Richard Pullen, EdD, MSN, RN, CMSRN, CNE-cl

CE 1.5 ANCC Contact Hours

Rx 0.5 Pharmacology Contact Hour

A Clinical Review of Primary Biliary Cholangitis

ABSTRACT

Primary biliary cholangitis is a slowly progressive immune-mediated cholestatic disease that causes a destruction of the intrahepatic bile ducts and may lead to cirrhosis of the liver, end-stage liver disease, and the need for liver transplantation. The disease is among the most common reasons why adults require liver transplantation. The primary signs of the disease include the presence of antimitochondrial and antinuclear antibodies, elevated alkaline phosphatase, hyperbilirubinemia, hypercholesterolemia, and histologic features, such as intense inflammation with a florid duct lesion and hepatic fibrosis. The patient's quality of life is impacted by fatigue, pruritus, malabsorption syndrome, sicca syndrome, osteoporosis, and challenges coping with chronic illness. Advanced practice registered nurses need to understand the pathophysiology, clinical presentation, diagnostic approaches, disease and symptom management, and priority nursing assessment and care in patients with this rare disease to differentiate it from primary sclerosing cholangitis, autoimmune hepatitis, obstructed bile duct lesions, drug-induced cholestasis, cholestasis in pregnancy, cholangiocarcinoma, hepatic malignancy, and peptic ulcer disease.

Primary biliary cholangitis (PBC) is an autoimmune disease that causes progressive destruction of the intrahepatic bile ducts leading to cholestasis (Tsuneyuma, Baba, Morimoto, Tsunematsu, & Ogawa, 2017; Wang, Bowlus, Wang, & Gershwin, 2017). The antimitochondrial antibody (AMA) is a hallmark feature in 90%–95% of PBC cases (Tsuneyuma et al., 2017; Wang et al., 2017). The primary immunological epitope recognized by AMA in the majority of people with PBC is pyruvate dehydrogenase complex (PDC-E2), which is an enzyme found in the mitochondria and plays an important role in metabolism (Tsuneyuma et al., 2017; Wang et al., 2017). Failure of immune tolerance to mitochondrial PDC-E2 causes a proliferation of autoreactive $CD4^+$ T-helper lymphocytes and $CD8^+$ cytotoxic T-lymphocytes and a reduction in T-regulatory lymphocytes (Wang et al., 2017). T-lymphocytes mediate an immune attack on bile duct epithelial cells and there is activation of inflammatory B-lymphocytes (Tsuneyuma et al., 2017; Wang et al., 2017). B-lymphocytes mediate inflammation through proinflammatory cytokines such as interleukin 6 (IL-6), interferon γ (IFN-γ), and tumor necrosis factor α (TNF-α) (Tsuneyuma et al., 2017; Wang et al., 2017). T- and B-lymphocytes infiltrate, damage, and destroy the intrahepatic bile ducts (Wang et al., 2017).

In addition to AMAs, 30%–50% of patients possess PBC-specific antinuclear antibodies (ANA) that mediate lymphocyte dysregulation including, but not limited to, Anti-gp210 and Anti-sp100, causing damage and destruction to the intrahepatic bile ducts (Tsuneyuma et al., 2017; Wang et al., 2017). Antinuclear antibodies are markers of a poor prognosis whereas AMAs are not generally reliable indicators of disease severity or progression (Wang et al., 2017). Approximately 50% of AMA-negative patients are positive for PBC-specific ANAs (Wang et al., 2017). Patients who do not have detectable antibodies may be diagnosed with the disease when they have laboratory and histological features of PBC (Chascsa & Lindor, 2018).

When the bile ducts are initially damaged, cholangiocytes normally proliferate and generate new ducts by hepatic progenitor cells (Levy, Carrion, & Mayo,

Received February 13, 2019; accepted May 13, 2019.

About the author: *Richard Pullen, EdD, MSN, RN, CMSRN, CNE-cl, is Full Professor, Texas Tech University Health Sciences Center School of Nursing, Lubbock, Texas.*

The author declares no conflicts of interest.

Correspondence to: *Richard Pullen, EdD, MSN, RN, CMSRN CNE-cl, Texas Tech University Health Sciences Center School of Nursing, 3601 4th St, STOP 6264, Lubbock, TX 79430 (Richard.Pullen@ttuhsc.edu).*

DOI: 10.1097/SGA.0000000000000480

2018). The extent of bile duct regeneration in PBC correlates with disease severity and prognosis (Levy et al., 2018; Tsuneyuma et al., 2017). The rate of damage and destruction of bile ducts may exceed that of regeneration of new ones (Levy et al., 2018; Tsuneyuma et al., 2017). The intrahepatic bile ducts gradually disappear (ductopenia) in PBC and bile becomes trapped in the liver (Levy et al., 2018; Tsuneyuma et al., 2017). Ductopenia occurs when less than 50% of the bile ducts are identified through imaging studies (Levy et al., 2018). Hepatocytes undergo cellular necrosis and apoptosis in response to intense inflammation from the toxic effects of the trapped bile and are replaced with fibrotic tissue (Assis, 2018; Levy et al., 2018). Fibrosis leads to cirrhosis because of distortion in hepatic structure and vasculature resulting in the liver's inability to form bile, absorb and metabolize bilirubin, synthesize protein, promote coagulation, metabolize carbohydrates, metabolize toxins and drugs, and store vitamins (Assis, 2018; Liberal & Grant, 2016).

