Eur Respir J 1997; 10: 2243–2249
DOI: 10.1183/09031936.97.10102243
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European Respiratory Journal
ISSN 0903 - 1936

The diagnostic capacity of forced oscillation and forced expiration techniques in identifying asthma by isocapnic hyperpnoea of cold air

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The diagnostic capacity of forced oscillation and forced expiration techniques in identifying asthma by isocapnic hyperpnoea of cold air. B. Schmekel, H-J. Smith. ©ERS Journals Ltd 1997.

ABSTRACT: The measurement of forced expiratory volume in one second (FEV_1) is often used to assess the effect of bronchial provocations, and deep inspiration is required beforehand. This may briefly alter the bronchial tone in a variable way in some subjects. The forced oscillation technique (FOT) is a test used to characterize the mechanical impedance of the respiratory system, and prior deep inspiration is not required. We tested the hypothesis that measurable bronchoconstriction would occur in all asthmatic subjects stimulated with isocapnic hyperventilation of dry cold air (IHCA).

Twenty patients with mild asthma and nine healthy controls were exposed to IHCA, at 70% of their maximal voluntary ventilatory capacity for 4 min and the results were assessed both by applying the FOT and by measuring FEV_1. Optimal cut-off levels were defined by receiver operating characteristic (ROC) curve analyses of the changes in respiratory resistance and reactance at 5–35 Hz, resonant frequency (f_{res}) and FEV_1.

A positive result was present in the asthmatics when measured by FOT, and using ROC analyses the discriminative capacity to correctly diagnose asthma was greatest for responses in f_{res}; the sensitivity was 89% and the specificity 100%. The sensitivity of FEV_1 to correctly diagnose asthma was only 73%, and the specificity 88%.

In conclusion, the results of this study suggest that the use of forced expiratory volume in one second for bronchial provocation tests by isocapnic hyperventilation of dry cold air may be misleading and that the bronchoconstriction thus elicited is measured with greater sensitivity and specificity by the forced oscillation technique than by forced expiratory volume in one second.

Eur Respir J 1997; 10: 2243–2249.

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Keywords: Asthma
cold air challenge
forced expiration technique
forced oscillation technique

Received: November 4 1996
Accepted after revision May 27 1997

This study was supported by The Swedish Medical Research Council B96-04X-11553-01A, The Heart and Lung Foundation, The Asthma and Allergy Foundation, Östergötlands läns landsting and Draco Pharmaceuticals AB.

Isocapnic hyperventilation is a physiological bronchoprovocation test useful in the diagnosis of asthma. It has been suggested that subjects with a decline in forced expiratory volume during one second (FEV_1) of at least 10% after isocapnic hyperventilation of dry cold air (IHCA) should be diagnosed as having asthma [1]. Measuring the effects of the test using FEV_1 requires that the subject performs a deep inhalation (DI) prior to the test, which is known to elicit changes in bronchomotor tone in some individuals [2]. The ability of FEV_1 measurements to correctly identify constriction or dilation of the bronchi elicited by either a bronchial provocation test or a bronchodilator might, therefore, be reduced. In support of this theory, it was reported that spirometry alone may fail to identify reversibility of airways obstruction and approximately 15% of responses recorded in an asthma population were false negatives [3]. Alternative tests must, therefore, be used to correctly identify changes in airway tone and a technique that does not require a preceding DI is preferable. The forced oscillation technique (FOT) for measuring bronchial responses is simple, requires only passive cooperation and a preceding DI is not required [4]. FOT is a method by which respiratory input impedance can be measured simultaneously at various frequencies by means of complex oscillations superimposed at the mouth during spontaneous quiet breathing. FEV_1, on the other hand, is a well-established method and highly reproducible values are obtained [5, 6], although the effort required by the patient may limit the feasibility, especially when repeated measurements are carried out on asthmatics.

