A Closer Look at the GI, Liver, and Nutrition PRN

Overview of the PRN

The GI/Liver/Nutrition (GILN) PRN was founded on October 25, 1999, in Kansas City, Missouri, to establish a network of clinical pharmacists interested in promoting and advancing practice, research, and education in the areas of gastrointestinal (GI) disease, liver disease, and nutrition. The founding officers, Rosemary R. Berardi (chair), William R. Garnett (secretary/treasurer), Rex O. Brown (Nominations Committee chair), and Susan Sorrells (Communication/Newsletter Committee chair), together with 25 participants, helped lay the foundation for the GILN PRN, which was officially recognized 84 days later, on January 17, 2000. The first official meeting of the GILN PRN reported 56 members.

The GILN membership is a tight-knit group of over 220 members, which include practitioners, fellows, residents, and students. Members of the GILN PRN have made significant contributions to the profession: 140+ papers written or cowritten by a PRN member, 44 book chapters written or cowritten by a PRN member, 100+ posters presented at meetings, and 300+ presentations at meetings. In addition, many of its members hold certifications, including BCPS, BCACP, BCNSP, and BCCCP. Many GILN PRN members have also received various honors, awards, and grants toward GILN-related research.

Opportunities for Resident and Fellow Members

The GILN PRN offers many opportunities for practitioners, residents, fellows, and students. These opportunities include travel awards for residents, fellows, and students. Travel award recipients are invited to present their research project at the ACCP Annual Meeting PRN networking and business meeting. The PRN also encourages networking with experienced practitioners and involvement in the PRN leadership.

Clinical Issues: Fatty Liver Disease – Considerations in Nutrition, the Microbiome, and Drug Dosing

Fatty liver disease, better known in the medical community as nonalcoholic fatty liver disease (NAFLD), is the leading cause of liver disease in the world. It consists of the infiltration of fat into the liver, which can be benign; however, it can also lead to nonalcoholic steatohepatitis (NASH), which in turn may lead to cirrhosis. Although its pathophysiology is not completely understood, NAFLD has been associated with excessive caloric intake, inactivity, and the metabolic syndrome, including visceral obesity dyslipidemia, hyperglycemia, and insulin resistance. It is not entirely clear whether the metabolic syndrome precedes NAFLD or NAFLD precedes the metabolic syndrome.[1] It is important to determine the cause of NAFLD so that effective treatments can be developed because NASH is a leading cause of cirrhosis in the world.

Currently, effective pharmacologic treatments for NAFLD are lacking. Cochrane reviews are available for using antioxidants, herbal products, and statins in patients with NAFLD and NASH; however, none has sufficient data to show benefit or harm.[2-4] Lifestyle modification is an important intervention, given the link of NAFLD with excessive caloric intake, obesity, and inactivity. Weight loss is an important step in reducing the impact of NAFLD; patients who lost 7% or more of their body weight had some recovery in liver function.[5] A combination of physical activity and a diet targeted at weight loss is preferred because patients are unlikely to maintain the weight loss initially obtained through diet alone.[6] Even without weight loss, physical activity has been shown beneficial for liver lipid levels.[7] Behavioral therapy is beneficial in assisting patients with NAFLD with adherence to diet, weight loss, and exercise.[8] The impact of specific nutraceuticals (e.g., glutamine, n-3 polyunsaturated fatty acids, vitamin E, resveratrol) is less clear, and further study is required to elucidate their usefulness.[5,9-11]

More recently, studies have shown a link between the development of NAFLD and a patient's GI microbiome.[12] Several mechanisms have been proposed to explain the link between the gut microbiota and the development of NAFLD, including (1) changes in the harvesting of energy from the diet[13]; (2) changes in intestinal permeability leading to endotoxemia and systemic and, specifically, hepatic inflammation[14]; (3) generation of endogenous toxic products such as ethanol[15]; and (4) modulation of bile acid homeostasis.[16] Some changes in the gut microbiota may be capable of drastically reducing or, in turn, increasing the risk of NAFLD. These changes can be made steadily with changes in diet or quickly with the use of antibiotics. They can also be made more specifically by modulating the microbiota with carbohydrates that stimulate the growth of beneficial microorganisms (known as prebiotics), through introducing beneficial microorganisms directly into the gut (known as probiotics), or a combination of the two (known as symbiotics). If any of these approaches are used, they must be used long term because the gut microbiota has a tendency to revert to its original state without continued modification and modulation (this can be beneficial when patients receive single short courses of antibiotics rather than prolonged or multiple courses). Data for using prebiotics, probiotics, and symbiotics are scarce, but there is much interest in the effects of these cocktails on the progression of NAFLD and NASH.