Epidemiology and Risk Factors

The prevalence of PBC ranges from 2 to 40 per 100 000 worldwide (Joshita, Umemura, Tanaka, & Ota, 2017; Levy et al., 2018). The prevalence of PBC may be higher because of a prolonged asymptomatic stage that escapes presentation (Levy et al., 2018). The female-to-male ratio is 10:1. The typical patient is a middle-aged female (Levy et al., 2018). There is a genetic predisposition to PBC in people who possess specific human leukocyte antigens (HLA), especially DRB1*8 allele family, and 27 non-HLA loci haplotypes, and the interleukin 12 (IL-12) inflammation pathways (Joshita et al., 2017; Levy et al., 2018). Factors that may trigger PBC in genetically susceptible individuals include bacteria, viruses, xenobiotics, heavy metals, vitamin D deficiency, cigarette smoke, hair dye, nail polish, and psychological stress (Joshita et al., 2017; Levy et al., 2018). Extrahepatic autoimmune disorders are present in 40%–70% of patients with PBC including Hashimoto's thyroiditis, Sjögren syndrome, celiac disease, scleroderma, lupus, and rheumatoid arthritis (Chalifoux, Kony, Choi, & Saab, 2017).

Clinical Presentation

Patients may have a spectrum of symptoms with initial presentation including advanced PBC with cirrhosis. However, approximately 60% of patients with PBC are asymptomatic during routine health screenings (European Association for the Study of the Liver [EASL], 2017; Levy et al., 2018; Lindor, Bowlus, Boyer, Levy, & Mayo, 2019). Liver chemistries provide early clues to PBC pathology including a disproportionately elevated alkaline phosphatase (ALP) to alanine aminotransferase (ALT) and aspartate aminotransferase (AST), elevated γ-glutamyl transferase (GGT), and (to a much lesser extent) elevated bilirubin (Lindor et al., 2019). Elevated levels of GGT in the presence of AMA are caused by chronic B-lymphocyte activation by the toll-like receptors signaling pathway (Levy et al., 2018; Lindor et al., 2019). Most asymptomatic patients become symptomatic within 2–4 years of diagnosis (Levy et al., 2018; Lindor et al., 2019).

Fatigue is present in approximately 80% of patients with PBC, is generally considered to be a multifactorial problem, and can be disabling (Lindor et al., 2019). Treatable causes of fatigue should be evaluated including anemia, medications, hypothyroidism, and other comorbidities such as pruritis, sleep disturbances, and depression (Lindor et al., 2019). Fatigue may be related to an increase in mitochondrial activity causing muscle fatigability from excessive acidosis with exercise (Lindor et al., 2019). Impaired autonomic function and baroreceptor response in PBC causes orthostatic hypotension which predisposes the patient to falls. Chronic fatigue may cause daytime sleepiness and cognitive dysfunction (EASL, 2017; Lindor et al., 2019).

Pruritis is reported in approximately 80% of patients with PBC and may be a major source of suffering (Levy et al., 2018). Patients with PBC have increased levels of bile acid that accumulate on the skin. The G-protein coupled bile receptor (TGR5) mediates neurotransmission of the cholestatic process to the skin (Carrion, Rosen, & Levy, 2018; Levy et al., 2018; Van Niekerk, Kersten, & Beuers, 2018). Increased levels of endogenous opioids and serotonin may also be pruritogenic substances (Carrion et al., 2018; Levy et al., 2018; Van Niekerk et al., 2018). The most recent evidence suggests that lysophosphatidic acid, a molecule that signals lipid production and is synthesized by the enzyme autotaxin (ATX), is the major cause of pruritis in PBC (Carrion et al., 2018; Levy et al., 2018; Van Niekerk et al., 2018). Increased levels of ATX correlate with the severity of pruritis. Pruritis in PBC tends to follow a circadian pattern with symptoms being more severe in the evening and late at night. Pruritis may be localized or diffuse and is often more severe on the arms, legs, feet, and hands (Lindor et al., 2019). Warmth, clothing, wool, and pressure exacerbate symptoms (Lindor et al., 2019). Chronic pruritis leads to sleep disturbances, fatigue, and depression (EASL, 2017; Levy et al., 2018; Lindor et al., 2019).

Malabsorption of fats and fat-soluble vitamins occur in 40% of patients with PBC from a reduction of bile in the duodenum (Assis, 2018; Lindor et al., 2019). Steatorrhea may accompany cholestatic disease and causes abdominal pain, bloating, cramping, diarrhea, and weight loss (Assis, 2018; Lindor et al.,

2019). The patient may have symptoms related to malabsorption of fat-soluble vitamins including, but not limited to, problems with night vision, dry and rough skin, rashes, decreased resistance to infection, immune system dysfunction, osteomalacia, osteoporosis, muscle weakness, anemia, and bleeding (Assis, 2018; Lindor et al., 2019). Patients with primary biliary cholangitis are at a risk for osteoporosis because there is an increase in bone resorption and a decrease in bone formation because of vitamin D deficiency in chronic cholestatic disease. Poor nutritional intake and darker climates contribute to a lack of vitamin D. Most patients with PBC are postmenopausal women who are already prone to osteoporosis. The incidence of osteoporosis in PBC is 20%–40% (Assis, 2018; Lindor et al., 2019).

