IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Scientific evaluation of different investigational methods used in diagnosing bronchial asthma in children aged between 2 and < 5 years[1]

Executive Summary

[1]Translation of the executive summary of the final report "Wissenschaftliche Bewertung verschiedener Untersuchungsmethoden zur Diagnosestellung eines Asthma bronchiale bei Kindern im Alter von 2 bis < 5 Jahren" (Version 1.0; Status: 20.05.2009). 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

Background

The German Joint Federal Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the reliability of asthma diagnosis in children aged between 2 and < 5 years and to assess the benefit of interventions resulting from these diagnostic procedures in this age group.

The commission comprises 3 research questions. The present report on commission V06-02C deals with the question of diagnostic accuracy and the patient-relevant benefit of different investigational methods used in diagnosing "bronchial asthma" in children in the relevant age group.

Research question

The aim of the present investigation was to scientifically evaluate the diagnostic accuracy and the patient-relevant benefit of procedures established in the German health care system for diagnosing bronchial asthma in children aged between 2 and < 5 years.

The following questions were investigated:

1. How valid and reliable (sensitivity, specificity, predictive power) are the diagnostic procedures identified by the search when compared to the reference standard?

2. How valid and reliable are the diagnostic procedures with reference to their discriminatory and predictive power, taking account of

    a) the time course and natural course of the disease,

    b) the course of the disease in comparative intervention studies in which a therapeutic benefit has been proven?

Methods

According to the research question formulated in the commission, the object of this report was the evaluation of the diagnostic accuracy of different investigational methods used in diagnosing "bronchial asthma" in children aged between 2 and < 5 years (goals 1 and 2a). In addition, the benefit of the test result to the patient was analysed in order to obtain a full appraisal of the diagnostic procedures (goal 2b).

Included in the investigation were studies on the diagnosis of children aged between 2 and < 5 years with bronchial obstruction, defined by medical diagnosis of bronchial asthma or by symptoms of obstructive respiratory tract disease. These include wheezing, dry cough and episodic dyspnoea.

Individual diagnostic measures and combinations consistent with a diagnostic algorithm were considered as diagnostic procedures. Corresponding to the commission formulation, the focus was on procedures established in Germany that are already recommended in the existing DMP for bronchial asthma or in the German CPGs and that can be applied in children aged between 2 and < 5 years.

Outcomes were established to determine diagnostic accuracy and predictive power. Clinical outcomes, such as "number and severity of symptoms", were used to assess the patient-relevant benefit.

To assess diagnostic accuracy and predictive power, Phase 2 and 3 diagnostic trials classified according to Köbberling [1] were collected. To assess the patient-relevant benefit of a diagnostic measure, a search was conducted for Phase 4 trials according to Köbberling. As such "direct evidence" is often not available, the "linked evidence" method was applied in order to indirectly derive indications on the benefit of a diagnostic measure. Consequently, by linking diagnostic studies and therapy studies, an attempt is made to derive the benefit of a diagnostic measure indirectly.

Results

Studies on diagnostic accuracy

The search and screening stages identified 6 diagnostic and cohort studies that were relevant to the project research question and another relevant cohort study was referred to during the commenting procedure. Procedures for pulmonary function tests were checked in the 2 diagnostic studies. In the 4 cohort studies, clinical indices or scores were developed based on medical history and examination data. These scores were evaluated for their ability to predict the later onset of asthma.

As no established, validated gold standard currently exists for diagnosing bronchial asthma, there is no consistent, comparable reference standard in the studies. No one procedure could be identified as being clearly superior to the other procedures. This was due, firstly, to the heterogeneity of the index tests and reference procedures and, secondly, to the often insufficient quality of the data. Particularly with regard to the calculated, predictive values, no procedure appears to be suitable for reliably establishing an "asthma" diagnosis. Furthermore, the information resulting from a negative test result is usually inadequate.

Studies on patient benefit

No randomized controlled trial could be identified from which the benefit of a diagnostic measure could have been directly derived. Strictly speaking, the "linked evidence" method could not be applied, as this would have required a uniform reference test. Using the "linked evidence" method as a basis, an attempt was made to link the identified diagnostic and cohort studies with the therapy studies identified in project V06-02B. However, in contrast to the "linked evidence", the linking should be performed via the index test, not the reference test.

Recognizable correspondence in the diagnostic criteria used could be found in the therapy studies and when compared with the diagnostic cohort studies, even though none were complete, thus not allowing direct reference. There are no diagnostic studies that allow an appraisal of the diagnostic accuracy or, more precisely, of the test strategy that was selected in the therapy studies for study inclusion.

No conclusions could be drawn concerning the clinical efficacy of the assessed diagnostic procedures. Due to the lack of a reference standard, the "linked evidence" methodology could only be applied in a rudimentary fashion.

Discussion

The evidence base for answering the research question proved itself to be of only limited robustness. Only a few relevant sources were identified, which moreover often revealed marked shortcomings in study and publication quality. The procedures for pulmonary function tests that were examined in the diagnostic studies assume the cooperation of the child, but not every child in the age group observed can manage this. In addition, these measures require special equipment, which may make a nationwide application difficult, e.g. as part of a DMP. In the 5 prospective cohort studies included, different combinations of symptoms, medical history data and information on clinical and family history were tested. It was difficult to group both them and the resultant comparison of indices and scores investigated, as other criteria were subsumed in each case. This could also explain the fluctuation range in generated values for sensitivity and specificity. An assessment of patient-relevant benefit was not possible either directly (through RCTs) or indirectly (through "linked evidence"). This is surprising given the relevance of the disease in the age group concerned and the frequency of interventions. This reveals a definite need for research.

With regard to the "linked evidence" method itself, there is no doubt that it could be applied in suitable studies. However, it should be noted that, even if all methodological requirements of the studies were met, it would still only be an indirect conclusion, whose validity has been little investigated up till now. The merging of diagnostic and therapy studies cannot replace the design of a Phase 4 trial in which the clinical efficacy of a test is directly examined. However, it may represent a useful add-on when only Phase 2 and Phase 3 trials are assessed.

Conclusions

The current evidence base for assessing nationally established investigational methods in the diagnosis of bronchial asthma in children aged from 2 to < 5 years is very small and the studies included in the analysis are characterized by shortcomings in the study and reporting quality. An evidence-based, robust recommendation for a valid, individual diagnostic instrument or an individual diagnostic method cannot be derived. Considering the data presented, no investigational procedure can be recommended as sufficiently certain, especially against the background of a possible diagnosis criterion for enrolment in a DMP.

No diagnostic and therapy studies could be linked for the purpose of "linked evidence". Based on the data available, no conclusions can be drawn on the quality of individual diagnostic procedures used in therapy studies or on the clinical efficacy of measures tested in Phase 2 diagnostic studies and cohort studies.

Keywords: bronchial asthma, children, diagnostics, disease management programme (DMP), linked evidence

The full report (in German) is available on http://www.iqwig.de/index.548.html