BRONCHODILATOR CHALLENGE TEST USING THE TIDAL RAPID THORACO-ABDOMINAL COMPRESSION TECHNIQUE AMONG INFANTS AGED 6-24 MONTHS WITH RECURRENT WHEEZING

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ABSTRACT

BACKGROUND: A definite diagnosis of asthma during infancy is difficult. Asthma Predictive Index (API) is used to predict asthma at school age, but does not determine who among these actually have asthma.

OBJECTIVES: This study aims to determine the bronchodilator response of infants with recurrent wheezing compared with normal control.

METHODOLOGY: This cross sectional study included asymptomatic subjects aged 6-24 months with history of recurrent wheezing and age/sex matched controls. After sedation with chloral hydrate (Odan) at 50-75 mg/kg, a bronchodilator challenge test was performed with single dose 400 mcg salbutamol (Ventolin) MDI inhalation delivered via a spacer (Philips Respironic OptiChamber Diamond). Baseline and 15 minutes after salbutamol inhalation Maximum Flow at Functional Residual Capacity (V'maxFRC) were determined using MasterScreen Paed/BabyBody Option Squeeze version 8.0. ANOVA and Pearson chi-square were used for the statistical analysis of data.

RESULTS: Sixty-nine infants (23 previous wheezers and positive API, 23 previous wheezers with negative API and 23 controls) were included. There was a significant difference in the post bronchodilator challenge test V'maxFRC between wheezers with positive API and controls (p= 0.047). There was no significant difference in other parameter among groups.

CONCLUSION AND RECOMMENDATION: Absolute values of V'maxFRC post bronchodilator challenge using the Tidal Rapid Thoracoabdominal compression technique may be used to identify current asthma among asymptomatic infants with recurrent wheezing. Further studies with patient follow-up are recommended to assess response to treatment.

KEY WORDS: Recurrent wheezing, Bronchodilator challenge test, Tidal Rapid Thoraco-abdominal compression technique

INTRODUCTION

A. Statement of the problem:

Wheezing in infancy is a common clinical problem (1). A definite diagnosis of asthma in the young age group has been challenging as it can be based largely on symptom patterns combined with a careful clinical assessment of family history and physical findings. It is also difficult to make a confident diagnosis of asthma in younger children because episodic respiratory symptoms such as wheezing and cough were also common without asthma, particularly in those 0-2 years old (2,3). In the year 2000, the Asthma Predictive Index (API) was developed using data in the Tucson Children's respiratory study to predict asthma at school age among those children with recurrent wheezing in the first 3 years of life. A positive stringent API score by the age of 3 years was associated with a 77% chance of active asthma from aged 6-13 years; children with a negative API score at the age of 3 years had less than 3% chance of developing active asthma during their school years (3). Using the API however only aids in predicting asthma later in life but does not determine at hand who among those infants with recurrent wheezing actually have or does not have asthma.

B. Significance of the study:

This study aimed to identify the presence of bronchodilator responsiveness among asymptomatic infants with history of recurrent wheezing. By being able to identify early on the reversal of an obstructive profile which is highly suggestive of asthma, therapies can be initiated for the secondary prevention of respiratory morbidity.

C. Review of Literature

Infant lung function (ILF) testing has evolved from a research technique into a diagnostic tool (5). It has been useful in the

early diagnosis of lung diseases (6), in serial monitoring of disease progression (7,8) and may improve the efficacy of therapeutic interventions (9). It was in the 1980s when prototypes of the infant pulmonary testing has been developed and was later enhanced in the mid 1990s (10,11). Series of standards for its use has been published in the year 2000 by the European Respiratory Society and American Thoracic Society. BabyBody-plethysmographic measurement reference values for Chinese and Taiwanese infants has also been published in 2017 (12,13). Relatively, the machine has been new in the Philippines and this study also aimed to establish reference data for Filipino infants.

Partial expiratory flow volume (PEFV) maneuvers obtained by the rapid thoracoabdominal compression technique have been used to assess airway function in infants (14). In this method, the result was expressed as the forced expiratory flow at the resting lung volume taken from the tidal breath before the inflation was applied and termed the forced expiratory flow at functional residual capacity, or V'maxFRC.

Because of the doubts about the stability of functional residual capacity and the apparently large intra-subject variability of VmaxFRC, an alternative technique was developed in which lung volume was first inflated several times to 20–30 cm H2O before inflating the compression jacket at the raised lung volume produced by these inflations. This technique generated a complete maximal forced expiratory flow volume (MEFV) curve (15) and allowed the measurement of parameters of expiratory flow at known proportions of the functional vital capacity as well as timed expiratory volumes such as the forced expiratory volume in the first 0.5 sec (FEV0.5) analogous to parameters obtained by standard spirometry in older children and adults.