Hypercholesterolemia is found in 75%–95% of patients with PBC (Assis, 2018; EASL, 2017; Lindor et al., 2019). High levels of high-density lipoproteins (HDL) and a subtype of low-density lipoprotein (LDL) called lipoprotein-X protect the patient with PBC from atherosclerosis (Assis, 2018; EASL, 2017; Lindor et al., 2019). Lipoprotein-X decreases LDL oxidation to protect the integrity of endothelial cells. Hypercholesterolemia in PBC is not treated unless the patient has comorbidities increasing cardiovascular risk. Patients and their family members who have a history of cardiovascular disease, high cholesterol, or low HDL should be under close surveillance. Hypercholesterolemia may also cause yellow, fatty lesions on the extremities (xanthoma) and around the eyes (xanthelasma), although these cutaneous manifestations are not specific to PBC (Assis, 2018; EASL, 2017; Lindor et al., 2019).

Sicca syndrome is present in 75% of patients with PBC. Sicca means "dry" in Latin. Dry eyes (keratoconjunctivitis sicca) and mouth (xerostomia) are common symptoms (Lindor et al., 2019). It appears that mitochondrial PDC-E2 mediates an immune attack on lacrimal tear ducts and salivary glands. Sicca syndrome is a major symptom of Sjögren syndrome, although this does not necessarily mean that the patient with PBC has the full extent of this disease (Lindor et al., 2019). Patients with Sjögren syndrome have dry mucous membranes that extend beyond the eyes and mouth, symptoms such as joint pain and rashes, are at risk for lymphoma, and possess the extractable nuclear antigens Sjögren syndrome Type A (SSA—sometimes referred to as Anti-Ro) or Sjögren syndrome Type B (SSB) (Both, Dylan, Van-Hagan, & Van-Daele, 2017).

Abdominal pain is experienced by many patients with PBC (Levy et al., 2018). Pain localized to the upper right quadrant may be caused by acute suppurative (inflammation from infection) cholangitis with fever, jaundice, and shock from a gallstone in the biliary tract (Assis, 2018; Levy et al., 2018). Approximately 30%–40% of PBC patients have cholelithiasis (Assis, 2018; Levy et al., 2018). Hepatocellular carcinoma, cholangiocarcinoma, and peptic ulcer disease should be in the differential diagnosis (Levy et al., 2018). Increasing hepatosplenomegaly in conjunction with hyperpigmentation of the skin and jaundice may indicate hepatic decompensation in PBC including the onset of portal hypertension (Liberal & Grant, 2016).

Most patients develop portal hypertension in late-stage disease with hyperbilirubinemia, jaundice, low serum albumin and proteins, peripheral edema, ascites, caput medusa, and gastric and esophageal varices (Liberal & Grant, 2016). An elevation of serum ammonia from protein catabolism may cause hepatic encephalopathy, which leads to changes in mental status (Liberal & Grant 2016). Priority nursing interventions include managing the patient's airway, mental status, fluid volume, nutrition, mobility, and any bleeding. A progressive loss of bile ducts and bridging necrosis (confluent necrosis of hepatic parenchyma) leads to cirrhosis and end-stage liver disease (ESLD) and the need for transplantation (Liberal & Grant, 2016).

Approximately 6% of patients with PBC develop portal hypertension before a diagnosis of cirrhosis because of nodular regenerative hyperplasia (NRH) (Kamath & Shah, 2018; Levy et al., 2018; Sclair & Levy, 2018; Wang et al., 2017). Nodular regenerative hyperplasia may develop from underlying autoimmune, neoplastic, hematological, and infectious disorders, and may also be medication-induced. In PBC, the interplay of antibodies, hepatic endothelial cells, and increased coagulation within the hepatic microvasculature transforms hepatic parenchyma into small regenerative nodules. These nodules mimic the fibrotic processes associated with cirrhosis of the liver. The absence of perinuclear collagen tissue differentiates NRH from the usual regenerative nodules in cirrhosis of the liver (Kamath & Shah, 2018; Levy et al., 2018; Sclair & Levy, 2018; Wang et al., 2017).

Diagnostic Approaches

The interprofessional team must correlate the patient's health history, signs and symptoms, laboratory data, imaging studies, and head-to-toe assessment to determine the presence of cholestatic disease. An assessment of antibodies, bilirubin level, and ALP to ALT and AST ratios is a priority. Elevated ALP is the hallmark biomechanical feature of cholestasis (Kouroumalis, Samonakis, & Voumvouraki, 2018). Ultrasound and magnetic resonance imaging cholangiography may be necessary to determine whether the elevated ALP is related to cholestasis from drug-induced biliary injury, infections, cystic fibrosis, or cholelithiasis. An elevated GGT is also a diagnostic feature in PBC (Kouroumalis

et al., 2018; Lindor et al., 2019). A normal GGT in the presence of an elevated ALP may indicate bone, intestine, and placental etiologies and not PBC (EASL, 2017; Lindor et al., 2019).

A differential diagnosis of primary sclerosing cholangitis (PSC) should be explored when there is disproportionately elevated ALP to ALT and AST in the absence of AMA (Bowlus, Assis, & Goldberg, 2018). Primary sclerosing cholangitis is associated with HLA B8 and DR3 and autoimmunity, causes inflammation and obliteration of the intrahepatic and extrahepatic bile ducts and cholestasis, has a predilection for males and individuals with inflammatory bowel disease, predisposes the patient to liver cancer, and may lead to cirrhosis of the liver, requiring transplantation (Bowlus et al., 2018). Diagnosing PSC is extremely different than that of PBC. Diagnosis of PSC requires magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde pancreatography (ERCP). Medication used in PBC disease management has not been successful slowing the progression of PSC. Liver transplantation is the best approach for PSC patients with advanced disease (Bowlus et al., 2018).

