Investigative bronchoscopy and endobronchial biopsy is well tolerated in hyperreactive asthma patients

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Abstract The tolerability of 57 non-smoking asthma patients inhaling salbutamol as needed (ATS, 18–60 years, 60% < FEV₁ < 100%, PDISFEV₁ < 0.4 mg histamine) to fibreoptic bronchoscopy (FOB) and endobronchial biopsy was studied. The FOB was done in local Lignocaine anaesthesia, and from five to eight biopsy specimens were taken from the bronchial mucosa of the right lung. The tolerability was measured as cough/bronchospasm during the procedure (from 0 = normal to 3 = interrupted procedure), success of the procedure, and untoward occurrences. Twenty-seven of the 57 patients (48%) had no cough or bronchospasm during the FOB (score 0). Few coughs of no importance (score 1) were documented in 23 patients (40%). Seven patients (12%) had cough and/or bronchospasm interfering with the FOB procedure (score 2). The FOB procedure was not interrupted because of cough and/or bronchospasm in any patient. Scores of cough and/or bronchospasm diminished progressively with the increase of PDISFEV₁ histamine. The success of the procedure was 100%. Two patients had untoward medical occurrences requiring additional rescue medication (3.5%). In conclusion, we found that hyperreactivity predicts cough and/or bronchospasm during the FOB. Cough and/or bronchospasm are frequently observed during the bronchial procedure, but they are mild and of minor clinical importance. An investigational endobronchial procedure can be successfully performed in mildly or moderately obstructive asthmatic patients, even in cases with severe bronchial hyperreactivity.

Keywords Investigative bronchoscopy; tolerability; asthma; hyperreactivity.

INTRODUCTION

Since the introduction of investigational endobronchial biopsy via fibreoptic bronchoscopy (FOB) in 1977, no serious adverse events have been reported in asthmatic patients (1). Laryngospasm and bleeding appear in fewer than 1/1000 patients (2). Half of the patients may have a fall in FEV₁, but only 15% of the subjects report breathlessness (2). The clinical significance of the changes of the pulmonary function in connection with the FOB procedure is difficult to assess. Bronchial obstruction and hypoxaemia have been reported in rare cases and are assumed to be more frequent in severely obstructive and/or hyperreactive patients (3). The impact of bronchial hyperreactivity on the tolerability of investigative FOB has not been studied. In a study with 10 mild asthmatics, the investigators calculated that approximately 60 patients would be needed to confirm the 10 ± 5% complication rate for bronchospasm with a power of 80% (4).

The aim of the present study was to investigate the tolerability of FOB and endobronchial biopsy among asthmatic patients with moderate or severe bronchial hyperreactivity.

METHODS

Subjects

The patients included to this analysis participated in a randomized double-blind study comparing the effects of long-acting beta2-receptor antagonist, disodium cromoglycate and inhaled corticosteroid. All patients entering the study underwent FOB before the treatment period.

Non-smoking 18–60-year-old asthmatic patients [ATS criteria (5)] were recruited. Patients included to the study had an FEV₁ from 60 to 100% of predicted value (6) and a moderate or severe bronchial hyperreactivity [provocative dose of histamine inducing a fall of 15% in the forced expiratory volume of 1s (PDISFEV₁) less than
0.4 and 0.1 mg, respectively (7)). The only medication used before the FOB was inhaled short-acting beta2-agonist when needed.

**Procedures**

The international consensus for the investigational FOB was applied (3,8). Premedication was 30 mg oxazepam perorally, 0.5 mg atropine intramuscularly, and inhaled salbutamol 0.2 mg. Lignocaine was given as local anaesthesia by inhalation and by pharyngeal and transbronchoscopic application up to a maximum dose of 500 mg. The bronchoscope (Olympus XT30, Tokyo, Japan) was introduced orally into the right main bronchus. The specimens were taken with a cupped forceps from the mucosa of the right upper lobe bronchus, the openings of the middle lobe bronchus and one of the basal bronchi of the lower lobe.

The patients were followed up for 4 h. Adverse events were recorded and gag reflex examined by a drinking test. Long-term adverse events were documented up to 2 weeks after the FOB.