In 98 healthy infants aged 1–69 weeks, the relationship between V'max FRC and the parameters derived from the MEFV curve in the same infants was compared.They noted that the VmaxFRC was most closely related to the forced expiratory flow at 85% of FVC (FEF 85) but with considerable variation between subjects (16). However , the study mentioned that if strict quality control criteria was applied, forced expiratory flows measured using Rapid Tidal Compression (RTC) were more variable than those measured using the Raised Volume Rapid Thoracic Compression (RVRTC) technique. By ensuring that RTC was performed during quiet sleep with steady end-expiratory levels, checking that the selected curves over lie the descending portion of the flow volume curve and ensuring an adequate driving pressure, the potential variability caused by an unstable FRC and lack of flow limitation can be minimized.

In another study done by Bar-Yishay et. al., the V'maxFRC derived from the partial expiratory flow volume maneuver was compared with expiratory flows and timed expiratory volumes derived from the MEFV curve in infants with a variety of respiratory problems. The study found out that despite the wide variety of diseases and the wide range in respiratory in airway function there was a good correlation between V'maxFRC and either FEF 75 or FEF 85. It further mentioned that a normal V'maxFRC virtually excludes abnormal lung function measured by more sophisticated methods like raised volume (17).

To illustrate whether there was an association between wheezing and bronchial responsiveness in infants, a study by Stick et. al. showed that the median V'max FRC of the wheezy group was 100.0 ml/S (95% CI:79 to133ml/s) compared with 182.0 ml/s (95% CI: 147 to 237 ml/s) for the normal group ($p<0.01$) The median difference in Vmax FRC between the wheezy infants and the control infants was-76ml/s (95%CI:-135 to -20mlls). There were no differences between the two groups with regards to the other baseline measurements of respiratory function. Despite the large difference in V'maxFRC between the two groups of infants, the geometric mean of the wheezy infants (1.8 mg/ml) was not significantly different from that of the normal infants (2.3 mg/ml). The data only indicate that recurrently wheezy infants do not have increased airway responsiveness to histamine compared with normal infants (18).

Similarly, Prendeville et.al. studied the effect of nebulized salbutamol on the bronchial response to nebulized histamine in five wheezy infants aged 3-12 months. The response to doubling concentrations of up to 8g/l of histamine was assessed by the change in maximum flow at FRC (V'maxFRc), measured by flow-volume curves produced during forced expiration with a pressure jacket.The concentration of histamine were required to provoke a 30% fall in V'max FRC (PC30) was measured. All of the infants responded to low concentrations of histamine during control tests before and after nebulised saline (mean PC 30 107 and 0-51g/l). On a separate day there was a similar response to histamine before salbutamol, but after salbutamol the response was completely abolished up to the maximum

concentration of histamine in all subjects. Thus wheezy infants have highly effective Beta adrenoceptors in the intrathoracic airways (19).

In a recent study by Shavit et. al., they evaluated the bronchodilator response of infants with recurrent wheezing or coughing and an obstructive profile on infant pulmonary function test. The study also assessed whether the existence of a positive response can help predict the course of the illness in early childhood. The study included 60 infants and results showed that 53% of whom demonstrated bronchodilator responsiveness defined as a mean post bronchodilator Vmax FRC exceeding the upper limit of the prebronchodilator confidence interval. Follow up data was then gathered after 2 years. It found out that infants in the responsive group had a significantly higher frequency of physician visits for wheezing than the non responders (3 mean visits/yr vs. 1.5) and had a higher likelihood of having received asthma medication in the last year of the follow up period (84% vs 50%). Also, at the end of the follow up period, more parents in the responsive group reported continued respiratory disease (71% vs 22%) (20).

II. OBJECTIVE OF THE STUDY:

General Objective:

The main objective is to determine if there is a significant difference in the bronchodilator response among group of asymptomatic infants with recurrent wheezing who fulfilled the criteria of the API, compared to those who did not fulfill the API and those normal healthy infants using the rapid thoracic compression technique.

Specific Objectives:

1. One of the specific objectives is to determine if there was a significant difference in the pre-bronchodilator V'maxFRC and post bronchodilator V'maxFRC among groups.

2. The second objective is to determine if there was a significant difference in the percent change of V'maxFRC post bronchodilator challenge test among groups.

III. METHODS

This is a cross sectional study. Asymptomatic infants ages 6 months to 24 months seen at Philippine Children's Medical Center and those from the local health centers were recruited in this study.

Sample Size computation

Sample size was computed as follows:

$$n = \frac{(Z_{L+\beta})^2 (SD)^2}{E^2}$$

$Z_{L=}$ 95% confidence level = 1.96
Z = 80% power of the study = 1.28
SD = standard deviation of the VmaxFRC:

$$\frac{0.94 + 0.7}{2} = 0.86$$

E= measure of effect, that was, difference in Vmax FRC

$$= -2.00 - (-1.36) = 0.64$$

$$= \frac{(1.96+1.28)^2 (0.86)^2}{(0.64)^2}$$

$$= 23$$

The number of samples collected was computed using 95% level of confidence and 80% power of the study. At least 19 subjects were needed to detect a 0.64 difference in the VmaxFRC among groups. A 20% allowance was added to account for lost to follow up subjects. A total of 23 subjects per group was needed.

