



Effects of Nesiritide in Patients with Acute Decompensated Heart Failure – A Review

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ABSTRACT

Acute decompensated heart failure is a major health problem that is associated with several million hospitalizations worldwide each year. ^[1] In such patients, the predominant symptoms are dyspnea and fatigue which are associated with pulmonary venous congestion and low cardiac output. ^[2, 3] The primary goal of therapy is the rapid relief of these symptoms. Nesiritide, an intravenous (IV) form of human B-type natriuretic peptide is the first in a new pharmacologic class of drug for treatment of decompensated congestive heart failure (CHF). Nesiritide, a recombinant B - type natriuretic peptide (BNP) with vasodilatory properties, ^[4-7] was approved in United States in 2001 for its use in patients with acute heart failure due to its ability to reduce pulmonary-capillary wedge pressure and improve dyspnea. Nesiritide is also well established as an agent for improving hemodynamics in patients with acute heart failure. Compared with other agents used in treatment of acute decompensated heart failure (ADHF), nesiritide is considered to be safer than inotropic agents such as dobutamine and milrinone. The overall effects of nesiritide in patients associated with acute decompensated heart failure is reviewed.

KEY WORDS: Acute decompensated heart failure, Dobutamine, Hemodynamics, Milrinone, & Nesiritide.

INTRODUCTION

Heart failure (HF) is a major and growing public health concern, significantly impairing quality of life and reducing years of age and is a primary hospital discharge diagnosis in approximately 1 million people of all ages each year. ^[8,9] Symptomatic decompensation is the most common reason for the hospitalization of patients with congestive heart failure due to left ventricular systolic dysfunction. In such patients, the

predominant symptoms dyspnea and fatigue are associated with pulmonary venous congestion and low cardiac output. Accordingly, the primary goal of treatment, which is the rapid relief of symptoms, is usually approached with the use of intravenous diuretics, vasodilators, and positive inotropic agents to decrease cardiac filling pressures and increase cardiac output. Dobutamine is a widely used inotropic therapy for decompensated heart failure. Although

dobutamine can cause early hemodynamic and symptomatic benefits, its use is limited by potentially serious side effects such as tachycardia, hypotension, myocardial ischemia and cardiac arrhythmias. [10-13]



Fig 1: Dobutamine

Generally it has been assumed that improved hemodynamic function will result in the resolution of symptoms in patients with decompensated congestive heart failure, most studies of new drugs for this purpose have focused on hemodynamic, rather than symptomatic, end points. One of such newer drug is the Nesiritide. Intravenous infusion of nesiritide, a brain (B-type) natriuretic peptide, has beneficial hemodynamic effects in patients with decompensated congestive heart failure. Brain (B-type) natriuretic peptide is synthesized in the ventricular myocardium, where its levels increase in patients with congestive heart failure. [14,15] Systemic infusion of nesiritide, a recombinant human brain natriuretic peptide, in patients with congestive heart failure results in beneficial hemodynamic actions, including arterial and venous dilatation, enhanced sodium excretion, and suppression of the renin-angiotensin-aldosterone and sympathetic nervous systems.



Fig 2: Nesiritide

EFFECTS OF NESIRITIDE IN ACUTE DECOMPENSATED HEART FAILURE

The infusion of nesiritide in patients with decompensated congestive heart failure resulted in improvements in hemodynamic function and rapid and sustained improvements in clinical status. Many studies demonstrate that nesiritide relieves the symptoms of decompensated congestive heart failure. When compared with standard therapy consisting primarily of dobutamine or milrinone. [16] Nesiritide causes a dose-related decrease in pulmonary-capillary wedge pressure. This effect was associated with a decrease in systemic vascular resistance and an increase in the cardiac index. Since nesiritide exerts no direct, positive inotropic action on the myocardium, the increase in cardiac output presumably reflects a reduction in left ventricular after load. [17] After six hours, the decrease in systemic vascular resistance was associated with mean decreases in systolic blood pressure. The decrease in blood pressure was not associated with reflex tachycardia or an increase in plasma norepinephrine levels. [18, 19] The observations made from various studies suggest that nesiritide may be helpful in the clinical management of fluid overload in patients with congestive heart failure. The most common adverse effect of nesiritide is dose-dependent hypotension, which is usually asymptomatic or associated with only mild symptoms. [20] The salutary clinical and hemodynamic profile of nesiritide and the relative absence of adverse effects associated with it circumvent several of these limitations.

EFFECTS OF NESIRITIDE ON RENAL FUNCTION

One of the main challenges in the treatment of acute decompensated heart failure (ADHF) is worsened renal function. Renal dysfunction independently predicts a worse outcome in heart failure in general and ADHF in particular. Renal dysfunction is a strong predictor of long-term risk in cardiovascular health as well as worsening of clinical outcome during hospitalization. [20-22]

Although the primary mechanism of action of nesiritide is systemic and pulmonary vasodilator, it has multiple effects on the kidneys, including promoting natriuretic, diuresis, and inhibiting the renin-angiotensin aldosterone axis.^[23-25]

Patients taking nesiritide do not develop significantly lower systolic and diastolic blood pressure, despite this lower blood pressure, patients on nesiritide did not develop worsened renal dysfunction. A possible reason may be the balance of “direct” and “indirect” effects of natriuretic peptides on renal function.^[24] Direct effects of natriuretic peptides serve to increase GFR by relaxing renal mesangial cells, dilating the afferent renal arteriole, and constricting the efferent renal arteriole; indirect effects serve to decrease GFR by inhibiting the renin-angiotensin-aldosterone and sympathetic axes and by lowering systemic blood pressures and circulating blood volume. It is likely the balance of these direct and indirect effects that causes GFR to increase, decrease, or stay the same in individual patients.^[25] Most of the studies have reported that 28% of patients developed worsening renal function during heart failure hospitalization, which they defined as an increase in serum creatinine of 0.3 mg/dL. Patients with worsening renal function were at increased risk of death.^[26] Further studies have also found the direct association between duration of nesiritide infusion and a rise in Serum Creatinine (SCr) or Blood urea nitrogen (BUN) in patients with ADHF. Worsening of renal function was significantly associated with duration of infusion 24 hours or more compared with less than 24 hours. Additionally, the incidence of SCr and BUN elevations was found to be highest in the 36 hour or more infusion group compared with the groups with shorter infusion duration. Shorter duration of infusion (<24 h) was not found to be associated with significant elevations of SCr and BUN, compared with longer infusion duration. Nesiritide infusion of 24 hours or more is associated with an increased risk of worsening surrogate markers of renal function in patients

with ADHF compared with infusions of less than 24 hours.^[27]

CONCLUSION

Nesiritide is widely used, largely because of its prompt improvement of pulmonary capillary wedge pressure and symptoms.^[28] In the current analysis of data rates of in-hospital mortality in patients treated with nesiritide were similar to those in patients treated with nitroglycerin, and nesiritide or nitroglycerin were associated with a significant survival benefit compared with either dobutamine or milrinone.^[29] These mortality data support the use of nitroglycerin or nesiritide rather than positive inotropic agents in the management of patients with ADHF who require IV vasoactive therapy. Positive inotropic agents should be considered only in patients who are refractory to treatment with vasodilators or nesiritide or in patients in impending cardiogenic shock. We therefore suggest that nesiritide would be a valuable addition to the initial treatment of patients admitted to the hospital for compensated congestive heart failure.^[30]

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