specialist appointment should be not more than 8 weeks
- The initial consultation for a patient with newly diagnosed viral hepatitis should be sufficient for an in depth discussion of the disease and should be not less than 20 minutes in length

c) Management of patients who do not attend for the first consultation

Many patients with chronic viral hepatitis are from disadvantaged, vulnerable groups – such as injecting drug users and ethnic minorities in whom literacy and English skills may be poor. A policy of automatic discharge from services following a failure to attend is inappropriate for such groups and robust policies to ensure that all those diagnosed with viral hepatitis have multiple opportunities to access services must be put in place. The local hepatitis network should audit management of patients who fail to attend and these data should be made publically available to facilitate comparisons and allow formal benchmarking.

2. Associated support

Guidelines on provision of ancillary services (pathology, virology, radiology, links to transplantation etc)

Overview

High quality care for patients with chronic viral hepatitis requires access to a variety of support services. Such services should be available to all who provide care for patients with viral liver disease but it is recognised that some degree of central service provision will be necessary for some of the more specialised services.

2.1 Virology:

Accurate diagnostic virology is the cornerstone of management of patients with chronic viral hepatitis. The range and value of diagnostic tests is changing rapidly (for example new assays for the quantification of HBsAg may improve management of patients with chronic HBV receiving pegylated interferon) and virological support for all those managing patients with viral hepatitis must be readily available. A named virologist with specialist interest in viral hepatitis must be available to all treating clinicians. The virologist should be responsible for the quality of the virological tests that are performed and should be responsible for the selection, evaluation, validation and appropriate interpretation of the diagnostic tests. The named virologist must have an appropriate level of knowledge to allow recommendations on sophisticated diagnostic testing (e.g. sequencing for drug resistance etc) The minimum requirement for a satisfactory virology service should be compliance with a documented external Quality Assurance scheme such as NQAS and CPA accreditation is recommended.

Appropriate funding must be available to support an adequate number of tests for every patient with chronic viral hepatitis.
Each patient with antibodies against the hepatitis C virus will require:-

- A diagnostic PCR test (which may need to be repeated on two further occasions to confirm or refute viral clearance) and a viral genotype
- A minimum of four quantitative measurements of HCV RNA during therapy
- Additional HCV RNA measurements should only be performed if there is a significant clinical change

Each patient with chronic hepatitis B will require:-

- Serial HBV DNA estimations – at least four tests are usually required during the first year to confirm the phase of the disease and two HBV DNA tests are needed annually thereafter in untreated patients.
- During antiviral therapy with oral antiviral agents HBV DNA testing should be performed every 3 to 4 months.
- Serological testing for eAg, eAb, sAg and sAb.

2.2 Pathology:

Full diagnosis and management of chronic viral hepatitis is often dependent upon pathological assessment of a liver biopsy. All clinicians treating patients must have access to a named pathologist with a special interest in liver pathology. There should be regular clinico-pathological meetings where biopsies can be discussed. The named pathologist must have significant experience in assessing liver biopsies and should take part in the national liver EQA scheme (http://www.virtualpathology.leeds.ac.uk/eqa/liver_circulations.php). He/she should attend appropriate local, national and international liver meetings at least once every two years to ensure that s/he remains up to-date. Specimen handling and reporting should be in accordance with the Royal College of Pathologist's Guidelines (http://www.rcpath.org/resources/pdf/g064tpliverandfocalmay08final.pdf). Pathologists working in smaller centres should have access to more specialist opinions from pathologists working in larger units.

The development of non-invasive markers of liver fibrosis is a welcome addition to the diagnostic options available for patients with viral liver disease. These tests should be viewed as being complementary to liver biopsy and it should be recognised that they will not replace liver biopsy. These tests do not replace the need for high quality pathological assessment of a liver biopsy but each network should ensure that patients have access to non-invasive fibrosis assessments.

2.3 Imaging:

Imaging of the liver is critical in patients with viral hepatitis and is of particular importance in those with cirrhosis where early diagnosis of hepatocellular carcinoma allows curative therapies. It is essential that all ultrasound examinations are performed by experienced ultrasonographers with regular training and supervision by consultant radiologists. Ultrasound scans performed by interested practitioners without specific training and supervision is not appropriate for the early recognition of liver cancer and should be avoided.
Specialist imaging of the liver, including CT scans and contrast enhanced MRI scans, must be available when required and all scans showing suspicious lesions should be reviewed at a properly constituted cancer MDT meeting.

2.4 Pharmacy:

Therapy for patients with viral hepatitis requires ready access to the NICE approved drugs. All those treating viral hepatitis should have ready access to a specialist pharmacist who is responsible for ensuring an appropriate drug supply. It is essential that robust mechanisms are in place to ensure that adequate supplies of drugs are available and funding for the NICE approved therapies must be made available by local PCTs.

