TIDAL BREATHING ANALYSIS AS A TOOL FOR ASTHMA DIAGNOSIS IN CHILDREN AGED SIX MONTHS TO FIVE YEARS

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ABSTRACT

BACKGROUND: The diagnosis of asthma is difficult to establish using spirometry in children below 5 years old. Tidal breathing analysis (TBA) can provide useful information about lung function in infants and young children, as it is effort-independent.

OBJECTIVES: To determine if baseline and post-bronchodilator ratios of the time and volume until peak expiratory flow to the total expiratory time and volume, (t_{PEF}/t_E and V_{PEF}/V_E) can distinguish asthmatics from normal children.

METHODS: This is a cross-sectional study wherein 146 children ages 6 months to 5 years old completed TBA before and 15 minutes after administration of 250µg of salbutamol via nebulization. Children 3 years old and below who did not cooperate were given sedation with oral diphenhydramine (1mg/kg/dose). The t_{PEF}/t_E and V_{PEF}/V_E were compared between the controls and asthmatics.

RESULTS: In children below 2 years old, the baseline t_{PEF}/t_E of asthmatics and non-asthmatics were 29.6 ± 13.8and 22.0 ± 6.6. The area under the curve (AUC) was 0.649 at$t_{PEF}/t_E$of 32.250, with a sensitivity and specificity of 50% and 97%. The baseline V_{PEF}/V_E of asthmatics and non-asthmatics were 32.7 ±12.4 and 26.0 ± 4.9.AUC was 0.661 atV_{PEF}/V_Eof34.500, with a sensitivity and specificity of 50% and 97%.In subjects 2 to 5 years old, the baseline t_{PEF}/t_E of asthmatics and non-asthmatics were 35.3 ± 14.7 and 35.0 ± 13.1. The baseline V_{PEF}/V_E were 37.0 ± 12.3 and 36.7 ± 10.7. After salbutamol nebulization, the t_{PEF}/t_E of asthmatics and non-asthmatics in all ages were 30.9±13.7 and 27.9± 10.8. The V_{PEF}/V_E were 34.1± 11.4 and 30.9± 9.0.

CONCLUSION: Baseline t_{PEF}/t_E and V_{PEF}/V_E can distinguish asthmatics from non-asthmatics in children below 2 years old. However, baseline t_{PEF}/t_E and V_{PEF}/V_E in children 2 to 5 years old and post-bronchodilator t_{PEF}/t_E and V_{PEF}/V_E in all ages could not distinguish asthmatics from non-asthmatics after nebulization with 250µg of salbutamol.

KEYWORDS: Tidal breathing analysis (TBA), ratio of time to peak tidal expiratory flow and expiratory time (t_{PEF}/t_E), ratio of volume at peak tidal expiratory flow and expiratory volume (V_{PEF}/V_E), tidal breathing flow volume (TBFV), bronchodilator challenge

INTRODUCTION

Asthma diagnosis is usually made clinically. In infants, clinical diagnosis is sometimes difficult, as they do not necessarily follow the classic symptoms that older children have.[1]Measurements of lung function are important to provide an assessment of the severity of airflow limitation and its reversibility, to provide confirmation of the diagnosis of asthma.[2] It is known that asthma is characterized by variable expiratory airflow limitation(i.e. expiratory lung function varies over time and in magnitude).[3] Lung function may vary between completely normal and severely obstructed in the same patient. Thus, bronchodilator challenge testing is recommended aside from studies of airflow limitation due to the possibility that asthmatics may have normal baseline lung function but still demonstrate reversibility. [4]

The common techniques in measuring pulmonary function are frequently used in older children and adolescents. In infants and young children, it is often difficult to measure pulmonary function because of lack of patient cooperation, short attention span and inability to follow instructions. [5]

Spirometry is the most frequently used method for measuring lung function. [6] This test requires cooperation from subjects, hence, cannot be used for infants and most preschoolers. Forced oscillation technique (FOT) or impulse oscillometry (IOS) requires passive patient cooperation.[7]On the other hand, body plethysmography and tidal breathing analysis (TBA) have the potential to provide useful information about lung function in infants and young children as it only needs quiet respiration, hence suitable for this age group.[8]

TBA is a non-invasive pulmonary function test that measures changes in the flow and volume at the airway opening or from body surface measurements. It has been used in several foreign and local studies in newborns, infants and pre-school children to establish reference values for tidal breathing.[9-14]It was used in several studies for assessing airway obstruction with varying results[15-18].

