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Executive summary

Early asthma prophylaxis, natural history, skeletal development and economy (EASE): a pilot randomised controlled trial

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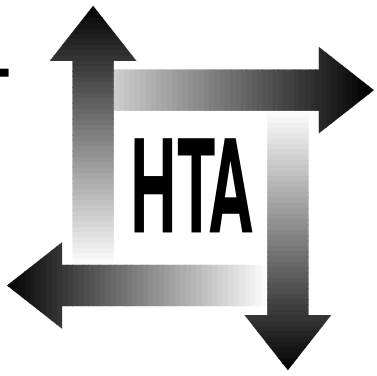

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Objectives

- To establish recruitment rates of newly presenting asthmatic children.
- To establish acceptability of study protocols.
- To pilot age-specific quality of life (QoL) assessment.
- To assess short-term (6 months) outcomes of inhaled corticosteroids (ICS) treatment.
- To refine sample size calculations for a definitive study.

Design

A randomised pragmatic longitudinal trial design was used, with no blinding or placebo, to examine early ICS introduction similar to its use in practice. Subjects were assessed at entry, 3 and 6 months.

Setting

Subjects were recruited from six general practices. Children under 6 years were assessed at the Craig Research and Investigation Unit, Royal Aberdeen Children's Hospital, or their family home, and subjects 6 years and over were assessed at their general practice.

Subjects

Children (aged 6 months–16 years) with symptoms suggestive of asthma/wheeze that had commenced no longer than 12 months before were identified retrospectively and prospectively from general practices. Subjects were also required to be naïve to prophylactic therapy with no other lung disease/ concomitant illness.

Interventions

Subjects were randomised to β_2-agonist (β_2-only group) or β_2-agonist and ICS (ICS group) for 6 months. Physicians could later prescribe ICS in controls if needed.

Main outcome measures

- Pulmonary function
- Asthma symptom diary
- Symptomatic health status questionnaire
- Caregiver's and child's QoL
- Growth
- Bone mass
- Bone turnover
- Economic issues

Results

Of over 15,000 children yielded from general practice records, 11% had symptoms suggestive of asthma/wheeze, and two-thirds of these already used ICS. Of the remaining, 141 subjects met the criterion of early asthma, and 86 were randomised. Two-thirds of those randomised were < 6 years old, the males:females ratio was 2:1, and 67% had a family history of atopy.

Physiological development

Pulmonary function did not significantly improve in the older children. Although tidal breathing measures in the pre-school children were significantly higher at 6 months in the β_2-only group, there was great variability. Incidence of wheeze and night-time cough reduced equally in both groups. Reduction of night-time symptom score and reliever use, and increase in symptom-free days were only significant in the β_2-only group. No significant differences were found in growth and bone mass between the two groups, but bone metabolism was significantly reduced at 6 months in the ICS group.

Psychological development

The caregiver's QoL questionnaire was sensitive to child symptom changes over 3 months, but absolute impact of child symptoms on their QoL varied, whereas the child-centred questionnaire was not sensitive to change.

Economics

There were no significant differences in medical consultation costs between the groups, but, as expected, prescription costs in the ICS group were higher over 6 months. Combined healthcare

costs were significantly higher for patients assigned to ICS, but there were no significant differences in any effectiveness measures between the groups.

Conclusions

Most (96%) of the proposed sample was recruited, and the low drop-out rate (8%) demonstrated acceptability of the study protocol. Most children first presenting with symptoms suggestive of asthma were < 6 years old and represented a group biased towards mild to moderate asthma, or virally induced wheeze. The caregiver's QoL questionnaire was found to better reflect a child's symptom changes than a child-centred instrument. In the short term, no adverse effects were seen on growth, but ICS treatment significantly reduced bone metabolism. Most of the young children with asthma/wheeze improved over time with β_2-agonist treatment alone, and clinical benefits of early ICS intervention amongst these children were not detected; however, there was inadequate power in this pilot study to establish this. Calculation from the outcomes indicated a trial of 300 children would be required to determine treatment effects at 90% power.

Recommendations for future research

A larger definitive study is recommended, ideally only including children with asthma and not virally induced wheeze, to confirm the pilot study results, and investigate long-term effects and cost–benefits of early ICS use in newly presenting wheezing pre-school children. In addition, it would be informative to determine the extent of ICS use in the total child population and any adverse effects of ICS on bone development that are separate from linear growth.

Publication

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NHS R&D HTA Programme

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The Standing Group on Health Technology advises on national priorities for health technology assessment. Six advisory panels assist the Standing Group in identifying and prioritising projects. These priorities are then considered by the HTA Commissioning Board supported by the National Coordinating Centre for HTA (NCCHTA).

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The views expressed in this publication are those of the authors and not necessarily those of the Standing Group, the Commissioning Board, the Panel members or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for the recommendations for policy contained herein. In particular, policy options in the area of screening will be considered by the National Screening Committee. This Committee, chaired by the Chief Medical Officer, will take into account the views expressed here, further available evidence and other relevant considerations.

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