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Chronic hepatitis B

A clinical audit of GP management

Background

Hepatitis B virus (HBV) infection represents a growing health burden in Australia. This clinical audit aimed to enhance general practitioner awareness of the recommended management for patients with chronic hepatitis B.

Objective

This article describes a clinical two-phase audit of 119 Australian GPs who contributed records retrospectively of patients with chronic hepatitis B.

Discussion

Patient records were examined for compliance with prevailing guidelines and GPs received education on guidelines. At completion of the audit 29% of patients were monitored at recommended intervals and 47% were managed according to the current guidelines. Recording of hepatitis B virus DNA results increased from 24% in phase 1 to 63% in phase 2. General practitioners reported increased knowledge of appropriate management and referral. Twenty-five percent of patients audited in both phases had been referred to a specialist. Participating GPs improved their management of patients with chronic hepatitis B. However, there remains considerable scope for enhancing GP understanding of hepatitis B virus and applying current guidelines to clinical practice.

Keywords: hepatitis b, chronic; general practice; clinical audit

Hepatitis B virus (HBV) infection represents a growing health burden in Australia. No individual with chronic infection should be considered a 'healthy carrier', but should be categorised as having either active or inactive disease.[1] It is estimated that in Australia by 2017 there will be a threefold increase in cases of HBV-induced liver cancer and a marked increase in deaths attributable to infection with the virus.[2]

In 2008, an estimated 187 000 people were living with chronic hepatitis B (CHB) infection in Australia.[2] Between 15 and 40% of those with CHB develop liver disease, including cirrhosis, liver failure and liver cancer. There is geographical clustering of hepatitis B cases, with higher rates in some localities than the national average.[3] A relatively slow rate of disease progression and ongoing migration from high HBV prevalence countries means that HBV related advanced liver disease will continue to be a major challenge for Australian healthcare providers for at least 2 decades.[4,5]

After infection, CHB passes through phases of relative inactivity followed by phases of activity that are associated with progressive liver damage (*Table 1*). There are four phases through which a patient can transition, ongoing regular monitoring is therefore needed.[1]

The role of the general practitioner in managing CHB is poorly defined. A hepatitis B national strategy has only recently been proposed.[6] Guidelines specifying risk assessment and referral criteria for HBV patients were published in 2008 (*Table 1, 2*)[4,7] and there is a critical role for primary care in detection, management and referral.[4,8] However, in a survey 70% of GPs reported a need to strengthen their skills in managing CHB patients.[8]

This clinical audit was undertaken to assess GP understanding of current recommendations for the management of patients with CHB, and to assist in identifying areas that require improvement.

Audit method

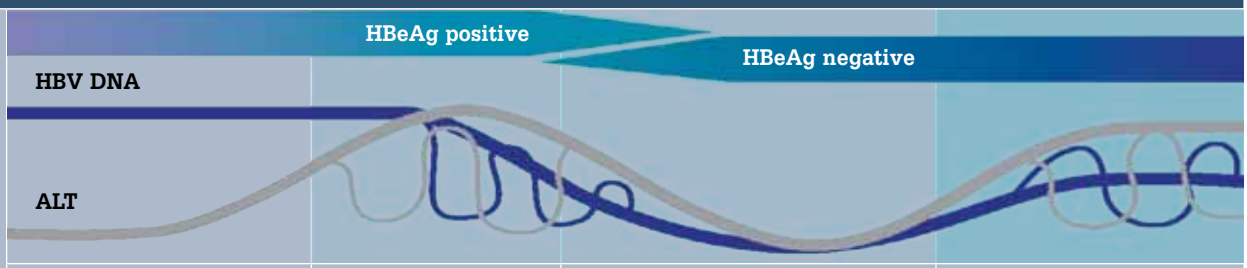
This clinical audit utilised the five step format[9] to aid in systematically reviewing clinical performance against best practice guidelines. Audit phase 1 took place in 2007–2008. General practitioners servicing communities with a high immigrant population from HBV endemic countries were targeted. Each GP identified a minimum of five practice patients that met the inclusion criteria of:

- diagnosis of CHB
- age over 18 years
- not currently under HBV specialist care
- no known co-infection with HIV, hepatitis C or hepatitis delta.

