Levalbuterol compared to racemic albuterol: efficacy and outcomes in patients hospitalized with COPD or asthma

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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 use of racemic albuterol (RA) versus levalbuterol (LEV) for the inpatient treatment of patients with chronic obstructive pulmonary disease (COPD) or asthma. The patients in the RA group were treated with a target care path of 2.5 mg every 4 hours and as medically necessary. The patients in the LEV group were treated with a target care path of 1.25 mg every 8 hours and as medically necessary.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adults hospitalised with COPD or asthma. Patients with concomitant diagnoses of cognitive disturbance or cancer were excluded.

Setting
The setting was secondary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered from July to December 1998 for the RA group, and from July to December 1998 for the LEV group. The price year could have been 1999.

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

Link between effectiveness and cost data
The costing was conducted retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations were not considered necessary due to the retrospective chart review. A sample of 231 patients identified in two seasonally matched periods was considered. All eligible patients were considered in order to avoid any bias. There were 125 patients in the RA group and 106 patients in the LEV group. The patients in the RA group had a mean age of 57.1 (+/- 21.5) years, 43.2% were men and 71.2% were white. Asthma was diagnosed in 28% and COPD in 72%. The patients in the LEV group had a mean age of 58.2 (+/- 16.1) years, 40.6% were men and 67.9% were...
white. The diagnosis was asthma in 17.9% and COPD in 82.1%.

**Study design**
This was a retrospective comparative study with historical controls that was conducted at a single centre, the Halifax Regional Hospital in Halifax County, VA. The patients were identified through a retrospective chart review. The patients were followed for 30 days after hospital discharge. No patient was lost to follow-up as complete patient data were considered.

**Analysis of effectiveness**
All the patients included in the initial study sample were accounted for in the effectiveness analysis. The primary outcome measure was the number of nebuliser treatments required in each group. The secondary outcomes were:

- pulmonary function, assessed using the forced expiratory volume in one second (FEV1);
- the use of adjuvant respiratory therapy with ipratropium bromide;
- the percentage of patients requiring rescue nebulisation for the treatment of acute exacerbations;
- the length of stay (LOS);
- discharge to home; and
- the rate of readmission within 30 days.

The study groups appear to have been comparable at baseline in terms of the demographic and clinical characteristics. A regression analysis was used to determine the impact of potential confounding factors (e.g. baseline FEV1, use of ipratropium bromide and diagnosis) on LOS and hospital readmissions.

**Effectiveness results**
The average number of nebuliser treatments required was 19 (+/- 12.7) in the LEV group and 30.8 (+/- 24) in the RA group, (p<0.001). LEV resulted in a 38% reduction in nebuliser treatments per hospital stay. The differences were even higher among asthma patients (14.1 +/- 9.2 versus 30 +/- 23.6; p<0.002).

The average number of days of nebuliser treatment was 3.9 (+/- 2.3) in the LEV group and 5.5 (+/- 4.3) in the RA group, (p<0.001). LEV resulted in a 29% reduction in days of nebuliser treatment. Again, the difference was even greater in the sub-group of asthma patients (2.6 +/- 1.2 days versus 4.6 +/- 3.7 days; p<0.008; 43% reduction).

The days of adjuvant respiratory therapy with ipratropium bromide were 2 (+/- 2.6) in the LEV group and 4.2 (+/- 4.3) in the RA group, (p<0.001).

The number of treatments with ipratropium bromide was 9.4 (+/- 11.5) in the LEV group versus 23.2 (+/- 25.1) in the RA group, (p<0.001).

The percentage of patients requiring rescue nebulisation for the treatment of acute exacerbations was 13.6% in the LEV group and 16.5% in the RA group. The difference was not statistically significant.

In the sub-group of asthma patients, no statistically significant differences were found in LOS (3.3 +/- 1.6 days with LEV versus 4.5 +/- 3.6 days with RA), discharge to home (94.7% versus 100%), and rate of readmission within 30 days (5.3% versus 0%).

In the sub-group of COPD patients, no statistically significant differences were found in LOS (5.1 +/- 3 days with LEV versus 6.1 +/- 4.4 days with RA) and discharge to home (96.6% versus 90%). However, the rate of readmission within 30 days was significantly lower in the LEV group (5.8%) than in the RA group (23%), (p=0.0012).
No statistically significant differences between the groups were observed in terms of pulmonary function.

The regression analysis showed that, after controlling for some baseline factors, LEV was associated with a 0.91-day saving in LOS, \( (p=0.015) \), and a 67% decrease in the likelihood of hospital readmission within 30 days of discharge \( (\text{odds ratio } 0.33; 95\% \text{ confidence interval: } 0.11 - 1.03; p=0.06) \).

**Clinical conclusions**
The effectiveness analysis showed that the use of LEV in place of RA led to a significant reduction in hospital stay and use of nebuliser therapy. A trend toward fewer hospital admissions postdischarge was also observed.

