ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Overview of Pruritus Management in Patients With Chronic Liver Disease

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G&H How common is pruritus in patients with chronic liver disease?

AB Overall, the incidence of pruritus or itching in patients with chronic liver disease has varied from 30% up to 70% depending upon the report. This wide range in incidence may be attributed to the underreporting of pruritus. Physicians may not commonly ask about pruritus, and there might be a stigma about it; patients may not wish to share that they are experiencing this symptom owing to the fear of being labeled as infectious or contagious. Physicians should do a better job asking about pruritus, and patients should be more upfront about telling physicians when they are experiencing this symptom so that both groups can be on the same page and treat pruritus as soon as possible.

> Pruritus can have a profound impact on a patient's quality of life by causing sleep disturbances, anxiety, and depression.

G&H Can all liver diseases make patients itch, or does pruritus mainly occur in specific liver diseases, such as primary biliary cholangitis?

AB Pruritus is a common and often distressing symptom experienced by individuals with liver disorders, including cholestatic liver diseases such as primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC). Pruritus is most prevalent in cholestatic liver diseases. For example, up to 50% to 70% of patients with PBC can develop itching at some point during their disease course. Interestingly, some studies suggest that pruritus in patients with cholestatic liver diseases is different from pruritus associated with other diseases, whereas other research suggests that there are more similarities than differences. Because pruritus is a common symptom with any type of liver disorder, it is important for physicians to take a good history of patients who have chronic liver disease to treat this symptom properly.

G&H What is the impact of pruritus on patients' quality of life?

AB Pruritus can have a profound impact on a patient's quality of life by causing sleep disturbances, anxiety, and depression. Furthermore, the presence of pruritus may indicate progression of liver disease or the development of complications. Therefore, it is crucial to routinely ask patients with liver disease about the presence of pruritus and its severity during clinical evaluations. Early identification and management of pruritus can significantly improve a patient's symptoms and overall well-being. Thus, I encourage physicians to include pruritus assessment as part of comprehensive liver disease patient care.

G&H How can pruritus be best evaluated in a patient with chronic liver disease?

AB Itching can be quite subjective. Several questionnaires have been identified in PBC to make this subjective symptom more objective. With the Visual Analogue Scale, the patient evaluates how much itching they have on a scale from 0 to 100, with 0 representing no itching and 100 representing the worst possible itching. With the 5-D itch scale, the patient also rates itching based on an objective scale for how many hours a day they have been itching during the past 2 weeks. Finally, the PBC-40 is a questionnaire in which one of the main parts relies on itching. Physicians can use these 3 objective measurements in the clinic to obtain objective values from a subjective symptom to help them decide on the best treatment for an individual patient. These measures are validated specifically for patients with PBC but have been used in patients with other conditions. For example, I use these scales to help give me an objective measurement of pruritus in patients with different liver diseases.

G&H What are the possible mechanisms of pruritus in chronic liver disease?

AB This is a topic of debate. There are multiple mechanisms, one of which involves bile acids. The elevation of bile acids is known to irritate nerve endings and the skin, which can cause itching. Another mechanism involves the serotonin pathway, which can lead to itching. Finally, patients with cholestatic liver diseases, specifically PBC and PSC, usually have lysophosphatidic acid (LPA) in autotaxin pathways. Although it has been possible to identify LPA and autotaxin pathways, it is not clear how they are related to itching. Because of these newly identified pathways, we have new potential different treatments for pruritus.

G&H What medical therapies are currently available for the management of pruritus in patients with chronic liver disease?

AB Based on the pathophysiology and different pathways for itching, various treatment options have been developed. For example, the first pathway I discussed involves bile acids. The bile acid–binding resins cholestyramine and colestipol can be used to treat pruritus because they decrease the absorption of bile acids in the terminal ileum. Although the data for these medications are poor, these agents are used as a first step because there are few side effects associated with them other than drug-drug interactions.

If itching persists, I often use rifampicin, which is an antituberculosis medication. Small studies have shown that rifampicin at a dose of 150 to 300 mg twice daily has been effective at treating itching. However, there may be a fear of the side effects of this medication, mainly liver toxicity. Therefore, it is important to make sure that patients who are starting this type of therapy undergo frequent liver testing so no liver toxicity is missed.