The hypothesis that we wished to test was that measurable bronchoconstriction was elicited in all asthmatics stimulated with IHCA for 4 min. We also intended to determine whether there was a difference in the ability to detect bronchoconstriction elicited by IHCA between measurements recorded using a special form of FOT, the impulse oscillation system (IOS), and FEV_1 in a mixed population of mild asthmatics and healthy

volunteers. To this end, the sensitivity and specificity of measurements, by means of IOS or FEV_1, were compared at different predetermined levels and evaluated by receiver operating characteristic (ROC) analyses. The capacity of the various parameters derived from IOS measurements, to identify bronchoconstriction elicited by IHCA, was evaluated to ascertain the presence or absence of a clinical diagnosis of asthma.

Methods

Patients

Twenty patients (thirteen women) with a clinical diagnosis of asthma, confirmed by a history of recurrent attacks of dyspnoea with perceptible wheezing, and meeting the American Thoracic Society clinical criteria [7], including prior demonstration of reversible airway obstruction of at least 15% or an abnormal bronchoprovocation challenge test. The subjects were randomly selected from a larger population of patients with asthma. All patients were in a stable clinical condition, and the resting value of FEV_1 was ≥80% of the predicted normal value [8, 9] in all but one of the subjects (78% pred). Exclusion criteria were airway infection or acute exacerbation 3 weeks prior to the test and any cardiorespiratory disease other than asthma. All asthmatics included in the test used short-acting beta-agonists on an "as-required basis" and no beta-agonist was allowed 8 h prior to the test. Twelve of the patients used inhaled glucocorticosteroids, none currently used non-steroidal anti-inflammatory drugs. Nine healthy volunteers (seven women) served as normal controls with no asthmatic symptoms and none of the exclusion criteria listed above. Demographic data are presented in table 1. A peak flow meter (Mini Wright, Clement Clarke Int Ltd, Harlow, Essex, UK) was given to all subjects 1 week prior to the test and the subjects were encouraged to measure peak expiratory flow rate (PEFR) twice daily for at least 5 days prior to the test. PEFR variability was calculated from the maximal minus the minimal value divided by the mean for the period. The PEFR variability was used as an independent indicator of bronchial hyperresponsiveness [10]. The study was approved by the local Ethics Research Committee and informed consent was obtained from all subjects before being included in the study.

Table 1. – Demographic data and pretest values of FEV_1 and PEF variability in patients with mild asthma and in healthy controls

	Asthmatics (n=20)	Controls (n=9)
Age yrs	32±10	37±8
Sex F/M	13/7	7/2
Height cm	169±6	170±9
Weight kg	64±10	66±11
FEV_1 % pred	91±7	97±14
PEF variability %	4.5±4.1	1.8±1.1

Values are means±SD, or absolute number for sex. There were no significant differences between groups for any parameter. FEV_1: forced expiratory volume in one second; PEF variability: peak expiratory flow rate variability over time.

Test technique

After baseline measurements of impedance and spirometry were taken, the subjects hyperventilated a dry gas mixture of 5% CO_2 and air during a single 4 min test, the target minute ventilation being set at 25 times baseline FEV_1 per minute (corresponding to ~70% of the maximal voluntary ventilation). A rotameter (Platon, Platon Parks Viables, Hants, UK) monitored the inhalation circuit flow rate. Air was directed through a balloon and a steady level of ventilation was achieved by visually observing the balloon size. The subjects breathed through a mouthpiece connected to a modified Respiratory Heat Exchange System (RHES, Erich Jaeger AG, Würzburg, Germany) and a Lauda UKT 800 refrigerator (Erich Jaeger AG), equipped with a two-way valve in the outlet which allowed the subjects to breath a dry cold air/CO_2 mixture. A thermistor was located 10 cm in front of the teeth in the inspiratory flow for measuring the temperature of the inhaled air (kept at -15°C during the test).

Relative humidity was measured by means of a hygrometer (Model 451, Testoterm GmbH, Germany) and using a Mollier diagram, the absolute humidity was calculated to be approximately 0.4 g water·kg dry cold air^{-1}.

Repeated challenges with hyperpnoea were performed in 14 patients with mild asthma and in seven healthy controls. The 95% confidence intervals for the differences in lung function measurements performed 7–8 min after the challenges, were -0.03–0.12 L for FEV_1 measurements and -3.06–0.33 Hz for measurements of resonant frequency (f_{res}). The coefficient of repeatability, as defined by SD/mean differences, was 3.6 for FEV_1 and 2.7 for resonant frequency.