**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 conducted.

**Direct costs**
Discounting was not relevant since the costs were incurred during a short time. The unit costs and the quantities of resources used were not presented separately. The health services included in the economic evaluation were respiratory therapy, in-hospital respiratory prescription drugs, and length of hospitalisation. The cost/resource boundary of the study was that of the third-party payer. Resource use was estimated using actual patient-level data, which were derived from the same sample of patients as that used in the effectiveness analysis. The drug costs came from average wholesale prices, while the hospital costs were estimated from Medicare reimbursement rates. The price year appears to have been 1999.

**Statistical analysis of costs**
Differences in the hospital costs were assessed using the Mann-Whitney test. A regression analysis was conducted to identify potential independent determinants of the costs, which were log-transformed because of their non-normal distribution.

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

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were not conducted.

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

**Cost results**
The total per patient costs of nebulisation therapy were $61 (+/- 43) with LEV and $112 (+/- 101) with RA, \( (p<0.001) \).

Similar results were observed in the sub-groups of COPD and asthma patients.

For asthma patients, the total hospital costs per patient were $1,856 (+/- 931) with LEV and $2,503 (+/- 1,994) with
RA. The corresponding costs for COPD patients were $2,952 (+/- 2,209) with LEV and $3,506 (+/- 2,908) with RA. The costs incurred by patients treated with LEV were 26% (asthma patients) and 16% (COPD patients) less than for those treated with RA.

These differences did not reach statistical significance.

When controlling for some baseline factors, the regression analysis showed that LEV was associated with $556 savings in total costs, (p=0.013).

Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant since, in effect, a cost-consequences analysis was conducted.

Authors’ conclusions
The use of levalbuterol (LEV) and racemic albuterol (RA) for the treatment of hospitalised patients with chronic obstructive pulmonary disease (COPD) or asthma resulted in equivalent improvements in pulmonary function. However, the use of LEV led to reductions in hospital stay and nebuliser treatments. A trend towards lower costs and fewer readmissions was also observed.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. RA represented standard care for a long time, while LEV was considered an alternative treatment because of the side effects associated with RA. The authors noted that the two drugs represented standard care at their institution in the two time periods considered (RA in 1998 and LEV in 1999). You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on a review of patient charts. This design has some limitations associated with its retrospective nature and the impact of bias. Further, the two groups were identified in two different timeframes. The authors attempted to reduce the limitations of the study in several ways. First, the same seasonal period was considered. Second, all eligible patients identified in the two periods were considered. Third, regression analyses, to control for the impact of potential confounding, were conducted and adjusted results were presented, although information on some relevant variables was unavailable. In addition, the study groups were quite comparable at baseline, despite the fact that no random allocation procedure was used. Since the study groups were not studied concurrently, time-related confounding factors could have affected the results of the analysis. However, the authors noted that there were no major changes in treatment protocols for asthma and COPD patients, and the attending pulmonologists were the same during the whole study period.

Power calculations were not conducted and no justification for the choice of sample size was provided. Power calculations were not considered necessary for a retrospective review, but the study could have been underpowered for some outcomes. The lack of blinding of the outcome assessment represents a further limitation to the validity of the study. The study sample appears to have been representative of the patient population as all eligible patients were included. Sub-group analyses were also conducted for some outcome measures. The authors stressed that this was a study based on real-world treatment patterns, as the chart review reflected actual choices of care.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because, in effect, a cost-consequences analysis was conducted.

Validity of estimate of costs
The perspective of the study was not explicitly stated, but it appears to have been that of the third-party payer. Accordingly, all the relevant categories of costs were included in the analysis. The sources of data were reported and a
breakdown of the items was provided. However, information on resource use and the unit costs were not presented separately. This limits the possibility of replicating the study in other settings. Statistical tests were used when the costs were compared, and a regression analysis was conducted to assess the impact of confounding factors. The price year was not clearly reported but it could have been 1999. This will facilitate reflation exercises in other settings. The authors noted that reimbursement rates were generally accepted as proxies for costs, and they have the advantage of being standard national values. Differences in the costs did not reach statistical significance, despite substantial savings being observed with LEV over RA. This could be explained by the study being underpowered to detect significant differences in the economic results.

Other issues
The authors made only a few comparisons of their findings with those from other studies and only clinical aspects were considered. The authors acknowledged that the evidence came from a single study, which reduces the generalisability of the study results to other settings. The study involved adults hospitalised with asthma or COPD, and this was reflected in the authors' conclusions. Some limitations of the study were noted. These have been highlighted elsewhere in this commentary.

Implications of the study
The study results supported the use of LEV as first-line therapy for hospitalised adults with COPD or asthma. Future studies should investigate the reasons for the differences in hospital readmission rates between the groups.

Source of funding
None stated.

Bibliographic details

PubMedID
12527613

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adrenergic beta-Agonists /therapeutic use; Albuterol /therapeutic use; Asthma /drug therapy; Female; Hospitalization; Humans; Male; Middle Aged; Pulmonary Disease, Chronic Obstructive /drug therapy; Retrospective Studies; Treatment Outcome

AccessionNumber
22003000291

Date bibliographic record published
31/01/2005
Date abstract record published
31/01/2005