Original Article

Early termination of exhalation: effect on spirometric parameters in healthy preschool children*

Efeito da terminação precoce da expiração nos parâmetros espirométricos em crianças pré-escolares saudáveis*

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Abstract

Objective: To evaluate the acceptability and reproducibility of spirometry in preschool children; to estimate the effect size of early termination of exhalation (ETE) on FVC, FEV_1 and $FEV_{0.5}$; and to evaluate the validity of $FEV_{0.5}$ in curves with ETE. **Methods:** Spirometric data were obtained from 240 healthy preschool children, who were selected by simple sampling. On the basis of the best curve from each child according to the end of exhalation, three groups were formed: no ETE (nETE); ETE and flow ≤ 10% of the highest PEF (ETE≤10); and ETE and flow > 10% of the highest PEF value (ETE>10). The reproducibility of FVC, FEV_1 and $FEV_{0.5}$ was compared among the three groups. The effect of ETE on FVC, FEV_1, and $FEV_{0.5}$ was assessed. **Results:** Of the 240 children tested, 112 (46.5%)—82 (34.0%) of those in the nETE group and 30 (12.5%) of those in the ETE≤10 group—had acceptable curves for all the parameters. In 64 (27.0%) of those in the ETE>10 group, the curves were acceptable only for $FEV_{0.5}$, increasing the proportion of children with valid $FEV_{0.5}$ to 73.0%. There were no significant differences between the nETE and ETE≤10 groups in terms of the mean values of the parameters assessed. **Conclusions:** Maneuvers with ETE and flow ≤ 10% of the highest PEF are valid. In individuals with a flow > 10% of the highest PEF value, these maneuvers are only valid for $FEV_{0.5}$.

Keywords: Spirometry; Child, preschool; Vital capacity; Forced expiratory volume; Reproducibility of results.

Resumo

Objetivo: Avaliar a aceitabilidade e a reprodutibilidade da espirometria em pré-escolares; estimar o tamanho do efeito da terminação precoce da expiração (TPE) nos valores de CVF, VEF_1 e $VEF_{0.5}$; e avaliar a validade do $VEF_{0.5}$ em curvas com TPE. **Métodos:** Espirometrias foram obtidas em 240 pré-escolares saudáveis, selecionados por amostragem simples. Três grupos foram formados com base na melhor curva de cada criança de acordo com o término da expiração: sem TPE (sTPE); com TPE e fluxo ≤ 10% do maior PFE (TPE≤10); e com TPE e fluxo > 10% do maior PFE (TPE>10). Foram comparadas a reprodutibilidade da CVF, VEF_1 e $VEF_{0.5}$ nos três grupos. Foi avaliado o efeito da TPE em CVF, VEF_1 e $VEF_{0.5}$. **Resultados:** Das 240 crianças testadas, 112 (46.5%) realizaram curvas aceitáveis para todos os parâmetros — 82 (34,0%) no grupo sTPE e 30 (12,5%) no grupo TPE≤10. Em 64 (27,0%) no grupo TPE>10, as curvas foram aceitáveis apenas para $VEF_{0.5}$, aumentando para 73,0% a proporção de crianças com $VEF_{0.5}$ válido. Não houve diferenças significantes nas médias dos parâmetros avaliados entre os grupos sTPE e TPE≤10. **Conclusões:** Manobras com TPE e fluxo ≤ 10% do maior PFE são válidas. Em indivíduos com fluxo > 10% do maior PFE, essas manobras são válidas somente para $VEF_{0.5}$.

Descritores: Espirometria; Pré-escolar; Capacidade vital; Volume expiratório forçado; Reprodutibilidade dos testes.

Introduction

For the last 10 years, spirometry has been used for the functional evaluation of preschool children.[1-9] The publication of reference values and study reports, showing that 40-90% of preschool children can perform spirometry appropriately, has promoted its use in clinical practice.[1-8] The acceptability criteria for spirometry in adults, standardized by the American Thoracic Society (ATS),[10] cannot be applied to children, especially because of the brevity of the expiratory maneuver, usually lasting less than 2-3 s. The major technical limitation is early termination of exhalation (ETE), characterized by the sudden interruption of exhalation. To allow for ETE, the following criteria for acceptable curves have been proposed[5,8,9]: minimum flows $\leq 25\%$ of the highest PEF; minimum flows $\leq 10\%$ of the highest PEF; and minimum flows ≤ 0.3 L/s. Considering the high frequency of ETE in the spirometric tests of preschool children, the ATS has proposed that the acceptability criteria be relaxed, and that curves with minimum flows $\leq 10\%$ of the highest PEF be accepted.[11] Although this relaxation of the criteria allows curves with ETE to be accepted, the clinical usefulness of such curves needs to be confirmed by determining their reproducibility.

