The role of physician extenders in managing patients with chronic hepatitis C

HARPREET GUJRAL, RN, MSN, CRNP; CARLA VISCOMI, RN, BSN; AND ROCHELLE COLLANTES, MD, MPH

ABSTRACT

The number of "physician extenders" (nurse practitioners and physician assistants) caring for patients with chronic hepatitis C is rising rapidly. Their growing role in the management of these patients promises greater efficiency in the delivery of care and more provider interaction with patients. This may yield benefits in terms of patient education and support, management of medication side effects, and patient adherence to treatment regimens. This article reviews the role of physician extenders in the management of patients with hepatitis C and outlines strategies for maximizing their contribution to the care of these patients.

The role of "physician extenders" (nurse practitioners and physician assistants) in primary care medicine and pediatrics has been extensively reported over the last 3 decades. However, literature on the role of physician extenders in subspecialty practices (including hepatology) is limited, even though the number of nonphysician personnel caring for patients with liver diseases is rising rapidly. This trend is evident in the management of patients with chronic infection with hepatitis C virus (HCV). There has been a sharp rise in the number of associate members of the American Association for the Study of Liver Diseases (AASLD) involved in patient care. This group includes registered nurses, nurse practitioners, and physician assistants. The AASLD's associate membership has more than quadrupled over a year and a half (from 39 in July 2002 to 173 in January 2004), and attendance at the AASLD Hepatology Associates Course rose from 272 in 2001 to 491 in 2003.[1]

This article describes the role that physician extenders have increasingly assumed in the management of patients with chronic hepatitis C, and shares strategies for how physician extenders can best serve to improve the efficiency and quality of that management.

PHYSICIAN EXTENDERS: HOW THE CONCEPT EVOLVED

In response to the shortage and uneven distribution of primary care physicians in the mid-1960s, a group of health care professionals now known as physician assistants came into existence. Initially, this group consisted largely of Navy corpsmen, also called Medex, who had extensive military medical training.[2] In the next decade, Medex and physician assistants (PAs) were classified under the same category,[3] and the 1970s also saw the advent of nurse practitioners (NPs) and nurse clinicians, who could deliver health care beyond the role of traditional registered nurses. PAs are licensed to practice medicine under the supervision of a physician,[2] whereas NPs may practice independently (in some states) or in partnership with other health care providers.[4]

The background, training, and certification requirements for the two professional groups also differ. NPs are registered nurses who receive 2 to 4 years of additional graduate nursing education, whereas PAs are graduates from a variety of disciplines who pursue at least 2 years of graduate education and training in primary medical care. NP certification is under the review of state boards of nursing, whereas state boards of medicine regulate the certification of PAs.

Despite these differences, the clinical roles of PAs and NPs overlap a great deal, justifying the combined designation "physician extenders." NPs have been trained to provide care in acute, ambulatory, or long-term care settings.[4] Their practice involves illness diagnosis and management, as well as health promotion and

From the Center for Liver Diseases (H.G. and R.C.), Inova Fairfax Hospital, Fall Church, Va.; and the Division of Gastroenterology (C.V.), MetroHealth Medical Center, Cleveland, Ohio.

Address: Harpreet Gujral, RN, MSN, CRNP, Inova Fairfax Hospital, Center for Liver Diseases, Department of Medicine, 3300 Gallows Road, Falls Church, VA 22042; e-mail: harpreet.gujral@inova.com.

Disclosure: Ms. Gujral reported that she serves as a consultant to the Schering-Plough corporation. Ms. Viscomi and Dr. Collantes reported that they have no commercial affiliations or interests that pose a potential conflict of interest with this article.

disease prevention. NPs may order, conduct, supervise, and interpret diagnostic tests, and they may prescribe certain medications. A major part of their practice is teaching and counseling individual patients, patients' families, and groups of patients. On the other hand, the comprehensive responsibilities of PAs include conducting physical examinations, illness diagnosis and treatment, ordering and interpreting diagnostic tests, counseling patients on preventive care, assisting in surgery, and, in most states, prescribing certain medications.[2]

