Comparison of the cost-effectiveness of budesonide and sodium cromoglycate in the management of childhood asthma in everyday clinical practice

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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
Two maintenance therapies for the management of childhood asthma were compared: budesonide and sodium cromoglycate, both recommended strategies in Sweden.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children, aged from 5 to 11 years suffering from bronchial asthma. Patients were included in the study if they were being treated with a beta2-antagonist at least 3 times per week, were awakened because of night symptoms at least once a week, and were candidates for prophylactic treatment with an inhaled glucocorticosteroid or cromoglycate. Patients were excluded if they had previously been treated with an inhaled glucocorticosteroid or sodium cromoglycate, had suffered from any serious respiratory, cardiovascular, renal, liver, or endocrine disease likely to interfere with the study, or were suffering from eczema requiring treatment with topical steroids group II or stronger on 2% or more of the body surface area.

Setting
The setting was hospital. The study was conducted at 10 secondary care centres in Sweden.

Dates to which data relate
The dates during which data on both effectiveness and resource use were collected were not reported. The price year was 1998.

Source of effectiveness data
Effectiveness data were derived from a single study.

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

Study sample
No power calculations were performed. A sample of 141 children were recruited at the study centres and participated in the study: 71 children were included in the budesonide group and 70 in the sodium cromoglycate group. Due to some
withdrawals during the run-in phase, the actual size of the two groups was 69 children (mean age: 7.57 years, range: 5 -
11 years; mean weight: 29.44 kg; 44 boys) in the budesonide group and 69 children (mean age: 6.96 years, range: 4 - 11
years; mean weight: 27.81 kg; 31 boys) in the sodium cromoglycate group.

Study design
This was a multi-centred, open-label, randomised, parallel group, clinical trial, carried out in 10 secondary care centres
in Sweden. After a period during which all patients received budesonide (200 microg), children were randomised in
balanced blocks using a computer programme through sealed coded envelopes assigned to each patient at the first visit.
The seal was broken after the completion of the run-in period when the investigator considered a patient's asthma to be
well controlled. Patients were followed for 1 year. Some missing data were reported at the end of the study period.

Analysis of effectiveness
The basis for the analysis (intention to treat or treatment completers only) was not stated. The analysis of the clinical
study was based on the comparison of the two treatment groups as defined after randomisation. However, 3 children in
the budesonide group and 5 in the sodium cromoglycate group did not provide valid data for the analysis, and it was not
clear whether these patients were included in the final analysis. The primary health outcomes were the control of
asthma and proportion of symptom-free days. The former was evaluated through specific criteria, such as daytime and
night-time asthma symptom scores, no exacerbation, rescue medication, etc. The latter was considered as the number of
days on which no beta2-antagonist was used and no day or night symptoms were experienced. The number of adverse
events was also recorded. Apart from a predominance of boys in the budesonide arm, study groups were comparable in
terms of demographics and clinical characteristics.

Effectiveness results
A total of 29 children in the sodium cromoglycate group switched to the budesonide arm of the study, mainly because
of the therapy's lack of effect, whereas the reverse situation did not occur, (p<0.001).

In children who continued on the same treatment, the percentage of those who reached asthma control was not
statistically significantly different in the study arms, although systematically higher in the group receiving budesonide.

The number of symptom-free days was similar in the two groups (76.02 +/- 25.43 days in the budesonide group and
74.63 +/- 22.24 days in the sodium cromoglycate group). However, children who switched from the sodium
cromoglycate group to the budesonide group reported a 14% increase in the number of symptom-free days after the
change (62.59 +/- 21.83 days before the change and 76.33 +/- 21.23 days after the change, (p<0.001).

The number of serious adverse events was greater in the budesonide group, but the adverse events were not related to
the treatment. Minor adverse events did not differ between the study groups.

Clinical conclusions
Although the two treatments were similar in terms of asthma control and number of symptom-free days, the therapy
based on sodium cromoglycate was less effective in that 42% of the children required switching to the budesonide
therapy.

Measure of benefits used in the economic analysis
Health outcomes were left disaggregated and no summary benefit measure was used, therefore a cost-consequences
analysis was conducted.

Direct costs
Discounting was not relevant due to the short time horizon of the study. Unit costs and quantities of resources were
reported separately. The quantity/cost boundary reflected the societal perspective adopted in the study. The direct cost
items included in the analysis were emergency visits, planned physician visits, house calls, telephone contacts with a physician, appointments with nurses, and hospital stay. The estimation of quantities was based on the resources consumed during the trial period, while the estimation of costs was mainly based on actual data obtained from official Swedish sources (such as the 1998 Swedish physicians' drug manual). Telephone contacts with a physician or other health care personnel were arbitrarily assigned a cost equivalent to 10% of a planned visit. The period during which the resource use data were gathered was not reported. The price year was 1998.

