Double-Blind, Placebo-Controlled, Multicenter Acute Study of Clinical Effectiveness of Nesiritide in Subjects With Decompensated Heart Failure

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Background

Nesiritide, a recombinant human B-type natriuretic peptide, is approved in the United States for improvement in dyspnea and reduction in pulmonary capillary wedge pressure in patients with acute heart failure. Prior meta-analyses have raised questions with regard to renal toxicity and mortality.

Methods

In a multi-center, double-blinded trial, 7,141 patients hospitalized with acute decompensated heart failure were randomly allocated to receive either intravenous nesiritide or placebo for 24 to 168 hours in addition to standard care. Co-primary endpoints were change in dyspnea at 6 and 24 hours as measured by a 7-point Likert scale, and heart failure rehospitalization or death within 30 days.

Results

Patients randomized to nesiritide reported improved dyspnea at 6 (P=0.03) and 24 hours (P=0.007) more frequently compared with placebo, but the pre-specified level for significance (P≤0.005 for both or P≤0.0025 for either) was not met. The rates of heart failure rehospitalization and all-cause mortality within 30 days were 9.4% in the nesiritide group and 10.1% in the placebo group (difference -0.7%; 95% CI -2.1% to 0.7%; P=0.31). The rates of 30-day all-cause mortality (nesiritide 3.6%, placebo 4.0% [difference -0.4%; 95% CI -1.3% to 0.5%] and worsening renal function as defined by >25% decrease in estimated glomerular filtration rate (nesiritide 31.4%, placebo 29.5%; OR=1.09, 95% CI 0.98-1.21, P=0.11) were not significantly different.

Conclusions

Nesiritide did not reduce death or heart failure rehospitalization in acute decompensated heart failure patients at 30 days. Nesiritide's effects on dyspnea were small and did not meet prespecified criteria for statistical significance at 6 and 24 hours. Importantly, nesiritide did not increase mortality or worsen renal dysfunction.

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