BVHG notes that for patients with HIV "package of care" funding in which drugs and support services are funded on a per patient basis has proven popular and allowed budget setting for support services to respond to changes in patient throughput. A similar model for viral hepatitis should be considered.

In some areas drugs for patients with viral hepatitis are supplied by companies that deliver drugs to the patient's home under contract to the NHS. BVHG supports increasing access to therapy by providing innovative services that increase the choice available but if such services are used appropriate quality controls and monitoring must be in place.

2.5 Further specialist services

All those treating patients with viral hepatitis must have ready access to liver transplantation and services for the management of liver cancer. Clear referral pathways must be in operation to ensure that patients requiring these specialist services have ready access and access should be monitored by the local network.

3. Provision of therapy

Guidelines on who should administer treatment and what monitoring is appropriate

Response to antiviral therapy is dependent upon compliance and, for chronic HBV infection, inadequate compliance may be associated with drug resistance that restricts future therapeutic options. It is essential that all patients with viral hepatitis receive adequate pre-treatment counselling and support during therapy.

3.1 Therapy for patients with chronic HBV infection:-

Therapy must be initiated by an appropriately trained specialist (see Section 1).

Prior to therapy the patient should receive appropriate education (both oral and written)

Therapy must be supervised by a competent health care provider, this may consist of a specially trained nurse, pharmacist or doctor.

Prescriptions must be provided for an adequate length of time (at least three months once treatment is established).

Monitoring should be conducted in accordance with clearly defined, written local protocols. It is recommended that:-

- A clear therapeutic goal is defined at the onset of therapy (e.g. HBeAg seroconversion, prolonged suppression of HBV DNA to undetectable)
- Patients with cirrhosis should be monitored by experienced care providers
- The treatment initiator should periodically review the investigations
- Complex cases should be reviewed at regular MDT meetings.
- Shared care protocols for stable patients should be developed to release capacity but all patients should be periodically reviewed by the treatment initiator

3.2 Therapy for patients with chronic HCV

Therapy must be initiated by an appropriately trained specialist (see Section 1)

Prior to therapy the patient should receive appropriate education (both oral and written)

Therapy must be supervised by a competent health care provider. Normally this will be a named specialist nurse but a named doctor or pharmacist may fulfil this role. It is important to ensure that appropriate arrangements are in place to provide continuous support during holidays etc.

Monitoring should be conducted in accordance with clearly defined, written local protocols. It is recommended that:-

- Patients with cirrhosis should be monitored by experienced care providers
- The treatment initiator should periodically review the investigations
- Complex cases should be reviewed at regular MDT meetings.

The number of patients managed by each treatment provider should be monitored. Traditionally a nurse:patient ratio of 1:50 has been considered appropriate but this should be reviewed in the light of other nursing activities and the reduction in monitoring required for patients who are stable on therapy. The BVHG recommends that further work is undertaken to determine the optimum time required to manage patients with viral hepatitis and appropriate numbers of nursing staff should be trained to manage the increasing number of patients who access therapy.

4. Community involvement

Guidelines on routine provision in the community

Community delivered care is being considered for many clinical services. The BVHG recognizes the advantages of delivering care close to the patient and supports the NHS goal of high quality care in the community. Service provision in the community should be safe, clinically and cost effective and must provide care of equal quality to that delivered in tertiary centres. A number of different models of community care should be considered and different models may need to be provided for different patient groups.

4.1 Community care for patients with viral hepatitis

Minimum service requirements for care in the community are:-

- Oversight and supervision by an appropriately trained specialist (usually a consultant) as defined in 1
- Treatment support by a competent health care provider engaged in an on-going program of medical education to ensure up to-date advice and support. This will usually be provided by a nurse specialist with clinical sessions at a local centre but alternative models may be considered provided that the health care provider has an appropriate period of in-depth training and regular (at least annual) updates along with a program of continuous medical education.
- A safe and confidential environment where patients can consult with health care professionals in comfort and with sufficient time to address their needs and concerns. This will include secure storage for notes and other confidential information, facilities for ensuring hygiene and safety and a suitable environment for physical and psychological examination.
- Access to on-site phlebotomy with facilities for venesection in patients with poor peripheral veins – it is essential that all patients undergoing therapy have access to a skilled phlebotomy service able to access veins in the neck and groin.
- Access to central laboratory reports to ensure that results of critical investigations (including viral loads etc) are available in real time. In view of the necessity for rapid dose modifications in patients undergoing antiviral therapy for chronic hepatitis C it is essential that local arrangements are in place to provide instant access to crucial investigations including full blood counts, liver and renal function tests.
- Patients treated in the community must have the same access to other network services, (such as psychiatric support) as patients undergoing therapy in tertiary referral centres.

