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This reference is a guide for Agrace clinicians who work with patients requiring palliative management of liver failure. Whether you are new to hospice care or simply new to Agrace, this resource provides a baseline understanding of the ways we work to keep patients with liver failure comfortable.

At Agrace, our aim is to support natural, comfortable dying, in union with our patients and their families. We use an inter-disciplinary approach as we attend to each patient and family's unique experience. With the patient and family as the drivers, we create Plans of Care that are specific, individualized and goal-oriented. Yet, there are some commonly seen symptoms and some shared experiences among people who require management of their liver failure. There are factors which, if integrated, make us knowledgeable end-of-life care practitioners.

Clinical Practice Guidelines

Palliative Management of Liver Disease

Contents:

Liver Failure and Hospice Eligibility

The liver is responsible for many bodily functions, including metabolism, detoxification, and creating and storing clotting factors. As a person ages, the liver's size and ability to break down drugs decreases, and it is less able to recover from injury. The only definitive treatment for liver disease is a transplant; however, patients may be treated with conservative measures on a short- or long-term basis. When liver disease worsens and can no longer be treated, the patient progresses to **liver failure,** which is associated with high mortality, frequent hospitalizations and a reduced quality of life.

Before palliative or hospice care: Before patients with liver disease enroll in hospice, many have had several procedures and diagnostics: lab draws, paracentesis for fluid removal, or upper endoscopy to diagnose or treat esophageal varices. They may have had a shunt placed that bypasses circulation through the liver to decrease portal hypertension. This procedure is called "transjugular intrahepatic portosystemic shunt" (TIPS). Unfortunately, some patients have suffered from social stigma, as liver disease is commonly caused by contagious liver infections (hepatitis) or excessive alcohol use.

Occasionally, patients with advanced disease will continue to receive aggressive care if there is any hope for liver transplantation. In these cases, they may not reach out for comfort care until death is near. Palliative management is aimed at treating the distressing symptoms of liver disease to provide comfort at end of life.

Hospice Eligibility: According to CMS guidelines for hospice eligibility, patients with liver disease are considered terminal (life expectancy of six months or less) if they meet the following criteria (1 and 2 should be present, factors from 3 will lend supporting documentation):

1. The patient should show both a and b:
    a. Prothrombin time prolonged more than 5 seconds over control, or International Normalized Ratio (INR) > 1.5
    b. Serum albumin < 2.5 gm/dl
2. End-stage liver disease is present and the patient shows **at least one** of the following:
    a. Ascites, refractory to treatment or patient non-compliant
    b. Spontaneous bacterial peritonitis
    c. Hepatorenal syndrome (elevated creatinine and BUN with oliguria [< 400 ml/day] and urine sodium concentration < 10 mEq/l)
    d. Hepatic encephalopathy, refractory to treatment, or patient non-compliant
    e. Recurrent variceal bleeding, despite intensive therapy
3. Documentation of the following factors will support eligibility for hospice care:
    a. Progressive malnutrition
    b. Muscle wasting with reduced strength and endurance
    c. Continued active alcoholism (> 80 gm ethanol/day)
    d. Hepatocellular carcinoma
    e. HBsAg (Hepatitis B) positivity
    f. Hepatitis C refractory to interferon treatment

A Note on Pain Management

Pain can be challenging to manage in patients with liver failure. One study showed that 60 percent of patients with end-stage liver disease experienced pain, and one in three of those patients said their pain was at least moderately severe most of the time (Potosek, Curry, Buss, & Chittenden, 2014, p. 1272). Pain may be the result of itching, skin disruption or pressure from ascites.

It is possible that the patient's pain has been undertreated in the past. There could be stigma associated with a history of alcohol or other drug abuse, which could lead providers to under-prescribe pain medication. Some physicians hesitate to prescribe medications that could worsen the patient's existing liver function, as could be the case with NSAIDs.

Many pain medications, including opioids, are cleared through the liver. Often, we will reduce opioid doses and increase dose intervals to account for delayed liver clearing. Acetaminophen should be limited to 2 – 3 g/day (Potosek, Curry, Buss, & Chittenden, 2014, p. 1273). So, care should be taken when managing pain, but if we dose carefully and titrate slowly, we can use these tools to effectively manage pain at end of life.