Measurement of lung function

Lung function was measured in duplicate at baseline. Spirometry and IOS measurements were performed using an MS-IOS Digital instrument (Erich Jaeger AG) and the results were processed on an ALR 486 computer (Evolution IV, Irvine, CA, USA). The oscillometry equipment fulfilled the standard recommendations [11] and flow and volume measurements were corrected according to body temperature and ambient pressure, saturated with water vapour (BTPS) conditions. Impedance measurements were performed according to principles previously published [12, 13] and data recorded during calm tidal breathing for periods of 30 s and 3, 5, 7, 11 and 13 min after IHCA. The IOS technique uses a simple on/off control of a loudspeaker to generate brief pressure pulses which form the test signal. These pressure pulses, with a frequency range up to 100 Hz, are generated at a rate of 3 pulses·s^{-1} and are superimposed on the spontaneous breathing of the subject. Pressure and airflow are recorded simultaneously at the mouth of the subject, by means of a Lilly type pneumotachograph (Erich Jaeger AG) connected to a differential pressure transducer (Sensym SLP 004, +/- 1 kPa; Sensym Inc, Fremont, CA, USA). The common mode rejection ratio of both transducers is 70 dB up to 50 Hz. Flow and pressure are analogue low-pass filtered at 50 Hz (-3 dB) and simultaneously sampled

at 200 Hz. Fast Fourier transformation of flow and pressure has a frequency resolution of 3.125 Hz in the range 0–50 Hz. For every determined frequency, the ratio between pressure and resulting airflow constitutes the impedance of the respiratory system (Z), which is characterized by its two cartesian components resistance (R) and reactance (X), where $Z=R+jX$. Apart from daily flow-volume calibrations, the equipment was regularly checked against a reference impedance of 0.2 kPa·L^{-1}·s^{-1}. Airway resistance at 5 Hz ($R5$), 20 Hz ($R20$) and 35 Hz ($R35$), as well as reactance at 5 Hz ($X5$), 35 Hz ($X35$) and $f$res were evaluated. The value of $f$res depends on the values of X at the various frequencies and is constituted by the frequency at which X is 0. The airway responses to IHCA were recorded in all subjects 8 min after the test was completed, using FEV1 measurements (fig. 1).

Data analysis

Data are expressed as mean±SD, unless otherwise indicated. All statistical calculations were carried out using a computer program (Statistica 5.0, Statsoft Inc, Tulsa, USA). The Student's t-test of independent and dependent values was used and the mean difference and standard deviation of the difference (SDdiff) were calculated on the duplicate measurements at baseline (table 2). There was no significant correlation between SDdiff and the baseline values in any of the parameters (the coefficients of correlation ranged -0.08–0.34, p>0.05). In this presentation, the predetermined levels of decision for responses were based on the size of the deviation from baseline divided by the SDdiff for the particular parameter, thus expressing deviation from baseline as the number of SD units. It was decided that the response decision levels for the various parameters should be determined for the range 0.5–6 SD units. The 7 min post-test sensitivity and specificity of responses of $R5$, $R20$, $R35$, $X5$, $X35$, $f$res and the 8 min FEV1 were registered on the computer and compared in order to ascertain the presence or absence of a clinical diagnosis of asthma, assuming that all asthmatics would respond to the test. The occurrence of positive or negative responses to the test and presence or absence of the clinical diagnosis of asthma [7] were calculated and compared between the two methods of evaluation using the ROC analysis. The relationship between true-positive and false-positive rate over a range of decision levels was then illustrated graphically. Changes in the true-positive rate (*i.e.* sensitivity) was shown as a function of the false-positive rate (*i.e.* 1 minus specificity) over the range of decision levels examined. A comparison of alternative techniques in similar conditions and over several decision levels may be carried out using this technique [14, 15], and it is possible to identify the optimal cut-off point that discriminates most efficiently between the absence or presence of a particular patient condition. The point closest to that at which both sensitivity and specificity are 1, *i.e.* 100% true-positive and no false-positive predictions, is the optimal cut-off point, and the distance to this point and any point on the ROC curve characterizes the test's discriminative ability at a given decision level. The distance of any point on a ROC curve from the ideal point may be measured and plotted against the decision levels, and the shorter the distance, the greater the method's capacity at any decision level. In this presentation the distance to the ideal point is expressed as distance units (DUs) and the decision levels expressed as deviation from baseline in number of SD units.

