Use of the Forced Oscillation Technique to Detect Bronchodilation in Children: Experience from the Schneider Children's Medical Center of Israel

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ABSTRACT: **Background:** The forced oscillation technique is a non-invasive and effort-independent technique that is well suited for lung function measurement in young children. FOT employs small-amplitude pressure oscillations superimposed on normal breathing. Therefore, it has the advantage over conventional lung function techniques in that it does not require patient cooperation for conducting respiratory maneuvers.

Objectives: To test the feasibility of the FOT test in preschool children and to compare the results to the commonly used spirometry before and after the administration of bronchodilator therapy.

Methods: Forty-six children (median age 4.9 years, range 1.8–18.3) attending the pulmonary clinic at Schneider Children's Medical Center tried to perform FOT and routine spirometry. Results were retrospectively analyzed.

Results: Of the 46 children 40 succeeded in performing FOT and only 29 succeeded in performing simple spirometry. All but one of the 32 children aged 4 years and above (97%) could perform both tests. Nine of 14 children (64%) aged 4 and less could perform the FOT but only 3 (21%) could perform spirometry. Baseline values of respiratory resistance measured at 6 Hz (R6) negatively correlated with body length ($r^2 = 0.68$, $P < 0.005$). Twenty-four children performed both tests before and after bronchodilator therapy. A significant concordance was found between the measured responses to bronchodilators by FOT and spirometry ($P < 0.01$). Only one child had a negative response by FOT but a positive response by spirometry.

Conclusions: The FOT is a simple, non-invasive technique that does not require subject cooperation and thus can be utilized for measuring lung function in children as young as 2 years old. Furthermore, the FOT was shown to reliably measure response to bronchodilator therapy.

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KEY WORDS: maximal expiratory flow-volume maneuver, forced expired volume in 1 second, bronchodilator therapy, preschool children

FOT = forced oscillation technique

The forced oscillation technique is a non-invasive and effort-independent technique that is well suited for lung function measurement in young children. FOT employs small amplitude pressure oscillations superimposed on normal breathing and therefore has the advantage over conventional lung function techniques in not requiring patient cooperation for performing respiratory maneuvers. According to the European Respiratory Society Task Force, the FOT is sensitive in detecting airway obstruction and bronchodilation response in children and is a reliable method to assess bronchial hyperresponsiveness in adults and children [1,2]. The most widely used parameter of the FOT is the resistance measured at 6 Hz, which reflects airways resistance [3].

We operate the first system available in Israel. The aims of the present study were to test the feasibility of the FOT test in preschool children and to compare the results with those of the commonly used spirometry before and after the administration of bronchodilator therapy.

PATIENTS AND METHODS

During the period July to December 2008, 46 children with various respiratory conditions, including recurrent pneumonia, chronic cough and asthma, were assessed consecutively from the outpatient pulmonary clinic in our medical center.

Each child tried to perform both FOT and routine spirometry. The FOT test always preceded the maximal expiratory flow-volume maneuver, which is known to affect the outcome of the FOT [1]. FOT measurements were performed in the sitting position with the head in a neutral or slightly extended position. During the measurement, the subject's cheeks were firmly supported by the technician or parent using both hands, and a nose-clip was worn. The subject was instructed to breathe quietly at functional residual capacity level. When testing very young children, the subjects were seated on their parents' laps.

Provided that the subject succeeded in performing both

tests, he/she was given two puffs of salbutamol pMDI, 100 µg/puff, using a valved spacer device with mask or mouthpiece (Aerochamber, Trudell Medical International, London, ON, Canada). FOT and spirometry were repeated 15–30 minutes later.

The FOT was conducted with the Chess i2m system (Chess mt NV, Oostakker, Belgium) as previously described [4]. Briefly, externally generated sinusoidal pressure oscillations superimposed on the spontaneous breathing of subjects enter the respiratory tract via the mouthpiece. The analysis of both signals, the external applied pressures and the induced flows, yield an estimate of the input impedance of the respiratory system Zrs, which is the ratio of the two corresponding signals: Zrs(f) = P(f) / Flow(f), both as a function of frequency. Depending on the level of respiratory resistance, the reflected airflow generates an oscillatory pressure, and the pressure and flow were sampled at the mouth with differential pressure transducers and pneumotachograph. All measurements were obtained over an 8 second sampling period and followed the international guideline recommendations [1,2].

Spirometry was performed with the Zan system (Zan 100, nSpire Health Inc., Germany), employing incentives that include stimulation of inspiratory and expiratory flows set by targets of predicted values for older children [5].

STATISTICAL ANALYSIS

Success in performing FOT was defined as having at least two acceptable 8 second recordings with coherence > 0.95 at every frequency. Success in performing simple spirometry was judged by inspecting the MEFV1curves for acceptable maximal inspiratory effort to total lung capacity and shape and smoothness of the expiratory phase. In some, mostly the very young, only one acceptable MEFV curve was obtained and this was included in the analysis.

Percent of predicted normal values were calculated based on Hordvik et al. for R6 [6] and Vilozni et al. for FEV_12[5]. Positive response to bronchodilators was defined as > 12% improvement in FEV_1 and > 28% fall in R6.

Statistical analysis was performed using paired Student's *t*-test for continuous variables and the 2 x 2 contingency table with two-sided Fisher's exact test for categorical variables. A $P < 0.05$ level was judged as significant.