Symptom Management in End-Stage Liver Disease

The following issues are common in patients with end-stage liver disease. The job of the hospice/palliative care clinician is to educate patients and families about these manifestations, normalize them when they occur, and offer strategies to manage discomfort.

Jaundice and Pruritis

Jaundice (also known as "icterus") is a yellow discoloration of body tissues caused by excessive bilirubin accumulation in the skin (Huether & McCance, 2017). Stool color may be gray or tan, and urine turns a dark brown. Tell your patients and their families about these expected changes.

Jaundice may also be accompanied by severe pruritis (itching). The most intense itching is often felt in the late evening. This itching often affects the limbs and soles of the palms and feet, but patients may also report more generalized itching (Hegade, Kendrick & Jones, 2015).

Care Considerations for Jaundice and Pruritis

Interventions	Rationale
Cholestyramine	Reduces bile acids in the body
Antihistamines	Decreases histamine response
Calamine lotion	Topical anti-itch lotion
Keep patient's nails short and clean	Prevents skin disruption when scratching
Baking soda or moisturizing bath oils	Helps to soothe itchy skin
Soft or old clothes and linens	Less irritating to the skin's surface
Temperature control (not too hot or too cold)	Decreases sweating
Recommend that patient scratch with knuckles rather than nails	Prevents skin disruption and infection

Hematologic Issues

Thrombocytopenia, leukopenia, anemia and coagulation disorders are thought to be the result of an enlarged spleen, which increases the removal of blood cells from circulation. Thrombocytopenia may be induced by an enlarged spleen secondary to portal hypertension (Murakami & Shimizu, 2013). Anemia can also be the result of inadequate RBC production and survival, poor diet, poor absorption of folic acid and variceal bleeding.

Coagulation issues result from the liver's inability to produce prothrombin and other clotting factors. Signs of coagulation issues may include epistaxis (nose bleeds), purpura (purplish discoloring of the skin), petechiae (red spots on the skin due to broken capillary vessels), easy bruising, bleeding of the gums and heavy menstrual periods (Lewis et al., 2017).

Care Considerations for Hematologic Issues

- Assess skin and oral mucosa for signs of bleeding.
- Educate patients and families on strategies to manage fatigue.
- Prepare patients and families for the possibility of severe bleeding so they can have a plan in place. See other interventions for bleeding in the section on esophageal varices, page 6.

Ascites

Ascites is an accumulation of excess fluid in the peritoneal cavity. It is characterized by abdominal distention and weight gain. Hypokalemia (low potassium) is also common and may result when diuretic therapy is used to treat the ascites (Lewis et al., 2017).

Ascites can have multiple causes:

- **Portal hypertension:** Proteins shift from blood into lymph, which can leak into the peritoneal cavity. The osmotic pressure created by the extra protein pulls additional fluid into the space.
- **Hypoalbuminemia:** The liver's decreased ability to create albumin reduces colloidal oncotic pressure, leading to water retention and swelling.
- **Hyperaldosteronism:** An increase in aldosterone causes an increase in sodium reabsorption by the kidney. Sodium retention, combined with an increase in ADH, causes water retention.

Patients with ascites can be at risk for spontaneous bacterial peritonitis, an infection in the ascitic fluid caused by bacteria normally found in the intestines. This is particularly common after a variceal hemorrhage or peritoneal drainage (Lewis et al., 2017). Signs and symptoms include fever, chills, abdominal pain, decreased bowel sounds and cloudy ascitic fluid (Huether & McCance, 2017).