Comparison of the baseline t_{PEF}/t_E and V_{PEF}/V_E between asthmatic and non-asthmatic children below 5 years old were only seen in foreign literature, but local studies on the normative values of t_{PEF}/t_E and V_{PEF}/V_E showed that Filipinos had lower t_{PEF}/t_E and V_{PEF}/V_E when compared with the corresponding reference data.[13, 14]A local study by Corpuz et al[20] assessed the reversibility of t_{PEF}/t_E and V_{PEF}/V_E between asthmatics and non-asthmatics using 15% change from baseline by computing for the sensitivity and specificity. The study neither determined the difference in the baseline t_{PEF}/t_E and V_{PEF}/V_E between the two groups nor computed for the specific percentage change that will distinguish the asthmatics from the non-asthmatics.

We aimed to determine the utility of tidal breathing analysis in diagnosing children with asthma. Specifically, we wished to determine the sensitivity and specificity of baseline t_{PEF}/t_E and V_{PEF}/V_E, and if reversibility of t_{PEF}/t_E and V_{PEF}/V_E to salbutamol respiratory solution could distinguish asthmatics from normal children.

METHODOLOGY

This was a cross-sectional study. We coordinated with the Quezon City Health Office to notify randomly selected heads of day care centers, pre-schools, and barangay health centers. Prospective subjects were sent to the Pulmonary Laboratory at Philippine Children's Medical Center. Demographic data and medical history were taken and recorded in a questionnaire evaluation form after purposive sampling of study participants. Physical examination was performed on each subject, and anthropometric measurements such as weight and height/length were recorded. Subjects who fulfilled the inclusion criteria were enrolled into the study after thorough explanation of the procedures to the parents and guardians, and after getting their informed consent.

Subjects aged 6 months to 5 years old were included if both parents were Filipino, asymptomatic at the time of enrollment, and had normal physical examination findings at the time of enrollment. Subjects with history of respiratory tract infection for the past 2 months, congenital malformation of the respiratory tract or chest wall or diaphragm, chronic lung disease, prematurity, cardiopulmonary or other systemic illness such as collagen diseases, nephropathies, any malignancy, neuromuscular disease such as Guillain-Barré Syndrome, myasthenia gravis and muscular dystrophies, thoracic and chest wall deformities, thoracic or abdominal surgery within the past 3 months, intake of any medication except vitamins for the past 4 weeks, exposure to tobacco smoke at home , and malnutrition (Weight for Length / Height Z score below -2 or above 3) were excluded from the study.

Physician-diagnosed asthmatics (re-evaluated by a pediatric pulmonologist) who were classified as intermittent asthmatic based

on the Philippine Consensus for the Management of Childhood Asthma (2002)[21] as reference standard were included. Other inclusion criteria for the asthmatic group were:1) any one of either parental asthma, physician diagnosis of atopic dermatitis, or evidence of sensitization to allergens in the air; and 2) any two of physician-diagnosed allergic rhinitis, wheezing unrelated to colds, and blood eosinophils >4%.

Subjects who used inhaled ß$_2$-agonists, ipratropium bromide or any other bronchodilating drugs, inhaled corticosteroids or disodium cromoglycate within12 hours before measurement, systemic ß$_2$-agonists or theophylline/aminophylline within 24 hours before measurement, and asthma controller medications (inhaled corticosteroids alone or in combination with long-acting ß$_2$-agonists, leukotriene receptor antagonists, herbal medications) in the past 4 weeks were excluded from the asthma group.

The performance of TBA followed the recommendations of the American Thoracic Society/European Respiratory Society statement on pulmonary function testing in pre-school children (2006).[6] Subjects rested for at least 10 minutes prior to the procedure**.** Children less than 3 years of age who did not sit quietly were sedated using oral diphenhydramine (1 mg/kg/dose, maximum: 50 mg) 30 minutes prior to the procedure. Those who vomited the said medication within 30 minutes after ingestion of the drug were given another dose. Patients not sedated after an hour from administration of the medicine were also given another dose, provided that the maximum dose was not yet reached.

