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Nesiritide Enhances Urine Output in Decompensated Advanced Heart Failure Patients

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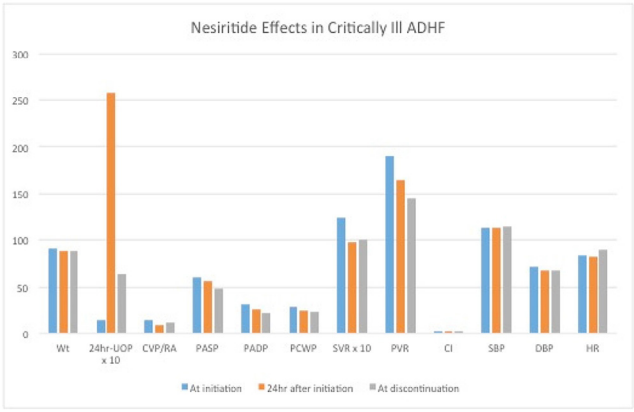
Nesiritide is not recommended for use in routine patients with acute decompensated heart failure (ADHF) based on current clinical evidence. However, patients with more advanced HF were not well represented in these clinical studies. IV vasodilators can be effective adjunctive treatments in advanced HF patients with acute decompensation and nesiritide is occasionally used for this purpose at our institution. The objective of this study was to review the clinical course of advanced HF patients with ADHF who received nesiritide infusion (NES) to assess efficacy and predictors of responsiveness. This was a single-center retrospective study approved by the study site's IRB. Electronic record review was performed on patients receiving NES from 9/1/15-12/31/16. Baseline characterisitcs and adverse events data were collected. Daily UOP and hemodynamic parameters were collected prior to NES initiation and 24 hr after initiation to assess efficacy. The primary endpoint was increase in UOP 24 hr after NES initiation. Logistic regression was performed to identify patient characteristics associated with a > 50% increase in UOP. A total of 35 patients received NES in addition to loop diuretics. Half of the patients were in the CCU with invasive hemodynamic monitoring and the majority were receiving inotrope and continuous loop diuretic infusions prior to NES initiation. The patient cohort had a mean EF of 25 ± 14%, BNP of 2879 ± 2900 pg/mL, and SCr of 2.3 ± 1 mg/dL. The average LOS was 30 ± 25 days and in-hospital mortality was 23%. NES was initiated 95 ± 20 hr from loop diuretic at a rate of 0.01 mcg/kg/min for an average of 62 hr. UOP significantly increased 24 hr after NES initiation (1407 (740–1863) mL v. 2580 (1450–3755) mL, $P < .001$). Additional variables collected are displayed in Figure. Predictors of NES responsiveness identified via univariate analysis which remained significant using a multivariable analysis included Na <135 mEq/L and female sex (Table 1). Nesiritide was associated with significant increase in UOP as an adjunct to loop diuretics in critically ill patients with ADHF. Female sex and low serum Na were predictors for efficacy. A prospective RCT in this patient population will be necessary to confirm these findings.