The American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) developed guidelines for a diagnosis of PBC (EASL, 2017; Lindor et al., 2019). These guidelines include: (1) A persistently elevated ALP for 6 months or longer; (2) A positive AMA or ANA; and (3) Histologic evidence of non-suppurative obstructive cholangitis involving the interlobular bile ducts (EASL, 2017; Lindor, et al., 2019). A diagnosis of PBC can be made when at least 2 of the 3 criteria have been met. A liver biopsy is necessary when the patient has a persistently elevated ALP and is negative for AMA and ANA (Levy et al., 2018). The term "autoimmune cholangitis" (AC) appears in the literature to denote patients who lack antibodies associated with PBC, but whose signs, symptoms, liver histology, treatment, and outcomes are nearly identical to antibody-positive patients (Levy et al., 2018). The research is inconclusive for evidence suggesting any substantial differences between PBC and AC (Levy et al., 2018).

Liver biopsy is not generally required to diagnose PBC (Levy et al., 2018; Tan & Goodan, 2018). However, a liver biopsy can confirm the extent of hepatobiliary damage. Primary biliary cholangitis is histologically characterized by nonsuppurative (inflammation from noninfectious causes) lesions that involve the interlobular and septal bile ducts (Levy et al., 2018; Tan & Goodan, 2018). Lesions may be in a florid duct pattern, which are intense areas of inflammation near the basal membrane of cholangiocytes causing necrosis by lymphocytes (Levy et al., 2018; Tan & Goodan, 2018). Epithelial granulomas are often present (Levy et al., 2018; Tan & Goodan, 2018). Intense inflammation causes compression and subsequent ischemia through the portal tracts leading to bridging necrosis, fibrosis, and cirrhosis (Levy et al., 2018; Tan & Goodan, 2018). Portal tracts are connective tissues that join the hepatic artery and portal vein to supply blood to the liver (Liberal & Grant, 2016). The Ludwig Histological Staging Criteria is commonly used in practice to stage the disease (Levy, et al., 2018); Stage 1: Portal inflammation with florid duct lesion; Stage 2: Ductular proliferation, interface hepatitis, no bridging necrosis; Stage 3: Decreased inflammation, septal fibrosis, bridging necrosis or fibrosis; Stage 4: Cirrhosis with generative nodules (Levy, et al., 2018). Stage 2 disease includes interface hepatitis that is characterized by cellular necrosis and apoptosis from the portal tracts through the hepatic parenchyma and is similar to what is seen in autoimmune hepatitis (AIH) (Levy et al., 2018). Patients should be evaluated for PBC and AIH overlap (To & Silveira, 2018; Zhang et al., 2018).

Medications to Prevent Disease Progression

The Food and Drug Administration (FDA) has approved ursodeoxycholic acid (UDCA) as the first-line therapy for disease management of PBC (Brown, 2018; Goel & Kim, 2018; Invernizzi et al., 2017). Ursodeoxycholic acid is a bile acid that is synthesized by the liver and is not toxic to hepatocytes like other bile acids. Supplemental oral administration of UDCA improves bile flow through the bile ducts, decreases damage to bile duct epithelial cells and hepatocytes from cholestasis, and decreases an immune-mediated attack on the intrahepatic bile ducts to slow the progression of the disease in most people (Brown, 2018; EASL, 2017; Goel & Kim, 2018). Ursodeoxycholic acid also helps prevent cholelithiasis and lowers cholesterol. Ursodeoxycholic acid is tolerated well by most patients. The patient should take the medication with food to promote absorption. Side effects are minimal, which may include diarrhea, rashes, and weight gain (Brown, 2018; Goel & Kim, 2018).

The FDA has also approved obeticholic acid (OCA) as a second-line agent for disease management of PBC (Brown, 2018; Levy et al., 2018; Lindor et al., 2019). Obeticholic acid is another bile acid that may be used when patients do not have a therapeutic response to UDCA or in combination with UDCA. Obeticholic acid reduces accumulation of toxic bile acids and damage to bile ducts and hepatocytes from cholestasis and has antifibrotic and anti-inflammatory properties (Brown, 2018; Levy et al., 2018; Lindor et al., 2019). The patient may take the medication with or without food. Patients may report minor side effects of gastrointestinal disturbances, rash, and constipation. However,

pruritis is a common side effect, which creates a challenge in the patient who is already suffering from PBC-related pruritis (Brown, 2018; Levy et al., 2018).

Ursodeoxycholic acid and OCA are more likely to have a therapeutic response in patients with Stage 1 and Stage 2 diseases when the bile ducts are still present and may have a normal life span (Brown, 2018; Levy et al., 2018). Normalization of liver enzymes and decreasing antibody titers are therapeutic outcomes (Levy et al., 2018). Disease-related fatigue does not generally improve with UDCA and OCA therapy (Lindor et al., 2019). The use of these medications has decreased the rate of liver transplantations. The GLOBE International Scoring System is one risk assessment tool healthcare providers can use to quantify PBC patients as at high and low risks for liver transplantation or death after 1 year of UDCA or OCA therapy (Lindor et al., 2019). The tool evaluates hepatobiliary function in relation to age, total bilirubin level, ALP levels, albumin level, and platelet level (Brown, 2018; Levy et al., 2018).

Medications in Clinical Trials

Clinical trials show promising evidence using fibric acid derivatives (lipid-lowering agents) and budesonide, a glucocorticoid, for PBC disease management in the future (EASL, 2017; Levy et al., 2018; Lindor et al., 2019). Clinical trials with azathioprine, mycophenolate, methotrexate, and B-lymphocyte depletion with rituximab continue to be evaluated for efficacy in PBC disease management, although they are usually highly effective in autoimmune diseases (EASL, 2017; Lindor et al., 2019; Molinara & Marschall, 2017). Primary biliary cholangitis patients who have severe interface hepatitis associated with AIH may benefit from immunosuppression (To & Silveira, 2018; Zhang et al., 2018).

