PALLIATIVE CARE CASE OF THE MONTH

"Use of IV Inotropes in Hospice"

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Volume 23, No. 134

Case: Ms. C. is a 60-year-old female with end-stage heart failure (ejection fraction of 10-15%) on home milrinone, status post biventricular implantable cardioverter defibrillator, coronary artery disease status post stenting, history of bioprosthetic mitral valve and tricuspid valve repair, and stage 4 chronic kidney disease, who is admitted with an acute exacerbation of chronic systolic heart failure.

The patient has had multiple hospitalizations in the past year for heart failure exacerbations and cardiogenic shock. She is not a candidate for heart transplant or a ventricular assist device (VAD). Ms. C. was unable to tolerate maximal oral goal-directed medical therapy. Dobutamine was started at a prior hospitalization, and she was discharged home on this medication because she could not be weaned off it. She recently transitioned from dobutamine to milrinone due to a nationwide dobutamine shortage.

The patient's health, functional status, and quality of life have progressively worsened in the past year. She is told by the heart failure team that her prognosis is less than six months. After palliative consultation and goals of care discussions with the patient and her family, the patient is considering hospice services at home. She asks, "Will I still be on milrinone if I go home with hospice?"

Background: Advanced or end-stage heart failure (HF) is classified by the American Heart Association as heart failure that is refractory to specialized interventions.1 There are limited treatment options for those with advanced HF. These options may include continuous intravenous inotropic support (CIIS) or more definitive surgical interventions such as cardiac transplant or mechanical circulatory support like VAD.2, 3, 4 Although intended as a bridge to the more definitive surgical options, a growing number of end-stage HF patients are receiving CIIS at home for palliation of their symptoms because many are not candidates for advanced surgical management.4, 5 Furthermore, these advanced surgical interventions may not align with the overall goals or values of the patient.4

Review of Pharmacology:

The two major classes of positive IV inotropic agents used in advanced heart failure are phosphodiesterase (PDE)-3 inhibitors (e.g., milrinone) and beta-adrenergic receptor agonists (e.g., dobutamine). Both work by increasing available calcium levels within myocardial tissue via cyclic adenosine monophosphate (cAMP) regulation, which subsequently increases cardiac contractility.6

Patients Who Benefit:

Those who benefit from CIIS are patients with end-stage HF on maximum tolerated oral medical therapy with refractory symptoms AND:

- Have failed trial of weaning inotrope support as an inpatient or were too sick to attempt wean
- Are able and willing to use an infusion pump and central line
- Are willing to undergo appropriate periodic monitoring
- Do not have refractory ventricular tachycardia or life threatening arrhythmias[6]

Outcomes and Risks:

Data is limited regarding the benefits of inotropic therapy, and the outcomes demonstrated are mixed.[6] Several studies suggest initial improvement in right heart catheterization hemodynamics, improvement in functional status and symptom burden/quality of life, and decrease in hospitalizations.[4, 5, 7, 8] There is a potential increase in tolerance for goal-directed medical therapy (GDMT)[8], but there does not seem to be evidence of an improvement in mortality. Most literature that exists suggests a potential increase in mortality due to fatal arrhythmias;[2, 4-6, 9-10] however, this is not well understood as most of the studies related to this were small trials on oral and intermittent IV inotropic therapy rather than continuous inotropic support. Further, these studies were conducted during a time when prophylactic ICD implantation was not the standard of care.[6]

Median survival for those on inotropic therapy who are not eligible for transplant or ventricular assistive device (VAD) is limited. Reports vary on time frame but are usually three to six months.[2]

Common side effects of IV inotropic therapy include tachycardia and hypotension. Dobutamine can cause angina, eosinophilia, and tachyphylaxis. Milrinone can cause headaches. Major risks of IV inotropes are catheter-related bloodstream infections (CRBSI), fatal arrhythmias, and sustained hypotension (which may confer shortened survival as discussed above).[4]

Potential Barriers:

There are several potential barriers for patients to receive palliative continuous IV inotropic therapy. These barriers may be particularly relevant for those planning on receiving continuous IV inotropic therapy at home for end-of-life (EOL) palliation of symptoms. From a practical standpoint, IV inotropes need to be started as an inpatient, typically in an ICU setting. IV inotropic management also requires a PICC or Hickman central catheter, which in turn requires ongoing and routine high-quality catheter-line care typically by an adequately trained home care team.[6]

Medicare will cover home inotropic therapy; however, strict guidelines are followed to qualify a patient for coverage. The patient must have uncontrolled symptoms, specifically dyspnea at rest despite maximum tolerated doses of GDMT. Hemodynamic studies are required within six months prior to initiation and must demonstrate a maximum cardiac index of 2.2L/min/m2 and/or a pulmonary capillary wedge pressure (PCWP) of 20mmHg prior to infusion on maximum tolerated oral medications.

