IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Scientific evaluation of therapeutic interventions in children aged from 2 to under 5 years with bronchial obstruction[1]

Executive Summary

[1] Translation of the executive summary of the final report "Wissenschaftliche Bewertung therapeutischer Interventionen bei Kindern von 2 bis 5 Jahren mit bronchialer Obstruktion" (Version 1.0; Status: 09.03.2009). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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Executive summary

Research question

The aim of this research was to obtain findings on the benefit and harm of therapeutic interventions in children aged from 2 to under 5 years presenting symptoms of bronchial obstruction (sub-goal 1). The definitive diagnosis of bronchial asthma cannot yet be made consistently in this age group, so a broad, symptom-oriented disease definition was used. By school age, many of these children no longer have symptoms and do not develop bronchial asthma, so that the weighing of benefit and, especially, harm of interventions for these children was to be studied as sub-goal 2.

The recommendations of the asthma DMP, which is approved for children from 5 years of age, formed the basis for selecting the drug and non-drug interventions investigated.

Methods

The evaluation was based on randomized, placebo-controlled intervention studies of at least 12 weeks' duration. For this purpose, systematic database searches were carried out (in MEDLINE, EMBASE, CENTRAL, BIOSIS, in addition to CINAHL, PsycINFO, PSYNDEX for non-drug interventions). If applicable, drug interventions were studied for the indications "maintenance therapy" and "reliever therapy". An operationalization of the prescribed age range was introduced, because of the frequent imprecise reporting.

IQWiG's preliminary benefit assessment, the preliminary report, was published on the Internet and the public invited to submit written comments (written hearing). Unclear aspects of these written comments were discussed in a scientific debate and the final report was subsequently produced.

Results

14 interventions (10 drug and 4 non-drug interventions) were investigated. The drug interventions (4 were used as reliever and 6 as maintenance therapy) included 8 different treatment options.

Drug interventions

- systemic corticosteroids
- inhaled corticosteroids
- leukotriene receptor antagonists
- short-acting beta-2 agonists (SABA)
- methylxanthines
- anticholinergics
- inhaled long-acting beta-2 agonists (LABA)
- specific immunotherapy / desensitization measures

Non-drug interventions

- education and training of children and/or carers
- sports and physical activity
- psychological, psychosomatic and psychosocial care
- allergen avoidance

Out of a total of 13 280 hits, no publication could be identified for 12 of the 14 interventions investigated that matched the age group and the other inclusion and exclusion criteria, and accordingly no statement can be made on benefit and harm.

Results for sub-goal 1

A statement on benefit and harm can be made for fluticasone propionate from the inhaled corticosteroids group and to a limited extent for montelukast from the leukotriene receptor antagonists group. Both substances were investigated in the included publications for the indication "maintenance therapy"; 2 studies were identified for each of the 2 drugs. The 4 studies differed substantially with regard to the patient population, study durations and selected outcomes as well as their operationalization.

Regarding montelukast, it should be noted that in the 2 studies considered this drug was not used in accordance with German drug approval status. This means that no final statement on the indication approved in Germany can be made in the conclusion. Due to the importance of the 2 studies and to the overall sparse data for children in this age group, the studies were included in full in the report and their results presented.

Summary of results for inhaled corticosteroids and leukotriene receptor antagonists

Symptom reduction: Both inhaled fluticasone propionate and montelukast p.o. reduced the symptoms of bronchial obstruction. An absolute improvement of 5% was shown when 88 µg of fluticasone propionate was administered twice daily. The improvements achieved in the studies for montelukast (4 mg) lay between 3% and 9% (absolute values).

Use of inhaled short-acting beta-2 agonists: The need for short-acting beta-2 agonists was less when using fluticasone propionate or montelukast than when using the placebo. Due to the different operationalization of the outcome, it is only possible to make a limited comparative representation and assessment of the results.

Exacerbations (with and without emergency treatment): The absolute values and percentages given in the studies can only be compared to a limited extent, as different units of measurement were used. In the 2 fluticasone propionate studies, exacerbations occurred less frequently than with the placebo. In one montelukast study, the exacerbation rate was the pre-defined primary outcome; the difference was statistically significant. In the second montelukast study, however, the proportion of patients with at least one exacerbation did not differ significantly between the treatment groups.

Hospital stays and outpatient treatments: In separate studies, both fluticasone propionate and montelukast helped to reduce both the number of required visits to the doctor and hospitalizations. Due to differing outcome definitions, there is very little comparability between the figures.

Frequency and seriousness of adverse events: In the 2-year fluticasone propionate study there was a reduction in growth of 1.1 cm with fluticasone propionate compared to the placebo. With montelukast, there were no clinically relevant reported differences between the treatment groups. No serious adverse events occurred in any of the studies using fluticasone propionate or montelukast therapies.

Activities of daily living: In one montelukast study, absences from preschool were reported with equal frequency.

Health-related quality of life: Due to the lack of data in the studies, no statement can be made on this outcome.

Deaths related to bronchial obstruction and/or total mortality: These outcomes were only reported in one fluticasone propionate study, in which no deaths occurred.

Effects of the disease on the parents: This outcome was only reported in one montelukast study. With regard to the parents' quality of life affected by asthma, there was no statistically significant difference between the treatment groups.

Results for sub-goal 2

None of the included studies comment on the percentage of children included for whom asthma could be definitely diagnosed by their fifth birthday according to the DMP criteria. It is not possible to differentiate the children into one group who developed asthma and one group who did not.

No definite statements can therefore be made for sub-goal 2.

Conclusions

- For 12 out of 14 drug and non-drug interventions established in the DMP on asthma, no study could be identified that could provide a statement on the benefit and harm to children aged from 2 to under 5 years. For the most part, the interventions established in the asthma DMP have been insufficiently investigated in children in this age group.
- Inhaled corticosteroids have been researched in children in this age group. 88 µg administered twice daily leads to an improvement in symptoms of bronchial obstruction, measured using various parameters (e.g. asthma-free days, 24-hour asthma symptom score). The rate of exacerbations is also reduced. The absolute reductions attained are small.
- In one 2-year study using inhaled fluticasone propionate (88 µg BID), there was an average reduction in growth of 1.1 cm compared to the placebo. Other significant differences in adverse event rates were not reported in patients using fluticasone propionate therapy.
- Overall, the benefit of inhaled corticosteroids appears to be limited, particularly in children with minor symptoms. This raises the question whether the impairment in growth during longer lasting cortisone administration should be accepted here.

- On the basis of the included studies, no statement can be made on the benefit and harm of treatment with the leukotriene receptor antagonist, montelukast, according to the indication approved in Germany.
- The question as to what extent children with bronchial obstruction who do not go on to develop asthma benefit from or are harmed by early drug intervention cannot be definitively answered, as none of the studies were designed to verify the diagnosis of bronchial asthma when children reached their fifth birthday.

Keywords: Bronchial asthma, bronchial obstruction, young children, disease management programme (DMP), maintenance therapy, reliever therapy

The full report (in German) is available on www.iqwig.de/index.645.html