Symptom Management

The nurse should consider the following questions to assess the underlying cause of fatigue: Is the fatigue related to (1) the PBC disease process, (2) comorbidities, (3) medication side effects, and (4) the patient's mental health? (Levy et al., 2018; Lindor et al., 2019). The interprofessional team should implement appropriate interventions to address these factors. Spreading activities evenly throughout the day and allowing for rest periods will conserve energy and lessen fatigue (Levy et al., 2018; Lindor et al., 2019). Patients with daytime sleepiness may benefit from modafinil, which is a central nervous system stimulant that improves daytime sleepiness and sleep apnea (Levy et al., 2018; Lindor et al., 2019). Common side effects are headache, nervousness, and nausea. The nurse should conduct a fall risk assessment (Levy et al., 2018; Lindor et al., 2019). Patients should rise slowly from a lying or sitting position to avoid orthostatic hypotension, and the environment should have sufficient lighting and be free of loose rugs (Levy et al., 2018; Lindor et al., 2019). Education and counseling for patients with chronic illness are important. The nurse should encourage the patients and their loved ones to join a PBC support group (Levy et al., 2018; Lindor et al., 2019).

The first-line therapy for pruritis is bile acid sequestrants, such as cholestyramine, which not only lower cholesterol in hypercholesterolemia but also metabolize excessive bile from the blood and improve pruritis in 90% of patients (Carrion et al., 2018; Trivedi, Liazola, Tapper, & Bonder, 2017). Patients must be educated to take the medication within 2–4 hours before or after taking other medications to promote absorption (Carrion et al., 2018; Trevedi et al., 2017). Bloating and constipation are common symptoms (Carrion et al., 2018; Trevedi et al., 2017). Rifampin, an antituberculosis medication, is the second-line therapy for pruritis because it increases bile acid excretion and decreases ATX levels (Carrion et al., 2018; Lindor et al., 2019). Rifampin has low toxicity potential and is generally well-tolerated. Liver enzymes, bilirubin, and white blood cell count should be monitored (Carrion et al., 2018; Trevedi et al., 2017). It is also important to monitor the international normalization ratio (INR) because rifampin affects vitamin K metabolism (Carrion et al., 2018; Trevedi et al., 2017). Opioid receptor blockers, such as naloxone, and selective serotonin uptake inhibitors, such as sertraline, may be effective in some patients (Carrion et al., 2018; Trevedi et al., 2017). Antihistamines are not generally helpful controlling pruritis in PBC and may exacerbate symptoms related to sicca syndrome (Carrion et al., 2018; Trevedi et al., 2017). Plasmapheresis has been effective in some cases. Comfort measures should be implemented by the nurse to promote quality of life (see Side Bar 1) (Blomberg, Griffiths, Wengstrom, May, & Bridges, 2016; British Columbia Interprofessional, 2019; Gallagher, 2017; Trevedi et al., 2017).

Nutritional deficits from malabsorption are best addressed by a dietician in collaboration with the nurse. Patients should avoid saturated fats (beef and pork) and foods high in sugar and sodium content (Assis, 2018). Low-sodium and restricted protein diet may be necessary if the patient has portal hypertension (Assis, 2018; Wu, 2017). Consuming fruits, vegetables, lean meats (chicken and turkey), and whole-grain products is a healthy choice in PBC (Assis, 2018). Patients should consume foods that provide sufficient vitamins A, D, E, and K. Vitamin supplements may be indicated (Assis, 2018).

Osteoporosis risk factors should be assessed including alcohol and tobacco use, poor nutritional intake of

SIDE BAR 1. Nursing Comfort Measures for Pruritis[a]

- Ask the patient to describe how pruritis has affected his or her quality of life and ability to obtain rest and sleep.
- Ask the patient to describe pruritis. Is it localized or generalized? What factors alleviate or aggravate the pruritis?
- Stay in a cool, comfortable environment that has air conditioning or a fan. Avoid humidity.
- Limit exposure to indoor lighting or the sun that is irritating to the skin.
- Wear loose clothing with soft and smooth fabric that feels comfortable to the skin.
- Bathe using cool-to-tepid water. Gently pat dry with a soft towel. Avoid rubbing the skin.
- Bathe in an oatmeal colloidal bath that is soothing to the skin.
- Use a moisturizer on the skin after bathing.
- Apply cool, damp compresses to the skin.
- Drink plenty of water to keep the skin moist.
- Avoid smoking and drinking alcohol.
- Avoid foods that are too hot in temperature or spicy.
- Keep fingernails trimmed and wear gloves to avoid breaking the skin if scratching.
- Reduce stress.

[a]From Blomberg et al. (2016); British Columbia Interprofessional (2019); Gallagher (2017); and Trevedi et al. (2017).

calcium, and a lack of exercise (Danford, Trivedi, Papmichael, Tapper, & Bonder, 2018). Bone density studies should be evaluated periodically in PBC patients (Danford et al., 2018). A balanced diet consisting of sufficient vitamin D and calcium should be encouraged. Weight-bearing exercises such as walking are important for bone modeling (Danford et al., 2018). Bisphosphonates may be helpful to reduce bone resorption and increase bone mass density in postmenopausal osteoporosis (Danford et al., 2018). Calcitonin has shown to be effective in osteoporosis (Danford et al., 2018). The use of hormone replacement therapy estrogens should be explored carefully (Danford et al., 2018). Estrogens increase skeletal bone mass in postmenopausal women and also increase the risk of vascular disease and malignancy (Danford et al., 2018).