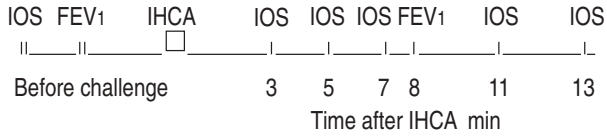

Fig. 1. – Schedule of investigational events. Measurements were taken in duplicate at baseline and after isocapnic hyperventilation of cold air (IHCA), by means of impulse oscillometry (IOS) and forced expiratory volume in one second (FEV1).

Table 2. – Lung function parameters measured in duplicate at baseline

	Replicate 1	Replicate 2	SDdiff
Impulse oscillometry			
$R5$ kPa·L^{-1}·s^{-1}	0.37±0.09	0.36±0.08	0.025
$R20$ kPa·L^{-1}·s^{-1}	0.34±0.08	0.34±0.08	0.019
$R35$ kPa·L^{-1}·s^{-1}	0.36±0.07	0.36±0.07	0.026
$X5$ kPa·L^{-1}·s^{-1}	0.11±0.03	0.10±0.03	0.016
$X35$ kPa·L^{-1}·s^{-1}	0.13±0.05	0.13±0.05	0.020
$f$res Hz	11.5±2.8	11.5±2.9	0.8
Spirometry			
FEV1 L	3.9±0.9	3.9±0.9	0.1

Values are mean±SD for replicates 1 and 2 and absolute values for the SD of the difference (SDdiff). $R5$, $R20$, $R35$: resistance at 5, 20 and 35 Hz, respectively; $X5$, $X35$: reactance at 5 and 35 Hz, respectively; $f$res: resonant frequency; FEV1: forced expiratory volume in one second.

Results

Analyses of the ROC curves for the best discriminative capacity (*i.e.* shortest distance to the ideal point) of the IOS parameters or forced expiration, recorded 7 min after IHCA, revealed that the shortest distances were obtained when data of $f$res and $R5$ were analysed. These parameters, therefore, had the greatest discriminative capacity for correctly identifying asthma by bronchial obstruction elicited by IHCA. The optimal cut-off level for $f$res was determined as 3 SD units (fig. 2) and sensitivity in detecting responses in asthma was 89% and specificity 100%. At the optimal cut-off level of 2 SD units, the sensitivity of $R5$ was 88% and specificity 89%. The power of FEV1 was much lower and at the optimal cut-off level of 2 SD units, the sensitivity of FEV1 to correctly diagnose asthma by bronchoconstriction elicited by IHCA was 73% and specificity 88%.

The frequency dependence of the responses of airway resistance elicited by IHCA was recorded in the patients 7 min after the test and significant differences between the post- and pretest airway resistance were recorded in the low frequency range among the asthmatics ($R5$, p<0.001, $R20$, p<0.001; table 3 and fig. 3). In contrast, there was no significant difference in airway resistance in the high frequency range ($R35$, p=0.31).

Frequency dependence of the airway response in asthmatics was also evident by comparing the post-test values obtained from patients and volunteers. Post-test