HOW AND WHY PHYSICIAN EXTENDERS MATTER

Physician extenders have an important positive impact on the quality, efficient delivery, and cost of health care. Because additional medical personnel can accommodate more patients and allow for more time with patients, physician extenders enable increased patient access to care, increased patient time with a health care provider, decreased waiting time, and greater continuity of care.[5] Physician extenders support efficient care delivery by attending to more minor and routine medical problems, allowing physicians to focus on cases requiring more expertise.[3] In an organized health care system, this ability to deliver expanded services at a lower cost also represents a financial advantage to the organization, especially since physicians can devote themselves to more complicated (and more high-cost) services.[2] Indeed, the financial benefits of physician extenders include cost containment, increased reimbursement, increased physician productivity, and a partial solution to workforce shortages.[5]

CHIEF FUNCTIONS OF PHYSICIAN EXTENDERS IN HEPATITIS C

Physician extenders have assumed a number of important responsibilities in the management of patients with chronic HCV infection.[6,7] These include:

- **Screening patients** with risk factors for HCV infection by ordering appropriate tests for HCV and excluding other causes of liver disease.
- **Taking detailed histories and performing comprehensive physical examinations.** This includes assessing for preexisting medical conditions, particularly depression, diabetes, heart disease, thyroid disease, and renal disease, and looking for signs of extrahepatic manifestations of hepatitis C and signs of cirrhosis or decompensated liver disease. These conditions have important implications for the treatment and monitoring of hepatitis C.
- **Educating patients and their families or partners about hepatitis C once the diagnosis is established.** This involves providing easy-to-understand information on the disease process, its natural history, and modes of transmission. The education is based on the patient's level of understanding and readiness to learn. It extensively covers the side effects of medications prior to treatment, as well as how they are managed. Patients are taught the self-injection technique and are asked to do a return demonstration during the first session. Working step-by-step on issues in the treatment process enhances adherence and promotes successful disease management. For example, a simple phone call from the physician extender may strengthen the patient's rapport with his or her health care providers, enabling continuation of treatment despite difficult side effects.
- **Collaborating with specialists, the primary care provider, the patient, and other health professionals to manage treatment challenges.** Physician extenders may find that consultation with a psychiatrist or dermatologist is necessary to address side effects of therapy, and collaboration with a nutritionist may be needed to manage weight loss related to therapy or cirrhosis.
- **Closely monitoring patients in a standard-of-care or protocol setting.** Physician extenders look for treatment side effects that may be evident from the patient's symptoms, physical examination, or laboratory data.
- **Mentoring the nursing staff** involved in managing patients with hepatitis C, to optimize care delivery.

In addition to these specific functions, physician extenders can be instrumental in various quality management activities specific to hepatitis C, given their intimate involvement in care delivery. Physician extenders also increasingly contribute to the general knowledge base in hepatitis C through participation in clinical research, contributions to scholarly works, presentations at professional and continuing education meetings, and active participation as associate members of the AASLD. Although certification for physician extenders in the subspecialty of hepatology is desired, it has not yet been put in place. Such certification would enable physician extenders to stay on the cutting edge of current treatments and better learn from their peers in hepatology.

STRATEGIES USED BY PHYSICIAN EXTENDERS FOR ENHANCING PATIENT MANAGEMENT

As previous articles in this supplement have made clear, managing patients with hepatitis C involves overcoming many challenges, such as the difficulty of ensuring adherence to treatment, the wide spectrum of treatment side effects, and the tendency for many

HCV-infected patients to have psychosocial or financial challenges. Physician extenders are well suited to play a prominent role in efforts to overcome these challenges, with the goal of enhancing adherence to therapy and thereby optimizing therapeutic outcomes **(Figure 1)**. This section details specific strategies that physician extenders can and do employ to overcome these challenges and improve patient management.

Identifying sources of social and financial support

Physician extenders are well positioned to help patients take advantage of their social support system, ie, family members, friends, community and church groups, and coworkers. This often includes identifying persons who can provide financial assistance, coordinate clinic visits, and help handle other practical matters. Physician extenders also frequently counsel patients on whether they may need a more flexible work schedule and assistance with household chores during their treatment. Similarly, they may need to discourage patients from starting a new job, business, or personal pursuit that could produce additional stress during therapy.

Because financial stability can be a stressful issue, physician extenders should be prepared to present and explain relevant worker-protection laws, such as the Family and Medical Leave Act and the Americans with Disability Act, if warranted. Discussion of the patient's financial resources may reveal a need to coordinate the source of payment for office visits, medical consultations, laboratory tests, and medications. The patient also should be made aware of industry-sponsored programs or specialty pharmacies that may provide assistance with medications on the basis of financial need.