Care Considerations for Ascites

- Intermittent paracentesis may relieve pain, pressure or difficulty breathing (Lewis et al., 2017). Let the patient/family know that fluid will re-accumulate because of portal hypertension and reduced albumin levels (Huether & McCance, 2017).
- Encourage semi-Fowler's or Fowler's position to improve respiratory efficiency.
- Use pillows to support arms and chest to increase comfort and ability to breathe.
- If it aligns with patient/family goals, a low-sodium diet can help manage fluid overload ("low" is less than 2 g/day, or for severe ascites, 250 to 500 mg/day). In addition to table salt, high levels of sodium can be found in foods such as canned soups, canned vegetables, frozen foods, salty snacks, nuts, smoked meats, crackers, breads, olives, pickles, ketchup and beer.
- Suggest seasonings other than salt to make food more palatable, such as garlic, parsley, onion or lemon juice.
- Consider spironolactone (Aldactone) or another potassium-sparing diuretic in combination with high-potency loop diuretic, such as furosemide (Lasix) (Huether & McCance, 2017).

Hepatic Encephalopathy

Hepatic encephalopathy is a potentially life-threatening spectrum of neurologic, psychiatric and motor disturbances. It results from the liver's inability to remove toxins, particularly ammonia, from the blood. A major source of ammonia is the breakdown of amino acids in the intestines. Normally the ammonia produced from this process travels to the liver through the portal circulation and is converted to urea before being excreted by the kidneys. When the liver is damaged or the blood is shunted past the liver through the collateral circulation, ammonia levels increase. It can then cross the blood brain barrier and cause neurologic changes (Lewis et al., 2017).

Early manifestations include changes in personality, memory loss, irritability, disinhibition and lethargy, as well as sleep disturbances. Later, the patient may show confusion, disorientation to time and space, a flapping tremor of the hands, slow speech, bradykinesia, stupor, convulsions and coma (Huether & McCance, 2017). Occasionally, hepatic encephalopathy is misdiagnosed in older adults as dementia.

Care Considerations for Hepatic Encephalopathy

- Assess risk of falls, level of responsiveness and sensory or motor abnormalities.
- Be aware of the possibility of fluid and electrolyte or acid-base imbalances.
- Lactulose reduces the production of ammonia in the intestines; the laxative effect expels the ammonia through the colon.
- Antibiotics (rifaximin or neomycin) may be given to patients who do not respond to lactulose treatment; this decreases ammonia-producing bacteria in the gut.
- Minimize constipation, which can increase ammonia levels.

Portal Hypertension

Structural changes can cause obstruction of blood flow in and out of the liver. This increases the pressure within the liver's circulatory system (Lewis et al., 2017), causing blood to back up. Portal hypertension is an increase in venous pressure in the portal circulation, splenomegaly, large collateral veins, ascites, and gastric and esophageal varices (Lewis et al., 2017).

Collateral circulation is the body's way of reducing pressure in the circulation. Collateral vessels typically form in the lower esophagus, anterior abdominal wall, parietal peritoneum and rectum.

Distended veins, known as varicosities, develop in areas where the collateral vessels and normal systemic circulatory vessels meet, resulting in varices and hemorrhoids.

Complications of portal hypertension and liver disease include hepatopulmonary syndrome and portopulmonary hypertension (Huether & McCance, 2017).

- Hepatopulmonary syndrome is manifested by vasodilation, intrapulmonary shunting and hypoxia.
- Portopulmonary hypertension is manifested by pulmonary vasoconstriction and vascular remodeling.
- There may be no signs of these disorders, but dyspnea, cyanosis and clubbing may occur.

Care Considerations for Portal Hypertension

- Beta-blockers can reduce the pressure in the portal venous system and help to prevent variceal bleeding (Huether & McCance, 2017).

Esophageal and Gastric Varices

Esophageal and gastric varices are enlarged, torturous veins at the lower end of the esophagus and upper portion of the stomach, respectively. Esophageal varices account for 80 percent of variceal bleeding, with the remaining 20 percent due to gastric varices (Lewis et al., 2017). They are fragile and cannot tolerate high pressure, so they can bleed easily.

Signs of variceal bleeding may include melena or hematemesis. While rupture of varices is typically painless, it can be a life-threatening complication of end-stage liver disease. Mortality from ruptured esophageal varices ranges from 30 percent to 60 percent (Huether & McCance, 2017). Nearly half of

liver failure patients will have at least one variceal bleed during their disease (Silva-Junior, Baiges, Turon, Hernandez-Gea & Garcia-Pagan, 2017).