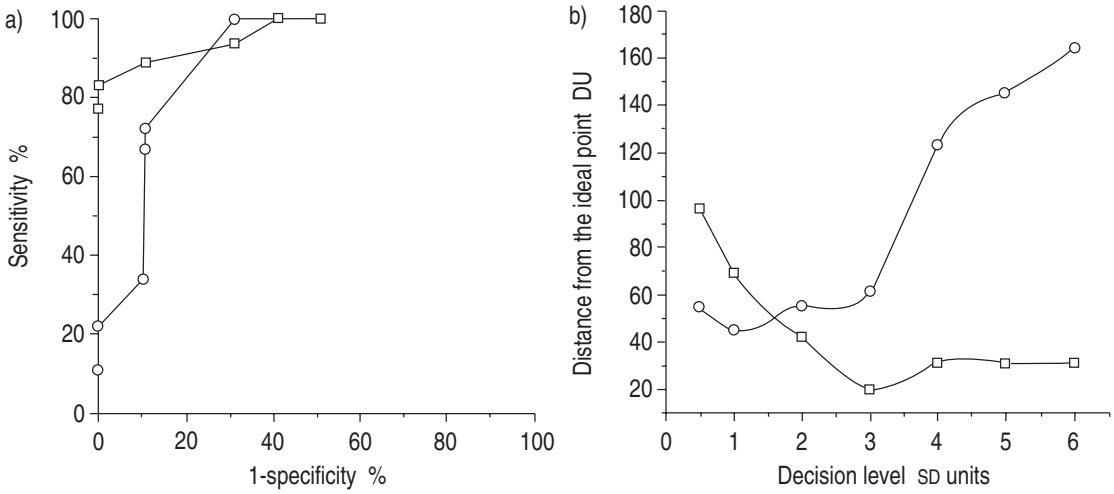

Fig. 2. – a) Receiver operating characteristic (ROC) curve; and b) distance to the ROC curve from the ideal point for various decision levels (0.5–6 SD units) of changes in resonant frequency (f_{res}; ❑) and forced expiratory volume in one second (FEV_1; ○). DU: distance unit. See text for further details.

Table 3. – Lung function data obtained from 20 asthmatics with no symptoms and nine healthy control persons, before and 7 and 8 min after isocapnic hyperventilation of cold air (IHCA)

	Asthmatics (n=20)		Controls (n=9)	
	Before IHCA	After IHCA	Before IHCA	After IHCA
Impulse oscillometry				
R_5 kPa·L^{-1}·s^{-1}	0.37±0.09	0.58±0.22###**	0.34±0.09	0.35±0.10
R_{20} kPa·L^{-1}·s^{-1}	0.34±0.08	0.39±0.09###	0.32±0.08	0.32±0.08
R_{35} kPa·L^{-1}·s^{-1}	0.35±0.06	0.36±0.08	0.38±0.09	0.36±0.08
X_5 kPa·L^{-1}·s^{-1}	-0.11±0.02	-0.22±0.13###**	-0.10±0.03	-0.10±0.03
X_{35} kPa·L^{-1}·s^{-1}	0.12±0.04	0.06±0.06###**	0.14±0.07	0.12±0.04
f_{res} Hz	12.0±3.0	24.4±8.4###**	10.5±2.5	11.6±3.1
Spirometry				
FEV_1 L	3.4±5	3.0±0.6###	3.6±0.9	3.5±1.0

###: p<0.001, *versus* before IHCA; **, ***: p<0.01, p<0.001, *versus* controls after IHCA. For definitions, see table 2.