Patients with PBC with sicca syndrome should stay well-hydrated to provide mucous membranes of the eyes and mouth with moisture to prevent infection. The first-line therapy for keratoconjunctivitis sicca is to lubricate the mucous membranes of the eyes with artificial tears or carboxymethylcellulose (Levy et al., 2018). Cyclosporin eye drops are also effective (Levy et al., 2018). Limiting exposure to irritants such as indoor lighting, sun, and smoke and wearing sunglasses are beneficial (Both et al., 2017; Levy et al., 2018). Periodic ophthalmic examinations should be conducted (Both et al., 2017; Levy et al., 2018). Patients should also avoid alcohol and smoking that irritate the oral mucous membranes (Both et al., 2017; Levy et al., 2018). Pilocarpine may be used to increase salivary production (Both et al., 2017; Levy et al., 2018). Frequent oral hygiene and periodic dental checkups are important (Both et al., 2017; Levy et al., 2018). Antihistamines should be used judiciously because they may exacerbate symptoms (Levy et al., 2018).

Patients with PBC have a poor prognosis when they have progressive hyperbilirubinemia, advanced histological stage, and decompensated cirrhosis with the onset of portal hypertension (Levy et al., 2018). The nurse should assess for ascites and peripheral edema. Fluid overload correlates with an increase in body weight and abdominal girth and a decrease in serum albumin and proteins (Kamath & Shah, 2018; Wu, 2017). Evaluating respiratory rate, depth, and lung sounds is important (Wu, 2017). A low-sodium diet and fluid restriction should be implemented (Wu, 2017). Fluid overload and anemia cause fatigue and environmental safety issues for the patient (Wu, 2017). Beta-blockers improve blood flow through the liver by reducing portal pressure and potassium sparing, and loop diuretics reduce fluid volume overload with a major goal of preventing bleeding gastric and esophageal varices (Kamath & Shah, 2018). Paracentesis may be necessary to improve respiratory status, reduce fatigue, promote safety, and enhance the quality of the patient's life (Wu, 2017). Changes in behavior or level of consciousness should be assessed that may indicate hepatic encephalopathy because of increased serum ammonia level and its impact on brain metabolism (Kamath & Shah, 2018; Liberal & Grant, 2016; Wu, 2017). Liver transplantation is necessary for patients in ESLD.

Liver Transplantation

Primary biliary cholangitis cases have increased in recent years whereas there has been a decrease of liver transplantations in PBC because of UDCA therapy preventing the progression to ESLD (Levy et al., 2018). The quality of life dramatically improves after transplantation. The survival rates after transplantation are excellent at 80%–90% at 5 years and 60%–70% at 10 years (Aguilar & Carey, 2018; EASL, 2017; Lindor et al., 2019). Primary biliary cholangitis may recur after transplantation because antibodies are still an integral part of the patient's immune system (Aguilar & Carey, 2018; Levy et al., 2018). The recurrence rate is 20%–40% (Aguilar & Carey, 2018; Levy et al., 2018).

Priority Assessment and Care

Patient care begins with an assessment of the patient's comfort level and mental status. For example, the nurse should ask the patient to rate fatigue, pruritis,

and abdominal pain on a 0 (No pain) to 10 (Severe pain) scale. Changes in mental status or behavior may indicate that the patient has unrelieved symptoms, is having difficulty coping with chronic illness, or has hepatic encephalopathy in advanced PBC. The nurse should perform an analysis and trending of laboratory data, vital signs, and the patient's responses to medications and treatment. A head to toe assessment should be conducted with a focus on the following components and liver enzyme analysis.

Evaluating respiratory rate, depth, and auscultation of lung sounds is critical to ensure optimal oxygenation, especially in patients with ascites from portal hypertension (Kamath & Shah, 2018; Wu, 2017). Fluid overload leads to an increase in respiratory effort. Correlating lung and heart sounds, the amplitude and equality of peripheral pulses, increasing abdominal girth from ascites, peripheral edema, and weight gain is a priority (Kamath & Shah, 2018; Wu, 2017).

Increasing jaundice and hyperbilirubinemia may correlate with fluid overload in portal hypertension and indicate the progression to ESLD (Wu, 2017). Patients should be placed into a position of comfort with the head not too low or high that would increase respiratory effort (Wu, 2017). Supplemental oxygen may be helpful (Wu, 2017). Patients must conserve energy.

Patients should be evaluated for gastrointestinal bleeding, including gastric and esophageal varices that may be manifested by sudden and massive blood loss or subtle, occult blood loss (Kamath & Shah, 2018; Wu, 2017). Stool should be assessed for bright red blood or blood that is dark and tarry (Kamath & Shah, 2018). The nurse should trend red blood cell count, hemoglobin, hematocrit, platelets, and clotting factors that indicate bleeding (Wu, 2017). Patients should use electric razors when shaving and soft toothbrushes when brushing their teeth to avoid bleeding (Wu, 2017). Patients should have sufficient fluid and fiber in the diet to avoid constipation. Straining at the stool may lead to variceal rupture (Kamath & Shah, 2018; Wu, 2017).

The nurse should monitor and trend liver enzymes. Decreasing liver enzymes are important indicators that UDCA and OCA are therapeutic (Levy et al., 2018). Liver enzymes in PBC follow a cholestatic pattern, which means that the ALP is disproportionately elevated to the ALT and AST (Levy et al., 2018). Conversely, ALT and AST that are disproportionately elevated to ALP in the presence of the smooth muscle antibody may indicate AIH and not cholestatic disease (Lohse & Weiler-Normann, 2018).