With the increasing incidence of liver disease and fatty liver disease in the Western world, providers need to take precautions to ensure safe and effective medication therapy. Although many drugs are metabolized by the liver, there is little information regarding the modifications to drug therapy needed by patients with severe liver disease, including cirrhosis and end-stage liver disease. This is of concern because hepatocyte metabolism is not the only alteration in cirrhosis that affects drug metabolism. Alterations in other pharmacokinetic parameters include decreased levels of proteins for protein binding, altered blood flow to the liver decreasing clearance beyond that expected from hepatocyte dysfunction, and altered volumes of distribution because of ascites or alterations in protein binding.[17,18] Bioavailability may be increased given the decreased metabolism of drugs through first-pass metabolism.[18] Patients with cirrhosis may develop hepatorenal syndrome and renal failure. One issue that makes hepatic dose adjustment more difficult than renal dose adjustment is the lack of a clear biological marker for the degree of liver impairment (i.e., serum creatinine and correlation of renal function). Many drugs can lead to liver failure, although the possibility of precipitating renal failure or GI bleeding or of provoking hepatic encephalopathy is of great concern in patients with cirrhosis as well. Even with the hepatotoxic potential of many drugs, some experts believe that using drugs with the potential for hepatotoxicity is reasonable with close monitoring.[19] It is opined that liver toxicity with these drugs may not be more common in patients with baseline liver dysfunction, but drug-induced hepatotoxicity may have more severe consequences.[20]

Some specific agents that require extra caution when used in patients with cirrhosis include sedatives, cardiac medications, and analgesics. For sedatives, benzodiazepines should be used cautiously. Many drugs in this class are metabolized by the liver to some degree and may precipitate hepatic encephalopathy; for this reason, propofol may be preferred for both long-term sedation if needed in the ICU and procedural sedation such as for endoscopy.[21] Benzodiazepines are still the preferred agents for treatment of alcohol withdrawal syndrome in patients with cirrhosis, although dose reductions are necessary to avoid oversedation and respiratory depression. Several cardiac medication classes are of concern. β-Blockers are used regularly in patients with cirrhosis both directly for portal hypertension and for comorbidities such as coronary artery disease. Labetalol has been reported to cause fatal drug-induced liver injury; thus, it should be used with great caution in patients with liver dysfunction.[22] Other β-blockers should be dose reduced to avoid adverse effects caused by decreased first-pass metabolism and bioavailability.[23] Angiotensin-converting enzyme inhibitors should be used with caution because of the risk of hyperkalemia when used in combination with aldosterone

antagonists and acute kidney injury.[24] With analgesics, there is much concern over the use of acetaminophen in patients with liver dysfunction; however, if used with caution at doses of 3 g/day or less (2 g/day or less if following U.S. Food and Drug Administration [FDA] recommendations), acetaminophen can be used safely in patients with cirrhosis.[25] Acetaminophen is actually preferred by most gastroenterologists to nonsteroidal anti-inflammatory drugs such as ibuprofen because of the increased risk of GI hemorrhage in patients with underlying coagulopathy and gastropathy and the risk of developing renal dysfunction, all of which are a concern for patients with cirrhosis.[26] The use of opiates can be challenging because they may induce hepatic encephalopathy.[27] Codeine requires activation to an active metabolite before it has analgesic effects; thus, it has reduced benefit when used in patients with liver dysfunction. Overall, the best sources of information for dose adjustment with liver dysfunction are the FDA and the package inserts.

To learn even more, please attend the GI/Liver/Nutrition PRN focus session at the ACCP Annual Meeting in October to hear from experts in fatty liver disease and liver pharmacokinetics.

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Submitted by:
Michael A. Smith, Pharm.D., BCPS
Clinical Assistant Professor of Pharmacy
University of Michigan College of Pharmacy
Ann Arbor, MI
Chair, GILN PRN

Michelle T. Martin, Pharm.D., BCPS, BCACP
Clinical Assistant Professor
University of Illinois at Chicago College of Pharmacy
Chicago, IL
Chair-Elect, GILN PRN

Johnathan Voss, Pharm.D., BCCCP
Overnight Critical Care/Emergency Medicine Clinical Specialist
John Peter Smith Hospital
Fort Worth, TX
Secretary/Treasurer, GILN PRN