Risk for hepatitis B and C virus reactivation in patients with psoriasis on biologic therapies: A retrospective cohort study and systematic review of the literature

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Background: Patients with psoriasis on biologic therapies and a history of viral hepatitis carry a risk for reactivation.

Objective: We evaluated safety of biologic therapies in psoriasis patients seropositive for hepatitis B or C viruses (HBV, HCV).

Methods: A retrospective cohort study design was used. Clinical and laboratory data for 30 patients undergoing biologic therapy who were seropositive for HBV or HCV were evaluated. Next, a systematic review was performed. Primary outcomes were hepatitis and viral reactivation during therapy. Treatment duration and antiviral prophylaxis were also recorded.

Results: Serology indicated HCV infection in 4 patients, past HBV infection in 17 patients, isolated core antibody in 8 patients, and chronic HBV infection in 1 patient. During follow-up (mean 4.85 ± 3.1 years), no patients experienced hepatitis or viral reactivation. The systematic review of the literature included 49 studies comprising 312 patients followed for a mean of 30.9 months. Viral reactivation occurred in 2/175 patients who were seropositive for core antibody and 3/97 with HCV infection (yearly rates, 0.32% and 2.42%, respectively) compared with 8/40 patients with chronic HBV infection (yearly rate, 13.92%). Three of these 8 patients with reactivated HBV infection received antiviral prophylaxis.

Limitations: We pooled heterogeneous studies evaluating different biologic therapies.

Conclusion: Biologic therapies pose minimal risk for viral reactivation in low-risk patients without hepatitis seropositive for HCV or HBV core antibody but are a considerable risk in patients with chronic HBV infection, highlighting the necessity of antiviral prophylaxis. (J Am Acad Dermatol 2017;77:88-97.)

Key words: biologic; HBcAg; hepatitis B virus; hepatitis C virus; psoriasis; reactivation; risk.

In the last 15 years, biologic therapies have been introduced for the treatment of moderate-to-severe psoriasis.[1] The main therapies available in Israel are anti–tumor necrosis factor-α (TNF-α), the interleukin (IL) 12/23 p40 monoclonal antibody ustekinumab, and the recently approved IL-17 antibody secukinumab.[2] Because these agents lack direct hepatic or renal toxicity,[3] these selective immunomodulatory treatments are appealing to patients with concurrent viral hepatitis.

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With the advent of TNF-α–inhibitor use in patients, so did reports on various disseminated and opportunistic infections.[4,5] TNF-α is an important cytokine in host antiviral defense.[6] Reports describing hepatitis B virus (HBV) reactivation following TNF-α–inhibitor use in patients with rheumatoid arthritis and spondyloarthropathies[7] prompted concerns regarding the safety of all biologics in psoriasis patients exposed to HBV or hepatitis C virus (HCV), but no systematic study addressing this issue has been conducted to date.

The aim of the present study was to evaluate the safety profile of biologic therapies among psoriasis patients with concurrent positive serology for HBV or HCV.

CAPSULE SUMMARY

- Patients with a history of viral hepatitis carry a reactivation risk, but it is uncertain how this is affected by biologic therapies for psoriasis.
- Patients positive for hepatitis C virus or hepatitis B virus (HBV) core antibody without evidence of hepatitis had a minimal risk for reactivation, whereas those with chronic HBV had a higher risk for reactivation.
- Select patients with a history of viral hepatitis may be safely treated with biologics.

METHODS

Retrospective cohort study

A retrospective cohort study design was used. The electronic database of the Dermatology Department of Rabin Medical Center, a tertiary referral hospital in Israel, was searched for patients treated with biologic agents for moderate-to-severe psoriasis since 2005. All patients were screened for HBV and HCV before initiation of biologic therapy. Positive HBV serology was subdivided into 3 categories according to the European Association for the Study of Liver Disease[8]: 1) resolved past HBV infection (HBV surface antigen [HBsAg] negative, HBV surface-specific antibody [HBsAb], and HBV core-specific antibody [HBcAb] positive), 2) chronic HBV infection (HBsAg positive), and 3) only core antibody positive (HBsAg negative, HBsAb negative, and HBcAb positive). Hepatitis was defined as an increase in the alanine transaminase level to 5 times the upper limit of normal.[9] Because no uniform diagnostic criteria are available for HBV reactivation, we adopted the definition commonly used by other researchers[10]: an increase in HBV replication of at least 1 log 10 copies/mL or conversion of serum HBV DNA results from negative to positive. HCV reactivation was defined as an increase of at least 1 log 10 copies/mL. According to Israeli guidelines, patients in whom pretreatment serology was suggestive of HBV or HCV infection were scheduled for clinical evaluation, which included measurement of transaminases, every 2-3 months until the end of follow-up. Patients with chronic HBV infection were serologically evaluated every 3-6 months. Because the best strategy for monitoring low-risk, only core antibody–positive patients is unknown,[11] the serologic status (HBsAg, HBcAb, and HBV DNA) of patients was evaluated at various intervals. The presence of HCV RNA was assessed at baseline and reassessed as part of antiviral therapeutic protocols, as suggested by the hepatologist. The demographic, clinical, and laboratory data were extracted onto a chart, which included the fields shown in Tables I-IV. The study was approved by the local ethics committee.

Systematic literature review

The systematic review was conducted and reported in accordance with the PRISMA (Preferred Reporting Items for Systemic Reviews and Meta-Analyses) statement.[12] We performed a search with no date limits using PubMed, our institute's search engine, and reference lists of included articles on May 13, 2016. The search criteria are shown in Appendix I (available at http://www.jaad.org).

Inclusion and exclusion criteria. We included articles written in English and excluded articles written in other languages. We selected articles describing the treatment of psoriasis with at least 1 biologic agent in the presence of a positive serologic or virologic marker for HBV or HCV before treatment onset that also had available serologic or virologic data on HBV or HCV at the end of follow-up. Any relevant study, regardless of design, was included. Literature reviews, expert opinions, and studies in which data of interest could not be extracted were excluded.

Data extraction and variables. One reviewer (IS) screened the titles and abstracts of all retrieved articles followed by the full text of the articles considered potentially eligible and extracted the data into a predefined form (Supplemental Table I; available at http://www.jaad.org)[13-60] that included the following items: 1) HCV and HBV infection status at the beginning of the study, 2) treatment factors, such as treatment duration, types, and quantities of different biologics, and 3) evidence of viral reactivation or hepatitis.

Studies were graded according to their level of evidence: (A) prospective controlled study, (B)