Nurses (provided by the audit coordinators) assisted with retrospective collection of data from patient notes that was recorded at diagnosis/initial assessment and during the three most recent consecutive visits. Surgery and GP demographics were also recorded.

Three predefined audit standards (*Table 3*) were adapted from international guideline recommendations,[10–13] as there were no Australian guidelines at the commencement of

Table 1. CHB phases and suggested management of patients not receiving treatment[4,7]



	Phase 1 Immune tolerance	Phase 2 Immune clearance	Phase 3 Immune control	Phase 4 Immune escape
HBsAg	+ for >6 months	+ for >6 months	+ for >6 months	+ for >6 months
HBeAg	+	+	–	–
ALT	Persistently normal	Persistently or intermittently elevated	Persistently normal	Persistently or intermittently elevated
HBV DNA*	≥20 000 IU/mL	Persistently or intermittently ≥20 000 IU/mL	<2000 IU/mL	Persistently or intermittently ≥2000 IU/mL
Liver histology	Minimal inflammation	Variable inflammation +/– fibrosis	Minimal inflammation and liver damage	Inflammation and often significant fibrosis
Natural history	Low risk of progression to advanced liver disease	Associated with hepatic flares and risk of progressive liver disease	• Low risk of advanced liver disease HBsAg loss: 1% per year • 10–20% have reactivation of HBV replication after many years	• Can enter this phase from immune clearance or immune control phase • High risk of progression to advanced liver disease
Suggested management	**If ALT levels <2 times ULN† (ULN = 30 U/L for men, 19 U/L for women)[10]** • No treatment • HBeAg and liver function tests every 12 months **If ALT levels increase to >2 times ULN** • HBeAg and liver function tests every 3–6 months **If ALT levels persistently >2 times ULN and if no HBeAg seroconversion within 6 months and/or age >40 years with ALT elevations 1–2 times ULN** • Consider referral to a specialist for consideration of liver biopsy and treatment	Consider referral to a specialist for consideration of liver biopsy and treatment	**ALT level normal** • No treatment • HBV DNA and liver function tests every 12 months **If ALT levels increase** • Check serum HBV DNA, exclude other possible causes of ALT elevation **If HBV DNA >2000 IU/mL and/or persistent ALT elevation and no other cause found** • Consider referral to a specialist for consideration of liver biopsy and treatment	Consider referral to a specialist for consideration of liver biopsy and treatment

* HBV DNA assay is available on the Medicare Benefits Schedule once per year for untreated CHB patients and four times per year for treated CHB patients;[14] † ULN = upper limit normal

the audit. Phase 1 data was used to determine whether GPs were meeting the audit standards. On completion of phase 1, individual GP results and an educational intervention were delivered by the nurses.

The interval between phase 1 and 2 data collection was approximately 9 months. This allowed GPs time to review the patient reports from phase 1 and determine whether further tests or referral to a specialist was appropriate. If phase 1 patient records could not be reaudited, a minimum of five new patients were audited. The end of phase 1 coincided with the publication of Australian GP guidelines on the management of CHB[4] and the availability of Medicare Benefits Schedule (MBS) reimbursement for HBV DNA testing.[14] Phase 2 data determined whether GPs were meeting audit standard 1 and 2 only.

Paired t-tests were performed to compare audit outcomes for GPs who completed both phases to assess changes in their management since phase 1.

According to the National Health and Medical Research Council checklist for quality assurance activities,[15] ethics committee approval was not required for this audit. Informed consent was sought from patients and doctors before inclusion in the audit.

Table 2. Recommended groups for HBV infection screening[4,7]

- People born in the Asia-Pacific region and other countries/groups with high/intermediate prevalence (eg. the Mediterranean, Africa, Indigenous Australians)
- Other high risk groups include:
  - patients undergoing chemotherapy or immunosuppressive therapy
  - household and sexual contacts of HBsAg positive people
  - inmates of correctional facilities
  - those with hepatitis C, HIV co-infection
  - renal dialysis patients
  - men who have sex with men
  - injecting drug users
  - people with multiple sexual partners or a history of sexually transmissible infections
  - people with chronically elevated ALT/aminotransferase
- All pregnant women should be screened for HBsAg, even if previously tested or vaccinated

