The Expanding Role of the Pharmacist in the Management of Hepatitis C Infection

Linda M. Spooner, PharmD, BCPS

Hepatitis C virus (HCV) infects approximately 3-4 million people per year worldwide. Overall, about 170 million people have chronic HCV infection, which can result in development of chronic liver disease, cirrhosis, and hepatocellular carcinoma. Of those with chronic HCV infection, the proportion with cirrhosis is expected to be 45% by the year 2030, and prevalence rates of hepatocellular carcinoma and hepatic decompensation are expected to increase over the next decade as well. These startling statistics underscore how crucial effective treatment and patient support are in the management of HCV infection. Pharmacists are in an ideal situation to assist with these endeavors, especially in light of new treatment options that recently became available. In this issue of JMCP, Tungol et al. provide a thorough review of the current status of treatment of genotype 1 HCV infection, along with suggestions for formulary management of new treatment options utilized in managing this chronic infection.

The Changing Face of HCV Management
Prior to May 2011, the standard treatment for chronic HCV infection involved use of peginterferon alfa, a weekly subcutaneous injection designed to boost the immune system’s response against the virus, and ribavirin, a twice-daily oral tablet or capsule designed to inhibit viral replication. A total of 48 weeks of therapy was required to treat genotype 1 (subtypes 1a and 1b) HCV, the most prevalent type in the United States, while 24 weeks is needed for the treatment of genotypes 2 and 3, the next most common types. The ultimate goal of treatment has always been to achieve a sustained virologic response (SVR), defined as an undetectable viral load (i.e., HCV ribonucleic acid [RNA]) 24 weeks following completion of treatment. Unfortunately, this goal was attained by only 40%-50% of patients with genotype 1 infection compared with 70%-80% of patients with genotypes 2 and 3 infection, emphasizing the need for improved treatment options in the former group of patients.

In May 2011, the U.S. Food and Drug Administration (FDA) approved 2 directly acting antivirals for genotype 1 HCV infection: the protease inhibitors boceprevir and telaprevir. This action changed the standard of care to triple drug therapy for patients with genotype 1 HCV infection who are treatment-naive or who have failed previous treatment with interferon. Depending on the individual characteristics of the patient, either of the protease inhibitors is combined with the “backbone” of peginterferon alfa and ribavirin. Timing of the addition of the protease inhibitor differs between the 2 agents; boceprevir is typically added 4 weeks after initial treatment with peginterferon alfa and ribavirin, while telaprevir is started simultaneously with the initiation of peginterferon alfa and ribavirin. Duration of treatment is dependent upon response for both regimens. Response rates with triple drug therapy are nearly twice those achieved with peginterferon alfa and ribavirin, truly revolutionizing the management of genotype 1 HCV infection. Of note, these agents are not approved for use in genotype 2 and 3 HCV infection, so dual treatment with peginterferon alfa and ribavirin remains the standard of care for these patients.

Where Does the Pharmacist Fit In?
The main caveats that practitioners must be aware of with these new protease inhibitors include their adverse effect profiles; extensive lists of drug interactions; potential for nonadherence secondary to high pill burden and frequency of dosing; and cost implications for insurers, managed care organizations, and patients. These are reviewed in detail by Tungol et al. in their review of these agents’ formulary management. Each of these areas provides a potential opportunity for pharmacist involvement in order to optimize care and improve the chances that a patient will complete therapy successfully and safely.

Adverse effects of HCV treatment have the potential to lead to nonadherence and frustration for the patient. The incidence of anemia was higher in the boceprevir and telaprevir groups in clinical trials than in the control regimens containing only peginterferon alfa and ribavirin. In our clinic’s experience, patients who become anemic on treatment will often complain of fatigue, dyspnea on exertion, and shortness of breath, depending on their hemoglobin and hematocrit values. This adverse effect can be managed through dose reductions of ribavirin or the addition of erythropoietin. Close monitoring and timely management can improve the patient’s quality of life. Additionally, telaprevir may cause increased frequency of rash and anorectal discomfort, while boceprevir can cause taste disturbances. Communication with patients regarding these adverse effects is essential, as each may impact quality of life in its own way. Pharmacists can provide counseling about adverse effects and suggestions for monitoring and managing.
them. Likewise, pharmacists can inquire about the occurrence of these adverse effects during patient encounters at the clinic and the pharmacy.