Subject Sampling:

Infants with a history of recurrent wheezing with or without the API and those normal healthy infants with no previous episode of wheezing were considered for inclusion.

The following were excluded: [a] any episode of upper and lower respiratory tract infection in the past 2 weeks prior to recruitment, and [b] with a significant co-morbid conditions affecting the respiratory system such as a physician-diagnosed congenital heart disease, presumptive interstitial lung disease, gastroesophageal reflux disease, upper airway obstruction, tracheoesophageal fistula, rib cage anomaly, kyphoscoliosis, history of prematurity (born <36 wks), cleft lip and palate and neurologic conditions such as seizure disorder and cerebral palsy.

Subjects were divided into three groups: Group 1 were Infants with recurrent wheezing who had a positive API; Group 2 were Infants with recurrent wheezing who did not fulfill the API, and Group 3 were normal healthy infants who never had an episode of wheezing and did not also fulfill the API. Informed consent was obtained prior to the study conduct.

To control for the influence of environmental temperature on respiratory pattern, room temperature was maintained between 20-25 C. The lights were also dimmed to encourage sleep. The equipments were checked before the test to avoid technical faults.

All infants were weighed, and their length were measured at the time of test. Feeding was also withheld at least 4 hours prior to testing. Vital signs such as cardiac rate, respiratory rate, temperature and oxygen saturation were recorded. Subjects were then sedated to facilitate positioning of the face mask and application of the jacket for thoracoabdominal compression. Chloral hydrate (Odan) 100mg/ml Syrup was given at 50 mg/kg per orem to facilitate moderate sedation (21).

Infants who woke up during the study conduct was given a smaller second dose of chloral hydrate at 25 mg/kg (max dose of 100 mg/kg) (22). However, infants who already achieved adequate volume curves were not resedated. Subjects with failed sedation and those who fail to have a technically acceptable manoeuvre after 3 trials were excluded in this study.

After the infants were sedated, a baseline measurement of the V'maxFRC using the rapid thoracoabdominal compression technique was obtained using the MasterScreen^{TM} Paed/BabyBody Option Squeeze version 8.0. The ATS/ERS statement on its current practice guidelines was used in this study. Measurements were made with the infant lying supine and the neck and/or shoulders supported in the midline in slight extension and the position was stabilized using a neck roll (23).

Partial expiratory flow volume curves were produced by wrapping a jacket around the infant's chest and abdomen. The infant's chest was wrapped in a suitably sized jacket. Small jacket size (Green in color) was used for infants weighing 8-13 kg; extra small (Blue) for 4-8 kg and extra extra small (yellow) for 2-4 kg (24). The outer expansive part of the jacket was firmly wrapped, while still being able to insert two adult fingers between the inner inflatable part and the infant's sternum. The mask was then placed with a silicon putty used to ensure that it was leak-free.

The jacket wrapping around the infant's chest and abdomen was inflated at the end of tidal inspiration to force expiration. An initial inflation pressure of 3 kPa (30 cm H20) was selected with the machine and applied at the end of tidal inspiration. A single squeeze maneuver was performed ensuring that the jacket remained inflated through out the entire expiration to be able to determine the flow at functional residual capacity (*V'max* FRC). The resultant changes in air flow were recorded through a pneumotachometer (PNT) attached to the face mask through which the infant breathed. The jacket pressure was subsequently increased by increments of 1 kpa until further increases did not elicit any further increase in forced expired flow at FRC. Three to five squeezes was performed at the first estimate of optimal pressure.

Once the optimal pressure has been determined with its corresponding V'maxFRC, a confirmatory determination of this pressure was done by decreasing at one pressure below and increasing at one pressure above it. If on confirmatory determination of the pressure the flows increased compared to the initial determination, subsequent incremental increase by 1 kpa was done until an airflow limitation was achieved. The determined pressure was then used after a bronchodilator challenge.

After the baseline V'max FRC has been determined, a bronchodilator challenge done using salbulatol inhalation. Infants were given Salbutamol (Ventolin) MDI 100 mcg/ inhalation, 4 puffs via a spacer (Philips Respironics OptiChamber Diamond) with face mask (25). After 15 minutes of salbutamol inhalation, a repeat rapid thoracoabdominal compression technique was taken. Vital signs such as cardiac rate, respiratory rate, temperature and oxygen saturations was monitored every 30 minutes until the patient was fully awake. Infants were only sent home when they were already active and were able to sustain wakefulness.

Outcome/ assessment, Data collection method, Instrument/s used

The MasterScreen^{TM} