Assessment of Bronchodilator Response in Preschool Children by Pulmonary Function Tests

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We performed pulmonary function test to document bronchodilator response by using tidal breathing flow volume loop (TBFVL), rapid thoracic compression (RTC), and raised volume rapid thoracic compression (RVRTC) techniques. Thirty-nine children (mean age 45.2 months) were evaluated. The parameters that showed significant improvement after bronchodilator administration included TEF10/ PTEF ratio in TBFVL, and $FEF_{25-75\%}$, FEV_1 and PEF in RVRTC. None of the parameters measured in RTC showed significant improvement. We conclude FEV_1, PEF and $FEF_{25-75\%}$ in RVRTC have greater sensitivity for detection of airways changes.

Keywords: *Bronchodilator, Infant, Pulmonary function test.*

Objective documentation of bronchodilator response in adults and older children may be carried out using forced expiratory maneuvers in spirometry, this may not be possible in infants and preschool children. In this age group, modified methods to assess airway status in form of tidal breathing flow volume loop (TBFVL), rapid thoracic compression (RTC), and raised volume rapid thoracic compression (RVRTC) techniques have been developed. It has been demonstrated that in RVRTC, flow limitation can be achieved during forced expiratory maneuvers in infants when initiated from near total lung capacity [1,2]. RTC and TBFVL were used for assessment of severity of airway obstruction [3]. These tests have been used to document air trapping in normal children and those with cystic fibrosis [4], and to document diminished pulmonary function test in infants with cystic fibrosis (CF) [5]. Documentation of bronchodilatory response is limited to a study in acute bronchiolitis [6] and in infants/children with recurrent episodes of wheezing [7,8]. No study has compared sensitivity of various indices to detect bronchodilatory response by these techniques. Therefore, we planned a study on infants and pre-school children with probable asthma to assess response to inhaled bronchodilator using clinical scores and to check sensitivity of various parameters obtained by TBFVL, RTC and RVRTC technique to identify bronchodilator response.

METHODS

This prospective cross-sectional study was carried out at a tertiary care center in India. Infants and pre-school children with probable asthma, weighing between 8-20 kg, who had presented to the pediatric out-patient department, were enrolled. Children presenting with acute onset cough without fever with past history of atleast more than two episodes of wheeze and family history of asthma (parents or sib) with or without wheeze were labeled as probable asthma. The study was approved by Institutional Ethics Committee. Detailed history and examination findings were recorded.

A previously validated clinical score, i.e. Respiratory Distress Assessment Instrument (RDAI) [4] including respiratory rate, heart rate, oxygen saturation, presence of wheeze and chest indrawing, was recorded before and after administration of bronchodilators. Pulmonary function tests (PFT) were performed on EXHALYZER/D (Eco Medics AG, Switzerland using standard guidelines [9]. The techniques used included: TBFVL, RTC, RVRTC. Procedure was explained to all participants and if child was not cooperative, sedation with triclofos (50 mg/kg) was used. After performing baseline PFTs, salbutamol was administered (100 µg/puff, 2 puffs) using a metered dose inhaler (MDI) and small volume spacer (350 cc) with a mask; PFTs and clinical scores were performed again after 15-20 minutes.

We considered the test values acceptable when at least 4 cycles in TBFVL and at least 3 curves of technically acceptable breath cycles in RTC and 2 acceptable breath cycles in RVRTC were obtained. For calculation of sensitivity for various parameters, an increase of more than 15% from baseline after salbutamol inhalation was considered significant [10].

As there was no similar study in literature, we planned to do this pilot study to include 30 preschool children. Data were analyzed using Stata 11 (StataCorp, College Station, TX). Data are presented in frequency percentage, mean ± SD, and confidence interval (95%). Paired *t*-test or Wilkoxon signed rank test were employed, for data following normal distribution or non-normal distribution, respectively.

