

On-Demand Clinical News

Focusing on End-Stage Cardiac Disease in the Hospice Patient

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Cardiac disease describes a wide range of conditions that can affect your heart. End-stage cardiac disease is the outcome to most heart diseases and includes heart failure. Factors affecting the prognosis of patients with heart failure include, but are not limited to, age, gender, left ventricular ejection fraction, renal function, natriuretic peptide plasma concentrations, diabetes, extent of underlying coronary artery disease, and uncontrolled blood pressure.

Since symptom management and comfort are the main goals in hospice patients, it is important to identify the most common signs and symptoms in a hospice heart failure patient. Those signs and symptoms include, but are not limited to, dyspnea, cough, edema and insomnia caused by refractory volume overload, depression, anxiety, low energy levels causing fatigue and weakness, pain, gastrointestinal disorders (i.e. nausea, anorexia, constipation), and hypotension/orthostasis.

Counteracting neurohormonal dysregulation with conventional therapies should continue on hospice since neurohormonal dysregulation results in a catabolic state, muscle remodeling, respiratory and skeletal muscle atrophy, and weakness. This results in worsening fatigue, dyspnea, and limited exercise capacity. Therefore, we want to assure maximization of these medications to minimize symptoms. Drugs that counteract neurohormonal dysregulation are angiotensin converting enzyme inhibitors (ACE inh, such as lisinopril), which improve exercise tolerance, fatigue, dyspnea, orthopnea and edema; aldosterone receptor blockers such as spironolactone, which improve fatigue and dyspnea, and may be used when ACE inh are not tolerated. Additionally, beta-blockers, such as metoprolol, improve physical exertional performance. Spironolactone has been associated with an improvement of these overall symptoms.

Nearly 70% of cardiac patients will experience moderate to severe dyspnea. The mainstay of therapy is diuresis and vasodilation to decrease pulmonary congestion by utilizing ACE inh and diuretics, which lead to improved exercise capacity, reduced fatigue, and edema. However, patients with advanced HF may have hypotension, renal dysfunction, or other factors that may limit the effective use of these therapies to diminish dyspnea. Keep in mind, maintenance of euvolemia can improve, but may not eliminate, dyspnea.

Continued on Page 3

Medication Management in Hospice and Palliative Care

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There are many factors to consider in medication management for the hospice and palliative care patient. Some that will be reviewed include drug interactions, renal and hepatic dosing, side effects/adverse drug effects, therapeutic duplication, and deprescribing.

The clinician must always be aware of possible drug interactions. They must monitor more closely than usual for drug interactions whenever starting or stopping drugs and increasing or decreasing drug doses. For many drugs with interactions, increased monitoring is required. For some interactions, it is recommended to avoid the combination of the drugs altogether. This is not a hard and fast rule, though. Some factors to consider include patient risk of clinically significant harm from the interaction, drug doses, alternative medications, and routine versus occasional use.

Common side effects/adverse drug reactions in our patients include drowsiness, sedation, stomach upset, and anticholinergic effects. To help manage side effects, discontinue the drug if it is not palliating symptoms, providing comfort, or if it is ineffective. If continued, use the lowest effective dose. Generally, the longer a patient is on a drug at a constant dose, the side effects should start to subside.

Using two or more drugs from the same drug class to treat the same symptom or indication is called therapeutic duplication. This can increase the risk of side effects or adverse reactions. The use of both drugs should be evaluated; sometimes one of the drugs can be discontinued and the dose of the other drug may be increased if not already at the maximum dose. Sometimes, the patient is no longer able to benefit from the use of certain medications – a good example is respiratory inhalers (such as Albuterol HFA). In the case of inhalers, when the patient is not able to use them adequately, they should be discontinued.

Continued on Page 2



The patient should then be started on the appropriate nebulizer and/or oral medication if needed.

Hepatic impairment can change a patient’s response to some medications. There is a large hepatic reserve, so the impairment must be severe before there are significant changes in drug metabolism. Unlike renal disease and CrCl, there is no easy way to calculate the best dose in liver impairment, though drug references provide general dosing recommendations for liver disease. See the below tables for information on renal/hepatic dosing in patients with impairment:

Common medications that require renal dosing

Miscellaneous	Miscellaneous continued	Antibiotics	Analgesics
Digoxin	H2 blockers - i.e. Ranitidine/Famotidine	Amoxicillin	Methadone - adjustment only required if the estimated CrCl is 10ml/min or less
Fluconazole	Magnesium - avoid in severe renal failure	Cephalexin	NSAIDs - avoid if the estimated CrCl is less than 30
Gabapentin	Rivaroxaban	Cefuroxime	Codeine - has active metabolites
Loratadine	Metformin - avoid if the estimated CrCl is less than 30ml/min	Ciprofloxacin	Morphine - has active metabolites
Lorazepam injectable	Glyburide - avoid in CKD stage 3-5	Levofloxacin	Tramadol - has active metabolites
Metoclopramide		Nitrofurantoin	Meperidine - avoid, has an active neurotoxic metabolite
		Trimethoprim/sulfamethoxazole	