Educating and empowering patients

The patient's level of education affects his or her understanding of hepatitis C and its management, especially antiviral therapy. The use of simple language without jargon can be key in explaining the medication regimen. By determining the patient's level of understanding of HCV infection and any preliminary information on the disease, the physician extender is able to appropriately build on that knowledge base. Patients can also be directed to reliable sources of information such as the National Institutes of Health, the Centers for Disease Control and Prevention, the American Liver Foundation, and the Hepatitis Foundation International.

Patient education must continue throughout therapy. It should elaborate on the natural history and prognosis of the disease, emphasizing modes of transmission and risk reduction as well as ways to improve general well-being (eg, increasing hydration, exercise, good nutrition, avoiding alcohol). Medication adherence also must be emphasized—specifically, maintaining more than 80% of the dosage of the drugs for more than 80% of the time to improve early virologic response and to enhance sustained virologic response.[8] Treatment-naïve patients require more information and support to deal with medication side effects.

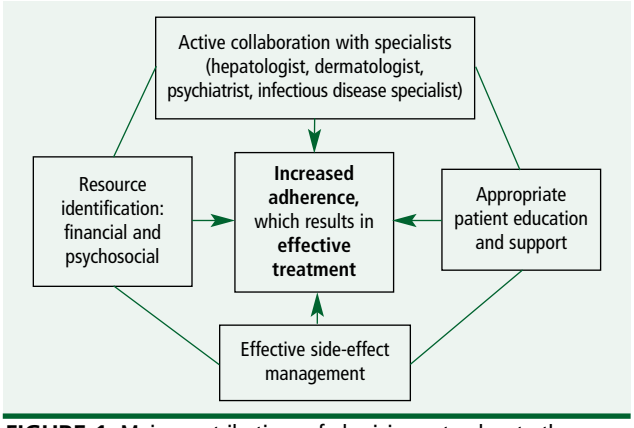

FIGURE 1. Major contributions of physician extenders to the management of patients with chronic hepatitis C.

All patients should be encouraged to take ownership of and accountability for their own care. All are asked to abstain from alcohol to improve their response to treatment, and cirrhotic patients require strict abstinence. Physician extenders should encourage participation in patient support groups, which can be extremely helpful. They also should provide ample opportunity for patients to ask questions and clarify myths. Knowledge is empowering: the more knowledge patients have, the more likely they are to adhere to treatment.

Managing side effects of combination antiviral therapy

A 2002 National Institutes of Health consensus conference on hepatitis C concluded that combination therapy with pegylated interferon alfa (peginterferon) and ribavirin results in the highest response rates of any therapy for chronic hepatitis C.[9] However, this combination can result in nonspecific, systemic, hematologic, neuropsychiatric, reproductive, cardiovascular, respiratory, dermatologic, and gastrointestinal side effects **(Tables 1 and 2)** that require effective management to ensure adherence to treatment. These side effects may diminish patients' quality of life[10] and reduce their productivity. Side effects are most intense during the initial few months of therapy. It is crucial that patients anticipate these side effects in an attempt to minimize them and to implement interventions to manage them.

Because of this wide spectrum of side effects and the long duration of therapy for chronic hepatitis C, close

TABLE 1
Practical strategies for managing side effects of combination therapy in patients with chronic hepatitis C*

Side effects caused by pegylated interferon

Flulike symptoms (fever, chills, myalgia, and headache are most common)
- Thoroughly educate and prepare patient for these symptoms
- Advise patient to take injection 2 to 3 hours before bedtime
- Advise patient that he/she may premedicate with acetaminophen or an NSAID (and may repeat as directed), but patients with cirrhosis should avoid NSAIDs
- Ensure adequate hydration (weight in kg = ounces of noncaffeinated fluids)
- Suggest that warm blankets may help with chills

Fatigue
- Assess at baseline and at follow-up visits. Exclude organic and psychiatric causes of fatigue (anemia, hypothyroidism, depression, etc).
- Encourage efforts to continue to work
- Advise that mild activity (eg, walking, swimming) can help reduce stress
- Tell patient to "listen to your body" and take breaks when possible
- Suggest taking one or two naps during the day
- Advise patient to delegate tasks if possible (eg, ask family or friends to do laundry)
- Advise patient to eat at regular intervals for adequate energy