The study consisted of measurements of tidal breathing flow volume (TBFV) loops: 1) at baseline and 2) 15 minutes after inhalation of salbutamol respiratory solution. A senior respiratory therapist measured the TBFV loops using MasterscreenPaed Jaeger Pediatric (Version 4.67 2012) in baseline condition and after inhalation of salbutamol respiratory solution. The respiratory therapist ensured that the respiratory pattern was stable and regular before starting data recording. A minimum of 30 seconds of tidal breathing was recorded to obtain a stable epoch of 20 tidal breaths per trial for a total of three consecutive trials. The computer calculated the final value, and the mean value was reported. Breaths were not included for analysis if they were obviously different in shape or size from surrounding breaths (e.g., sighs), if there were doubtful points of zero flow (e.g., pause between inspiration and expiration), or if there was more than one peak of expiratory flow. Indices obtained were calculated for 20 consecutive individual breaths per trial.

The nebulized solution was salbutamol (*Ventolin Respiratory Solution*), 250 µg placed in *DevilbissPulmo-Aide* compressor/nebulizer with a flow of 9L/min, attached to a face mask. The output of the nebulizer was 0.15mL/min with particles having a diameter below 5µm. The senior respiratory therapist measured the TBFV loops again, as previously described. Gathered data were recorded in a data sheet by the principal investigator.

The measurements were performed between 0800h and 1200h at the Pulmonary Laboratory of the Philippine Children's Medical Center in a cool and quiet environment. The average duration of each measurement of lung function was 10 minutes, and the entire sequence of lung function measurements before and after nebulization of salbutamol, including nebulization time took approximately 45 minutes.

A total sample size of 144 subjects achieved 82% power to detect a difference of -6 in t_{PEF}/t_E and V_{PEF}/V_E if the mean ratio of t_{PEF}/t_E and V_{PEF}/V_E for the control group was 31.77 with a standard deviation of 12.38. This calculation was based on a significance level of 0.05 using a 2-sided two-sample T-test based on a previous study done by Carlsen KH et al. [19]

Descriptive statistics was used to summarize the clinical characteristics of the patients. Frequency and proportion was utilized for nominal variables, and mean and SD for interval/ratio variables. Independent sample T-test was used to determine the significant difference between respondents with and

without asthma on interval/ratio scale type of data, while Chi-square analysis for the frequency of two groups. All valid data were included in the analysis. Missing variables were neither replaced nor estimated. Null hypotheses were rejected at 0.05 α-level of significance. Statistical analysis (SSPS Statistics 15.0) was used for data analysis.

RESULTS

There were one hundred and ninety-three (193) children recruited from health centers and day care centers in the Quezon City area, as well as in the private and out-patient clinics of Philippine Children's Medical Center. Participating barangay health centers were drawn at random from a list provided by the city health office. Six subjects were excluded due to malnutrition. TBA was attempted in all subjects, but twenty were entirely not subjected to the procedure due to the following reasons: infants unable to sleep despite sedation, and preschoolers who refused to do the test. Among those who completed the baseline measurements, two refused to undergo the post-bronchodilator determination and nineteen infants awakened during and/or after nebulization. The failure rate was 11.2%.

A total of 146 patients were included, 38 of whom were asthmatics. The patients without asthma were significantly younger, and subsequently had lower weight and height. Gender distribution was similar between groups (Table 1).

Table 1. Demographic Profile of Patients

Age Group	n	Demographic Characteristics	Control n (sd)	Asthmatic n (sd)	p-value
0 to < 2 years old	35	Female (14)/Male (21)	13 (44.8)/16 (55.2)	1 (16.7)/5 (83.3)	0.366 (NS)[a]
		Age (years)	0.83 (0.21)	1.00 (0.00)	0.000**[d]
		Weight (kg)	8.52 (1.60)	10.22 (1.55)	0.023*[c]
		Height (cm)	72.97 (7.87)	79.83 (5.27)	0.050 (NS)[c]
2 to 5 years old	111	Female (61)/Male (50)	44 (55.7)/35 (44.3)	17 (53.1)/15 (46.9)	0.805 (NS)[b]
		Age (years)	3.62 (1.14)	4.19 (0.93)	0.008**[d]
		Weight (kg)	14.27 (2.90)	15.38 (2.60)	0.064 (NS)[c]
		Height (cm)	96.63 (9.77)	101.47 (7.95)	0.015*[c]
All ages	146	Female (75)/Male (71)	57 (52.8)/ 51 (47.2)	18 (47.4)/ 20 (52.6)	0.566 (NS)[b]
		Age (years)	2.87 (1.58)	3.68 (1.45)	0.006**[c]
		Weight (kg)	12.72 (3.66)	14.56 (3.10)	0.006**[c]
		Height (cm)	90.28 (14.03)	98.05 (10.98)	0.002**[c]