Care Considerations for Esophageal and Gastric Varices

- Observe for signs of bleeding varices, such as bloody emesis or bloody stools.
- Have a plan in place in case of rupture; consider having black/dark towels or clothes at the bedside to lessen/mask the appearance of blood.
- An upper endoscopy may be considered to check for varices. Endoscopic band ligation may be performed to prevent bleeding.
- A non-selective beta-blocker (e.g., propranolol) can reduce the incidence of hemorrhage.
- Octreotide (Sandostatin) or Vasopressin cause vasoconstriction of the mesentery, which decreases portal blood flow/hypertension (Baik et al., 2005, p. 1).

Peripheral Edema

Peripheral edema (swelling) is a common issue because a damaged liver is less able to create albumin, a protein that pulls fluid into blood vessels from the body's tissues. As a result of lower albumin, fluid remains in the tissues and creates peripheral edema (Lewis et al., 2017).

Care Considerations for Peripheral Edema

- Suggest a low-sodium diet.
- Assess extremities and abdominal girth to monitor severity of edema.
- Provide patient with alternating air pressure mattress or other special mattress to prevent skin breakdown to edematous tissue, and promote an every-two-hour turning schedule.
- Elevate the legs if necessary.
- A scrotal support may provide relief for males with scrotal edema.

Hepatorenal Syndrome

Hepatorenal syndrome, rapid deterioration in kidney function, is caused by changes in renal perfusion and blood vessel tone due to worsening liver disease (Potosek, Curry, Buss, & Chittenden, 2014, p. 1272). In a patient with liver failure, this syndrome typically follows treatment with diuretics, a GI bleed or paracentesis (Lewis et al., 2017). Signs include increased serum creatinine, urine sediment and oliguria (UptoDate, 2018).

Care Considerations for Hepatorenal Syndrome

Treatment usually requires liver transplant, but palliative treatment may include administering albumin to replace blood volume and terlipressin to promote vasoconstriction (Huether & McCance, 2017).

Malnutrition

Malnutrition is common in patients with liver failure, and commonly involves a protein deficiency (Lewis et al., 2017). Anorexia, nausea, vomiting, pressure from ascites and poor eating habits can all contribute to malnutrition.

Care Considerations for Malnutrition

- Encourage oral hygiene before a meal to improve patient's taste sensation.
- Encourage snacks between meals so the patient can eat when food is tolerable.
- Let the patient eat what they like, when possible.
- Oral supplements with proteins from branch-chained amino acids that are broken down by the muscles may be indicated. The type of protein found in these supplements is more easily metabolized by the liver.

Alcohol Withdrawal Syndrome

A person can develop alcohol withdrawal syndrome when alcohol use is stopped abruptly. Onset varies, depending on quantity, frequency, pattern and duration of alcohol use. Signs typically start within a few hours after the person's last drink, peak after 24 to 48 hours, and disappear unless withdrawal progresses to delirium. Classic symptoms include agitation, anxiety, increased heart rate and blood pressure, sweating, nausea, tremors, insomnia and hyperactivity.

Care Considerations for Alcohol Withdrawal Syndrome

- Benzodiazepines to prevent seizures or delirium
- Thiamine to prevent Wernicke-Korsakoff syndrome
- Multivitamins (e.g., folic acid, B vitamins)
- Magnesium sulfate to treat low serum magnesium
- IV glucose to treat hypoglycemia, and/or beta-blockers or alpha-2 agonists to stabilize vital signs (Lewis et al., 2017)

Alcohol Withdrawal Delirium

If unmanaged, alcohol withdrawal may progress to alcohol withdrawal delirium. This serious complication can develop two to three days after a patient's last drink and last for two to three days. Risk for developing withdrawal delirium is related to how dependent a patient is on alcohol. Symptoms include disorientation, seizures, and visual, tactile or auditory hallucinations. Death can result from hyperthermia, sepsis, aspiration pneumonia or peripheral vascular collapse.