**Outcome measures of tolerability**

**Cough and/or bronchospasm:** Cough and bronchospasm during the FOB procedure were graded 0–3. Score 0 stood for no changes from the normal situation, 1 for few coughs of no importance, 2 for cough and bronchospasm interfering with FOB procedure, and 3 for FOB interrupted because of cough and bronchospasm.

**Adverse events:** All untoward medical occurrences experienced by the patient were recorded as adverse events (short-term during the 4-h polyclinical follow-up after the FOB and long-term during the following 2 weeks).

**Statistical methods:** The T-test was used to compare the difference in the scores of cough/bronchospasm at the different levels of bronchial hyperreactivity. The confidence interval for the occurrence of adverse events was estimated.

**RESULTS**

Fifty-seven consecutive patients entering the study were analysed. All patients completed the FOB procedure with the number of specimens ranging from five to eight.

**Cough and/or bronchospasm**

Twenty-seven of the 57 patients (48%) had no cough or bronchospasm during the FOB (score 0). Few coughs of no importance (score 1) were documented in 23 patients (40%). Seven patients (12%) had cough and/or bronchospasm interfering with the FOB procedure (score 2). The FOB procedure was not interrupted because of cough and/or bronchospasm (score 3) in any patient. Score 2 was found mainly among severely hyperreactive patients (PD15FEV1 histamine less than 0.1 mg). The scores of cough and/or bronchospasm diminished progressively with the increase of PD15FEV1 histamine. The difference between patients with cough/bronchospasm (scores 1 and 2) and without (score 0) (Fig 1) was statistically significant (p=0.02).

**Adverse events**

Four of the 57 patients (7.0%, 95% confidence interval 3–17%) had a short-term adverse event documented on the FOB visit. One patient with PD15FEV1 histamine 0.14 mg had slight throat irritation and cough. Another patient with PD15FEV1 histamine 0.02 mg had mild haemoptysis. These symptoms resolved spontaneously. Two patients had dyspnoea. One of them had PD15FEV1 histamine 0.03 mg and the other had PD15FEV1 histamine 0.24 mg. Both patients quickly responded to salbutamol taken as rescue medication. The follow-up time of the patients was not prolonged because of any of these adverse events.

The most common long-term adverse events during the 2-week (post-bronchoscopy days 0–13) period following the FOB were headache (nine episodes), respiratory infection (four episodes), and increase in asthma symptoms (three episodes), which responded to rescue medication (inhaled salbutamol).

**DISCUSSION**

Fifty-seven hyperreactive asthma patients completed the investigative FOB protocol with endobronchial...
biopsy without complications interfering with the procedure. Severe cough and/or bronchospasm or severe short-term adverse events were not detected. Bronchial hyperreactivity predicted cough and/or bronchospasm during the FOB.

The present study suggests that adverse events immediately related to the FOB procedure are present with a frequency of 3–17%. In this study they were mild and resolved rapidly without prolonging the stay at hospital. During the 2-week follow-up, only three patients reported increase in asthma symptoms which responded to rescue medication (inhaled salbutamol). The most frequent adverse events during the two-week follow-up in our study, i.e. headache and respiratory infection did not have any fixed relationship to the bronchial procedure. Our finding is thus comparable with that of Humbert et al. who reported no delayed effects on asthma control up to 2 weeks after FOB (9).

The present results with 57 patients as well as some previous studies suggest that the investigative FOB can be safely performed in mildly or moderately obstructive asthma patients (9,10). This study also shows that FOB with endobronchial biopsy is well tolerated in pre-medicated asthmatics with a mild-to-moderate obstruction, even in cases of severe bronchial hyperreactivity. Pre- and rescue medication were sufficient to treat all clinical consequences of the investigative FOB and endobronchial biopsy in the present study. Asthmatics with severe obstruction and extreme bronchial hyperreactivity are not recommended to be taken into studies including investigative FOB (3).

In conclusion, we found that hyperreactivity predicts cough and/or bronchospasm during the FOB. Cough and/or bronchospasm are frequently observed during the bronchial procedure, but they are mild and of minor clinical importance. An investigational bronchial procedure can be successfully performed in mildly or moderately obstructive asthmatic patients, even in cases with severe bronchial hyperreactivity.

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REFERENCES