a using Fisher's Exact test
b using Pearson Chi-square test
c using ANOVA F test
d using t-test for equality of means
* significant at the 0.05 level of significance
** significant at the 0.01 level of significance
(NS) not significant

To check whether the baseline tidal breathing analysis parameters were different between asthmatics and non-asthmatics, ANOVA F-Test was used. Table 2 compares the average baseline tidal flow parameters between patients with and without asthma. Only children less than 2 years old had statistically significant difference when baseline tidal flow parameters were compared.

Table 2. Comparison of Baseline Tidal Flow Parameters in the Controls and Asthmatics

Tidal Flow Parameters	n	Control (n = 108)	Asthmatics (n = 38)	p-value
t_{PEF}/t_E				
0 to < 2 years old	35	22.0 ± 2.4	29.6 ± 11.0	0.046*
2 to 5 years old	111	35.0 ± 2.9	35.3 ± 5.1	0.903 (NS)
V_{PEF}/V_E				
0 to < 2 years old	35	26.0 ± 1.8	32.7 ± 9.9	0.031*
2 to 5 years old	111	36.7 ± 2.4	37.0 ± 4.3	0.911 (NS)

* significant at the 0.05 level of significance
(NS) not significant

Receiver operating characteristic (ROC) curves were drawn for diagnosing asthma in children below 2 years old based on baseline TBA. At t_{PEF}/t_E, the AUC was 0.649 (95% CI: 0.305 to 0.993). Using the cutoff point of 13.300, the sensitivity and specificity of the t_{PEF}/t_E to diagnose asthma were 83% and 3%, respectively. Using the cutoff point of 23.550, the sensitivity and specificity of the t_{PEF}/t_E to diagnose asthma were 67% and 62%, respectively. Using the cutoff point of 32.250, the sensitivity and specificity of the t_{PEF}/t_E to diagnose asthma were 50% and 97%, respectively (Figure 2a). At V_{PEF}/V_E, the AUC was 0.661 (95% CI: 0.302 – 1.000). Using the cutoff point of 19.250, the sensitivity and specificity of the V_{PEF}/V_E to diagnose asthma were 83% and 3%, respectively. Using the cut off point of 28.050, the sensitivity and specificity of the pre-bronchodilator at V_{PEF}/V_E to diagnose asthma were 67% and 66%, respectively. Using the cutoff point of 34.500, the sensitivity and specificity of the V_{PEF}/V_E to diagnose asthma were 50% and 97%, respectively (Figure 2b).

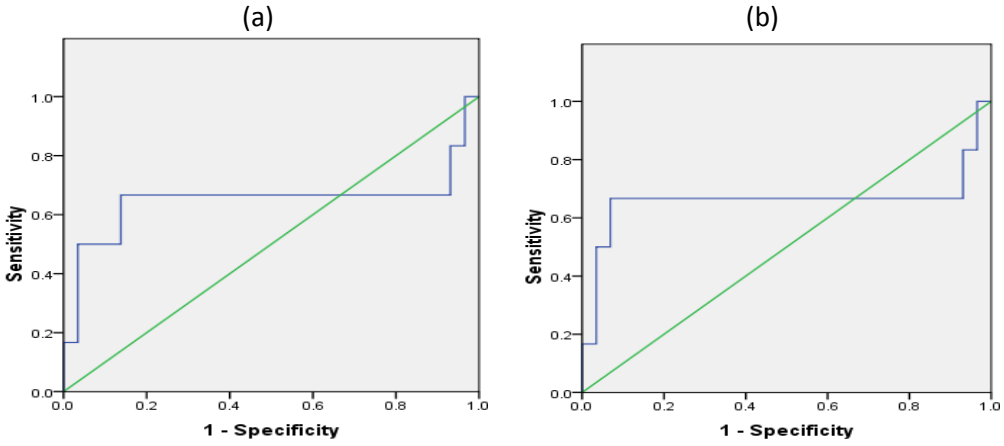

Figure 1. ROC Curve for children less than 2 years old at baseline (a)t_{PEF}/t_E [AUC 0.649 (95% CI: 0.305 to 0.993)] **and (b)V_{PEF}/V_E**[AUC 0.661 (95% CI: 0.302 – 1.000)]