In a recent paper focusing on preschool children, it was recommended that, for FVC and FEV_1, the reproducibility criterion be a flow ≤ 0.10 L or $\leq 10\%$ of the highest PEF, whichever is greater.[11] Regarding the reproducibility of $FEV_{0.5}$, only two studies have evaluated it, and they did not reach a consensus regarding the criterion adopted for curve termination.[3,4]

The disagreement among the authors of the various studies cited regarding whether or not curves with ETE are valid is explained by the lack of studies testing this validity. The limit of 10% of the PEF has been adopted arbitrarily and has not been validated experimentally. The objectives of the present study were to evaluate the acceptability and reproducibility of spirometry in preschool children (3-6 years of age); to estimate the effect size of ETE on FVC, FEV_1, and $FEV_{0.5}$; and to evaluate the validity of $FEV_{0.5}$ in curves with ETE > 10% of the highest PEF, but with forced expiratory time (FET) ≥ 0.5 s.

Methods

This was a prospective cross-sectional study. The target population consisted of healthy preschool children, 3-6 years of age, selected by simple sampling at public schools, private schools, and public day care centers in the city of Recife, Brazil, and evaluated between February of 2005 and December of 2006. Of the 682 schools and day care centers, 17 were selected by random sampling. From those 17 facilities, a total of 315 children were recruited. Because the present study also aimed to generate reference values, only the children considered to be free of respiratory diseases (asthma and other acute and chronic respiratory diseases) underwent testing. For classifying children as normal, we used the ATS questionnaire known as ATS-DLD-78-C, which is recommended by the Epidemiology Standardization Project and has been adapted and validated for use in Brazil[12] The questionnaire was completed by the parents or legal guardians of the children. For calculating the sample size, we considered the value of 70% as the expected frequency for tests with good reproducibility, in accordance with the study conducted by Nystad et al.[4] Accepting an error of 6%, with a confidence level of 95%, we calculated the minimum sample size to be 225 children. To compensate for losses due to any cause, we increased the sample size by 40%, and we therefore initiated the study with 315 children. After administration of the questionnaire, 240 children were considered to be free of respiratory abnormalities and were consequently included in the study.

Children with a birth weight < 2,500 g were excluded, as were those born at a gestational age < 37 weeks, those who had respiratory distress at birth, those who had previously performed spirometry, and those with previous or current heart disease.

The study was approved by the local research ethics committee. The parents or legal guardians of the children gave written informed consent.

All tests were performed with MultiSPIRO™ spirometers (WinDX Revelation 1.0.64; Creative Biomedics, San Clemente, CA, USA). At the time of testing, each child was trained individually. With a nose clip in place, the children were instructed to perform the test standing up, in accordance with the standard technique.[13] The test sessions were suspended if the acceptability

criteria were not met after an average of twelve attempts or, before that, if the child showed fatigue or disinterest.

All tests were performed by one of the study authors, who is experienced in performing spirometry in children. Only tests with at least two acceptable curves were included in the analysis. The acceptability criteria were independently evaluated by two other study authors.

The parameters evaluated were as follows: PEF; FVC; FEV_1; $FEV_{0.5}$; and $FEF_{25-75\%}$. The FVC and FEV_1 values were obtained from the best curves, in accordance with standard recommendations.[13] The $FEV_{0.5}$ values were obtained from the curves with the highest FEV_1 value or the highest $FEV_{0.5}$ value, when FET was < 1 s.

The acceptability criteria for the expiratory curves were as follows: FET ≥ 0.5 s; no artifacts (no cough and no early glottal closure); no inspiratory pause (hesitation); evidence of maximal effort (PEF showing a clear and reproducible peak); and back-extrapolated volume < 5% of FVC.

Because there is no consensus regarding the criterion for curve termination in this age group,[5,6,8,9] the acceptable tests were divided into three groups, based on the criterion for curve termination, in order to determine the validity of partial maneuvers—no child was classified as belonging to more than one group. For the analysis, we selected only the tests with at least two acceptable curves and with reproducible FVC and FEV_1 values ≤ 10% or ≤ 0.1 L. The best curve from each child was classified according to the end of exhalation as follows:

- No ETE (nETE): a full exhalation was clearly seen in the flow-volume curve, with a plateau of at least 1 s in the volume-time curve
- ETE and flow ≤ 10% of the highest PEF (ETE≤10%): this point was determined by grading the flow axis of the flow-volume curve with the use of a millimeter ruler
- ETE and flow > 10% of the highest PEF (ETE>10), with FET ≥ 0.5 s

Examples of the three types of acceptable flow-volume curves are shown in Figure 1.