Statistical analysis of costs
Statistical analyses of total costs were conducted to test for statistical significance of the results.

Indirect Costs
Work income losses were included in the cost analysis. Discounting of indirect costs was not relevant. Unit costs and quantities of resources were reported. The indirect cost items included in the analysis were the days off work attributable to the child's asthma, days the patient was away from nursery or school, time spent by the parent/guardian in caring for the child, sleep disruption caused to the caregiver, and cost of home help related to asthma. The estimation of quantities of resources was based on actual data obtained from the trial. The estimation of work income for men and women was based on Statistics Sweden. The price year was 1998.

Currency
Swedish kroner (Sek). In December 1999, US$ 1 = Sek 1.82 and Euro 1 = Sek 8.65.

Sensitivity analysis
Two sensitivity analyses were carried out. First, hospitalisations were excluded from the analysis since they had a disproportionately large effect on the results, due to the small sample size. Second, the analysis was conducted twice in the sodium cromoglycate group considering the initial sample and the sample consisting of children who switched to the budesonide group. An ordinary least squares regression analysis was also conducted to keep constant as many as possible of the variables that could influence costs levels such as age, height, weight, sex, years with asthma, etc.

Estimated benefits used in the economic analysis
See effectiveness results above.

Cost results
There was no statistically significant difference in terms of quantities of resources used in the two groups.

In the budesonide group, costs were Sek 1,914 for asthma medication, Sek 5,237 for personnel, Sek 939 for hospitalisation, and Sek 5,151 for indirect expenses.

In the sodium cromoglycate group, costs were Sek 3,911 for asthma medication, Sek 6,586 for personnel, Sek 285 for hospitalisation, and Sek 6,653 for indirect expenses.

The cost for asthma medication was the only item which reached statistical significance.

Total annual cost per patient was Sek 13,240 in the budesonide group and Sek 17,436 in the sodium cromoglycate group. Therefore, the average annual cost per patient was Sek 4,195 (95% CI: -2,340 - 10,731) lower in the budesonide group than in the cromoglycate group. However, the difference was not statistically significant.

Excluding hospitalisations, total cost was Sek 4,849 lower in the budesonide group in comparison with the sodium cromoglycate group (95% CI: -1,083 - 10,781).

The cost for the children who remained on sodium cromoglycate during the entire study period was Sek 18,762, while
the cost for the children who switched to budesonide was Sek 15,606, mainly due to a difference in asthma drug cost of Sek 2,495, \( p<0.001 \).

The regression analysis indicated that taking study treatment into account in the model, the cost in the budesonide group was 43% lower than in the sodium cromoglycate group, \( \text{NS, } p=0.059 \).

**Synthesis of costs and benefits**
Costs and benefits were not combined due to the cost-consequences approach adopted.

**Authors' conclusions**
The authors concluded that the strategy based on budesonide was more cost-effective than that based on sodium cromoglycate in the maintenance of childhood asthma control: it was less costly (although not significantly) and resulted in no treatment switches during the 1-year study period.

**CRD COMMENTARY - Selection of comparators**
The rationale for the selection of the comparators was clear. The two strategies were selected because they represented recommended therapies in Sweden. You, as a user of this database, should assess whether they represent widely used health interventions in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness was based on a single study, whose randomised design appears to be appropriate to the study question. Furthermore, the authors stated that the design of the study was robust because it attempted to represent real-life clinical practice. Since the measurement of the treatment outcome represents a controversial issue in the case of asthma treatment, the authors discussed a set of 7 criteria to be used as a comprehensive evaluation tool. However, power calculations were not performed and no evidence was provided that the initial sample size was appropriate for the clinical study question. The authors noted that the sample size was small and data were somewhat skewed, therefore the lack of statistically significant differences between the treatment groups could have been due to lack of statistical power. In addition, the period of collection of the effectiveness evidence was not reported, an issue that could limit the internal validity of the analysis.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the economic analysis and a cost-consequences analysis was conducted. However, it would have been helpful to consider the impact of the therapies on health status through a benefit measure reflecting the quality of life of patients (and caregivers).

**Validity of estimate of costs**
The perspective adopted in the study was that of the society, for which all-relevant categories of direct and indirect costs appear to have been included in the analysis. Unit costs and quantities of resources were clearly reported as well as the price year. Appropriate currency conversions and statistical analyses of total costs and quantities were conducted. Since all costs were incurred in one year, discounting was not relevant. However, the period during which the resource use data were gathered was not reported.

**Other issues**
The issue of the generalisability of the study to other settings was not addressed and few sensitivity analyses were conducted. The authors compared their findings with those from another study, which showed that budesonide was more effective than sodium cromoglycate.
**Implications of the study**
The findings of this study suggest that budesonide should be recommended in everyday clinical practice in the management of childhood asthma.

**Source of funding**
None given.

**Bibliographic details**

**Indexing Status**
Subject indexing assigned by NLM

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