Common medications to avoid or adjust in hepatic impairment

DRUG	RECOMMENDATION
Acetaminophen	Avoid doses greater than 2-3gm/day; if active alcohol use, try to avoid or limit use to the short-term and maximum dose of 2gm/day
Apixaban	Avoid in severe impairment. Use with caution in moderate impairment
Azithromycin	Avoid, may cause jaundice
Buspirone	Avoid in severe impairment. Use with caution in mild to moderate impairment
Carvedilol	Avoid in severe impairment. Use with caution in mild to moderate impairment
NSAIDS	Increased risk for GI bleeding, can cause fluid retention, use with caution or avoid in severe liver disease
Metoclopramide	Reduce dose in moderate and severe impairment
Nitrofurantoin	Jaundice and chronic active hepatitis reported
Promethazine	Adults-use with caution, Pediatric-avoid if signs and symptoms of hepatic disease
Roflumilast	Avoid in moderate to severe impairment. Use with caution in mild impairment
Rivaroxaban	Avoid in moderate to severe impairment and any impairment with coagulopathy
Sulfamethoxazole/Trimethoprim	Avoid in severe liver disease
Valproic Acid	Avoid in severe disease, not recommended for use in mild to moderate disease
Warfarin	Avoid in severe disease; mild to moderate disease: monitor INR closely due to increased sensitivity
BENZODIAZEPINES	
Alprazolam	Immediate release formulation 0.25mg 2-3 times daily
Clonazepam	Avoid in significant hepatic impairment
Diazepam	Avoid oral tablets in severe hepatic impairment
Lorazepam	Oral-severe impairment and/or encephalopathy-may require lower doses, use with caution. Parenteral-Avoid in severe impairment or failure. Use with caution in mild to moderate impairment



Opioids are the first-line adjuvant therapy to treat dyspnea in HF. Benzodiazepines should be reserved for the treatment of dyspnea caused by anxiety.

Patients with advanced HF may have persistent lower extremity edema and ascites, which if severe, may be associated with considerable discomfort. Guideline-recommended sodium restriction to less than 3 grams per day seems feasible in some cases to reduce edema. Also, avoidance of fluid retaining medications (i.e. NSAIDs, aspirin, etc.), leg elevation and/or compression stockings, or bandage wraps can be beneficial. Finally, loop diuretics (such as furosemide) plus thiazides or thiazide-like diuretics (such as metolazone) can be utilized at the lowest effective dose, adjusting doses according to individual needs over time.

Up to 63% of patients with cardiac failure have clinical depression. Options for treating depression in patients approaching end-of-life include cognitive behavioral therapy, spiritual support, and medications. Selective Serotonin Receptor Inhibitors (SSRI's), such as sertraline and paroxetine, have been found to be safe and effective as first-line therapy for depression in patients with heart failure. These medications should be started at a low dose and increased until depression improves or until recommended dose is achieved. These drugs can induce fluid retention and hyponatremia in patients with renal insufficiency, and some prolong the QTc interval. The onset of effects is 1-2 weeks with SSRI's. Mirtazapine is also a great option for those with depression and insomnia along with poor appetite. Low-dose methylphenidate or dexamethasone may be options for a faster onset of relief, keeping in mind methylphenidate may increase heart rate. Dexamethasone is preferred over prednisone, because dexamethasone only stimulates glucocorticoid activity, and therefore water retention/edema is not as prevalent as with prednisone.

Up to 70% of our cardiac failure patients experience fatigue and weakness. Fatigue and weakness in patients with advanced HF are usually multifactorial, related in part to cardiac insufficiency, loss of muscle mass, deconditioning, and co-morbid conditions (i.e. anemia, thyroid dysfunction, sleep disorders, and depression), which should be ruled out and treated if appropriate. Stimulants, such as methylphenidate, may be beneficial in some cases, but must be weighed against the potential risk of HF exacerbation.

Up to 75% of patients with advanced HF will experience pain. Consider addressing unrecognized psychological, social, and spiritual needs that will often explain a nonresponding physical pain. Of the non-opioid pain medications, acetaminophen has the most favorable safety profile for patients with HF with mild to moderate somatic pain. Oral opiates may be used for management of moderate to severe pain in patients with HF. Nonsteroidal anti-inflammatory drugs (NSAIDs) are generally contraindicated in patients with HF due to propensity for causing fluid retention and exasperating renal dysfunction. Many NSAIDs, such as cyclooxygenase (COX) inhibitors, also carry black box warnings for patients with cardiovascular disease.

For more in-depth information on heart failure and management of the heart failure patient receiving hospice care, the corresponding presentation to this article is available on the ProCare HospiceCare website, and, as always, ProCare Clinical Pharmacists are available 24-hours a day/7-days a week to assist in symptom management of your patients.

References:

1. Thompson, Keith A. Heart Failure therapy: beyond the guidelines. *Journal of Cardiovascular Medicine*. 11(12):919-927, December 2010.
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Deprescribing to optimize medication therapy is a planned and monitored process where drug doses are reduced or discontinued. At the end-of-life, drugs can cause harm and may no longer be beneficial. Goals of deprescribing are to reduce the risk of harm, reduce pill burden, and improve quality of life. Some reasons to stop medications or reduce doses include noncompliance with no negative health effect; using incorrectly with no negative health effect or no benefit; no indication or a relative contraindication; no longer indicated; an inappropriate choice for a geriatric patient; and changed goals of care or life expectancy.

Drugs and drug classes to target for deprescribing include but are not limited to: amiodarone, anticoagulants, antilipemic agents, antihyperglycemics, antihypertensives, bisphosphonates, acetylcholinesterase inhibitors, memantine, digoxin, BPH and overactive bladder medications, inhalers, levothyroxine, multivitamins and supplements, and proton pump inhibitors.

We have reviewed many factors to consider in medication management for the hospice and palliative care patient. For optimal patient care, we must monitor for drug interactions, side effects/adverse drug effects, and therapeutic duplication. Some drugs require dose adjustments or even avoiding use in renal and or hepatic impairment. Finally, deprescribing medications is another tool we use to ensure the best use of medications and an improved quality of life for our patients and their families.

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1. Farrell et al., (2017). Deprescribing Proton Pump Inhibitors, Evidence-based clinical practice guideline. Canadian Family Physician, 63,354-364.
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