Hepatitis B reactivation: reducing the risk in patients with inflammatory bowel disease

We would like to congratulate Lamb *et al* for the production of such a comprehensive guideline for the management of inflammatory bowel disease (IBD).[1] Further clarification is warranted regarding screening for hepatitis B virus (HBV) prior to immunosuppression and subsequent management to reduce the risk of virus reactivation.

The guidelines recommend screening for HBV at diagnosis and before immunomodulatory/biologic therapies. We strongly recommend that screening includes hepatitis B surface antigen (HBsAg), antibody to hepatitis B core antigen (anti-HBc) and antibody to hepatitis B surface antigen (anti-HBs) as outlined in the European Crohn's and Colitis Organisation Opportunistic Infections Consensus.[2] Lamb *et al* advise seeking specialist input prior to commencing immune-modifying therapy for those patients with active HBV (i.e. HBsAg positive). In line with national and international guidelines, all HBsAg positive patients should be managed in a specialist setting regardless of planned treatment for IBD. HBsAg positive patients who will receive immunosuppressive drugs for treatment of IBD should be offered prophylaxis against reactivation regardless of the disease phase of HBV.

Lamb *et al* do not comment on the management of patients who are HBsAg negative and anti-HBc positive, a profile indicative of past exposure to HBV that confers an ongoing, although low, risk of reactivation in the context of immune suppression. Studies of patients receiving rituximab in urban areas have estimated a seroprevalence of 6% (Newcastle)[3] and 10% (East London).[4] Anti-HBc detection will be higher in populations with risk of exposure to the virus, including migrants from endemic areas and people who inject drugs.

We recommend the following steps in the management of HBsAg negative, anti-HBc positive patients:

TEST FOR HBV DNA AT BASELINE

Positive HBV DNA with undetectable HBsAg (occult HBV) occurs in 0%–27% of patients with anti-HBc positivity, although studies are heterogeneous.[5] Patients with detectable HBV DNA should be managed as if they are HBsAg positive and referred for specialist review.

RISK STRATIFY BASED ON THE POTENCY OF IMMUNE SUPPRESSION AND ANTI-HBS TITRE

Biologics confer a moderate risk of reactivation to patients who are anti-HBc positive (2%–10%).[6] This risk will be higher if multiple immunosuppressive agents are given simultaneously, or if the patient has suspected immune compromise due to age, malnutrition or comorbidities.

Most patients with IBD and evidence of past infection to HBV will not require antiviral prophylaxis to prevent HBV reactivation. They should be monitored at least 3 monthly with HBV DNA, HBsAg and ALT. Pre-emptive therapy with an antiviral should be commenced if HBV DNA and/or HBsAg is detected.[7]

Emerging evidence suggests that reactivation is most likely in those with low or undetectable anti-HBs levels[8]. As such, antiviral prophylaxis could be considered for HBsAg negative IBD patients requiring biologics who are anti-HBc positive but have low titres of anti-HBs (e.g. <50mIU). The cost of antiviral prophylaxis has fallen significantly with availability of new generic formulations, but further studies are needed to ascertain whether this is a cost-effective strategy in comparison to treating in response to HBV reactivation.

The use of biologics is a long-term management strategy for IBD patients. There are no data to suggest that monitoring, or indeed antiviral prophylaxis, could safely be stopped during this treatment. Cost-effectiveness analyses comparing monitoring versus empirical use of antiviral prophylaxis therefore must be performed in the context of long-term immune suppression and should include measures of quality of life.

Reactivation of hepatitis B is an infrequent but potentially serious complication of immunosuppressive treatment. We urge clinicians managing IBD to formulate robust policies for screening and management, as appropriate for their local population and healthcare resource.

Grace Elizabeth Dolman ,[1]
Patrick T F Kennedy[1]

Barts Liver Centre, Barts and The London School of Medicine and Dentistry, London, UK

Correspondence to Prof Patrick T F Kennedy, Barts Liver Centre, Barts and The London School of Medicine and Dentistry, London E1 2AT, UK; p.kennedy@qmul.ac.uk

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ORCID iD
Grace Elizabeth Dolman http://orcid.org/0000-0002-1302-4066

REFERENCES

1 Lamb CA, Kennedy NA, Raine T, *et al*. British Society of gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut* 2019;68:s1–106.
2 Rahier JF, Magro F, Abreu C, *et al*. Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. *J Crohns Colitis* 2014;8:443–68.
3 Dyson JK, Jopson L, Ng S, *et al*. Improving testing for hepatitis B before treatment with rituximab. *Eur J Gastroenterol Hepatol* 2016;28:1172–8.
4 Dolman GE, Theocharopoulos I, Kennedy P, *et al*. PTU-089 hepatitis B screening prior to rituximab and subsequent management to reduce the risk of reactivation. *Gut* 2019;68:AA235.
5 Allain J-P. Global epidemiology of occult HBV infection. *Ann Blood* 2017;2:7.
6 Koffas A, Dolman GE, Kennedy PTF, *et al*. Hepatitis B virus reactivation in patients treated with immunosuppressive drugs: a practical guide for clinicians. *Clin Med* 2018;18:212–8.
7 European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu, European Association for the Study of the Liver. EASL 2017 clinical practice guidelines on the management of hepatitis B virus infection. *J Hepatol* 2017;67:370–98.
8 Schwaneck EC, Krone M, Kreissl-Kemmer S, *et al*. Management of anti-HBc-positive patients with rheumatic diseases treated with disease-modifying antirheumatic drugs-a single-center analysis of 2054 patients. *Clin Rheumatol* 2018;37:2963–70.