Table 3. Hepatitis B management standards specified at the outset of the audit

Standard 1: Monitoring
Follow up at regular intervals as defined by patient's HBeAg status, HBV DNA and ALT levels*
Standard 2: Management
Patients should be considered for referral who have ALT levels ≥2 times upper limit of normal or are ≥35 years, with high HBV DNA levels* or who have a family history of HCC†
Standard 3: Counselling
This standard covered counselling on the following topics: • explanation of disease and outcomes • lifelong follow up • potential transmission risks and preventive measures • vaccination for family members • alcohol use • lifestyle advice

* In phase 1 and 2 if HBV DNA was unknown high results were assumed

† In phase 1 this question was worded, 'Family history of liver disease or HCC'; phase 2 requested information about HCC only and included whether patient notes had any detail regarding family history of HCC in the previous 12 months. If this was unknown, it was assumed to be positive for this standard

Audit results

Demographics

A total of 119 GPs participated in phase 1. They were based in urban practices in Sydney (49), Melbourne (41), Brisbane (26) and Perth (3). Of the 1042 patients audited and analysed, most (73.3%) were born in Vietnam or China, and 73.8% were aged 35 years or older (*Table 4*). More patients were identified as HBeAg negative than HBeAg positive (65% vs. 12%). Phase 2 included 106 of

Table 4. Demographics of patients evaluated in phase 1 and 2 of the audit

Variable	Phase 1 n (%)*	Phase 2 n (%)*
Total number patients analysed	1042**	729†
Age (years)		
• 18–34	272 (26.1)	128 (17.6)
• 35–54	568 (54.5)	417 (57.2)
• >55	201 (19.3)	182 (25.0)
• Unknown	1 (0.1)	2 (0.3)
Gender		
• Female	566 (54.3)	391 (53.6)
• Male	474 (45.5)	334 (45.8)
• Not recorded	2 (0.2)	4 (0.6)
Country/region of birth††		
• Vietnam	548 (52.6)	
• China	216 (20.7)	
• Asia (other)	64 (6.1)	
• Hong Kong	60 (5.8)	
• Taiwan	33 (3.2)	
• Australia	23 (2.2)	
• Cambodia	16 (1.5)	
• Malaysia	16 (1.5)	
• Pacific	16 (1.5)	
• Europe	15 (1.4)	
• Africa	12 (1.2)	
• Unknown	23 (2.2)	

* Percentages may not add to 100% due to rounding

** Two patients were excluded from analysis as they were under 18 years of age

† Of the 729 patients audited at phase 2, 540 were audited at phase 1

†† Data on country of birth was not collected at phase 2

the original GPs and a total of 729 patients, with 540 (74%) re-evaluated from phase 1. In phase 2, 74% of patients were HBeAg negative and 10% were HBeAg positive.

Hepatocellular carcinoma risk awareness

Data from time of diagnosis/initial assessment collected at phase 1 showed 41% of patients were screened for hepatocellular carcinoma (HCC) by abdominal ultrasound or α-fetoprotein test. For 74% of patients, no notation was made regarding family history of liver disease or HCC. These figures, along with increased awareness of the rising incidence of HCC after the completion of phase 1, resulted in an increased focus on how GPs consider HCC risk in phase 2. From phase 2 data, 22% of patient notes included information on HCC family history (positive, negative or unknown) recorded in the preceding 12 months. A total of 61% of audit patients had undertaken an HCC check in the past 3 years, however, from the data collected it was not possible to evaluate the percentage of high risk patients receiving recommended 6 monthly checks.

GP management and monitoring of CHB

Phase 1 results showed that 2% of patients were monitored at the appropriate intervals, as set out in audit standard 1 (*Table 3*). By phase 2, 29% ($p<0.001$) of patients were appropriately monitored. Likewise, 34% of patients were managed according to the defined audit standard 2 at phase 1, significantly increasing to 47% at the end of the audit cycle ($p<0.0001$).

The main reason for GPs not meeting audit management standard 2 at audit completion was because of not referring for specialist assessment the following at risk patients:

- aged ≥35 years with high HBV DNA (66 patients) or without HBV DNA testing in which case it was presumed high (183 patients)
- alanine transaminase (ALT) ≥2 x upper limit of normal (ULN) (12 patients)
- positive family history of HCC (27 patients) or unknown family history (242 patients).