Establishing Outcome Measures

The interprofessional team should establish target outcomes that reflect PBC disease management and symptom control. Outcomes should include the following: (1) liver enzymes and bilirubin will normalize, (2) antibody titers will decrease or be negative, (3) histological improvement through repeat liver biopsy will be achieved, (4) physical and psychological symptoms will be controlled, (5) optimal nutritional status will be maintained, and (6) optimal activity level will be maintained.

Conclusions

Early diagnosis with aggressive treatment is crucial to managing symptoms and preventing the progression of PBC. Primary biliary cholangitis progresses slowly in most cases. Medications and lifestyle management can control symptoms and promote quality of life. Most patients with PBC who are in Stage 1 or Stage 2 disease achieve a therapeutic response to treatment and do not progress to cirrhosis and ESLD. The prognosis is excellent for patients who require liver transplantation. ✪

REFERENCES

Aguilar, M. T., & Carey, E. J. (2018). Current status of liver transplantation for primary biliary cholangitis. *Clinics in Liver Disease*, *22*, 613–624. doi:10.1016/j.cld.2018.03.011

Assis, D. N. (2018). Chronic complications of cholestasis: Evaluation and management. *Clinics in Liver Disease*, *22*, 533–544. doi:10.1016/j.cld.2018.03.014

Blomberg, K., Griffiths, P., Wengstrom, Y., May, C., & Bridges, J. (2016). Interventions for compassionate nursing care: A systematic review. *International Journal of Nursing Studies*, *62*, 137–155. doi:10.1016/J.ijnurstu.2016.07.009

Both, T., Dalm, V. A. S. L., Van Hagan, P. M., & Van Daele, P. L. A. (2017). Reviewing primary Sjogren's syndrome beyond the dryness: From pathophysiology to diagnosis and treatment. *International Journal of Medical Sciences*, *14*(3), 191–200. doi:10.7150/ijms.17718

Bowlus, C., Assis, D., & Goldberg, D. (2018). Primary and secondary sclerosing cholangitis. In J. Sanyal, T. D. Boyer, K. D. Lindor, & N. A. Terrault (Eds.), *Zakim & Boyer hepatology: A textbook of liver disease* (7th ed., pp. 626–647). Philadelphia, PA: Elsevier.

British Columbia Interprofessional Palliative Symptom Management Guidelines. (2019). *British Columbia center for palliative care*. Retrieved from http://www.bc-cpc.ca/cpc/wp-Content/uploads/2017/11/04.-SMG-Clinical-Best-Practices-print-BW-pruritis.pdf

Brown, R. S. (2018). Use of obeticholic acid in primary biliary cholangitis. *Gastroenterology and Hepatology*, *14*(11), 654–657.

Carrion, A. F., Rosen, J. D., & Levy, C. (2018). Understanding and treating pruritis in primary biliary cholangitis. *Clinics in Liver Disease*, *22*, 517–532. doi:10.1016/j.cld.2018.03.005

Chalifoux, S. L., Konyn, P. G., Choi, G., & Saab, S. (2017). Extrahepatic manifestations of primary biliary cholangitis. *Gut and Liver*, *11*(6), 771–778. doi:10.5009/gnl16365

Chascsa, D. M., & Lindor, K. D. (2018). Anti-mitochondrial antibody-negative primary biliary cholangitis: Is it really the same disease? *Clinics in Liver Disease*, *22*, 589–601. doi:10.1016/j.cld.2018.03.009

Danford, C. J., Trivedi, H. D., Papamichael, K., Tapper, E. B., & Bonder, A. (2018). Osteoporosis in primary biliary cholangitis. *World Journal of Gastroenterology*, *24*(31), 3513–3550. doi:10.3748/wjg.v24.i31.3513

European Association for the Study of the Liver (EASL). (2017). EASL clinical practice guidelines: The diagnosis and management of patients with primary biliary cholangitis. *Journal of Hepatology*, *67*(1), 145–172. doi:10.1016/j.jhep.2017.03.022

Gallagher, D. L. (2017). Assessment of the integumentary system. In S. L. Lewis, L. Bucher, M. M. Heitkemper, M. M. Harding, J. Kwong, & D. Roberts (Eds.), *Medical-surgical nursing: Assessment and management of clinical problems* (10th ed., pp. 422–424). St Louis, MO: Elsevier.

Goel, A., & Kim, W. R. (2018). Natural history of primary biliary cholangitis in the ursodeoxycholic acid era. *Clinics in Liver Disease*, *22*, 563–578. doi:10.1016/j.cld.2018.03.007

Innerizzi, P., Floreani, A., Carbone, M., Marzioni, M., Craxi, A., Muratori, L., ... Alvara, D. (2017). Primary biliary cholangitis: Advances in management and treatment of the disease. *Digestive and Liver Disease*, *49*, 841-846. doi:dx.doi.org/10.1016/j.dld.2017.05.001

Joshita, S., Umemura, T., Tanaka, E., & Ota, M. (2017). Genetic contributions in the pathogenesis of primary biliary cholangitis. *Journal of Immunology Research*, *2017*, 3073504. doi:10.1155/2017/3073504

Kamath, P. S., & Shah, V. H. (2018). Portal hypertension related to bleeding. In J. Sanyal, T. D. Boyer, K. D. Lindor, & N. A. Terrault (Eds.), *Zakim & Boyer hepatology: A textbook of liver disease* (7th ed., pp. 233–261). Philadelphia, PA; Elsevier.