Table 3 shows the comparison in reversibility of t_{PEF}/t_E and V_{PEF}/V_E between patients with and without asthma. Results showed that there was a significant difference between the baseline and post-bronchodilator T_{PEF}/T_E in the older age group, but not in the younger patients of both asthmatics and non-asthmatics. Results for V_{PEF}/V_E showed that there is no difference in all subjects except for the 2 to 5 years old non-asthmatics.

Table 3. Comparison of Reversibility of t_{PEF}/t_E and V_{PEF}/V_E in Controls and Asthmatics

Tidal Flow Parameters	n	Controls (n = 108)		p-value	Asthmatics (n = 38)		p-value
T_{PEF}/T_E		Baseline	Repeat		Baseline	Repeat	
0 to < 2 years old	35	22.0 ± 2.4	20.0 ± 5.8	0.064(NS)	29.6 ± 11.0	24.1 ± 15.8	0.266 (NS)
2 to 5 years old	111	35.0 ± 2.9	30.8 ± 10.8	0.001**	35.3 ± 5.1	32.2 ± 13.1	0.023*
V_{PEF}/V_E							
0 to < 2 years old	35	26.0 ± 1.8	24.4 ± 4.7	0.065(NS)	32.7 ± 9.9	28.1 ± 13.8	0.196 (NS)
2 to 5 years old	111	36.7 ± 2.4	33.2 ± 9.1	0.001**	37.0 ± 4.3	35.2 ± 10.8	0.136 (NS)

Statistical Analysis used: Paired T-test
* significant at the 0.05 level of significance
** significant at the 0.01 level of significance
(NS) not significant

The use of percent change after bronchodilation measured the reversibility of t_{PEF}/t_E and V_{PEF}/V_E in each individual. Table 4 shows that neither t_{PEF}/t_E nor V_{PEF}/V_E was significantly different between children with and without asthma.

Table 4. Comparison of means of tidal flow parameters between the asthmatics and controls using percent change of reversibility

Tidal Flow Parameter	n	Change from baseline in controls (%, sd)	Change from baseline in asthmatics (%, sd)	p-value
T_{PEF}/T_E				
0 to < 2 years old	35	-6.3 (23.1)	-13.8 (34.7)	0.511(NS)
2 to 5 years old	111	-6.1 (34.0)	-6.3 (19.3)	0.984(NS)
All ages	146	-6.2 (31.4)	-7.5 (22.0)	0.817(NS)
V_{PEF}/V_E				
0 to < 2 years old	35	-4.8 (16.3)	-12.8 (21.8)	0.312(NS)
2 to 5 years old	111	-6.1 (24.6)	-2.8 (16.3)	0.478(NS)
All ages	146	-5.8 (22.6)	-4.4 (17.4)	0.722(NS)

Statistical test used: independent T-test
* significant at the 0.05 level of significance
** significant at the 0.01 level of significance
(NS) not significant

DISCUSSION

TBA is a non-invasive pulmonary function test that measures changes in the flow and volume at the airway opening or from body surface measurements. The breathing pattern obtained during tidal breathing contains significant physiological information pertaining to a number of processes related to respiratory control and pulmonary mechanical function.[8] Most published data measured the flow and volume, and related this to timing of peak tidal expiratory flow namely: (*1*) Time to peak tidal expiratory flow (t_{PEF}) (s), (*2*) total expiratory time (t_E) (s), (*3*) the ratio of these (t_{PEF}/t_E), (*4*) volume at peak tidal expiratory flow (V_{PEF}) (ml), (*5*) expired tidal volume (V_E) (ml), and (*6*) the ratio of these (V_{PEF}/V_E). The peak tidal expiratory flow measures, t_{PEF}/t_E and V_{PEF}/V_E are commonly used in the assessment of obstructive pulmonary diseases.[6] t_{PEF}/t_E and V_{PEF}/V_E were also correlated to other parameters of airway obstruction including FEV1[22] hence, the present study used these parameters.