Since boceprevir and telaprevir are potent inhibitors of the cytochrome P450 (CYP450) 3A4 isoenzyme,\(^8,9\) the potential for drug interactions is quite high, necessitating numerous contraindications and precautions. Similar concerns are observed with protease inhibitors used for human immunodeficiency virus (HIV) infection; coadministration of concomitant medications must be carefully considered. Pharmacists are in an excellent position to assist with drug interaction checking; their knowledge of substrates and inhibitors of the CYP450 system, online tools for drug interaction assessment, as well as their efficient methods of gathering complete medication histories permits careful determination of which concomitant medications are safe and which require avoidance or dosage adjustment.

Nonadherence is a potential issue with both boceprevir and telaprevir, owing to their 3 times daily dosing frequency.\(^8,9\) Each agent requires dosing every 7-9 hours, posing a challenge to patients who need to fit this regimen into their daily routines. In our clinic’s experience, many patients work second- and third-shift jobs that require unique sleeping hours and naps that may vary from day to day. Working closely with patients to determine their schedules and the optimal way to fit HCV treatment into their day is an important job for the pharmacist; pharmacists are experienced in assisting with adherence to treatments that must be administered multiple times per day. During initial teaching sessions on HCV treatment, pharmacists can help facilitate the use of alarms, handheld devices, and other reminder tools.

Additionally, pill burden with the protease inhibitors may be overwhelming to patients. Boceprevir is packaged in a carton of 28 bottles, each containing 12 capsules, which are dosed as 4 capsules every 7-9 hours,\(^8\) while telaprevir is available in either a bottle of 168 tablets or a package containing 4 weekly cartons of 7 blister strips of 6 capsules, to be taken as 2 capsules every 7-9 hours.\(^8\) Providing strategies for organizing and managing all components of triple drug therapy is a key role a pharmacist can play to ensure proper administration and adherence to the regimen.

The cost of genotype 1 HCV infection treatment is quite high, owing to the high prices of each component of triple therapy as well as the costs of management of adverse effects, both of which are addressed by Tungol et al. in their review.\(^3\) This cost may be offset by the prevention of complications of HCV infection when the virus is eradicated, including prevention of cirrhosis, hepatocellular carcinoma, and death.\(^2\) In our clinic’s experience, most payers require prior authorizations to be completed in advance of treatment initiation. Pharmacists can counsel patients on the requirements that their prescription plans have for HCV treatment, providing insight on length of time required for a response from the payer, what the out-of-pocket costs will be, and other pharmacy benefit management information. Pharmacists can also identify potential sources of financial assistance for patients who have difficulty affording their prescription deductibles or copayments. As Tungol et al. reiterate in their review, adherence to therapy is essential to ensure cost-effective use of these new agents for management of HCV infection.\(^3\)

**Strategies for Maximizing Pharmacist Involvement in HCV Management**

Our clinic’s experience involving a pharmacist participating within the outpatient HCV clinic setting has been successful for the patients as well as for the practitioners and students involved in the practice. A pharmacist specializing in infectious diseases and affiliated with a school of pharmacy attends the weekly HCV clinic, held on Friday afternoons. Following initial assessment of vital signs and weight, the pharmacist interviews each new patient referred for HCV infection management, gathering such information as past medical history, any prior treatment for HCV, social history, allergies, and current prescription and nonprescription medications. This pertinent information is then entered into the electronic medical record. Assessment of patient readiness for treatment and drug interactions screening are also performed by the pharmacist. All of this information is presented to the HCV clinic attending physician, who then interviews and examines the patient and determines which further assessments are necessary (e.g., laboratory work up, liver biopsy) to determine candidacy for treatment.

When a patient is ready to start treatment, medications are prescribed by the attending physician and prior authorization requests are completed by the physician and clinic staff. The medications are either picked up by the patient or delivered to the clinic. The patient visits the clinic for a 45- to 60-minute teaching session with the pharmacist. At that time, the pharmacist verifies that the patient has received all prescribed medications and that the doses and strengths of each medication are appropriate. Each medication is reviewed with the patient with respect to proper handling, storage, administration, adverse effects, drug interactions, and refill instructions. Additional emphasis is placed on teaching proper injection technique for the interferon alfa component of the regimen; patients are encouraged to self-administer their first dose during the visit, following demonstration and teaching by the pharmacist. Adherence recommendations are provided based on the individual needs of the patient, including use of diaries, timers, pill boxes, or other devices. Additionally, the pharmacist outlines the plan for follow-up care with the patient, including a schedule of follow-up appointments and laboratory work, as well as
what to expect over the coming weeks. At the end of the visit, the attending physician and pharmacist wrap up and address any questions that have arisen during the session.