Table 1. Predictors of Nesiritide Responsiveness

Characteristic at Nesiritide Initiation	Increase UOP >50% (n = 15)	Increase UOP <50% (n = 19)	univariate *P*	multivariable *P*
Age, yr	61.6 (45,67)	64.9 (57,69)	.228	
Female Sex, n(%)	10 (52.6)	3 (20.0)	.052	.008
White Race, n(%)	12 (63.2)	11 (73.3)	.426	
Nesiritide bolus, n(%)	4 (21.1)	2 (13.3)	.672	
Nesiritide duration, hr	114.0 (62,157)	49.0 (34,69)	.011	.780
Total mg received	5.7 (3.5,10.3)	2.8 (1.5,4.9)	.015	.646
EF <40%, n(%)	15 (83.3)	13 (100)	.245	
Loop Continuous Infusion, n(%)	16 (88.9)	9 (64.3)	.195	.427
Time from Loop, hr	37.9 (8.5,74.0)	78.2 (52.3,151.4)	.089	.074
24-hr UOP, mL	823.0 (550,1664)	1600.0 (1200,2160)	.056	.120
Na <135 mEq/L, n(%)	10 (52.6)	3 (20)	.052	.008
CVP/RA	16 (8,19)	10.5 (6,18)	.463	
PASP	64 (57,70)	56.5 (51,68)	.442	
PADP	31 (28,38)	28.5 (24,34)	.382	
PCWP	29.5 (28,33)	24.5 (23,32)	.279	
SVR	1517 (1273,–)	1028 (692,1140)	.117	.078
PVR	137 (117,–)_	196 (172,249)	.381	
CI	2.5 (1.8,2.7)	2.0 (1.8,2.2)	.328	
SCr, mg/dL	2.13 (1.31,2.72)	2.06 (1.62,3.4)	.336	



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Oral Metolazone Increases Urine Output Comparable to Chlorothiazide IV as an Adjunct to Loop Diuretics in HFrEF Patients with ADHF

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Thiazide diuretics are often utilized to overcome loop diuretic resistance when treating ADHF. In addition to a large cost advantage, several pharmacokinetic advantages exist when administering oral metolazone (MT) compared to IV chlorothiazide (CT); yet many providers are reluctant to utilize an oral formulation to treat ADHF. Several studies have found no difference in efficacy between the agents, however these studies had limited patients, utilized net UOP which can be misleading if patients are intubated or fluid restricted, and included HFpEF patients which may not have comparable UOP goals to HFrEF patients. The purpose of this study was to compare the increase in 24 hr total UOP after adding MT or CT to IV loop diuretics (LD) in patients with HFrEF. This was an IRB-approved, single-center retrospective chart review. Inclusion criteria were EF ≤40% and >24 hr use of LD with recorded UOP prior to administration of MT ≥ 5 mg or CT ≥ 500 mg. Patients with dialysis, no oral or per tube medications within 24 hr, or an overlap of MT/CT therapy were excluded. Baseline characteristics and safety data were collected in addition to 24 hr UOP prior and post drug administration. A subgroup analysis of patients receiving vasopressors was conducted *a priori*. From 9/2013-8/2016, 961 patients received either MT or CT in addition to LD. Most patients were excluded for HFpEF (n = 469), < 24 hr LD or UOP

Table 1. Baseline Characteristics for HFrEF Utilizing Thiazides for ADHF with Loop Resistance

Baseline Characteristic	IV Chlorothiazide (n = 108)	Oral Metolazone (n = 60)	*P*
Age, yr	64 (54,69)	63 (54,74)	.558
Male Sex, n(%)	74 (69)	41 (68)	.98
White Race, n(%)	68 (63)	34 (57)	.621
EF, %	22 (15,30)	23 (17,30)	.293
BNP, pg/mL	1371 (830,2230)	1517 (825,3313)	.620
SCr, mg/dL	1.5 (1.0,2.1)	1.6 (1.2,2.1)	.328
cCrCl, mL/min	47 (30,68)	43 (30,61)	.390
Total UOP, mL	1693 (863,2388)	1675 (1113,2591)	.330
Net UOP, mL	-350 (±1217)	-552 (±1205)	.303
Hospital LOS, days	16 (9,28)	13 (8,32)	.502
Loop Continuous Infusion, n(%)	67 (62)	25 (42)	.011
IV Inotropes, n(%)	53 (49)	24 (40)	.258
ICU, n(%)	77 (71)	38 (63)	.287
ICU LOS, days	4 (0,10)	2 (0,8)	.088
Vasopressor, n(%)	34 (32)	16 (27)	.892
Mechanical Ventilation, n(%)	15 (14)	2 (3)	.033
APACHE II, score	12 (9,15)	10 (7,14)	.099
Inhospital Morality, n(%)	21 (19)	1 (2)	.001