The Epi Info software, version 6.04, and the Statistical Package for the Social Sciences, version 11.0 (SPSS Inc., Chicago, IL, USA), were used for the statistical analysis. The values are expressed as means and standard deviation. For the comparison of the three types of curves adopted, we used F-tests (ANOVA), Student's t-test, and Duncan's test. For a better evaluation of the results of these tests, we performed multiple linear regression analysis of the nETE and ETE≤10 groups, using FVC as the dependent variable; the independent variables were weight, age, group, gender, and height. The kappa coefficient was used for evaluating inter-rater reliability in the selection of acceptable curves. The variability of the measurements performed
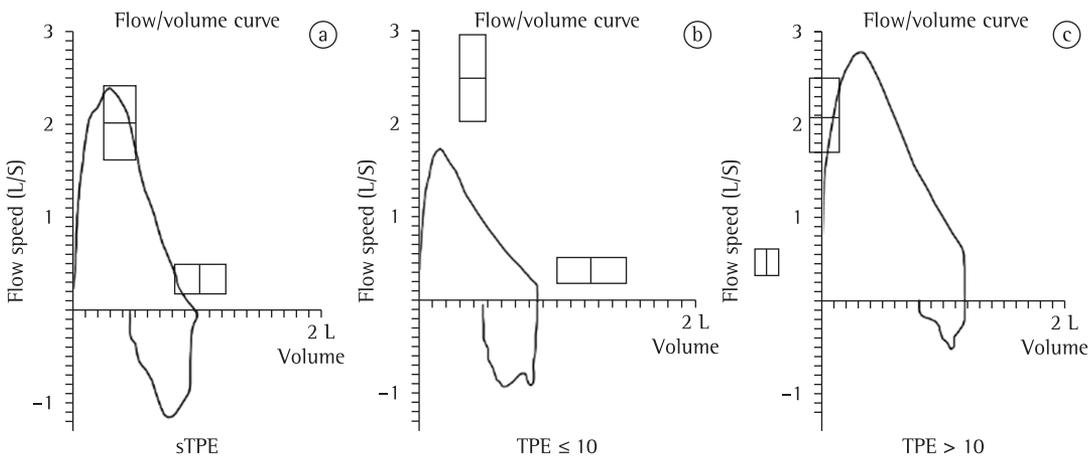
Figure 1 – Flow-volume curves, in accordance with the acceptability criteria for each group. In a, no early termination of exhalation (nETE), with a plateau of at least 1 s in duration. In b, early termination of exhalation, with the end-expiratory point at a flow ≤ 10% of the highest PEF (ETE≤10). In c, early termination of exhalation, with the end-expiratory point at a flow > 10% of the highest PEF and a forced expiratory time ≥ 0.5 s (ETE>10).

Table 1– Characteristics of the study population.[a]

Characteristic	Value
Age, months	56.61 ± 9.12
Height, cm	105.69 ± 7.42
Male, %	45.0
White, %	69.2
Weight, kg	18.91 ± 4.29
Weight percentile, %	
< 3rd	3.7
[≥ 3rd < 10th]	6.7
[≥ 10th ≤ 90th]	70.4
[> 90th < 97th]	12.5
≥ 97th	6.7

[a]Values expressed as mean ± SD, except where otherwise indicated.

was assessed by calculating the mean and standard deviation of the difference between the highest and second highest values for each parameter analyzed (PEF, FVC, FEV_1, and $FEV_{0.5}$), separated by type of curve, with the Kruskal-Wallis and Mann-Whitney tests.

Results

Of the 315 children initially evaluated, 56 (18%) were excluded because of a diagnosis of asthma and 19 (6%) were excluded for various reasons (e.g., preterm birth, low weight, heart disease, and declining to undergo testing). Therefore, 240 children underwent testing and were distributed by age as follows: 3 years, 39 (16%); 4 years, 81 (34%); 5 years, 107 (45%); and 6 years, 13 (5%). The characteristics of the sample are detailed in Table 1.

Among the 240 children tested, we obtained at least two acceptable curves in 82 (34.0%) of those in the nETE group; in 30 (12.5%) of those in the ETE≤10 group; and in 64 (27%) of those in the ETE>10 group (Table 2). In

the last group, only the $FEV_{0.5}$ and PEF values were considered. Analyzing the first two groups together, we found that 112 children (46.5%) performed acceptable maneuvers, in accordance with the current guidelines of the ATS and of the European Respiratory Society (ERS).

