Effect of nesiritide versus milrinone in the treatment of acute decompensated heart failure

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Nesiritide was compared with milrinone in the treatment of acute decompensated heart failure (ADHF). Nesiritide was administered as an intravenous (IV) bolus of 2 microg/kg followed by a fixed dose by IV infusion of 0.01 microg/kg per minute. Milrinone was administered as an IV infusion at an average rate of 0.4 microg/kg per minute.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adults admitted to a hospital cardiology service with a diagnosis of heart failure. Patients were excluded from the study of adherence to the nesiritide protocol if they had signs of low cardiac output syndrome, a systolic blood pressure less than 90 mm Hg, or cardiogenic shock. Patients were included in the comparative study if they received either milrinone or nesiritide to treat ADHF during hospitalisation, but were excluded if they had received therapy inconsistent with ADHF.

Setting
The setting was tertiary care. The economic study was carried out in Kentucky, USA.

Dates to which data relate
The effectiveness and resource use data were collected from September 2001 to March 2002. The price year was not reported.

Source of effectiveness data
The evidence for the final outcomes was derived from a single study.

Link between effectiveness and cost data
The link between the effectiveness and cost data was not stated. The effectiveness data were derived from patients who had been identified from the hospital(s cost-accounting database. It is likely that the cost data were gathered from the same source.

Study sample
No power calculations were reported. Investigators compiled a database of cases from the hospital’s accounting records, cross-referenced with pharmacy records, which met the study inclusion criteria for the study period. All 130 patients
who were treated with nesiritide in the study period were assessed for compliance with the protocol. For the comparative study, 55 patients met the inclusion criteria. Of these, 29 received nesiritide and 26 received milrinone. Physician preference dictated which drug a patient received.

**Study design**
The comparative study used a retrospective cohort design and was conducted in a single centre. Patient data were collected for 30 days following discharge.

**Analysis of effectiveness**
The basis of the analysis was treatment completers only. Adherence to the nesiritide protocol was based on administration of IV diuretics prior to nesiritide and the need to the increase the dose of nesiritide. For the comparative study, the primary health outcomes were overall hospital length of stay (LOS), intensive care unit (ICU) LOS and readmission within 30 days of discharge for any cause. The authors did not state whether any patients were excluded because of incomplete data. At the start of the trial, the group were shown to be comparable in terms of mean age, weight and haemodynamic data, but the nesiritide group had significantly higher levels of serum creatinine.

**Effectiveness results**
IV diuretics were administered to 93% of patients prior to nesiritide. The dose of nesiritide was increased for 3.3% of the patients.

The total hospital LOS was not significantly different between the two groups. The average LOS was 7.0 (+/- 0.84) days for patients treated with nesiritide and 8.2 (+/- 0.59) days for those treated with milrinone, (p=0.328).

The average LOS in the ICU was significantly shorter in the nesiritide group (3.9 +/- 0.39 days) than in the milrinone group (5.9 +/- 0.52 days), (p=0.007).

The percentage of patients readmitted within 30 days of discharge (for any cause) was not significantly between the two groups, 16% for nesiritide versus 28% for milrinone, (p=0.306).

**Clinical conclusions**
The authors concluded that adherence to the nesiritide protocol was within the hospital's limits. A shorter ICU stay and a trend towards decreased overall LOS and readmission rates were observed in the nesiritide group.

**Measure of benefits used in the economic analysis**
The authors did not derive a summary measure of benefit. In effect, a cost-consequences analysis was performed.

**Direct costs**
The costs and resource use were not reported separately. Only the direct costs to the hospital were included in the analysis. The costs reported were for hospital stay (including bed cost and floor supplies) and drug therapy (nesiritide and milrinone). The source of the cost data was not stated, but it seems likely that the data were gathered from the hospital's cost-accounting database. It was unclear whether hospital costs or charges were reported. The drug cost was based on the average wholesale price. For milrinone, the costs were calculated using generic drug pricing. Discounting was not relevant as the cost data covered less than one year. The average costs were reported. The price year was not reported.

**Statistical analysis of costs**
The cost data were deterministic. No statistical analysis of the costs was reported.
Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was undertaken.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
For the nesiritide group, the total mean cost was $4,155. Of this, $3,409 was for hospital stay and $746 was for the drug.

For the milrinone group, the total mean cost was $4,553. Of this, $4,273 was for hospital stay and $280 was for the drug.

Overall the cost of therapy was $398 less per patient receiving nesiritide.

The cost of adverse effects was not addressed in the study.

Synthesis of costs and benefits
Not applicable.

Authors' conclusions
Using nesiritide with a fixed-dose approach was safe and effective and, with proper monitoring, it could be initiated and administered outside the intensive care unit (ICU). Although the cost of using nesiritide was greater than using milrinone, nesiritide was associated with a lower overall cost. This was because of the shorter ICU stay, and a trend towards a lower overall hospital length of stay (LOS) and decreased readmission rates among patients with acute decompensated heart failure (ADHF).

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used. Milrinone was an approved treatment for moderate to severe exacerbation of heart failure, and was used in the practice setting. You should decide if the use of milrinone represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a retrospective cohort design which, as the authors noted, is associated with some limitations given the study question. In particular, there is the risk of confounding by other patient co-morbidities, baseline characteristics, disease severity, or therapies that were not considered for these patients. The study referred to patients with ADHF, but it was not clear whether the study sample was representative of the study population because insufficient details of the patients were provided. The patient groups were shown to be comparable at analysis in all but one measure. However, it should be noted that the comparison was limited to mean age, weight, serum creatinine levels and haemodynamic data. The retrospective nature of the study represents a limitation to its internal validity. A statistical analysis was performed on each of the end points. No power calculation was reported, thus it is not possible to ascertain
whether the results obtained were due to the intervention or to chance.

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of health benefit. In effect, a cost-consequences analysis was performed.

**Validity of estimate of costs**
The cost analysis was performed from the perspective of a hospital. As such, it appears that all the relevant categories of costs have been included in the analysis. Some relevant costs were omitted from the analysis, for example, the costs of other drugs or procedures undertaken. It was unclear whether the omission of such costs would have affected the authors' conclusions. The costs and the quantities were not reported separately, thus limiting the reproducibility of the study in other settings. The authors reported measures of variance and the results of a statistical analysis of LOS and hospital readmission data, but did not report such details or any statistical analysis of the prices. This introduces possible uncertainty into the results. Discounting was not applied, which was appropriate given that the cost data covered less than one year. It was unclear whether hospital costs or charges were reported. Drug charges were based on the average wholesale price. The price year was not reported.

**Other issues**
The authors made limited comparisons of their findings with those from other studies and noted the lack of data comparing the two drugs. The issue of the generalisability of the results to other settings was not directly addressed. The authors do not appear to have presented their results selectively. The authors did not report any further limitations to their study.

**Implications of the study**
The authors noted the potential of new therapies to create considerable annual cost-savings in this large patient group. However, their findings need to be confirmed by large, prospective randomised trials that concurrently compare the safety and efficacy of nesiritide and milrinone in the treatment of patients with ADHF.

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