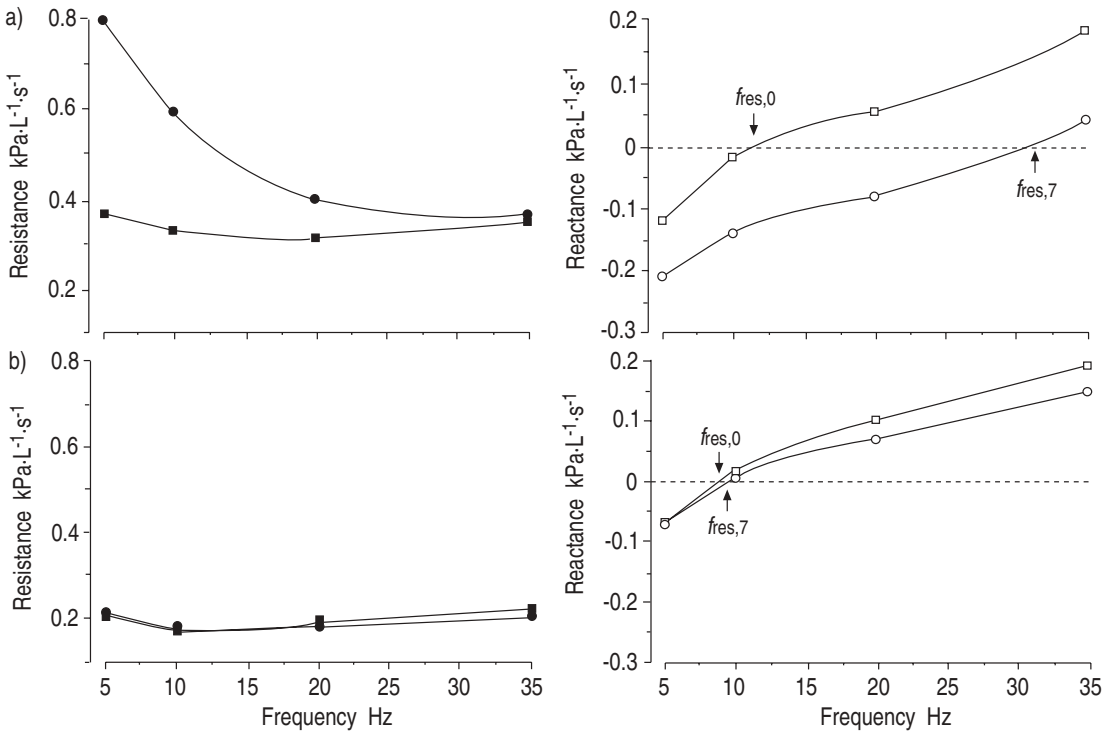

Fig. 3. – Example of impulse oscillometry system (IOS) data recorded in: a) one subject with asthma; and b) one healthy control. Resistance obtained in the frequency range 5–35 Hz, before (■) and after (●) isocapnic hyperventilation of cold air, and reactance obtained in the frequency range 5–35 Hz, before (❑), and 7 min after (○) isocapnic hyperventilation of cold air are given. Resonant frequencies recorded before ($f_{res,0}$) and 7 min after ($f_{res,7}$) the challenge, are indicated by the frequency at which the reactance is zero.

values of R_5 were significantly higher in the asthmatics than in the healthy volunteers (p=0.005), while this was not so for R_{20} (p=0.07) and R_{35} (p=0.95) (table 3). Significant responses in airway reactance (X_5, X_{35} and f_{res}) were recorded in the asthmatics 7 min after IHCA (p<0.001, all comparisons) and all the values recorded after the test were significantly different in the asthmatics and volunteers (p<0.01, table 3). The healthy volunteers showed no significant response to IHCA in the measurements of FEV_1 or impedance (p>0.05, all comparisons) and no differences between asthmatics and healthy volunteers were seen at baseline in any of the lung function parameters (table 3).

Peak expiratory flow (PEF) variability before the test tended to be higher in the asthmatics than in the volunteers and was significantly correlated to the magnitude of response in f_{res} elicited by IHCA (r=0.46, p<0.05), but not to any of the remaining lung function parameters. Significant correlation was also obtained between the responses in FEV_1 and those in R_5 (r = -0.79, p<0.01), f_{res} (r = -0.73, p<0.01) and X_5 (r=0.89, p<0.01), but not in the other parameters obtained by IOS.

Effect of forced movement on bronchial tone

Fifteen of the asthmatics were evaluated with regard to how the bronchial tone is affected by a forced expiratory manoeuvre preceded by a DI, by taking impedance measurements 11 and 13 min after the IHCA, *i.e.* 3 and 5 min after the final FEV_1 measurement (fig. 1). Temporary and partial bronchodilation was recorded in most of the asthmatics after the forced action and the decreases of airway tone, recorded by a fall in f_{res} 3 min after the FEV_1 (-4.4±5.8 Hz) were followed by a mean increase in f_{res} 5 min after this action (+1.7±4.2 Hz). A retrospective analysis of these asthmatics was carried out in order to evaluate whether there were any characteristics that could distinguish the asthmatics who responded to forced actions with more pronounced bronchodilation, from those who did not. The asthma population was divided into two groups depending on whether their change in f_{res} from the third to the fifth minute after the forced action was above or below the median value for the whole group of asthmatics, as only those who exhibited an increased bronchial tone after some minutes could claim reversal of the induced bronchoconstriction elicited by the forced action. The two groups contained eight (seven females) and seven (five females) individuals each, and there was no difference in the demographic data between the groups. The level of bronchial tone, as reflected by f_{res}, measured before and after IHCA and FEV_1 is illustrated for the two subgroups of asthma patients (fig. 4). Significantly higher values of R_5 (p<0.01), R_{20} (p<0.01) and R_{35} (p<0.05) were recorded at baseline in the groups of asthmatics who did not respond to DI with reversal of the bronchial contraction. For these asthmatics, the data indicate higher baseline airways tone. Similarly, the values of X_5 were lower in this group of asthmatics, but the difference did not reach statistical significance (p=0.07).The difference in baseline tone was also reflected in a difference between f_{res} at baseline, the difference was not, however, statistically significant (p=0.06).