Considering the nETE and ETE≤10 groups collectively and by age (% of those in the sample as a whole), we obtained at least two acceptable curves in 9 children in the 3-year-old group (7.4%); in 36 children in the 4-year-old group (29.5%); and in 65 children in the 5-year-old group (53.3%), demonstrating that acceptability increases with age. Considering the ETE>10 group alone, we obtained at least two acceptable curves in 14 children in the 3-year-old group (22.0%); in 35 children in the 4-year-old group (54.7%); and in 15 children in the 5-year-old group (23.4%). Therefore, nearly 77% of the children producing at least two acceptable curves were below 5 years of age. The proportion of children producing at least three acceptable curves was 76%, 64%, and 58% in the nETE, ETE≤10, and ETE>10 groups, respectively. The proportion of children producing at least two acceptable curves was higher than 84% in all three groups.

Regarding the reproducibility of FVC and FEV_1, the nETE group, as well as the ETE≤10 group (with at least two acceptable curves), had a rate above 90% when the reproducibility criteria were flows ≤ 0.1 L and ≤ 10% of the highest PEF (Table 3). Regarding the reproducibility of $FEV_{0.5}$ in relation to the criterion of a flow ≤ 10% of the highest PEF in the children who had at least two acceptable curves, the rate was ≥ 95% for the three groups. In the children who had at least three acceptable curves, the rate was ≥ 81% (data not shown).

Table 2 – Distribution of the 240 children in the study by the acceptability criteria adopted for the curves obtained in relation to the number of acceptable curves.[a]

Number of acceptable curves	Groups		
	nETE	ETE≤10	ETE>10
	(n = 82)	(n = 30)	(n = 64)
	n (%)	n (%)	n (%)
2	15 (18)	8 (27)	22 (34)
3	67 (82)	22 (73)	42 (66)

nETE: no early termination of exhalation; ETE≤10: early termination of exhalation and flow ≤ 10% of the highest PEF; and ETE>10: early termination of exhalation and flow > 10% of the highest PEF, with a forced expiratory time ≥ 0.5 s. [a]Of the 240 children included in the study, 64 (27% of the sample as a whole) had fewer than two acceptable curves.

Table 3 – Evaluation of the reproducibility of FVC, FEV$_1$, and FEV$_{0.5}$ among the children who had at least two acceptable curves, by group.

Variable	Groups		
	nETE	ETE≤10	ETE>10
	(n = 82)	(n = 30)	(n = 64)
	n (%)	n (%)	n (%)
FVC ≤ 0.10 L	79 (96.3)	29 (96.7)	-
FEV$_1$ ≤ 0.10 L	78 (95.1)	29 (96.7)	-
FVC ≤ 10.0%	79 (96.3)	30 (100.0)	-
FEV$_1$ ≤ 10.0%	80 (97.6)	29 (96.7)	-
FEV$_{0.5}$ ≤ 10.0%	81 (98.8)	30 (100.0)	61 (95.3)

nETE: no early termination of exhalation; ETE≤10: early termination of exhalation and flow ≤ 10% of the highest PEF; and ETE>10: early termination of exhalation and flow > 10% of the highest PEF, with a forced expiratory time ≥ 0.5 s.

The mean values of the parameters assessed were compared among the three groups. Between the nETE and ETE≤10 groups, there was a statistically significant difference only for FVC (data not shown). In order to confirm this difference, we performed multiple linear regression analysis. However, the analysis reviewed no significant difference between the nETE and ETE≤10 groups in terms of FVC (p = 0.346). On average, the FVC values were 27 mL lower in the ETE≤10 group curves than in the nETE group curves. Because the mean FVC value of the latter group was 1,082 mL, this error corresponds to less than 3% (Table 4). Therefore, the ETE≤10 group curves can be considered valid, even in relation to the FVC values.

For the independent selection and classification of curves, we found good inter-rater reliability (kappa coefficient = 0.72), in accordance with the various acceptability criteria adopted. In terms of variability, there were no significant differences among the three types of curves (data not shown).

Table 4 – Multiple linear regression analysis of the differences between the group with no early termination of exhalation group and the early termination of exhalation/flow ≤ 10% of the highest PEF group, in terms of FVC.[a]

Variable	Coefficient		Standardized coefficient
	β	SE	β
Constant	−1.065	0.242	
Height	0.020	0.003	0.572
Female gender	−0.125	0.024	−0.250
Group	−0.027	0.029	−0.047
Weight	0.010	0.004	0.168
Age	0.001	0.002	0.047

[a]Dependent variable.