Follow-up appointments are structured in a manner similar to initial visits; the pharmacist interviews the patient and documents the findings in the electronic medical record. Specific questions are asked during this time, including identification of missed doses, presence of adverse effects, initiation of new medications since last visit, and difficulties acquiring medications from the pharmacy. Questions regarding medications and laboratory results are answered, and physical assessments of the skin and injection sites are performed, documented, and discussed with the attending physician, who also interviews and examines the patient. Potential drug interactions are assessed during the visit by the pharmacist so they can be resolved appropriately.

Numerous advantages result with the involvement of a pharmacist at the HCV clinic. First, patients view the pharmacist as a resource for drug information, not only about their HCV treatments, but also about other medications they utilize for comorbidities. Many come armed with questions specifically for the pharmacist; many concerns are derived from misinformation acquired on the Internet. Often, these patients read blogs written by people with chronic HCV infection who may have had extreme difficulty managing treatment and its adverse effects. This can result in noncompliance when patients become fearful of the side effects of the treatment they have either started or plan to start. The pharmacist can reassure patients that individuals can each have very different experiences with drug treatment. Additionally, patients often read about complementary and alternative medicines touted to cure HCV infection. The pharmacist can provide honest feedback regarding the ineffectiveness and potential hazards of the use of these agents. As the relationship develops between the pharmacist and patient, a level of comfort can be attained that permits nonjudgmental, open discussion of current drug and alcohol use, noncompliance, and social concerns. It is likely that regular follow-up visits with the pharmacist will enhance adherence to therapy, and we hope to assess the relationship of pharmacist intervention with adherence to HCV drug therapy and clinical outcomes.

Second, the presence of a pharmacist in the HCV clinic permits real-time checking for drug interactions. This is especially important for patients infected with genotype 1 HCV who require treatment with protease inhibitors, as they have extensive drug interaction profiles necessitating careful assessment for contraindicated combinations and dose adjustments. This checking can be done efficiently by the pharmacist at the point of care and immediately discussed with the attending physician, thereby preventing adverse effects or potential treatment disruption.

Third, the pharmacist provides informal teaching on HCV medications to resident physicians, medical students, and pharmacy students participating in the clinic. Discussion occurs between patient visits, permitting review of medication initiation, dosing, and adverse effects. Pharmacy and medical students often attend teaching sessions with patients in order to learn the proper approach for educating patients about a large amount of information regarding HCV treatment. Student participation fosters additional discussion following each teaching session, including double-checks for drug interactions that students will perform. Additionally, since the pharmacist is a faculty member and is fully funded by a school of pharmacy, the clinic and patients do not incur the costs of this member of the health care team. Overall, this arrangement results in a true multidisciplinary collaboration that benefits the patient and clinic through the provision of quality patient care.

The Bottom Line

Due to the changing face of HCV infection management, it is essential that pharmacists become more involved in the care of these patients. This can involve HCV clinic providers seeking out pharmacists who can provide teaching to their patients within their clinics. Additionally, many specialty pharmacies that dispense these medications provide HCV resources that can be offered to patients, including trained pharmacists who provide telephone counseling and printed educational materials upon dispensing of HCV treatments. HCV clinic providers should draw upon these resources to improve adherence rates in their patients. Additionally, pharmacists need to take a more active role in the development of patient educational resources, such as pamphlets that detail how to take these medications effectively, and suggest dietary recommendations, options for medication scheduling, and information detailing possible adverse effects. Pharmacists are assets for both practitioners and patients, ensuring proper prescribing and understanding of the complexity of HCV regimens in order to provide the greatest opportunity for patients to succeed with their treatment for HCV infection.

Author

LINDA M. SPOONER, PharmD, BCPS with Added Qualifications in Infectious Diseases, is Associate Professor of Pharmacy Practice, Massachusetts College of Pharmacy and Health Sciences, School of Pharmacy-Worcester/Manchester, Worcester, Massachusetts.

AUTHOR CORRESPONDENCE: Linda M. Spooner, PharmD, BCPS, Massachusetts College of Pharmacy and Health Sciences, 19 Foster St., Worcester, MA 01608. Tel.: 508.373.5696; E-mail: linda.spooner@mcphs.edu.
DISCLOSURES
The author reports no financial or other potential conflicts of interest related to the subject of this commentary.

REFERENCES