On the other hand, ursodeoxycholic acid has not been shown to be effective at treating symptoms such as itching. Many patients coming to my practice have been prescribed ursodeoxycholic acid as part of their itching management, but that should not be the case.

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Finally, data from a recently published paper in *The New England Journal of Medicine* on the use of fibrates, which are peroxisome proliferator-activated receptor agonists, showed improvement in itching in patients with PBC and, in my opinion, will revolutionize PBC treatment. Elafibranor (Iqirvo, Ipsen) was recently approved by the US Food and Drug Administration, and seladelpar will likely be approved in the next several weeks. Both of these medications have shown significant improvement in patients with PBC and moderate pruritus.

G&H Are any agents in the development pipeline showing promise for the management of pruritus in chronic liver disease?

AB I think ileal bile acid transporter inhibitors, which target the absorption of bile acids at the terminal ileum, will be game changers for patients with itching. These medications are now undergoing phase 3 clinical trials and have shown very promising results. One of these agents recently reported significant improvement in itching with just 12 weeks of treatment.

G&H What nonpharmacologic approaches have been studied to treat pruritus in patients with chronic liver disease?

AB Ultraviolet light has been studied, as it can help metabolize bilirubin, which is often elevated in patients with cholestatic liver diseases, along with alkaline phosphatase. I have used this therapeutic approach several times. Before the recent wave of new therapies, plasmapheresis was also used to treat itching. Liver transplantation should still be considered in patients whose pruritus cannot be controlled with the pharmacologic therapies currently available. With recent improvements in the understanding of pruritus in patients with cholestatic liver diseases as well as recent advances in therapies, I think the indication of liver transplant in these patients will significantly decrease.

Finally, there are a number of common measures that patients can use to help control their pruritus. For example, I usually ask my patients to make sure they have short nails. I also ask them to wear cotton clothes and make sure they do not use soaps or anything that might damage or dry their skin. These recommendations may not be supported by clinical data but may make a difference in patients with chronic liver disease who have pruritus.

Disclosures

Dr Bonder has done consulting for Intercept/Alfasigma, Chemomab, Ipsen, GSK, Guidepoint, and Alnylam. He also has served as a primary investigator for Gilead, Ipsen, Intercept, Mirum, CymaBay, Genfit, and Chemomab; on the editorial board for DynaMed and Journal of Clinical Medicine*; as a medical reviewer for Pfizer; and on the medical advisory board for Tharimmune, PBC Foundation, and PBCers.*

Suggested Reading

Ebhohon E, Chung RT. Systematic review: efficacy of therapies for cholestatic pruritus. *Therap Adv Gastroenterol*. 2023;16:17562848231172829.

Hirschfield GM, Bowlus CL, Mayo MJ, et al; RESPONSE Study Group. A phase 3 trial of seladelpar in primary biliary cholangitis. *N Engl J Med*. 2024;390(9):783-794.

Kowdley KV, Bowlus CL, Levy C, et al; ELATIVE Study Investigators' Group. Efficacy and safety of elafibranor in primary biliary cholangitis. *N Engl J Med*. 2024;390(9):795-805.

Marenco-Flores A, Sierra L, Goyes D, Kahan T, Patwardhan VR, Bonder A. Managing pruritus in chronic liver disease: an in-depth narrative review. *Clin Liver Dis (Hoboken)*. 2024;23(1):e0187.

Medina-Morales E, Barba Bernal R, Gerger H, et al. Pharmacological therapy of pruritus in primary biliary cholangitis: a systematic review and meta-analysis of randomized clinical trials. *J Clin Gastroenterol*. 2023;57(2):143-152.

Schattenberg JM, Pares A, Kowdley KV, et al. A randomized placebo-controlled trial of elafibranor in patients with primary biliary cholangitis and incomplete response to UDCA. *J Hepatol*. 2021;74(6):1344-1354.

Smith HT, de Souza AR, Thompson AH, et al. Cholestatic pruritus treatments in primary biliary cholangitis and primary sclerosing cholangitis: a systematic literature review. *Dig Dis Sci*. 2023;68(6):2710-2730.