Neuropsychiatric side effects†

Depression/mood disturbance
- Obtain a baseline assessment for depression
- If a patient is depressed or has a history of depression, consider antidepressants
- Investigate and manage other neuropsychiatric side effects (anxiety, mania, etc)
- Encourage patient to consider support groups or relaxation techniques
- If symptoms do not improve, refer to a psychiatrist

Headaches
- Assess for various etiologies (eg, migraine, allergy status, hydration, drug interaction, infection, insomnia)
- Thorough neurologic exam warranted. Refer to neurologist if headaches worsen.
- Advise patient to avoid alcohol and caffeinated beverages

Insomnia
- Advise patient to maintain good sleep hygiene and stay awake during the day
- Suggest light exercise during the day
- Suggest that patient drink a warm glass of milk at bedtime
- Evaluate for depression
- Consider use of mild sedatives

Impaired concentration
- Provide reassurance ("It's usually temporary."). Involve family members if needed.
- Advise patient to make lists and check off completed tasks
- Suggest keeping a diary and writing notes to self
- Advise patient that short naps may help

Side effects caused by ribavirin

Cough (generally nonproductive)
- Assess at baseline and monitor thereafter
- Investigate for infection or allergy
- Suggest a humidifier or hard candy
- Encourage smokers to quit smoking
- If worsening or severe, exclude other causes (pulmonary fibrosis, cardiac, etc)

Rash/dry skin/itching
- Perform baseline and subsequent skin assessments. Consider extrahepatic manifestation of HCV infection.
- Suggest tepid showers or baths, followed by patting the skin dry
- Advise keeping skin well mosturized. Suggest soaps with moisturizers, sunscreen, products for sensitive skin.
- Consider topical antipruritics, such as diphenhydramine cream
- Use hydrocortisone ointment sparingly
- Suggest oatmeal baths to ease itching
- Consider dermatology consult for uncontrolled rash

Teratogenic/embryocidal effects
- Require patient to practice two methods of contraception during treatment and 6 months thereafter
- Do baseline and monthly pregnancy tests for women of childbearing age

* Adapted in part from "Guiding Patients Through Chronic Hepatitis C Therapy," Schering Hepatitis Innovations, Schering Corp., Copyright © 2002.
† Refer to article by Crone and colleagues in this supplement for more detail on management of these side effects.

monitoring and continued support of patients is essential to maintaining adherence. Physician extenders can facilitate simple interventions that may ameliorate some of these side effects. When gastrointestinal symptoms such as nausea, diarrhea, anorexia, or dyspepsia occur, patients should be encouraged to avoid fatty and spicy foods, follow the "BRAT" (banana, rice, applesauce, toast) diet, try ginger tea or candy, and eat small but frequent meals. For alopecia, patients can be advised to avoid harsh hair treatments, wear hats or hairpieces, or use hair products that minimize hair loss. If a patient has diarrhea, stool examinations should be done to rule out infection. If chest pain or palpitations occur, a cardiology evaluation is mandatory.

Cytopenias are a common challenge during treatment. Approximately 10% of patients experience reversible hemolytic anemia from ribavirin therapy, and interferon or peginterferon therapy may induce anemia and neutropenia. According to the package insert for ribavirin, the dose should be reduced if the patient's

hemoglobin falls below 10 g/dL and the drug should be permanently discontinued if the hemoglobin falls below 8.5 g/dL. However, the use of erythropoietic growth factors (epoetin alfa or darbepoetin alfa) may allow clinicians to manage anemia proactively. These growth factors may increase hemoglobin levels and thus improve anemia-related symptoms and health-related quality of life, as reported in several studies detailed by Ong and Younossi earlier in this supplement.

