Pharmacoeconomic evaluation of a combination of ipratropium plus albuterol compared with ipratropium alone and albuterol alone in COPD


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
Pharmaceutical technology: ipratropium combined with albuterol in a single inhalational canister (Combivent; Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, USA).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with COPD. Further details are given in the study sample field below.

Setting
Hospital. The economic study was performed in New Orleans, USA.

Dates to which data relate
The effectiveness and resource data were collected in 1994. 1998 prices were used.

Source of effectiveness data
Effectiveness data were based on a single study (based on two multi-centre safety and outcome trials).

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
1,067 patients were randomised to albuterol alone (n=347), ipratropium alone (n=362) and albuterol plus ipratropium (n=358). A power calculation was used to determine the sample size. Patients included in the trials had a diagnosis of COPD, were aged over 40 years of age and had a history of smoking more than 9 packs of cigarettes per year. Excluded patients included those with asthma, allergic rhinitis, atrophy, an oesinophil count > 500 cubic mm or who were taking cromolyn or more than 10 mg prednisone daily.

Study design
This was a double-blind, randomised controlled trial designed to compare bronchodilating efficacy and safety of the
inhalation aerosol form of ipratropium, albuterol and combination over an 85-day treatment period. The studies shared a common study design and protocol and were based on multi-centre participation. The two trials were part of the same clinical development programme of the drug manufacturer.

**Analysis of effectiveness**
The analysis appears to be based on the intention to treat principle. The clinical outcomes assessed included changes in forced expiratory volume (FEV1) and disease exacerbation (defined as worsening of COPD-related symptoms (i.e. cough, wheezing, dyspnea, sputum production, etc for 3 consecutive days or longer).

**Effectiveness results**
The improvement in forced expiratory volume in one second (FEV1) and the area under the FEV1 response time curve from time 0 - 4 hours (FEV1 AUC 0-4) was significantly greater for the combination of albuterol plus ipratropium than either albuterol or ipratropium alone on all test days.

The mean (FEV1 AUC 0-4) for albuterol, ipratropium and ipratropium plus albuterol was:

- 0.78, 0.63, 1.01 (day 1);
- 0.66, 0.68, 0.89 (day 29);
- 0.64, 0.63, 0.88 (day 57) and
- 0.66, 0.66, 0.89 (day 85).

The inclusion of ipratropium in the pharmacologic treatment regimen was also associated with a lower rate of exacerbations. 62% of patients receiving albuterol experienced exacerbations compared to 45% receiving ipratropium and 44% receiving ipratropium plus albuterol, (p < 0.05). Albuterol patients had 770 patient days of exacerbations compared to 504 patient days for ipratropium patients and 554 for combination patients, (p < 0.05). Increased exacerbations in the albuterol only group were associated with a greater total number of hospital days (103 days) than albuterol plus ipratropium (46 days) and ipratropium alone (20 days), (p<0.05) and greater antibiotic and corticosteroid use.

**Clinical conclusions**
The inclusion of ipratropium in a pharmacological treatment regimen is associated with a lower rate of exacerbations.

**Measure of benefits used in the economic analysis**
Changes in forced expiratory volume (FEV1) and disease exacerbation were the benefit measures.

**Direct costs**
Quantities and costs were analysed separately. Only health service costs were considered: number and length of acute pulmonary exacerbations of COPD, the number and length of hospitalisations due to exacerbations, and the number of patient days of increased doses or additions of corticosteroids and antibiotics. The basis for the acquisition costs of the drugs was the 1998 PC-Price Chek average wholesale price. The price date was 1998.

**Statistical analysis of costs**
A statistical analysis (analysis of covariance) was performed.

**Indirect Costs**
Not considered.
Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
The mean (FEV1 AUC 0-4) for albuterol, ipratropium and ipratropium plus albuterol was

0.78, 0.63, 1.01 (day 1);
0.66, 0.68, 0.89 (day 29);
0.64, 0.63, 0.88 (day 57) and
0.66, 0.66, 0.89 (day 85) respectively.

Cost results
The acquisition costs per patient for ipratropium alone were $94, for ipratropium plus albuterol were $106 and for albuterol alone. The costs of hospitalisation were estimated to be $600/day. However, the mean total per patient costs over the 85-day follow-up for ipratropium alone were $156 (+/- 69), for ipratropium plus albuterol were $197 (+/- 84) and for albuterol alone were $269 (+/- 108). Adjusted total costs were also presented taking into account the percentage of combined number of days both exacerbation free and hospital free. Adjusted total costs were $277 for albuterol, $159 for ipratropium and $201 for albuterol plus ipratropium.

Synthesis of costs and benefits
Ipratropium alone ($236 per mean FEV1AUC0-4) and the albuterol/ipratropium combination ($221 per mean FEV1AUC0-4) were significantly more cost-effective than albuterol alone ($408 per mean FEV1AUC0-4)(p<0.05) at day 85. Ipratropium alone and the albuterol/ipratropium combination were also more cost-effective than albuterol alone at days 1, 29 and 57.

Authors' conclusions
The authors concluded that long-term use of ipratropium alone or the combination of ipratropium plus albuterol was associated with fewer exacerbations of COPD than the use of albuterol alone. As the number of exacerbations did not differ significantly between the two treatment arms, the inclusion of ipratropium in a pharmacologic treatment regimen alters the rate of exacerbations in COPD.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used. The comparators chosen: a beta-adrenergic receptor agonist (albuterol) and quaternary ammonium anticholinergic agent (ipratropium) are commonly used regimens for the treatment of COPD. You as a user of this database, should consider whether these are appropriate comparators.

Validity of estimate of measure of benefit
The study was based on an overview of two randomised controlled trials. However, the trials only provided data for up to 85 days. The 85 day results may not be an accurate representation of effectiveness over an extended period.
Validity of estimate of costs
Adequate details were given of the sources of estimates, of resource use and prices and price date, although more information would have been useful on the nature of the hospital costs.

Other issues
The cost data may not be generalisable to other settings or countries.

Implications of the study
Lower rates of exacerbations associated with the long-term use of ipratropium or the combination of ipratropium plus albuterol leads to lower treatment costs and improved cost-effectiveness.

Source of funding
The post hoc pharmacoeconomic analysis was supported by Boehringer Ingelheim.

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