Kouroumalis, E., Somonakis, D., & Voumvouraki, A. (2018). Biomarkers for primary biliary cholangitis: Currect perspectives. *Hepatic Medicine: Evidence and Research*, *2018*(10), 43. doi:10.2147/HMER.S135337

Levy, C., Carrion, A. F., & Mayo, M. J. (2018). Primary biliary cholangitis. In E. R. Schiff, W. C. Maddrey, & K. R. Reddy(Eds.), *Schiff's diseases of the liver* (12th ed., pp. 523–545). Oxford, England: Wiley-Blackwell.

Liberal, R., & Grant, C. R. (2016). Cirrhosis and autoimmune liver disease: Current understanding. *World Journal of Hepatology*, *8*(28), 1157–1168. doi:10.4254/wjh.v8.i28.1157

Lindor, K. D., Bowlus, C. L., Boyer, J., Levy, C., & Mayo, M. (2019). Primary biliary cholangitis: 2018 practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*, *69*(1), 394–419. doi:10.1002/hep.30145

Lohse, A. W., & Weiler-Normann, C. (2018). Autoimmune hepatitis. In J. Sanyal, T. D. Boyer, K. D. Lindor, & N. A. Terrault (Eds.), *Zakim & Boyer hepatology: A textbook of liver disease* (7th ed., pp. 594–609). Philadelphia, PA: Elsevier.

Molinara, A, & Marschall, H. U. (2017). Why doesn't primary biliary cholangitis respond to immunosuppressive medications? *Current Hepatology Reports*, *16*(2), 119–123. doi:10.1007/s11901-017-0345-y

Sclair, S. N., & Levy, C. (2018). Primary biliary cholangitis. In J. Sanyal, T. D. Boyer, K. D. Lindor, & N. A. Terrault (Eds.), *Zakim & Boyer hepatology: A textbook of liver disease* (7th ed., pp. 610–625). Philadelphia, PA: Elsevier.

Tan, D., & Goodan, Z. D. (2018). Liver biopsy in primary biliary cholangitis: Indications and interpretation. *Clinics in Liver Disease*, *22*, 579–588. doi:10.1016/j.cld.2018.03.008

To, U., & Silveira, M. (2018). Overlap syndrome of autoimmune hepatitis and primary biliary cholangitis. *Clinics in Liver Disease*, *22*, 603–611. doi:10.1016/j.cld.2018.03.010

Trivedi, H. D., Lizaola, B., Tapper, E. B., & Bonder, A. (2017). Management of pruritis in primary biliary cholangitis. A narrative review. *The American Journal of Medicine*, *130*(6), 744-e2-744-e6. doi:10.1016/j.amjmed.2017.01.037

Tsuneyuma, K., Baba, H., Morimoto, Y., Tsunematsu, T., & Ogawa, H. (2017). Primary biliary cholangitis: Its pathological characteristics and immunopathological mechanisms. *Journal of Medical Investigation*, *64*(7), 7–13. doi:10.2152/jmi.64.7

Van Niekerk, J., Kerstein, R., & Beuers, U. (2018). Role of bile acids and the biliary $HC0_3$– umbrella in the pathogenesis of primary biliary cholangitis. *Clinics in Liver Disease*, *22*, 457–479. doi:10.1016/j.cld.2018.03.013

Wang, L., Bowlus, C. L., Wang, F. S., & Gershwin, M. E. (2017). Primary biliary cholangitis: Its science and practice. In G. Hirschfield, D. Adams, & E, Liaskou (Eds.), *Biliary disease: From science to clinic* (pp. 129–182). New York, NY: Springer.

Wu, K. H. (2017). Cirrhosis. In S. L. Lewis, L. Bucher, M. M. Heitkemper, M. M. Harding, J. Kwong, & D. Roberts (Eds.), *Medical-surgical nursing: Assessment and management of clinical problems* (10th ed., pp. 986–998). St. Louis, MO: Elsevier.

Zhang, W., De, D., Mohammed, K. A., Munigala, S., Chen, G., Lai, J. P., & Bacon, B. R. (2018). New scoring system classification for primary biliary cholangitis—autoimmune hepatitis overlap. *Hepatology Communications*, *2*(3), 245–253. doi:10.1002/hep4.1148

For 10 additional continuing education articles related to liver disease, go to www.NursingCenter.com.

Instructions for Taking the CE Test Online:

- Read the article. The test for this CE activity can be taken online at www.nursingcenter.com. Tests can no longer be mailed or faxed.
- You will need to create a free login to your personal CE Planner account before taking online tests. Your planner will keep track of all your Lippincott Professional Development online CE activities for you.
- There is only one correct answer for each question. A passing score for this test is 13 correct answers. If you pass, you can print your certificate of earned contact hours and the answer key. If you fail, you have the option of taking the test again at no additional cost.
- For questions, contact Lippincott Professional Development: 1-800-787-8985.

Registration Deadline: March 4, 2022

Disclosure Statement:
The authors and planners have disclosed that they have no financial relationships related to this article.

Provider Accreditation:
Lippincott Professional Development will award 1.5 contact hours, including 0.5 pharmacology credit, for this continuing nursing education activity.

Lippincott Professional Development is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. This activity is also provider approved by the California Board of Registered Nursing, Provider Number CEP 11749 for 1.5 contact hours. Lippincott Professional Development is also an approved provider of continuing nursing education by the District of Columbia, Georgia, and Florida, CE Broker #50-1223. Your certificate is valid in all states.

Payment:

- The registration fee for this test is $10.50 for members; $15.00 for nonmembers.

DOI: 10.1097/SGA.0000000000000522