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For palliative care consultations please contact the Supportive and Palliative Care *programs at PUH/MUH, 412-647-7243, pager # 8511, Shadyside, 412-647-7243, pager # 8513, Perioperative/ Trauma Pain, 412-647-7243, pager # 7246, UPCI Cancer Pain Service, pager 412-644-1724, Magee Women's Hospital, pager 412-647-7243 pager # 8510, VA Palliative Care Program, 412-688-6178, pager # 296. Hillman Outpatient: 412-692-4724. For ethics consultations at UPMC Presbyterian-Montefiore and Children's pager 412-456-1518*
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Following initiation of inotrope infusion, follow-up hemodynamic studies must show a 20% increase in cardiac index and/or at least 20% decrease in PCWP. There also must be documentation of improvement in patient "well-being" at time of discharge and with follow up. "Well-being" is defined in this instance as decreased dyspnea, increased diuresis, improved renal function, reduction in weight, and overall improvement in quality of life. Medicare coverage additionally requires documentation of deterioration with attempts to discontinue and/or wean therapy. Any potentially fatal arrhythmias must be controlled and addressed prior to hospital discharge, and efforts to maintain the patient on the lowest practical dose must be made and documented within the first three months of therapy. Finally, Medicare only covers specific dose ranges for dobutamine and milrinone.[6]

Another major barrier to continuous IV inotropic therapy is cost. Although it varies depending on drug and insurance type, IV inotropic therapy is expensive. Dobutamine can cost $1000-3000 per month. Milrinone is even more costly and can cost anywhere between $4500 to $21,000 per month. This is solely the drug cost and not the cost of ancillary costs like home nursing visits.[6]

Discussion:

In considering patients like the one described above who are on CIIS and decide to receive hospice services at home, there is limited evidence and data to help inform management and decision-making strategies regarding IV inotropic therapy in hospice settings at the end of life.[4] Many hospice agencies may not accept patients on continuous IV milrinone or dobutamine due to cost and need for advanced training/staffing.[3, 7, 10] Medicare reimburses hospice agencies at a fixed daily rate regardless of the complexity of care involved.[10,11] This means that hospice agencies are left to cover remaining expenses related to the primary hospice diagnosis. Hospice agencies thus may not be able to afford the cost of expensive IV inotropes. One study that looked at perspectives on cardiac medications in hospice cited providing inotropic therapy as a challenge mostly because of cost, but also due to IV access issues, lack of clinician knowledge, lack of caregiver support, or lack of proven efficacy to relieve symptoms. This same study noted that just over half of agencies (57%) were able to provide IV inotropic therapy in any hospice setting, implying that the initial setting of hospice care on CIIS may not be at home given agency resources.[12]

Despite limited resources, it is possible for those receiving CIIS to be transitioned to hospice successfully;[13] however, hospice agencies often need a plan to discontinue or wean therapy before patients are accepted.[10] There are no standard guidelines for weaning or discontinuing CIIS, although inotropic therapy may itself cease to provide symptomatic relief for the patient or its risks and side effects may be too burdensome (e.g. cause tachyarrhythmias).[14] These instances may subsequently lead to discussions with patients and families about discontinuation of inotropic therapy as it ceases to be effective.

Patients and families should be informed that while on hospice, the infusion rate of inotropic support will not be increased. There should also be an agreement regarding a taper plan for eventual discontinuation. Once weaned off, alternate agents can be used for management of dyspnea.[9] When weaned off at the EOL, the prognosis of patients varies–patients often survive at least one day with some surviving more than 72 hours.[13]

Despite the various barriers to CIIS, patients with advanced HF note the benefits of symptom control. It is worth asking how we can provide this type of support to patients on hospice. For instance, could we implement a similar program to the Concurrent Hospice-Dialysis Program for advanced HF? In fact, there was a study in 2020 published in the American Journal of Hospice and Palliative Medicine that described the implementation of a cardiac home hospice program in New York City. Patients admitted into this program were receiving complex therapies including CIIS. Among other things, it included partnerships with contracted infusion companies for IV therapies and CIIS at home. The study's aim was mainly to demonstrate how specific care practices can increase awareness and enrollment of patients with HF and better control EOL symptoms, so it did not specifically discuss the benefits of CIIS at home for hospice patients; however, it did show that advanced HF patients do benefit from tailored support in general at the end of life.[15]

Back to the case:

Our team had an open discussion with Ms. C. regarding weaning therapy once home with hospice. We explained what a taper would look like and the potential negative effects of continued home milrinone therapy. After discussing risks and benefits, the patient and her family opted to defer hospice until a later time. Her plan was to go home on milrinone and then transition to hospice care once she clinically worsened.

This case highlights the importance of discussing goals with patients and families regarding the use of palliative inotropic therapy. By having early and ongoing discussions about the benefits and burdens of this therapy (including how it may change the course of a patient's EOL), we can help lessen patient and family distress and help them make more informed decisions. Furthermore, any major clinical change that indicates EOL should trigger reevaluation and discussion regarding possible cessation of therapy.[4,10]

Conclusion:

CIIS is increasingly being used in palliative care for advanced HF patients. As these patients transition to end-of-life care, hospice agencies run into barriers for providing this type of advanced support, which in turn leads to questions about whether CIIS should be implemented into a hospice care plan. Palliative clinicians should thus help patients and families think about the symptomatic benefit versus the harms and risks associated with CIIS before implementation as palliative therapy.

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Once CIIS has been started, it is imperative to have ongoing discussions of goals of care and the benefits and burdens of CIIS to help guide patients and families on what to expect at the end of life and how this might look in a hospice setting.

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