

Expanding HCV Care Beyond The Specialty Setting:

A Series for Primary Care Clinicians



Combatting Alert Fatigue

Chronic hepatitis C virus (HCV) infection, dubbed the “silent killer,” is largely asymptomatic until progression results in noticeable, often irreversible health effects. Fortunately, the advent of modern direct-acting antiviral (DAA) therapies offers nearly all patients the opportunity for a cure with minimal side effects and regimens that are substantially easier for both clinicians and patients compared with historical interferon-based treatment. However, it is important that clinicians are aware of the potential for drug-drug interactions and the Food and Drug Administration boxed warning for hepatitis B virus (HBV) reactivation.

Case Description

A 44-year-old man with a history of chronic HCV, HBV, hypertension, and type 2 diabetes mellitus was referred to a hepatologist/gastroenterologist for potential treatment of HCV. The patient had a history of multiple prior blood transfusions.

The physician reviewed the patient’s records, performed a physical examination, and, based on the patient’s history, ordered lab studies. The patient was found to have chronic genotype 1b HCV without cirrhosis. The physician recommended the initiation of DAA treatment, specifically the combination of ledipasvir and sofosbuvir for 12 weeks.

The patient’s current medications included metformin, glipizide, amlodipine, and lisinopril. When the physician ordered the patient’s medications electronically, several alerts popped up in the electronic health record (EHR) warning of multiple drug interactions, including the risk of HBV reactivation in patients receiving DAA treatment. Faced with numerous similar alerts each day, he dismissed the alerts without reading them

individually. The physician reviewed medication instructions with the patient and explained the follow-up labs that would be necessary per protocol during the 12-week course of treatment.

The patient took the ledipasvir/sofosbuvir combination as prescribed. At week 4 of treatment, he appeared to be responding to the treatment well. At week 8, however, the patient developed weakness and jaundice. Lab studies revealed elevated transaminases (ALT, 2,500; AST, 3,000) with a viral load of 30,000,000. Liver biopsy showed severe hepatitis with extensive necrosis, inflammation, and fibrosis. Despite the initiation of tenofovir, the patient developed worsening encephalopathy, requiring transfer to the intensive care unit. He subsequently required liver transplant and experienced a complicated postoperative course.

The patient and his family sued the physician, alleging that he failed to recognize the potential for HBV reactivation with DAA treatment for chronic HCV, resulting in the need for liver transplantation and resulting postoperative complications. Moreover, the patient argued that the physician ignored alerts of this potential risk and failed to inform him of the risk of HBV reactivation when prescribing the medications. The physician argued that, although he was alerted to the potential risk of reactivation, he did not believe that risk was significant enough to alter his treatment recommendations or counsel the patient about the risk. The physician further argued that he received hundreds of such alerts each week.

Case Discussion and Lessons for the Future

It is estimated that providers using an EHR system may encounter more than 100 alerts daily. These alerts are intended to promote patient safety by drawing a physician's attention to potential risks. However, such a high volume of alerts may lead to alert fatigue, which can result in missing potentially critical alerts. Indeed, research by the Agency for Healthcare Research and Quality suggests that providers override the vast majority of warnings, even critical alerts. One strategy to prevent alert fatigue is for a physician to customize his/her alerts to try to minimize the number of unnecessary alerts, allowing a physician to focus on fewer alerts—specifically, those most likely to prevent patient harm. This may entail restricting certain levels of alerts or specific types of alerts that have limited relevance to a physician's specific practice. Because EHR customization options may be institution-specific, physicians should consult their information technology departments for alert customization options and support.

In this case, the physician received numerous alerts each day through his EHR system. He had become so accustomed to alerts that he routinely “clicked through” them, often without reviewing them closely or even at all. As a result, the physician did not appreciate the alerts that popped up when he attempted to prescribe a DAA for a patient with HBV/HCV coinfection. Although the risk may have been relatively low, the patient's history made him susceptible to HBV reactivation. Because of alert fatigue, the physician missed the opportunity to warn and/or prevent the patient's liver failure. Had the physician customized his alert settings to minimize unnecessary alerts and, as a result, allow him to review more critical alerts, this patient's acute liver failure due to HBV reactivation and associated need for liver transplant as well as

postoperative complications may have been prevented.

Primary care clinicians are well-poised to reverse the tide of rising HCV infections and provide a cure for infected patients. Safety profiles of HCV treatments have improved greatly from the days of interferon-based therapy, which was poorly tolerated and minimally effective. However, clinicians need to continue to be mindful of the risks associated with treatment in patients with HBV/HCV coinfection.

Suggested Readings

1. Ende AR, Kim NH, Yeh MM, Harper J, Landis CS. Fulminant hepatitis B reactivation leading to liver transplantation in a patient with chronic hepatitis C treated with simeprevir and sofosbuvir: a case report. *J Med Case Rep*. 2015;9:164.
2. US Food and Drug Administration. FDA Drug Safety Communication: FDA warns about the risk of hepatitis B reactivating in some patients treated with direct-acting antivirals for hepatitis C. October 4, 2016. www.fda.gov/downloads/Drugs/DrugSafety/UCM523499.pdf. Accessed November 27, 2018.
3. Ou P, Fang Z, Chen J. Hepatitis B reactivation in a chronic Hepatitis C patient treated ledipasvir and sofosbuvir: a case report. *Clin Res Hepatol Gastroenterol*. 2017;41(2):e17-e18.
4. American Association for the Study of Liver Diseases and Infectious Diseases Society of America. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. www.hcvguidelines.org. Accessed November 27, 2018.
5. National Institutes of Health. LiverTox Drug Record: Sofosbuvir. <https://livertox.nih.gov/Sofosbuvir.htm>. Accessed November 27, 2018.

Developed in Collaboration