NICE National Institute for Health and Care Excellence

Surveillance report 2017 – Hepatitis B (chronic): diagnosis and management (2013) NICE guideline CG165

Surveillance report

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Contents

Surveillance decision

We will not update the guideline on hepatitis B (chronic): diagnosis and management at this time.

During surveillance editorial or factual corrections were identified. Details are included in appendix A: summary of evidence from surveillance.

Reason for the decision

Assessing the evidence

We found 59 studies through surveillance of this guideline.

This included evidence on the effectiveness of antiviral therapy (tenofovir disoproxil, telbivudine, entecavir, adefovir and peginterferon alfa-2a) to treat people with chronic hepatitis B viral infection. Evidence was also included on the diagnostic accuracy of non-invasive methods (transient elastography, FibroTest, FIB-4 index and FibroScan) to assess the severity of necro-inflammatory activity and liver fibrosis. The evidence was considered to support current recommendations.

We asked topic experts whether this evidence would affect current recommendations. Generally, the topic experts agreed that the new evidence would not impact recommendations in these areas.

We did not find any evidence related to patient information, assessment and referral in primary care, genotype testing and frequency of monitoring tests for chronic hepatitis B infection markers or early hepatocellular carcinoma detection.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

After considering all the evidence and views of topic experts and stakeholders, we decided that no update is necessary for this guideline.

See how we made the decision for further information.

Commentary on selected evidence

With advice from topic experts we selected 1 study for further commentary.

Research recommendation – Long-term safety of tenofovir disoproxil in chronic hepatitis B

We selected a randomised controlled trial by Buti et al. (2015) for a full commentary because this is a new piece of evidence that relates to one of the research recommendations from the original guideline.

What the guideline recommends

The research recommendation was to determine the long-term safety of tenofovir disoproxil, including the risk of clinically significant hypophosphataemia and related bone toxicity, in people with chronic hepatitis B. The cost effectiveness of routine monitoring for phosphate loss and bone disease in people with chronic hepatitis B who are receiving tenofovir disoproxil treatment was also considered to need further evaluation.

Methods

Study participants (n=641) included people who were hepatitis B e antigen (HBeAg)-positive or HBeAg-negative chronic hepatitis B (CHB), 18–69 years of age with compensated liver disease and Knodell necroinflammatory score C3. Participants were randomised to receive either tenofovir disoproxil fumarate (TDF) or adefovir dipivoxil (ADV) daily for 1 year, after which all participants received TDF for up to 7 years.

Results

At study completion, 68% of the participants remained with the other 32% discontinuing treatment due to withdrawal of consent; loss to follow-up; investigator discretion; safety, tolerability, or efficacy reasons; HBsAg or HBeAg seroconversion; protocol violation; or sponsor decision. Among the participants who had abnormal serum alanine aminotransferase (ALT) at the beginning of the study, 80% of them experienced ALT normalisation by the end of year 7. Of the HBeAg-positive participants who remained on

the study at year 7, 55% experienced HBeAg loss and 40% experienced seroconversion to anti-HBe indicating that TDF was both an effective and safe treatment for chronic hepatitis B.

Strengths and limitations

Strengths

The study population matched those within the current guideline, also the methodology was fully and clearly reported along with the majority of the outcomes. Patient disposition details at year 7 were also reported in full, which aimed to add to the evidence base on the long term safety of treatment.

Limitations

The study methodology described measuring several outcomes throughout the duration of the open label phase but these were not fully reported in the published paper. Also, baseline measurements at the beginning of the open-label phase were not reported as a comparison to the end of study (year 7) results indicating reporting bias within the study.

Impact on guideline

The population, intervention and outcomes measured were all of relevance to the clinical guideline. As the reported outcomes do not fully answer those posed by the research recommendation (i.e. bone toxicity and cost effectiveness of monitoring) there is no anticipated impact on the guideline at this time.

How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 4 years after the publication of NICE's guideline on hepatitis B (chronic): diagnosis and management (NICE guideline CG165) in 2013.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Evidence

We found 58 studies in a search for randomised controlled trials and systematic reviews published between 10 October 2012 and 9 March 2017. We also included 1 relevant study identified by members of the guideline committee who originally worked on this guideline.

From all sources, we considered 59 studies to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A: summary of evidence from surveillance for details of all evidence considered, and references.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline.

Views of stakeholders

Stakeholders commented on the decision not to update the guideline. Overall, 7 stakeholders commented. See appendix B for stakeholders' comments and our responses. Six stakeholders commented on the proposal to not update the guideline with 3 agreeing and 3 disagreeing with the decision.

Two stakeholders referred to a recently published recommendation by the European Association for the Study of the Liver (EASL) as a reason to update the guideline. The EASL guideline recommends: 'patients with HBeAg-positive chronic HBV infection, defined by persistently normal ALT and high HBV DNA levels, may be treated if they are older than 30 years regardless of the severity of liver histological lesions'. This contradicts the current recommendation in NICE's guideline on diagnosis and management of hepatitis B, which states that persistently elevated ALT serum levels (greater than or equal to 30 IU/litre in males and greater than or equal to 19 IU/litre in females) on 2 consecutive tests conducted 3 months apart are an indication for treatment. The EASL recommendation was, by its own grading criteria, a weaker recommendation with less certainty based on the opinions of respected authorities and descriptive epidemiology whereas the NICE recommendation was determined from a full systematic review of all the relevant published evidence. As the difference between the EASL recommendation and the NICE guideline is not driven by new evidence, no impact on NICE's guideline on hepatitis is anticipated at this time.

Comments received by several stakeholders were about testing for hepatitis B and as such were outside the scope for this guideline. Recommendations on testing can be found in NICE's guideline on hepatitis B and C testing in people at risk of infection.

Several stakeholders highlighted published studies or feedback from clinical practice as part of their challenge to the proposal to remove 3 prioritised research recommendations from the NICE guideline and the NICE research recommendations database (research recommendation 1 in particular) with the majority stating that they are ongoing questions which should be retained. Upon review of this and previous evidence, we propose to retain all 4 of the current research recommendations.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

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