

FAST FACTS AND CONCEPTS #283
USE OF HOME INOTROPES IN PATIENTS NEAR THE END OF LIFE

Mallory Strickland Ciuksza MD, Randy Hebert MD, and George Sokos DO

Background Some patients with end-stage heart failure causing symptoms at rest are placed on continuous infusions of cardiac inotropes in an attempt to improve symptoms and avoid hospitalizations. Among end-stage heart failure patients who are ineligible for advanced cardiac therapies (such as heart transplant or a ventricular assist device), mean life expectancy with inotrope-dependent medical therapy is estimated at 9.4 months, with 26% surviving to 1 year. Hence, the home use of continuous inotrope therapy may be commonly encountered by clinicians who care for the seriously ill.

Pharmacology Both major classes of inotropic agents, adrenergic agonists (i.e. dopamine and dobutamine) and phosphodiesterase inhibitors (i.e. milrinone), increase contractility by increasing available calcium levels within myocardial tissue via cAMP regulation (2).

Patient Selection Patients on maximal medical therapy who continue to have refractory symptoms at rest (New York Heart Association Class IV) may benefit from home IV inotrope therapy. Eligible patients must have either failed a trial of weaning inotropic support in the inpatient setting or been too ill to attempt weaning (3,4). Patients should not receive home inotropic therapy if they are not maximized on their oral medications, unable or unwilling to utilize an infusion pump and central line, unwilling to undergo appropriate monitoring, or have refractory ventricular tachycardia or life threatening arrhythmias (5).

Outcomes and Risks Available data assess the number of hospitalizations, symptom control, mortality, and quality of life (6-13). Unfortunately, the strength of the data is relatively weak and the outcomes are mixed as very few studies utilize the same methods or measure the same outcomes. The prevailing literature suggests trends of hastened death with dobutamine and milrinone administration largely due to arrhythmias (10,11, 14-18). However, the majority of this data is based on data from small trials on oral and intermittent IV inotropes (not continuous therapy), and, importantly, are from an era in which prophylactic ICD implantation was not the standard of care. The most recent guidelines advocate against the use of intermittent therapy altogether. Despite these risks, if the patient's goal is to be at home, there is evidence that *continuous* outpatient inotrope infusion may shift the remaining survival time to a home setting through marked improvements in symptom control and therefore may be an excellent treatment for the well selected patient (9).

Practical Concerns Inotropes are started during an inpatient hospitalization. This typically occurs in the setting of the intensive care unit where doses can be titrated to allow for a weaning trial if the patient is clinically stable enough to do so. Patients will require a PICC line or Hickman catheter for infusion with regular, high quality line care to prevent infections. Patients on home inotropes require ongoing care by an adequately trained home care team and an experienced physician (typically a cardiologist) so that their medications can be adjusted as needed. The most common side effects are hypotension and arrhythmias. For this reason electrolytes should be regularly followed, as well as renal function through regular serum creatinine monitoring in order to anticipate dosing changes that may be necessary if changes in creatinine clearance should occur.

Medicare Coverage Requirements: Medicare has strict coverage guidelines for home inotropes, which greatly affect how they are used in the US. Below are the criteria that need to be met in order for inotrope therapy to be covered (5).

- Symptoms must be uncontrolled; specifically, **dyspnea at rest** must be present despite maximum tolerated doses of digoxin, loop diuretics, ACEIs, or other vasodilators.
- **Hemodynamic studies** must be performed within six months prior to initiation of home inotropic therapy that show both:
 - **Cardiac index of 2.2 L/min/m²** (maximum) and/or **pulmonary capillary wedge pressure of 20 mmHg** before infusions while on maximum tolerated oral medications.
 - A **20% increase in cardiac index**, and/or at least a **20% decrease in pulmonary capillary wedge**

pressure during inotrope infusion.

- **Improvement in patient “well-being”** (i.e., decreased dyspnea, increased diuresis, improved renal function, or reduction in weight) must be shown with the **absence of dyspnea at rest** at the time of discharge and with outpatient follow up.
- There must be **documented deterioration** with attempts to discontinue/wean the patient from inotropes while in the hospital.
- Any life-threatening **arrhythmia must be controlled** and addressed prior to discharge. Some evidence suggests that oral amiodarone may benefit these patients who experience ectopy but are still benefiting from inotrope therapy (17,19).
- Covered inotrope dosing must be within the following **ranges**:
 - Dobutamine 2.5-10 mcg/kg/min.
 - Milrinone 0.375-0.75 mcg/kg/min.
 - Dopamine may also be used at a rate of 2 mcg/kg/min.
- Efforts to maintain the patient on the **lowest practical dose** must be made and documented during the first three months of therapy.

Cost Cost of these therapies varies significantly depending on choice of drug and insurance type. Milrinone cost per month ranges between \$4500-\$21,000 and dobutamine between \$1140-\$2790 (estimates are based on a 75 kg patient with infusions of 0.5 mcg/kg/min and 5mcg/kg/min for milrinone and dobutamine respectively) (20). Medicare will reimburse for these therapies and for associated equipment such as infusion pumps, however nursing visits are not included in these estimates.

Home Care and Hospice Many hospices will not accept inotrope-dependent patients given the cost and need for advanced training (12). Some communities have specialized home-care agencies or programs for patients on home inotropes, which may or may not be part of a hospice program.