t_{PEF}/t_E measures the delay between the initiation of expiratory flow and peak expiratory flow during tidal breathing. In healthy patients, peak flow occurs at approximately one-third of the expiratory phase.[23] With airway obstruction, the round tidal loop takes on a more triangular appearance as the peak expiratory flow occurs closer to the beginning of expiration.[23]

Both the t_{PEF} and t_E influence the final value of the ratio t_{PEF}/t_E. Among patients with symptomatic bronchiolitis, slow exhalation secondary to an increased expiration time constant will increase t_E. In addition, active laryngeal breaking is diminished, leading to decreased $t_{PEF.}$[15] These patients with airflow obstruction are therefore expected to have decreased t_{PEF}/t_E. Behavior of the parameters t_{PEF} and t_E were comparable with that of V_{PEF} and V_E.[18]

There is only one foreign study and one local study in the literature comparing the baseline t_{PEF}/t_E and V_{PEF}/V_E between asthmatics and non-asthmatics less than 2 years old.[19, 21] Both showed that the baseline t_{PEF}/t_E and V_{PEF}/V_E of asthmatics were lower than those of non-asthmatics, which is in contrast with that of the present study. Clarke and associates showed that in healthy infants t_{PEF}/t_E values were significantly higher at 1 month than at 6 months and did not alter between 6 and 12 months.[25] This change seems to be entirely due to an increase in t_E, whereas the t_{PEF} remains constant during the 12 months.[26] The increase in t_E is caused by a gradual decrease in respiratory rate during the first year of life.[27] Thereafter, t_{PEF}/t_E values in infants gradually become similar to those obtained in older children and adults.[28] These physiologic changes could explain why t_{PEF}/t_E and V_{PEF}/V_E values in the present study differ from that of previous studies. None of the asthmatics were below 12 months old, and majority of the non-asthmatics were less than 1 year old.

ROC curves were used to determine baseline cutoff values of t_{PEF}/t_E and V_{PEF}/V_E to discriminate asthmatics from non-asthmatics. Three values were presented each for t_{PEF}/t_E and V_{PEF}/V_E. Using a cutoff value of 23.550 for t_{PEF}/t_E and 28.050 for V_{PEF}/V_E may not discriminate asthmatics from non-asthmatics. Using a cutoff value of 13.300 for t_{PEF}/t_E and 19.250 for V_{PEF}/V_E may miss out asthmatics in 17% of cases. Using a cutoff value of 32.250 for t_{PEF}/t_E and 34.500 for V_{PEF}/V_E will diagnose asthmatics correctly in 97% of cases, but may misdiagnose 3% of non-asthmatics as having asthma. Only for this purpose, to rule in asthma, use a higher t_{PEF}/t_E and V_{PEF}/V_E cutoff value.

There are two studies assessing reversibility of t_{PEF}/t_E and V_{PEF}/V_E after administration of salbutamol respiratory solution to children less than 2 years old.[19,21] Both studies show that there is a significant difference in the t_{PEF}/t_E and V_{PEF}/V_E at baseline and after bronchodilation between asthmatics and non-asthmatics. This is also in contrast with the result of the present study. The differences in ethnicity, inclusion/exclusion criteria, state of arousal, and TBA software used could have been sources of differences in the results of the present study from the previous studies. In the study by Carlsen and colleagues, participants

were all Caucasians and asymptomatic. Asthmatic children were in different grades of severity, some on controller medications. They were measured awake (in sitting position), using Sensor Medics 2600 system. The nebulized solution was 500 μg of salbutamol respiratory solution. In the study by Corpuz et al, participants were symptomatic Filipino children with recent use of systemic corticosteroids, sedated at the time of measurement using an older version of MasterscreenPaed Jaeger Pediatric, and were nebulized with 250 μg of salbutamol respiratory solution. Investigators of the present study did not follow the inclusion/exclusion criteria of the previous studies because presence of symptoms at the time of enrollment and use of controller medications could affect the results of the TBA. Participants of the present study were asymptomatic; asthmatic subjects were only those who were classified as intermittent asthmatics, without recent use of systemic corticosteroids. All subjects less than 2 years old were sedated hence measured in the supine position, the rest were awake and seated. The software used was MasterscreenPaed Jaeger Pediatric (Version 4.67 2012).