Discussion

In the present study, we observed that, with the use of stricter acceptability criteria, based on the acceptance of full exhalation curves exclusively, only 34% of the preschool children were able to perform acceptable maneuvers. With the use of more flexible criteria, such as those currently recommended by the ATS/ERS (equivalent to those applied to the ETE≤10 group), that rate was 46.5%. With the acceptance of curves that were less complete (equivalent to those of the ETE>10 group), 73% of the children tested were able to perform maneuvers with reliable and reproducible FEV$_{0.5}$. The ETE≤10 group curves were valid, reliable, and reproducible for FVC, FEV$_1$, and FEV$_{0.5}$. The ETE>10 group curves, with FET ≥ 0.5 s, were only valid for FEV$_{0.5}$.

The proportion of acceptable curves in the nETE group (34%) was lower than that reported in a previous study (40%),[6] possibly because of the lower mean age of the children in our study (4.7 years vs. 5.1 years). A recent study, in which the 2007 ATS/ERS recommendations were used, found that 56% of preschool children (4-6 years of age) were able to produce acceptable and reproducible spirometry results.[14] In the present study, that rate was only 46.5%, possibly because our sample was younger, with a predominance of children 3-5 years of age (6-year-olds accounted for only 5% of our sample). A recent study evaluating spirometry results in 76 preschool children with asthma found a high percentage of acceptability (82.4%), with a mean age of 4.8

years, similar to that observed in our sample[15]; the differences in the criterion adopted for curve termination might be the explanation for the higher percentage of acceptability (the authors reported that there was a plateau only in the final second). In preschool children, we often observe a plateau in the volume-time curve. However, inspection of the flow-volume curve reveals no correspondence of full exhalation. This is due to a fault in the spirometer program, which maintains the record of a plateau even after the end of exhalation. In some studies of preschool children, the criterion adopted for curve termination is unclear, making it difficult to assess that criterion more accurately, as well as to make comparisons across studies.[2-4] Acceptability was found to increase with age, a finding that is in accordance with data in the literature.[4,6]

Although the number of small children who were able to perform maneuvers in accordance with the 2007 ATS/ERS acceptability criteria was small (7.4% of those aged 3 years and 29.5% of those aged 4 years), with the acceptance of the ETE>10 group curves, $FEV_{0.5}$ could have been assessed in 20% more of the children tested, raising the proportion of preschool children with available $FEV_{0.5}$ data to 73%, which would justify the use of spirometry in this age group.

The high reproducibility and low variability of FVC, FEV_1, and $FEV_{0.5}$ in the three groups demonstrates that the measurements performed are reliable. The evidence that the ETE≤10 group curves, which were similar to those recommended by the ATS/ERS in 2007, were reliable and reproducible, validates this standard. Although the confirmed reliability of curves with ETE is a recommended criterion for curve termination in preschool children in the ATS/ERS document,[11] there have been no studies testing that reliability.

The observation that the curves of the ETE>10 also showed high reproducibility and low variability demonstrates that the PEF and $FEV_{0.5}$ values are reliable and can be used in clinical practice. Other studies have demonstrated that $FEV_{0.5}$ is reproducible and can be used in the assessment of bronchodilator response.[3,4,9] Vilozni et al. assessed the effect of bronchodilators in children with moderate or severe asthma and observed that, in those with moderate asthma (n = 62), there was, in relation to the baseline value, a response in the mean FEV_1 and in the mean $FEV_{0.5}$ of, respectively, 14% ± 10% and 15% ± 11%, suggesting that the latter would be useful in the assessment of bronchodilator response.[9]

The good inter-rater reliability in the analysis and classification of the maneuvers by group indicates the reliability of the tests.

For younger children who cannot make a full exhalation, curves with partial exhalation, with measurements of FEV_1 or only of $FEV_{0.5}$, can be used in the assessment of respiratory symptoms because they have been proven to be reliable, reproducible, and useful in the assessment of bronchodilator response. The sensitivity of this parameter for the detection of functional abnormalities should be tested in future studies. Similarly, there is a need for studies that will specifically assess cut-off points for bronchodilator response measured by $FEV_{0.5}$.

It was evident in the present study that, in order to calculate the cut-off point for acceptability of curves with ETE more accurately, more appropriate spirometry programs are necessary, with screens with larger flow-volume curves and two axes with a millimeter ruler. These findings show the need for adapting the spirometry programs to the preschool age group.

Acknowledgments

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