USEFULNESS OF BRONCHOSCOPY IN CHILDREN: CLINICAL OR RESEARCH TOOL?

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INTRODUCTION
Evaluation of children with chronic respiratory problems commonly includes blood tests, radiological analysis (thorax x-ray and occasionally high resolution computerized tomography) and lung function tests while bronchoscopy with or without endobronchial biopsy is rarely needed in diagnostics. When symptoms imply structural abnormalities, bronchoscopy provides the only reliable means to examine the anatomy of the larynx and main bronchi. Moreover, analysis of endobronchial biopsies and bronchoalveolar lavage (BAL) can provide information about inflammation and infection. The quality (size and composition) of endobronchial biopsies is of uttermost importance. It has been shown that endobronchial biopsies obtained by rigid bronchoscopy are larger in size but those obtained from fiberoptic bronchoscopy are similarly valuable (1).

SAFETY OF BRONCHOSCOPY AND ENDOBRONCHIAL BIOPSY
Although diagnostic bronchoscopy is an invasive procedure, it is safe in hands of an experienced bronchoscopist. Rigid bronchoscopy is as safe as flexible, providing that the operator has appropriate training and the guidelines for safe anaesthesia are followed (2). Recently the safety of performance of endobronchial biopsy in 33 children under five years old undergoing flexible bronchoscopy was evaluated. There were no incidences of significant bleeding or pneumothorax neither in the biopsy group nor in the control group for whom only bronchoscopy was done (3). Only a few patients become pyretic in both groups. However, operative bronchoscopy (such as endobronchial toilet in cystic fibrosis or treatment of tracheal and bronchial strictures) carries more risk of complications, depending on the primary condition and the age of the child.

ETHICAL ASPECTS OF BRONCHOSCOPY AND ENDOBRONCHIAL BIOPSY
Ethical guidelines for research in children conclude that only research procedures of no or minimal risk can be performed, unless the individual child will benefit of the research procedure (4). In young children, therefore, bronchoscopy cannot be performed solely for research purposes. This principle inherently limits our understanding of the normal development of the airway wall structure (such as thickness of reticular basement membrane (RBM)) and presence of inflammatory
and structural cells in the absence of a disease. In order to collect healthy control material, for example from children undergoing bronchoscopy for removal of foreign body or autopsy samples, international collaboration should be encouraged.

**FINDINGS WITH BRONCHOSCOPY IN SYMPTOMATIC CHILDREN**

Only few studies have been published where a substantial number of children with different indications and symptoms were evaluated with bronchoscopy. Indications and results of 386 pediatric bronchoscopies were retrospectively investigated by Puhakka et al. (5). The most common indications for bronchoscopy in children < 1 year of age were dyspnea or anomaly and in children > 1 year of age, foreign body or respiratory infection. Laryngomalacia with or without an abnormal epiglottis, subglottis stenosis or tracheal compression were commonly confirmed whereas 17% showed normal findings.

Schellhase et al. studied infants, 0-18 months of age, referred to a tertiary centre for further evaluation of recurrent wheezing by flexible bronchoscopy and BAL (6). They found airway abnormalities in 17/30 (57%) infants. Differential cellular analysis of BAL was abnormal in 11/27 (41%) while positive bacterial growth was confirmed in 11% of the samples.

In another study on young children with severe recurrent wheeze, the patients were referred to a tertiary centre for investigations and studied with bronchoscopy, endobronchial biopsy and BAL (7). A total of 47 children, 3 months to 5 years of age, refractory to conventional asthma therapy were included. An abnormal bronchoscopy was found in 79% of the patients, including structural abnormalities (36%) such as enlarged tonsils and adenoids, laryngo-, tracheo- or bronchomalacia, foreign body or tracheal compression and increased mucus (54%). A qualitatively good biopsy was received from 36 patients and eosinophilic inflammation and thickening of the RBM were present in 44% and 28% of the patients, respectively. Bacterial growth in BAL was confirmed in 27% of the cases. The usefulness of bronchoscopy in severe recurrent wheeze was shown to be unanimous: abnormal findings were present in 79% by Saglani et al. and in 57% by Schellhase et al.
EARLY INFLAMMATORY AND STRUCTURAL CHANGES

Only recently we have learned about the early onset of structural airway changes in infants with recurrent respiratory symptoms. We measured the lung function by body plethysmography for infants with recurrent respiratory symptoms, including dyspnea, cough and wheeze; whereafter bronchoscopy with endobronchial biopsy was performed (8). A total of 53 steroid-naïve children, aged 3 months to 2 years, were included. Neither a reticular basement thickening nor an eosinophilic inflammation characteristic of asthma in older children and adults was present in symptomatic infants with reversible obstruction, even in the presence of atopy.