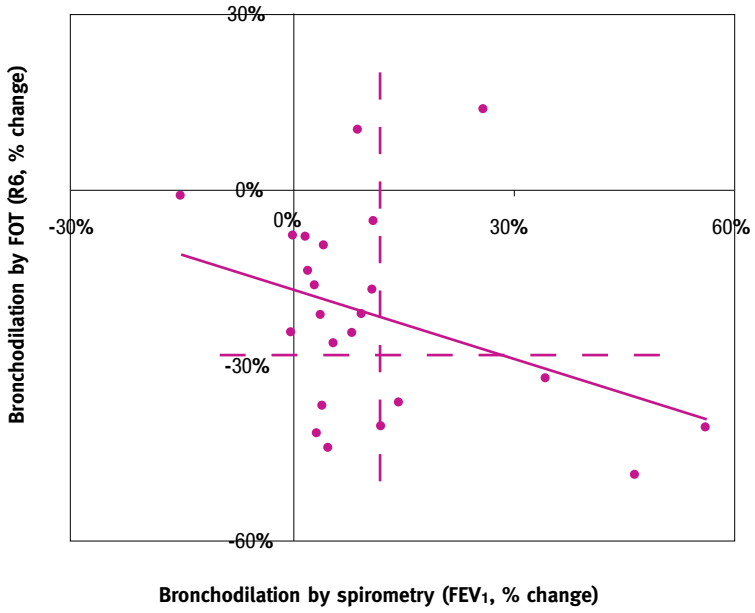
RESULTS

The study population included 46 children with a median age of 4.9 years (range 1.8–18.3 years), height 109 cm (range 81–163 cm), and weight 19.5 kg (range 11–96 kg). Forty children had asthma or suspected asthma, and the others were evaluated for recurrent pneumonia episodes. Twenty-eight children were in the preschool age range.

All but one child older than 4 years (31/32, 97%) succeeded in performing both tests. In the preschool age, 6 years old or younger, 22 of the 28 children (79%) succeeded in performing the FOT maneuver but only 17 (61%) succeeded in performing spirometry. In the very young children, aged 4 years and less, 9 of 14 (64%) could perform the FOT but only 3 (21%) could perform spirometry.

In 38 of the children, baseline respiratory resistance at 6 Hz (R6) as measured by the FOT could be obtained. As expected, R6 value negatively correlated with height (r^2 = 0.68, $P < 0.005$). Only 32 of them succeeded in doing spirometry, and only 24 were successful in completing the full protocol with measurements of both maneuvers before and after the administration of bronchodilators. Percent change in R6, as measured by the FOT, versus percent change in FEV_1, as measured by the simple spirometry are plotted in Figure 1. As can be seen, there is a good concordance between R6 and FEV_1 with a two-sided $P < 0.01$ (Fisher's exact test). Of the 24 children who repeated the tests after bronchodilators, 5 had a positive bronchodilator response and 15 had no response as judged by both methods. An additional child had a positive response by spirometry only, and three more by FOT alone.

Figure 1. Bronchodilatation response by FOT (R6) versus spirometry (FEV_1). Percent change in R6, as measured by the FOT, versus percent change in FEV_1, as measured by the simple spirometry in 24 children following bronchodilator therapy. The dashed lines represent threshold for positive response.



MEFV = maximal expiratory flow volume
FEV_1 = forced expired volume in 1 second

DISCUSSION

We report here our initial experience in operating the first system in Israel to utilize the forced oscillation technique, FOT. Routine lung function tests require subject cooperation and, in the case of performing maximal expiratory flow volume maneuvers, generating maximal effort is mandatory. It is therefore not surprising that alternative technologies are being continuously sought. Since the FOT requires very little subject cooperation its use in very young subjects is particularly attractive. Indeed, we have shown that preschool children as young as 2 years old are capable in most cases of performing the test. The feasibility of achieving acceptable results in children aged 4 and younger is even more favorable when comparing the FOT with spirometry. About half of the children could perform FOT (8 of 15), while only 27% could perform spirometry. This encouraging finding is as good as or even better than success rates published in the past [7-9].

The correlations between baseline values of R6 and FEV_1 ($P < 0.02$) and between the two measures of bronchodilation response were somewhat lower than these previously reported in the literature [9,10]. One possible reason for this is an initial learning curve in applying the technology within our laboratory. However, when analyzing the second half of the results, the correlation between baseline values and the concordance between the two measures R6 and FEV_1 did not improve, despite the fact that the correlation between the two measures of bronchodilation response improved ($r^2 = 0.45$, $P < 0.02$). In this context, it should be noted that although the literature is quite robust when dealing with older children and adults, it is scarce for the preschool age range.

We acknowledge the fact that our study is preliminary in nature, describing our initial experience in adopting a new technology. In this respect, it is anticipated that with further practice and improved know-how, very basic information such as the determination of the normal range for healthy Israeli children can be obtained.

In conclusion, our initial experience is encouraging since we found the FOT system to be very simple to operate and acceptable to the subjects. These factors contributed to a high success rate when studying preschool children as young as 2 years old and significantly better than those achieved with the commonly used spirometry. Furthermore, the FOT was shown to reliably measure response to bronchodilator therapy.

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Capsule

People with mutation in apolipoprotein CIII less prone to cardiovascular disease

High blood levels of triglycerides, a major form of dietary fat, have been linked to human heart disease. To identify genes that contribute to inter-individual differences in the body's handling of dietary triglycerides, Pollin and co-workers performed a genome-wide association study of volunteers from the Lancaster (U.S.) Amish population whose blood triglyceride levels had been measured before and after consumption of a milkshake. Individuals with the lowest levels of blood triglycerides were found to be heterozygous carriers of a null mutation in the gene encoding an inhibitor of triglyceride hydrolysis, called apolipoprotein C-III (apoC-III). These individuals, who produce half the normal amount of apoC-III, also had a favorable cholesterol profile and coronary calcification score, suggesting that they are less likely to develop cardiovascular disease.

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