Neutropenia and thrombocytopenia have also been noted in HCV-infected patients receiving combination antiviral therapy. Neutropenia is more frequent than thrombocytopenia, although the latter is more pronounced in patients with cirrhosis. Both of these side effects may require antiviral dose reduction, which may have implications for the likelihood of sustained virologic response, but their management varies. Some clinicians use growth factors such as filgrastim (granulocyte colony-stimulating factor) to treat neutropenia,[11] although it is not currently approved for use in HCV-infected patients receiving interferon or peginterferon. Other clinicians may accept lower neutrophil counts and prefer close monitoring over peginterferon dose reduction. However, unlike in patients with chemotherapy-induced neutropenia, evidence of an increased risk of infections among patients with hepatitis C is currently lacking. Oprelvekin (IL-11) has not been accepted with any enthusiasm for thrombocytopenia related to hepatitis C therapy, owing to its high incidence of side effects. Moreover, thrombocytopenia-related bleeding episodes are not common.

The exact role of physician extenders in managing cytopenias in HCV-infected patients depends on the practice setting. Large centers may have protocols in place for consideration of hematopoietic growth factors for anemia and neutropenia. In such a setting, physician extenders can follow the protocol established by a multidisciplinary team. Indeed, it has become increasingly necessary that physician extenders follow established protocols or seek the advice of the treating physician before reducing the dose of antiviral therapy.

TABLE 2
Practical strategies for managing cytopenias due to combination therapy for chronic hepatitis C*

Anemia (caused by ribavirin and interferons)
- Take complete blood cell count at baseline, at weeks 2 and 4 of therapy, and monthly thereafter
- Discuss with patient the signs and symptoms of anemia, including fatigue, shortness of breath, etc
- Instruct patient to notify provider if dyspnea develops
- Consider use of epoetin alfa or darbepoetin alfa

Neutropenia (caused by interferons)
- Advise frequent hand-washing
- Advise avoidance of crowds
- Consider use of granulocyte colony-stimulating factor

Thrombocytopenia (caused by interferons)
- Advise use of a soft-bristled toothbrush
- Discourage shaving of large areas; urge use of electric razor
- Suggest use of a humidifier to keep nasal mucosa moisturized and to minimize nose bleeds
- Instruct patient to notify provider of any signs of bleeding and to seek emergency treatment if uncontrolled

* Refer to article by Ong and Younossi in this supplement for more detail on management of these hematologic abnormalities.

SUMMARY

Over the past 3 decades, physician extenders have become increasingly involved in subspecialty practices such as hepatology, and particularly in the management of patients with hepatitis C. In general, their roles include diagnosis and disease management, health promotion, and disease prevention. Physician extenders' participation in hepatitis C management and active collaboration with clinical specialists may help to ensure adequate patient education, better identification of resources for patients, and effective management of medication side effects. In these ways, physician extenders can facilitate patient adherence to therapy, which is crucial for enhancing the efficacy of treatment for hepatitis C.

REFERENCES

1. **American Association for the Study of Liver Diseases.** Unpublished data, 2004.
2. **American Academy of Physician Assistants.** Information about PAs and the PA profession. Available at: www.aapa.org/geninfo1.html. Accessed March 3, 2004.
3. **Fottler MD.** Physician attitudes toward physician extenders: a comparison of nurse practitioners and physician assistants. Med Care 1979; 17:536–549.
4. Scope of practice for nurse practitioners. Austin, Tex.: American Academy of Nurse Practitioners; 1993 (revised 1998 and 2000).
5. Physician extenders are cost-effective approach. Physician Relations Update 1998(Jan):7–8.
6. **Clark CH, Ghalib RH.** Hepatitis C: role of the advanced practice nurse. AACN Clin Issues 1999; 10:455–463.
7. Position statement: role delineation of the advanced practice nurse in gastroenterology/hepatology and endoscopy. Society of Gastroenterology Nurses and Associates. Gastroenterol Nurs 1996; 19:216–217.
8. **McHutchison JG, Manns M, Patel K, et al.** Adherence to combination therapy enhances sustained response in genotype-1-infected patients with chronic hepatitis C. Gastroenterology 2002; 123:1061–1069.
9. **National Institutes of Health.** National Institutes of Health Consensus Development Conference Statement: Management of hepatitis C: 2002—June 10–12, 2002. Hepatology 2002; 36(5 suppl 1):S3–S20.
10. **Martin LM, Sheridan MJ, Younossi ZM.** The impact of liver disease on health-related quality of life: a review of the literature. Curr Gastroenterol Rep 2002; 4:79–83.
11. **Van Thiel DH, Faruki H, Friedlander L, et al.** Combination treatment of advanced HCV associated liver disease with interferon and G-CSF. Hepatogastroenterology 1995; 42:907–912.