References

1. Long EF, Swain GW, & Mangi AA. Comparative survival and cost-effectiveness of advanced therapies for end-stage heart failure. *Circulation: Heart Failure*. 2014; 7:470-478
2. Felker GM, O'Connor CM. Inotropic therapy for heart failure: an evidence-based approach. *Am. Heart J*. 2001; 142(3):393-401.
3. Lewis EF. End of life care in advanced heart failure. *Curr Treat Options Cardiovasc Med*. 2011; 13(1):79-89.
4. Young JB, Moen EK. Outpatient parenteral inotropic therapy for advanced heart failure. *J Heart Lung Transplant*. 2000; 19(8 Suppl):S49-57.
5. Gorski LA. Positive inotropic drug infusions for patients with heart failure: current controversies and best practice. *Hom Healthc Nurs*. 2002; 20:244-53.
6. Oliva F, Latini R, Politi A, et al. Intermittent 6-month low-dose dobutamine infusion in severe heart failure: DICE multicenter trial. *Am. Heart J*. 1999; 138(2 Pt 1):247-53.
7. Marius-Nunez AL, Heaney L, Fernandez RN, et al. Intermittent inotropic therapy in an outpatient setting: A cost-effective therapeutic modality in patients with refractory heart failure. *American Heart Journal [Internet]*. 1996; 132(4):805-8.
8. López-Candales A, Vora T, Gibbons W, Carron C, Simmons P, Schwartz J. Symptomatic improvement in patients treated with intermittent infusion of inotropes: a double-blind placebo controlled pilot study. *J Med*. 2002; 33(1-4):129-46.
9. López-Candales AL, Carron C, Schwartz J. Need for hospice and palliative care services in patients with end-stage heart failure treated with intermittent infusion of inotropes. *Clin Cardiol*. 2004; 27(1):23-8.
10. Krell MJ, Kline EM, Bates ER, et al. Intermittent, ambulatory dobutamine infusions in patients with severe congestive heart failure. *Am Heart J*. 1986;112(4):787-91.
11. Cesario D, Clark J, Maisel A. Beneficial effects of intermittent home administration of the inotrope/vasodilator milrinone in patients with end-stage congestive heart failure: a preliminary study. *Am Heart J*. 1998;135(1):121-9.
12. Hershberger RE, Nauman D, Walker TL, Dutton D, Burgess D. Care processes and clinical outcomes of continuous outpatient support with inotropes (COSI) in patients with refractory endstage heart failure. *J Card Fail*. 2003; 9(3):180-7.
13. Gheorghiade M, Gattis WA, Klein L. OPTIME in CHF trial: rethinking the use of inotropes in the management of worsening chronic heart failure resulting in hospitalization. *Eur J Heart Fail*. 2003

- Jan;5(1):9–12.
14. Elis A, Bental T, Kimchi O, Ravid M, Lishner M. Intermittent dobutamine treatment in patients with chronic refractory congestive heart failure: a randomized, double-blind, placebo-controlled study. *Clin Pharmacol Ther.* 1998; 63(6):682–5.
 15. Amsallem E, Kasparian C, Haddour G, Boissel JP, Nony P. Phosphodiesterase III inhibitors for heart failure. *Cochrane Database of Systematic Reviews.* 2005, Issue 1. Art. No.: CD002230. DOI: 10.1002/14651858.CD002230.pub2.
 16. Thackray S, Easthaugh J, Freemantle N, Cleland JGF. The effectiveness and relative effectiveness of intravenous inotropic drugs acting through the adrenergic pathway in patients with heart failure—a meta-regression analysis. *Eur J Heart Fail.* 2002; 4(4):515–29.
 17. Toma M, Starling RC. Inotropic therapy for end-stage heart failure patients. *Curr Treat Options Cardiovasc Med.* 2010; 12(5):409–19.
 18. Ewy GA. Inotropic infusions for chronic congestive heart failure: medical miracles or misguided medicinals? *J Am Coll Cardiol.* 1999; 33(2):572–5.
 19. Nanas JN, Kontoyannis DA, Alexopoulos GP, et al. Long-term intermittent dobutamine infusion combined with oral amiodarone improves the survival of patients with severe congestive heart failure. *Chest.* 2001; 119(4):1173–8.
 20. Vantage Home Infusion Therapy Services. prepared by Dr. Robert Buzas. <http://www.vhcn.com/vantage-home-infusion-services/>

Authors' Affiliations: Allegheny Health Network, Pittsburgh, PA

Conflicts of Interest Statement: The authors have disclosed no relevant conflicts of interest.

Version History: First published August 2014. References updated and copy-edited in September 2015 by Sean Marks MD.

Fast Facts and Concepts are edited by Sean Marks MD (Medical College of Wisconsin) and associate editor Drew A Rosielle MD (University of Minnesota Medical School), with the generous support of a volunteer peer-review editorial board, and are made available online by the [Palliative Care Network of Wisconsin](#) (PCNOW); the authors of each individual *Fast Fact* are solely responsible for that *Fast Fact's* content. The full set of *Fast Facts* are available at [Palliative Care Network of Wisconsin](#) with contact information, and how to reference *Fast Facts*.

Copyright: All *Fast Facts and Concepts* are published under a Creative Commons Attribution-NonCommercial 4.0 International Copyright (<http://creativecommons.org/licenses/by-nc/4.0/>). *Fast Facts* can only be copied and distributed for non-commercial, educational purposes. If you adapt or distribute a *Fast Fact*, let us know!

Disclaimer: *Fast Facts and Concepts* provide educational information for health care professionals. This information is not medical advice. *Fast Facts* are not continually updated, and new safety information may emerge after a *Fast Fact* is published. Health care providers should always exercise their own independent clinical judgment and consult other relevant and up-to-date experts and resources. Some *Fast Facts* cite the use of a product in a dosage, for an indication, or in a manner other than that recommended in the product labeling. Accordingly, the official prescribing information should be consulted before any such product is used.