Three previous studies in children above 2 years old have shown differences in the baseline t_{PEF}/t_E and V_{PEF}/V_E and their reversibility among asthmatics and non-asthmatics.[19,21,24] Most of these studies were done in subjects who presented with signs of airflow obstruction. Only 2 of these studies were definite with the technique in performing TBA, the software used, dose of the bronchodilating agent and the state of arousal of participating subjects. All 3 studies showed that the baseline t_{PEF}/t_E and V_{PEF}/V_E of asthmatics were lower compared to controls, and that there was significant reversibility after bronchodilation in asthmatic subjects. Again, these were in contrast with that of the present study, wherein controls had lower t_{PEF}/t_E and V_{PEF}/V_E values and that there was no significant change in reversibility between asthmatics and non-asthmatics. Theoretically, sedation may reduce t_{PEF}/t_E by diminishing active laryngeal breaking.[15] This theory was in contrast to the study of Stocks and coworkers, that although there were no statistically significant differences in t_{PEF}/t_E or t_E between sedated and awake children, sedated children had higher tidal volume, higher PTEF, and a higher breathing frequency.[27] Higher t_{PEF}/t_E and V_{PEF}/V_E may be explained by arousal state, as awake infants seem to have higher tidal flows than sleeping infants, as shown in previous studies.[8] It must be noted that in the present study, most of the asthmatic population belong to the older age group. Only those 3 years old and below who did not cooperate were given sedation. This may explain the lack of significant differences in t_{PEF}/t_E and V_{PEF}/V_E between the asthmatic and control groups. A study by Cutrera and associates found out that under baseline conditions, V_{PEF}/V_E did not differentiate between asymptomatic asthmatic children and control subjects.[29]

The present study used 250 μg of salbutamol to assess reversibility based on the Global Initiative for Asthma Global Strategy for Asthma Management and Prevention 2012.[2] There was evidence of reversibility in subjects greater than 2 years old, both in asthmatics and non-asthmatics (Table 4). But when post-bronchodilator t_{PEF}/t_E and V_{PEF}/V_E between asthmatics and non-asthmatics were compared, the difference was not significant. Although a standard method of aerosol delivery and standard dose of bronchodilator were used, altered respiratory mechanics due to airflow obstruction in asthmatics may have lead to a decrease in the delivered dose of bronchodilator resulting in a lack of significant difference in the reversibility between asthmatics and non-asthmatics in the present study. A comparison of lung function methods for assessing dose-response effects of salbutamol was done by Houghton et al.[29] in adult subjects, showing that with 100 μg the asthmatic group already showed improvement in pulmonary function.

This study had the following limitations: only asymptomatic subjects were included since presence of symptoms could affect the tidal breathing parameters. This could be one reason why the t_{PEF}/t_E and V_{PEF}/V_Ecould not distinguish asthmatics from the non-asthmatics in the older age group, where the greater bulk of asthmatics subjects belonged. Another limitation of the

study was the use of only one dose of salbutamol respiratory solution. An earlier study that made use of 500 µg of salbutamol respiratory solution was able to distinguish asthmatics from non-asthmatics.[19] The authors made use of 250 µg of salbutamol respiratory solution since the local study done by Corpuz et al was also able to distinguish between the two groups by having greater than 15% reversibility post-bronchodilator in the asthmatic group.[20]Although the dose of bronchodilating agent was within the recommended dose based on the Global Initiative for Asthma Global Strategy for Asthma Management and Prevention 2012[2], physiologic changes in the infant airways may contribute unpredictability of the response to bronchodilating agents. Since the post-bronchodilation values of t_{PEF}/t_E and V_{PEF}/V_E were not statistically significant between the two groups, studying dose-response curve to salbutamol respiratory solution in this age group could help determine the appropriate amount that must be administered.

CONCLUSIONS

Baseline t_{PEF}/t_E and V_{PEF}/V_E could distinguish asthmatics from non-asthmatics in children less than 2 years old, but not in older children. The cutoff point of 32.250 for $t_{PEF}/t_E$and 34.500 for V_{PEF}/V_E may be used to rule in asthma, both with a specificity of 97%. Post-bronchodilator t_{PEF}/t_E and V_{PEF}/V_E in children 6 months to 5 years old could not distinguish asthmatics from non-asthmatics after nebulization with 250 µg of salbutamol.

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