health professionals, particularly when considering pharmacotherapy.

Nausea and vomiting

Nausea is experienced by over half of patients with cirrhosis attributable to a number of potential etiologies, including medications (e.g., lactulose, opioids), adrenal insufficiency, electrolyte imbalance (e.g., hyponatremia, hypercalcemia), uremia, reflux, and constipation.[35,43] LD can also be associated with gastroparesis and increased intra-abdominal pressure (e.g., with tense ascites). Thus, nonpharmacological approaches to the management of nausea and vomiting can include behavioral avoidance (e.g., avoiding triggering smells and tastes), removal of triggering medications, treatment of underlying physiological causes, use of ginger, guided imagery or relaxation techniques, and acupuncture (Table 6).[278,279]

First-line pharmacotherapy for nausea and vomiting in patients with cirrhosis may include a trial of a histamine H2 antagonist or proton pump inhibitor in patients with suspected reflux-associated nausea. Ondansetron (a serotonin 5-HT_3 antagonist) can be used in patients with liver impairment at a dose of up to 8 mg/d, though patients should be monitored for constipation and QTc prolongation.[111] A small, randomized trial of 8 patients with cirrhosis and mild encephalopathy were treated with metoclopramide (up to 60 mg daily) versus placebo for nausea over a period of 2 weeks; all patients also received neomycin.[280] Although metoclopramide was associated with reduced nausea and heartburn in this small study, the risk of extrapyramidal side effects limits its long-term use, and a 50% dose reduction is recommended for patients with hepatic impairment.[280,281] Other medications for the palliative treatment of nausea may include olanzapine, haloperidol, or prochlorperazine; however, all have significant side-effect profiles (Table 4); prochlorperazine should be avoided in the setting of jaundice given case reports of cholestatic liver injury.[282]

Cannabinoids are another potential treatment for nausea and vomiting. Because of media coverage and conflicting data, clinicians should be prepared to discuss the benefits and potential harms of medical marijuana and other cannabinoids with patients with cirrhosis and their caregivers. The strongest supportive data for the use of medical marijuana are for nausea and vomiting. However, although one meta-analysis found that cannabinoids were associated with a reduction of nausea and vomiting of >50%, the data, particularly in cirrhosis, are limited.[283] Adverse effects of cannabinoids in the general population include dizziness, dry mouth, nausea, fatigue, somnolence, euphoria, vomiting, disorientation, drowsiness, confusion, loss of balance, and hallucination.[283] Some observational studies identified associations between cannabis and accelerated hepatic fibrosis, encephalopathy, and ascites in patients with chronic LD attributable to HCV and fatty liver disease.[284–287] However, other observational studies, including two meta-analyses of marijuana use and HCV, did not find a significant association between cannabis and hepatic fibrosis.[288–291] Trials of medical cannabinoids/marijuana have generally excluded patients with cirrhosis, given their vulnerability to neuropsychiatric symptoms. Thus, cannabinoids should be used with caution and with attention to institutional protocols for its use. When cannabinoids are used, edible formulations are favored over inhaled because of the potential infectious and respiratory effects of smoking.

Guidance statements

58. For patients with cirrhosis who suffer with nausea and/or vomiting, an evaluation should include assessment of electrolytes, adrenal insufficiency, and pharmaceutical causes as well as assessment for and treatment of gastroesophageal reflux disease.
59. First-line pharmacotherapy for nausea and vomiting is ondansetron (maximum 8 mg/d), using caution given constipating effects; most antiemetics require monitoring for QTc prolongation.
60. Medical marijuana is not first-line management for any symptom for patients with DC. However, providers should be able to engage in an educated conversation about its risks and benefits.

END-OF-LIFE CARE

The burden of symptoms and distress that patients with DC experience at the end of life is comparable to that of patients with advanced colorectal and lung cancer.[30] Symptoms commonly include pain, lack of energy, drowsiness, insomnia, and difficulty concentrating.[35] Eliciting treatment preferences for EoLC and addressing palliative needs based on priority are critical to ensuring that care at the end of life is patient and caregiver centered.

Patients and caregivers often want to know what to expect nearing the end of life; thus, health care teams should provide education about prognosis and help them develop plans for addressing infection, hemorrhage, and encephalopathy, which are the most common scenarios leading to death.[30] Care plans developed based on these discussions may often require balancing goals that are simultaneously aggressive and nonaggressive. This can be a particular challenge for patients and caregivers who wish to pursue EoLC at home or in the community, though the majority of patients with cirrhosis die in a health care facility.[292,293] There are a number of scenarios that are important to