An important part in early childhood asthma is the viral-driven inflammation. Knowing that most asthma exacerbations are caused by viral infections, the role of human rhinovirus (HRV) has been of interest to many investigators. HRV was first detected from lower airways during experimental infection in adult asthmatics (9, 10). Our study group used in situ hybridization to detect HRV from endobronchial biopsies from the group of infants with recurrent respiratory symptoms. HRV was detected in 21 of 47 (45%) specimens and abnormal lung function was found in 18 of 21 (86%) HRV+ infants (11).

FINDINGS IN PEDIATRIC ASTHMA

Investigations of pediatric asthma by bronchoscopy and endobronchial biopsy are justified only in children with poorly controlled disease in order to clarify the diagnosis and to guide treatment. This means that the findings from bronchoscopy and biopsy in pediatric asthma are done mostly among severe asthmatics. There are a few studies, which have found thickening of the RBM and presence of inflammatory cells on the bronchial mucosa (12-14). A part of the severely asthmatic children have eosinophilic inflammation characteristic of adult asthma and in one study, the eosinophils were even associated with persistence of symptoms (14).

Barbato et al. measured the RBM and eosinophils from the endobronchial biopsies in children with asthma and in children with atopy (15). Interestingly, they found
eosinophilic inflammation both among non-asthmatic atopic and asthmatic children.

Until now, only one follow-up study looking into development of structural abnormalities in children has been published (16). The inflammation and remodeling were present already before asthma could be diagnosed based on clinical symptoms. Since there may be a therapeutic window before irreversible structural changes occur, more data about the proinflammatory events are needed.

To summarize the findings of BAL-studies in infants and preschool children with wheeze, an overall increase in inflammation has been reported (17, 18) but eosinophils are rarely observed (18, 19).

It is important that opportunities for obtaining tissue for research during clinically indicated procedures are maximized (20). New markers of immunological mechanisms are constantly found which can be later analyzed in the correctly preserved tissue blocks.

**Clinical Indications for Bronchoscopy**

There are clear clinical indications for bronchoscopy to identify conditions (other than asthma) such as foreign body, aortic ring, primary ciliary dyskinesia, gastro-oesophageal reflux, structural airway abnormalities, lower respiratory tract infections, tuberculosis, bronchiectasis and obliterative bronchiolitis. Bronchoscopy can also be used in the diagnosis and follow-up of conditions such as severe laryngo-, tracheo- and bronchomalacia, and esophageal atresia with respiratory symptoms.

In contrast, most children with recurrent respiratory symptoms such as cough, wheeze, dyspnea and excess of mucus are in first line suspected for asthma, respiratory infections, enlarged adenoid and so on and other investigations than bronchoscopy are carried out. Only when these symptoms are prolonged, severe and/or refractory to conventional asthma therapy, bronchoscopy and endobronchial biopsy are considered. In such cases, direct examination of
bronchial tissue may confirm asthma and give reassurance for the need to modify medication.

**CONCLUSIONS**

There is an obvious and unfulfilled need for understanding pathological mechanisms of wheezy disorders in young children. Although non-invasive means to obtain information about inflammation in lower airways are being developed, we also need to study the structural and pathological changes present in the bronchial wall of children with chronic symptoms. Pediatric bronchoscopy is a safe procedure in hands of a-well-trained operator. Bronchoscopy is not needed for most cases of childhood asthma but it should be used both as a clinical and a research tool for clearly defined respiratory indications and for children with recurrent, undiagnosed respiratory symptoms at a specialist unit.
REFERENCES