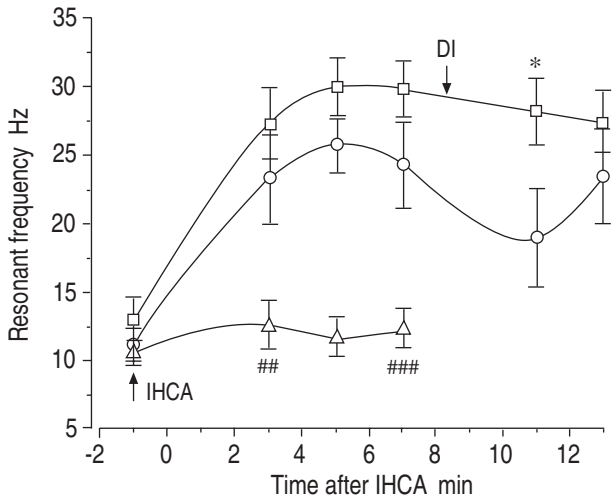

Fig. 4. – Resonant frequency before and after isocapnic hyperventilation of cold air (IHCA) and one deep inspiration (DI) and forced expiratory volume in one second (FEV_1) manoeuvre, in eight asthmatics where the bronchoconstriction did not reverse after a forced action (Group A; ❑) and in seven asthmatics who exhibited temporary bronchodilation after a forced action (Group B; ○). Data obtained from nine healthy controls are also given (Controls; Δ). Values are presented as mean±SEM. *: p<0.05, *versus* Group B; ##,###: p<0.01, p<0.001, *versus* patients.

Impedance measurements were discontinued for five asthmatics, four individuals for technical reasons and one individual for safety reasons (excessive bronchial response). Retrospective analysis of the status at baseline for the four subjects who were not evaluated, revealed that they tended to have lower bronchial tone in relation to the remaining asthmatics, determined by higher values of FEV_1 (p<0.001) and lower values of R_5 and R_{20} (p<0.05 and p<0.001, respectively). The bronchial responses to IHCA also tended to be milder in the four asthmatics in whom the impact of forced action was not studied; significantly lower responses to IHCA were recorded in f_{res} and FEV_1 in relation to the remaining asthmatics (both p<0.01). Furthermore, except for treatment with glucocorticosteroids in the asthmatics, there were no statistically significant differences at baseline between these patients and the control subjects.

Discussion

All the asthmatics exhibited significant bronchial obstruction after IHCA, provided the response was measured by FOT and recorded at the optimal cut-off level. This was not true when the airway response was measured by the FEV_1 technique. The hypothesis that bronchial constriction was induced in all asthmatics was, therefore, proven only for the FOT method of measuring the airway response. The discriminative capacity, sensitivity and specificity of impedance measurements, *i.e.* f_{res} and R_5, were, therefore, shown to exceed that of FEV_1 in correctly diagnosing asthma by airway responses elicited by IHCA and recorded 7–8 min after the test. The finding that FOT was a more sensitive method than the forced expiration technique is in agreement with recent observations of higher sensitivity of FOT than flow-volume recordings [16]. The reason for the