Care Considerations for Alcohol Withdrawal Delirium

- Benzodiazepines to treat delirium and prevent seizures
- Carbamazepine to treat seizures
- Antipsychotic drugs, such as chlorpromazine or haloperidol
- Chlordiazepoxide if psychosis continues despite other benzodiazepines (Lewis et al., 2017).

Medication Reference: Commonly Used Medications

Medication	Rationale
Medications to Manage Edema and Ascites	
Spironolactone	• Potassium-sparing • Used alone, has limited diuretic effect (typically paired with another diuretic, such as furosemide)
Furosemide	• Useful in patients with severe renal impairment (Burcham & Rosenthal, 2016)
Medications to Manage Portal Hypertension	
Nadolol (the preferred non-selective beta-blocker)	• Used to manage portal hypertension, varices. • Blocking beta2 receptors in the liver can inhibit glycogenolysis and block signs of hypoglycemia, which can be dangerous for diabetics. • Dosing can be difficult and need adjustment based on patient response; responses vary widely and little correlation exists between blood levels and therapeutic responses.
Medications to Manage Itching	
Cholestyramine	• First-line treatment for pruritus related to liver disease • Unpleasant taste; improves when combined with juice • Binds to bile acids within in the hepatic circulation ,which are then excreted in the feces (Hegade, Kendrick & Jones, 2015)
Hydroxyzine	• Antihistamine • Can also promote drowsiness, reduce anxiety, reduce nausea and vomiting (Burcham & Rosenthal, 2016)
Medications to Manage Hepatic Encephalopathy	
Lactulose	• Osmotic laxative • Increases intestinal excretion of ammonia • May cause flatulence and cramping
Rifaximin or Neomycin	• Used commonly in community; replaced with oral Neomycin in hospice patients due to cost • Broad-spectrum antibiotic • Kills ammonia-producing gut bacteria

Medication Reference: Commonly Used Medications, *continued*

Medication	Rationale
Medications to Manage Esophageal Varices	
Octreotide	• Used to treat varices • Somatostatin analog • Reduces pressure in the portal circulation by inducing splanchnic vasoconstriction (Silva-Junior, Baiges, Turon, Hernandez-Gea & Garcia-Pagan, 2017)
Vasopressin	• Used to treat varices • Also known as antidiuretic hormone • May cause excessive water retention • Stimulates contraction of vascular smooth muscle (Burcham & Rosenthal, 2016)
Medications to Manage Hepatorenal Syndrome	
Terlipressin	• Synthetic derivative of vasopressin • Improves renal function and increases survival time
Albumin	• Replaces lost blood volume (Nassar Junior et al., 2014)
Medications to Manage Alcohol Withdrawal	
Thiamine	• Also known as Vitamin B1 • Used in the prevention of Wernicke-Korsakoff syndrome (if Wernicke-Korsakoff syndrome is suspected, parenteral thiamine should be started immediately) • Dietary sources include whole-grain breads, cereals and pork
Benzodiazepines	• Stabilize vital signs, reduce withdrawal symptom intensity, reduce seizure risk and risk for delirium tremens • Common side effects include sedation and psychomotor slowing; side effects subside in seven to 10 days (Burcham & Rosenthal, 2016)

Medication Reference: Commonly Used Medications, *continued*

Medication	Rationale
Medications to Manage Alcohol Withdrawal Delirium	
Carbamazepine	• Anti-epileptic • Reduces withdrawal symptoms and reduces the risk for seizures
Chlorpromazine	• Antipsychotic • Can increase risk for seizures • May intensify response to benzodiazepines
Haloperidol	• Antipsychotic • Used to treat acute psychosis
Chlordiazepoxide	• Benzodiazepine • Useful if other benzodiazepines fail to control psychosis

Psychosocial Considerations of End-stage Liver Disease

It is always important to complete a thorough psychosocial assessment for patients with end-stage liver disease. It is *imperative* when the patient has a history of substance-use disorders (SUD), including alcohol use disorder (AUD). Various psychological, emotional and social impacts associated with prolonged substance abuse may complicate a patient's end-of-life journey. **The goal of this section is to guide assessment and conversation and to avoid harmful stereotyping.**

Understand the patient's current social support system. Stigma is a major issue for people with AUD. According to the World Health Organization (WHO), stigmatization of AUD is a global issue; the socioeconomic impacts include poverty, unemployment, homelessness and marginalization. Many people with SUD/AUD have a limited support system, limited family involvement and/or complex family dynamics.