4.2 Community care for patients with viral hepatitis and on-going substance abuse.

All patients with chronic viral hepatitis have a right to high quality care regardless of lifestyle. Therapy for patients with addictive disorders poses particular challenges but a number of studies have shown that provision of therapy in the community is effective. BVHG recommends that all networks consider provision of specialist services in the community to provide care for those with addictive disorders. It is essential that all community services adhere to the standards outlined in Section 4.2.

4.3 Other patients not engaged with services (e.g. ethnic minorities):

There is an urgent need for novel approaches to therapy for patients from difficult to reach groups (including ethnic minorities who, to-date have failed to engage with current services).

Further research is needed to identify effective approaches and BVHG welcomes initiatives and examples in this area.

4.4 Children:

Chronic HBV infection can be prevented in children born to infected mothers by immunization. It is imperative that immunization strategies are in place to ensure that all at risk children are protected and PCTs must take responsibility for delivering effective immunization to all at risk infants. Hepatitis networks should audit the uptake of immunization.

Children with chronic viral hepatitis should have access to all community and Network services. Paediatric keyworkers may play a key role in encouraging access from disadvantaged and difficult to reach children and they should be appropriately educated.

5. The Hepatitis Network

Local networks play a key role in developing local services and ensuring that high quality care is available to all. Networks should be multidisciplinary involving liver and infectious disease specialists as well as associated services.

The central function of the hepatitis network is to inform commissioning and to monitor outcomes. Additional functions include**:**
- Support for clinical research
- To provide practical standards (informed by the multidisciplinary network meeting)
- To provide supervision and training to the specialist nurses
- To collate and provide data to commissioners. Data should include information on local outcomes, treatment rates and estimates of future treatment needs.
- Health promotion – awareness and education
- Development of local guidelines, which ensure that national guidelines are modified to meet local needs and circumstances

Outputs to commissioners:

Networks should provide feedback to local commissioners. Data to be reported should include:-
- Local prevalence, referral and treatment rates on HBV and HCV for children and adults
- Local Service Level Agreement (SLA) on delivery of the BVHG guidelines
- Health Protection Agency engagement
- An annual report
- Summary and details of research activity within the network

The following list should be available to local services for a minimal multidisciplinary network (in alphabetical order):
- Commissioner
- Dental service
- Dermatology
- Endocrinology
- Gastroenterology
- Haematology
- Health Protection Agency
- Hepatology
- Histopathology
- Infectious Diseases
- Nutrition
- Obstetrics/gynaecology
- Oncology
- PCT
- Pharmacy
- Prison services
- Psychiatry
- Radiology

- Sexual health
- Transplantation
- Virology

6. Research, audits and wider engagement

Clinical audit is pivotal to the provision of high quality clinical care. Research has been identified as "a core part of the National Health Service" in the NHS Constitution. All those involved in managing patients with viral hepatitis must commit to a program of regular audit and should actively contribute to on-going research programs**.**

6.1 Audit:

The following key outcome measures should be audited regularly:

- Diagnostic rates
- Referral and attendance rates
- Treatment :-
- For HCV monitoring must include data on:-
    - Non-responders, rapid responders, sustained virological response rates, compliance and completion rates.
- For HBV monitoring must include data on
    - Proportion of patients with HBeAg+ disease, proportion treated and proportion achieving HBe and HBs antigen loss
    - Compliance and adherence with interferon based therapies
    - Proportion of patients receiving oral anti-viral therapy
    - Proportion of patients achieving undetectable HBV DNA within 6 and 12 months of starting therapy.
- For all patients data on rates of cirrhosis, HCC, hepatic decompensation, transplantation and death should be provided

BVHG supports the development of national databases and suggests that all patients with viral hepatitis are recorded on national databases – such as The Sciensus database and HepSeq.

BVHG recognises that there is no central funding, support or enthusiasm for national databases in England, although such support services are available in Scotland and Wales. To overcome these barriers in England BVHG suggests that local funders consider a requirement for data to form part of the network performance monitoring and consider including data provision in Service Level Agreements.

6.2 Research

Key priorities for research include

- Natural history (with intervention)
- Demography of the patient population in the UK
- Approaches to improve diagnostic rates
- Methods to prevent/reduce transmission
- Patient experience
- Long term safety and tolerability of antiviral medications
- Optimal, cost effective strategies to reduce drug resistance

All those involved in managing patients with chronic viral hepatitis should endeavour to support local and national clinical trials and must engage and register with Comprehensive Local Research Networks (CLRNs). It is essential that all patients are given the opportunity to participate in clinical trials and all patients should be aware of the research opportunities that are available to them.