difference in discriminative capacity of the IOS and FEV_1 techniques is not known. Agreement between the responses recorded through forced expiration and impedance was not anticipated, since these techniques do not measure the same airway properties or events. Transient reversal of the airway constriction induced by DI, may contribute to the differences. Whether the DI itself, performed as a part of a hyperpnoea test, also contributes to a loss of bronchoconstriction at an early phase after the test is not known, since we did not measure impedance earlier than 3 min after completion of the test. A temporary constriction reversal was recorded in most of the asthmatics during the period directly after the test. The time pattern of several minutes for the dilation and constriction elicited by DI, as recorded in this study, agrees with previously reported patterns [17], but disagrees with others, where bronchodilation, which rapidly passed, was recorded [18]. All the asthmatics presented in this study had mild asthma and those who responded with the greatest reversal of the bronchial obstruction elicited by hyperpnoea also had the mildest asthma, indicated by the lowest airway resistance values prior to the test. Airway diameter is known to influence responses to various types of bronchial challenges [19, 20], but such differences at baseline cannot explain the differences between the two subgroups of asthma. The results agree with previous reports of mild asthmatics [2, 21, 22] and the findings that the bronchomotor effect of DI corresponds to the severity of asthma, was suggested to represent a physiological indicator of peripheral obstruction due to inflammation in mild asthmatics [23].

The mechanisms of the fall in bronchomotor tone by DI are not fully understood, but may include differences in hysteresis of airway and lung parenchyma [24], which, in turn, may depend upon differences in airway inflammation. Volume history responses differed between equally constricted guinea-pigs tested with either isocapnic hyperpnoea, methacholine or antigen [25]. A reversal of the constriction was observed only in animals tested with hyperpnoea and methacholine, and differences in the concentration of inflammatory mediators were observed in bronchoalveolar lavage fluid obtained from these groups of animals, suggesting a difference in airway and/or parenchymal microvascular leakage and cellular inflammation between the tested animals.

Peak expiratory flow rate (PEFR) variability may reflect bronchial hyperresponsiveness by means of an independent technique [10]. The level of PEFR variability was low in the present material, which indicates that the asthmatics had a mild form of the disease and a low level of unspecific bronchial hyperresponsiveness. The response rate to IHCA, as assessed by the FOT, *i.e.* f_{res}, was, however, high and the magnitude of the responses correlated significantly to PEFR variability. The relative discrepancy in the levels of PEFR variability and responses to IHCA may depend on an underestimation of the variability of PEFR, as previously reported [26], or, alternatively, it may reflect different aspects of asthma.

In agreement with previous reports of tests subjecting asthma patients to cold air, we found frequency dependence of the airway responses, suggesting events within the peripheral compartments of the lung [27]. Movement of the upper airway wall during the forced oscillation may underestimate the resistance values, but providing firm support of the cheeks, as performed by the present subjects, effectively reduces the error due to movement of the upper airway wall [28]. Despite the fact that the two different techniques to measure airway responses do not measure the same properties, significant correlation was obtained between responses in FEV_1 measurements and those of IOS within the low frequency range, which supports the notion that these parameters reflect events in the intrathoracic airway, presumably peripheral.

The sensitivity and specificity of f_{res} were highest in all comparisons and, provided that the optimal cut-off level was used, this parameter seemed suitable for serial or single airway response measurements in bronchoprovocation studies. Sensitivity and specificity of similar magnitudes were reported in studies on the reversibility of airway obstruction [29, 30] but tended to be higher than in one particular study of induced bronchoconstriction [31]. Due to variations in patient selection, testing methods and analysis, however, the data cannot be compared completely.

In conclusion, measurements of bronchoconstriction elicited by isocapnic hyperventilation of dry cold air by the impulse oscillation system are sensitive and the capacity to diagnose asthma is greater when the impedance technique is used (*i.e.* resistance at 5 Hz and resonant frequency) than when the forced expiratory volume in one second technique is applied. It can also be concluded that forced actions may conceal airway responses and in measuring the responses to bronchial tests, the choice of technique must include one that is not dependent on forced expiration and a preceding deep inhalation. The use of forced expiratory volume in one second for bronchoprovocation tests may be misleading and it is therefore recommended that alternative methods to detect airway responses, such as the impulse oscillation system, be employed due to the consequences of bronchodilation in asthmatics during the test.

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