People with SUD/AUD often have a history of issues with access to housing and health care. There is a domino effect: SUD increases homelessness, which may limit access to health care and community resources (Nooe & Patterson, 2010). Learning about the patient's social support system and history with housing and health care access will help clinicians identify areas of needed services and potential resources to meet those needs. Connecting the patient with the resources they need may be difficult if they have a negative personal history with medical professionals and government agencies.

There is a high correlation between SUD/AUD and mental health disorders. One study found that people with SUD also presented with depression, personality disorder, adjustment disorder, schizophrenia or bipolar disorders (Brems, Johnson, Wells, Burns, & Kletti, 2002). Another report stated that 90 percent of people age 65 and older who have AUD also have a history of depression. People with a history of AUD may also have a history of suicidal ideation. According to one report, when partnered with depression and anxiety disorder, AUD accounts for over 70 percent of suicides (Caputo et al., 2012). Different emotional and psychiatric care may be needed for a person with situational depression as compared with a person with chronic depression, a personality disorder or suicidal ideation.

Understanding past trauma can help clinicians address care needs across all care areas. There is a high incidence of PTSD associated with SUD (Caputo et al., 2012). Trauma may have been physical, sexual or emotional abuse/neglect, or the person may have witnessed or participated in violence (e.g., as a member of the armed forces). According to one study, AUD affects over 40 percent of U.S. veterans. There is also increased likelihood of psychiatric conditions—including suicidality—for veterans with AUD. Veterans are up to four times more likely to have PTSD or depression if they also had a SUD (Fuehrlein et al., 2016). When managing PTSD, consider the patient's triggers as well as coping mechanisms.

Care Considerations for Psychosocial Needs

- Have a clear understanding of the patient's current and past mental health needs: Are these needs due to their current situation or is this a long-standing issue? Understanding the symptoms of a patient's preexisting psychiatric disorders will help identify an acute exacerbation.
- Learn the patient's history of access to housing and health care needs, and assess for any current needs. Identify resources in the community to assist patients who have housing issues, limited social support and/or limited health care access.
- Assess for suicidal risk/ideation; this is critical for people with a SUD/AUD.

Collaboration/IDT

- Work collaboratively to build the patient's trust; this will be key in meeting needs across all areas of care.
- Identify patient's support system. Patients may be estranged from their family. They may have redefined who their family is or feel the need to reconnect with estranged family members.
- Finding placement for a person with alcohol and/or substance abuse issues may be difficult; be proactive and coordinate care.
- A patient with a history of housing issues and health care access issues may have limited financial resources and may need to apply for benefits. Learn the patient's financial needs and start any needed applications to ensure coverage for needed services.
- Remember that alcohol or substances abuse may be how a patient self-medicates for a psychiatric condition.

- Ask about the patient's history with psychiatric care (medications, hospitalization, outpatient care, etc.) as well as their coping methods. They may have felt stigmatized in receiving past psychiatric care.
- While working with a patient with a preexisting psychiatric condition, maintain consistent, healthy boundaries.
- It may help to request a consultation from a psychiatrist or doctor familiar with the patient and/or their presenting psychiatric condition.
- Each veteran's experience is unique to their service time, rank and branch of service. Ask for information that will help identify possible interventions, such as matching the patient with a volunteer who has military service.
- Be aware of the stress felt by the family caregivers of a patient with alcohol or substance abuse issues. Provide them additional emotional support and resources, if needed, and be aware of your own self-care.

Teaching Tip

Some clinicians find emotional and mental health assessments challenging. Help patients open up about their feelings by normalizing the discussion of emotional and mental health. Practice asking these types of questions, and make emotional and mental health assessments a regular part of your practice. You can start by saying: "Many people struggle with _____, especially at end-of-life. Do you have a similar experience? Is there anything that you are struggling with? I'm here for you and want to help you.

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