The use of B-type natriuretic peptide in the management of patients with diabetes and acute dyspnoea

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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
The study examined the measurement of B-type natriuretic peptide (BNP) levels for the management of patients with diabetes presenting with acute dyspnoea. BNP is a cardiac marker. The results of BNP measurement were integrated with other clinical results in order to decide on patient management. To differentiate heart failure from other causes of dyspnoea, two BNP cut-off levels were considered (100 and 500 pg/mL). In patients with a BNP level below 100 pg/mL, heart failure was considered unlikely and alternative causes of dyspnoea were investigated. In patients with a BNP level above 500 pg/mL, heart failure was considered likely and therapy was recommended. For patients with BNP levels between 100 and 500 pg/mL, the protocol recommended clinical judgement and possible further diagnostic testing.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population of the BASEL trial comprised patients with shortness of breath as the primary complaint and no obvious traumatic cause of dyspnoea. Patients with severe renal disease (serum creatinine > 250 micromol/L), patients in cardiogenic shock, and patients who requested an early transfer to another hospital were excluded. The current study focused on the sub-group of patients with diabetes, which was defined as a known history of diabetes currently being treated with diet, oral glucose-lowering agents, or insulin.

Setting
The setting was an ED. The economic study was carried out in Switzerland.

Dates to which data relate
The effectiveness and resource use data were gathered from May 2001 to April 2002. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness analysis.
Study sample
Of the 665 patients initially screened, 213 were ineligible or did not consent to participate. Therefore, a total of 452 patients were enrolled in the BASEL trial, of which 225 were in the BNP group and 227 in the control group. In the current sub-study, there were 47 patients (64% men) in the BNP group and 56 patients (64% men) in the control group. The mean age was 72 (+/- 10) years in the BNP group and 73 (+/- 11) years in the control group. Diabetic patients included in the current study were comparable with non-diabetic patients in terms of their age and gender, but differed in other respects (cardiovascular and renal disease, and haemoglobin, albumin, serum creatinine and BNP levels). Other details on sample selection were not reported. The use of power calculations was not stated.

Study design
The BASEL study was a prospective, randomised single-blind trial that was carried out in the ED of the University Hospital in Basel, Switzerland. Randomisation was based on a computer-generated sequence without stratification. The patients were followed for 30 days after their initial presentation to the ED. No patient was lost to the follow-up assessment. Physicians who were not involved in patient care and were blinded to the assigned group evaluated the clinical outcomes.

Analysis of effectiveness
The analysis of the clinical study was conducted on an intention to treat basis. The primary outcome measure was time to discharge, which was defined as the time interval from presentation to the ED to hospital discharge. Other clinical end points were time to treatment, hospital admissions, in-hospital mortality, 30-day in-hospital days, and 30-day mortality. The study groups were well matched at baseline in terms of their clinical and demographic factors.

Effectiveness results
The median time to discharge was 13 days (interquartile range, IQR: 8 to 22) in the control and 9 days (IQR: 2 to 16) in the BNP group, (p=0.016).

The median time to treatment was 71 minutes (IQR: 17 to 207) in the control group and 61 minutes (IQR: 13 to 133) in the BNP group, (p=0.151).

The rate of hospital admissions was 95% in the control group and 81% in the BNP group, (p=0.036).

The rate of in-hospital mortality was 7% in the control group and 4% in the BNP group, (p=0.686).

The median number of 30-day in-hospital days was 16 (IQR: 6 to 24) in the control group and 9 (IQR: 2 to 19) in the BNP group, (p=0.008).

The 30-day mortality was 9% in the control group and 6% in the BNP group, (p=0.724).

The authors stated that similar benefits were observed in non-diabetic patients.

Clinical conclusions
The effectiveness analysis showed that BNP patients were discharged faster, had a lower rate of hospital admission, and spent fewer days in hospital than patients in the control group.

Measure of benefits used in the economic analysis
The health outcomes were left disaggregated and no summary benefit measure was used in the economic analysis. In effect, a cost-consequences analysis was carried out.

Direct costs
The perspective chosen for the analysis of the costs was not explicitly stated, but only hospital costs were considered. A detailed breakdown of the cost items was not provided and the unit costs were not presented separately from the quantities of resources used. Only the unit cost of a BNP measurement was given. Resource consumption was estimated from the sample of patients included in the clinical trial. The costs were obtained from hospital charges collected at the authors’ institution for patients with general insurance living in Basel. Discounting was not relevant since the costs per patient were incurred during a short time period. The price year was not reported.

**Statistical analysis of costs**
Standard analyses of were carried out to test the statistical significance of cost-differences.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were not carried out.

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

**Cost results**
The initial treatment costs were $5,940 (IQR: 3,641 to 10,371) in the control group and $5,538 (IQR: 1,200 to 8,673) in the BNP group, (p=0.093).

The 30-day treatment costs were $7,420 (IQR: 4,194 to 11,966) in the control group and $5,705 (IQR: 2,285 to 9,137) in the BNP group, (p=0.036).

**Synthesis of costs and benefits**
A synthesis of the costs and benefits was not relevant as a cost-consequences analysis was carried out.

**Authors’ conclusions**
B-type natriuretic protein (BNP) measurement in the emergence department (ED) used in conjunction with other clinical information improved the management of diabetic patients presenting with acute dyspnoea, thus reducing time to discharge, hospital days, and total treatment costs in comparison with standard care.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear as patients in the control group were managed according to clinical practice guidelines. Details of the measurement of BNP were accurately described. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness evidence came from a clinical trial, which was appropriate for the study question. Since the main trial was published in a previous study, limited information on the design and other aspects of the current study were
The method of randomisation was described, but few details of the method of sample selection were reported. The use of power calculations was not stated. The study groups were well matched at baseline, although randomisation was not stratified for diabetes. This enhances the robustness of the comparison. Statistical analyses were carried out to test the significance of differences between the groups. The length of follow-up, although short, was appropriate. The evidence came from a single centre, thus caution will be required when extrapolating the results of the analysis to other settings. Given the random allocation of patients to the study groups and the single-blinded design, the impact of confounding and bias should have been limited. The use of intention to treat in the analysis of the clinical end points improved the internal validity of the study.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
Few details of the cost analysis were provided. The perspective of the study appears to have been that of the hospital, although this was not explicitly stated. A breakdown of the cost items was not provided and the unit costs and quantities of resources used were not presented separately. This limits the possibility of replicating the analysis in other settings. The cost estimates were specific to the study setting. The impact of using alternative cost estimates was not investigated. Statistical tests were carried out but only to assess the significance of the cost comparison. The price year was not reported, which will make reflation exercises in other time periods difficult.

Other issues
The authors stated that their findings corroborated the results from previous research. However, explicit comparisons were not made. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not carried out. Therefore, the external validity of the analysis is low. The authors also stated that the study sample included in the BASEL study was highly representative of the elderly diabetic population currently presenting to the ED in the USA and Europe.

Implications of the study
The study results support the use of BNP measurement in the assessment of diabetic patients presenting with acute dyspnoea. The authors suggested that future studies should evaluate whether improvement in patient management associated with the rapid BNP measurement can reduce mortality.

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