RESULTS

A total of 39 (30 boys) preschool children were enrolled in the study over a period of 12 months. The mean age of enrolled subjects was 45.2 ± 14.6 months (range 9 to 58 months); their mean height was 96 ± 9.5 cm (range 68 to 111 cm) and mean weight was 13.6 ± 2.6 kg (range 8.2 to 19.2 kg). Family history of asthma was present in either parents in 22 (57%) and only in sibs in 17 (43%). Wheezing was audible in 63% of patients.

Baseline RDAI scores (mean + SD) was 2.48 (2.15) and improved to 1.17 (1.95) ($P<0.05$). Of the 39 patients, TBVFL could be performed in all patients, RTC in 38/34 (pretest/post test) and RVRTC in 34/31(pretest/post test). ***Table* I** shows changes in various indices before and after administration of the bronchodilator. ***Web Table* I** shows association between changes in clinical scores and changes in various indices of PFTs. A significant association was found between ≥2 change in RDAI score and ≥15% change in test result in RTC (V70%: P=0.04) and RVRTC (VPEF/VE%: P= 0.015).

We reanalyzed data (not shown here) after excluding infants and children without wheeze. The results did not change. However sensitivity of some indices [(TBVFL): t_E/t_tot, TEF75, TEF25, (RVRTC): TEF10/PTEF, VmaxFRC2, V70%2, PEF] showed improving trends without statistically significant deference.

DISCUSSION

In the present study, we observed that FEV_1 and PEF in RVRTC have more sensitivity to detect changes in airways diameter but various indices in RTC were not a sensitive test for same purpose. RTC maneuver works at a fraction of vital capacity and therefore it has less sensitivity than RVRTC. Other reason for low sensitivity of indices obtained from RTC include high intra individual variability due to lack of achieving flow limitation [11,12]. RTC has been reported to be less useful than RVRTC in infants with cystic fibrosis [4,5]. Modl, *et al*. [6] studied 17 infants with acute bronchiolitis and compared RTC and RVRTC and found significant difference in $VMax_{FRC}$ and $FEV_{0.5}$ after bronchodilators. However, we found FEV_1 as a sensitive test in our study but it was feasible in 36% of our patients. Mekus at al also observed that a calculation of FEV1 was rarely feasible in young infants [13].

We observed increased coefficient of variability in RTC as well RVRTC because we used less pressure (10-20 mm Hg) as recommended by manufacturer and used sedation in only 4 infants as compared to other reports [6,7] that used more pressure and sedation in all patients [6,7]. Lower ratio of TPTEF/TE has been studied as a potential tool for detecting airway obstruction [3,4,15]. We found TEF10/ PTEF ratio more useful (P= 0.0047). We could find association of ≥2 change in score and ≥15% change in test result in $V_{70\%}$ (RTC) and VPEF/VE% (RVRTC) but these parameters weren't recognized as sensitive tests for detection of airways changes.

Strengths of our study include demonstration of bronchodilator response objectively by using various parameters and documented sensitivity of indices for detection of bronchodilator response. Limitations include: inclusion of children without wheeze at time of performing test, not using sedation in all the patients and not measuring FRC. These limitations are likely to affect the measurements.

We conclude that pulmonary function test in infants and preschool children are feasible and are evolving. More studies are required to assess the utility of various indices.

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TABLE I *CHANGES IN VARIOUS PARAMETER MEASURED BY VARIOUS TEST INSTRUMENT BEFORE AND AFTER BRONCHODILATOR*