Hepatitis B virus DNA testing significantly increased from 24% of patients in phase 1 to 63% in phase 2 ($p<0.0001$). Of these, 44% had HBV DNA levels >2000 IU/mL.

Advice and counselling

Audit standard 3 required that patients be counselled at diagnosis about transmission minimisation and lifelong follow up (*Table 3*). During phase 1, GPs reported providing the full recommended range of counselling for 57% of patients. In a subset analysis, GPs believed that the majority of their patients understood most of the topics discussed. As this standard retrospectively assessed counselling provided around the time of diagnosis it was not appropriate to reassess at phase 2.

Referral outcomes

At phase 2, 25% of the 540 reaudited patients were referred to a specialist. Of these, 60% remained under specialist care at the time of phase 2 data capture.

Discussion

Over 90% of GPs reported that participating in the clinical audit improved their knowledge of CHB management. Baseline results from phase 1 suggested low levels of appropriate monitoring of patients with HBV infection and only one-third of patients potentially being managed according to prevailing guidelines. Phase 2 results showed significant increases in appropriate patient monitoring and management, and this positive result can be attributed both to active participation in the clinical audit cycle and to recent national initiatives addressing the growing burden of CHB.

It should be noted, however, that the true proportion of patients monitored correctly or who were appropriate for specialist referral (audit standard 2) may have been affected by the assumptions made when interpreting audit data. In particular, if no HBV DNA results or family history of HCC were reported, high or positive results were assumed.

A clear relationship has been demonstrated between serum HBV DNA levels and HCC risk.[16] The mid audit MBS rebate changes for HBV DNA testing illustrated the value of reimbursement for clinically informative investigations: HBV DNA assay results increased from 24% to 63% of patients once this test received an MBS Item Number (and the GPs had received the educational intervention). Current guidelines recommend considering referring all patients who are HBsAg positive, particularly if HBV >2000 IU/mL, ALT is elevated or there are features of significant liver damage.[4]

Providing pre- and post-test information at the point of diagnosis is important to ensure patients understand the disease and respond effectively.[8] Audited doctors reported providing some counselling to most patients, however, only 57% of patients received the full range of recommended counselling.

The provision of a nurse to assist the GPs in identifying and assessing the management of patients with CHB greatly increased the frequency of monitoring and referral. This highlights the need for support, information and education aimed at general practice to assist with effective monitoring and recall systems in CHB, as well as the appropriate use of a management plan and specialist referral and liaison. It would be valuable to further explore the potential benefits of utilising nurses in identifying patients for screening, and for providing ongoing patient counselling and follow up.

Although these findings are from a retrospective clinical audit rather than an observational, prospective study and the sample cannot be considered representative of the breadth of Australian general practice, the deficits identified suggest that there may be scope for a coordinated strategy that encompasses public and professional education. Such a strategy would also need to consider how to optimise patient access to specialists once identified for referral.

Conclusion

In the setting of HBV management in general practice, participation in this clinical audit enhanced awareness of current best practice guidelines and facilitated these being adopted in a clinical setting. Improved monitoring and management contribute to the therapeutic management goals for HBV infection, which are accurate monitoring of disease to prevent progression to cirrhosis and HCC.[7] By encouraging regular testing and clinical assessment, in addition to specialist referral where indicated, initiatives to enhance GP engagement may help stem the growing burden of HBV infection.

Key points for practice

- No patient with CHB should be considered a healthy carrier – terms such as active and inactive disease should be used.
- Monitoring and management of a patient with CHB should be lifelong, whether or not the patient's disease appears inactive.
- HBV DNA testing is available on the MBS (one test per year for untreated patients, up to four tests per year for those on antiviral therapy).
- All patients positive for surface antigen (HBsAg), should be considered for referral to a specialist, particularly if HBV DNA >2000 IU/mL, ALT levels are elevated or they have features of significant liver damage.
- High risk CHB patients (those with cirrhosis, Asian men >40 years, Asian women >50 years, African men and women >20 years, family history of HCC) should be screened for HCC with liver ultrasound and serum α-fetoprotein every 6 months.

Resources

- The Gastroenterological Society of Australia (GESA): www.gesa.org.au
- The Australasian Society for HIV Medicine (ASHM): www.ashm.org.au
- Hepatitis Australia: www.hepatitisaustralia.com Helpline 1300 437 222
- HepB Help: www.hepbhelp.org.au.

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