

Results from a Pilot Study to Determine the Feasibility in Transitioning Outpatient CHF Patients from Intermittent Intravenous Inotrope Therapy to Nesiritide

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Introduction

The goal of any heart failure outpatient clinic is to improve or stabilize a patient's clinical symptoms by reducing hospitalizations and mortality and improving quality of life. Serial infusions of inotropes have been used for several years to treat heart failure in the outpatient setting. However there is controversy on the effectiveness of this application of inotropes, and in many cases patients fail to improve.

Recent studies have indicated that inotrope use may be associated with increased mortality. Recently an alternative therapy for the treatment of heart failure has become available and that has the potential to be effectively used in the outpatient setting to manage patients with advanced heart failure. Nesiritide (Natrecor[®]) is a recombinant form of human B-type natriuretic peptide (BNP). BNP is secreted by the myocardium in response to left ventricular stretch, which occurs with volume overload often associated with congestive heart failure. Results from acute care studies with nesiritide suggest that it offers some unique properties that may be especially beneficial in this setting.

Among the available pharmacotherapeutic agents, nesiritide offers the unique ability to affect positively both the hemodynamic and neurohormonal responses in the CHF patient without creating the potential for proarrhythmic effects as observed with inotropes. We hypothesized that, in addition to its benefits in the acute care setting, nesiritide would be equally efficacious in stabilizing hemodynamics and symptoms in end-stage CHF in the intermittent outpatient setting.

As a secondary hypothesis, we suspected that patients switched from inotrope to nesiritide serial therapy would have improved quality of life scores. We report here the results from an open label pilot study conducted in our clinic, where we offered 30 patients currently receiving inotrope serial infusion therapy the opportunity to switch to nesiritide therapy and followed them for 12 weeks.

Methods

- Open label, 2-arm pilot study conducted in 30 patients for 12 weeks.
- Patients were NYHA Class IIIb or IV patients currently being treated for advanced heart failure with serial infusions of milrinone and/or dobutamine.
- Patients were asked if they would be willing to try a new therapeutic agent in place of their current inotrope therapy. All other standard care medications were continued in both groups and adjusted throughout the study at the physician's discretion.
- Patients identified as high risk for rehospitalization showed greatest benefit from nesiritide treatment with (1) reduced incidence of worsening heart failure, hypotension, and kidney function AEs, and (2) reduced mortality.
- Patients who remained on inotrope therapy continued with their current regimen.
- All patients continued to receive all their other current standard care medications. ACEI/B-blockers were titrated to achieve normal hemodynamic parameters utilizing bio-impedance cardiography (BioZ[®]).
- Patients switched to nesiritide received infusions twice a week for 4 hours each at the current recommended dose: a 2 µg/kg bolus followed by 0.01 µg/kg/min continuous infusion.
- At each visit patients were seen by clinical nursing staff for assessment of their symptomology and for standard education follow up.
- Hemodynamics were collected weekly using standard bioimpedance measurement (BioZ[®], CardioDynamics):
 - CI - Cardiac Index
 - SVRI - Systemic Vascular Resistance Index
 - TFC - Thoracic Fluid Content
 - LCWI - Left Coronary Work Index
- Short form 36 questionnaires (SF36) were administered every six weeks for monitoring of quality of life issues.

Results

Patient Population

- 14 of the 30 NYHA class IIIb/IV patients agreed to switch to nesiritide for this pilot study.
- There were no substantial differences in baseline demographics between the two groups (Table 1).
- Patients received either nesiritide 2 times per week or inotropes 2–3 times per week (Table 2).

Hemodynamics

- All 30 patients entering the study were hemodynamically stable. During the 12-week study period, no significant changes in hemodynamic stability were observed following the transition from inotropes to nesiritide.

Quality of Life

- Patients in the nesiritide group had substantially lower baseline Quality of Life scores compared to the inotrope group, suggesting they were more symptomatic than patients in the inotrope group.
- However with respect to the physical component score (PCS), patients on nesiritide showed a significant improvement in PCS while the patients on inotropes continued to decline.

Clinical Outcomes

- One patient in each group was hospitalized for congestive heart failure as a result of volume overload; non-compliance to fluid restriction was suspected in each admission.
- No CHF related deaths occurred in either group.
- One death occurred in the nesiritide group, which was unrelated to therapy. The patient expired due to surgical complications from an elective aortic valve replacement surgery.

Renal Effects and Diuretic Use

- There were no clinically significant differences in BUN/Creatinine in either group over the 12-week period.
- There were no significant changes in diuretic use at 3 months compared to baseline.
- Some adjustment (reduction in dose) of diuretics was noted in the nesiritide group during the first two weeks of administration.

Table 1. Patient Demographics

Parameter	Nesiritide (n = 14)	Inotrope (n = 16)
Age (years)		
Mean	66.6 ± 9.4	72.5 ± 9.3
Range	48 - 82	52 - 87
Gender (% male)	6 (43%)	9 (56%)
Type of Heart Failure		
Systolic	13 (93%)	15 (94%)
Diastolic	1 (7%)	1 (6%)
Etiology of Heart Failure		
Ischemic	8 (58%)	12 (75%)
Primary	3 (21%)	1 (6%)
Other	3 (21%)	3 (19%)
Concomitant Medications		
Beta-blockers	14 (100%)	13 (81%)
ACEI	10 (71%)	11 (69%)
ARB	5 (36%)	2 (12%)
ACE or ARB	13 (93%)	12 (75%)
Digoxin	10 (71%)	14 (88%)

Table 2. Drug Doses

Treatment Group	Dose Regimen
Nesiritide (n = 14)	2 µg/kg bolus followed by 0.01 µg/kg/min infusion for four hours, twice per week
Inotropes (n = 16)	
Milrinone	4-5 hours, twice a week (n = 5) OR 4 hours, three times a week (n = 7)
Dobutamine	2.5 to 3.5 hours, 1-2 times a week (n = 3)
Milrinone and Dobutamine	4 hours, twice a week (n = 1)

Conclusions

While this pilot study had significant limitations including a small sample size, being an open label and a non randomized study, a number of interesting findings suggest that nesiritide has the potential to be of significant value in the outpatient treatment of advanced heart failure patients:

- Nesiritide appears to be as efficacious as inotropes in maintaining hemodynamic stability when given intermittently in the outpatient setting.
- Switching patients from inotrope therapy to nesiritide was found to be safe in an outpatient setting.
- The replacement of inotrope serial infusion therapy with nesiritide serial infusion therapy was found to rapidly increase physical functioning.
- BUN and serum creatinine levels remained stable during the 12-week period.

Further study is warranted to determine the potential beneficial effects of nesiritide on clinical symptoms and quality of life.