	Pre test	*Post test*	*Percentage change*	*CI (95%)*	*P value*
TBFVL					
PTEF	0.23 ± 0.145	0.24 ± 0.011	16.06	(-3.10, 35.24)	0.2641
t_E/t_tot	55.71 ± 5.18	54.86 ± 5.15	-1.14	(-4.00, 1.70)	0.2784
t_PTEF/t_E	34.73 ± 12.31	33.3 ± 11.54	2.64	((-9.08, 14.37)	0.4735
MTEF	0.142 ± 0.053	0.154 ± 0.071	13.56	(-3.48, 30.61)	0.2358
TEF75	0.193 ± 0.071	0.215 ± 0.10	17.72	(-1.56, 37.02)	0.1391
TEF50	0.189 ± 0.072	0.212 ± 0.093	19.76	(1.55, 37.97)	0.08
TEF25	0.160 ± 0.0640	0.172 ± 0.078	14.76	(-1.03, 30.56)	0.2397
TEF10	0.129 ± 0.051	0.132 ± 0.066	8.49	(-7.27, 24.26)	0.741
TEF50/TIF50	84 ± 19.68	89.26 ± 30.67	8.75	(-2.31, 19.83)	0.2782
TEF75/PTEF	90.45 ± 7.41	88.64 ± 10.48	1.85	(-5.49, 2.002)	0.2517
TEF50/PTEF	88.49 ± 6.69	88.63 ± 5.0	0.582	(-2.01, 3.18)	0.897
TEF25/PTEF	75.13 ± 10.44	72.73 ± 8.20	-1.91	(-6.50 , 2.678)	0.1057
TEF10/PTEF	61.55 ± 13.11	55.5 ± 12.66	-7.96	(-14.99, -.93)	0.0047
PTEF/V_TE	1.450 ± 0.530	1.556 ± 0.466	12.22	(3.60, 20.84)	0.1133
RTC					
Vmax FRC	375.7 ± 152.2	411 ± 204.4	56.6	(13.53, 99.70)	0.5154
V50%	387.2 ± 26.7	411 ± 35.06	12.3	(-3.00, 27.75)	0.5289
V70%	330 ± 179.7	339.5 ± 209	22.2	(-13.53,58.04)	0.5784
PEF	440.6 ± 140.4	477.7 ± 165.5	13.7	(-.20, 27.66)	0.2855
RVRTC					
Vmax FRC2	210 ± 141.6	315 ± 242.35	139.0	(-59.8, 337.9)	0.5846
V50% 2	281.2 ± 216.1	349.8 ± 246.68	151.8	(-106.5, 410.2)	0.0703
V70% 2	219.8 ± 196.7	291.5 ± 257.55	139.2	(-91.4, 369.8)	0.2286
FEV	1.92 ± 104	196 ± 101	30.18	(-3.22, 63.59)	0.2989
MEF25%	289.8 ± 190.3	335.6 ± 187.58	85.47	(7.30,163.6)	0.118
MEF10%	279.7 ± 200.6	296 ± 213.25	78.1	(-7.03,163.2)	0.3764
MEF25%/FEV	1.52 ± 0.731	3.07 ± 6.81	43.4	(-.78 ,87.77)	0.1203
FEF25-75%	293 ± 192.94	364 ± 198.70	86.61	(23.5, 149.7)	0.0598
FEV0.5	134.6 ± 76.3	159.9 ± 86.9	118.2	(11.59, 224.8)	0.1579
FEV.75	181 ± 100.4	181.7 ± 83.2	99.82	(22.97, 176.6)	0.2787
FEV 1	221± 129	201 ± 82	71.6	(20.87,1 22.3)	0.018
PEF	393.3 ± 189.1	482.9 ± 210.7	76.2	(-1.93, 154.45)	0.0205
VPEF/VE%	35.7 ± 27.9	29.42 ± 31	9.59	(-47.65, 66.84)	0.3876

Paired t-test / Wilcoxon signed rank; AVF: Area of flow volume loop , EEL: End expiratory level , ERV: expiratory reserve volume, MTEF: Mean tidal expiratory flow, MTIF: Mean tidal inspiratory flow, PTEF: Peak tidal expiratory flow, PTIF: Peak tidal inspiratory flow, t_E: Expiratory time, t_I: Inspiratory time, t_PTEF :time to PTEF, t_PTIF: time to PTIF; t_tot: total breath time ,TEF: tidal expiratory flow, TPEF/TE: time ratio of peak-TEF in time of expiration , V_T: Tidal volume

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WHAT THIS STUDY ADDS?

- Pulmonary function tests can be used to document bronchodilator response in preschool children with wheeze.
- FEV_1, PEF and $FEF_{25-75\%}$ in RVRTC have greater sensitivity for detection of airways changes.

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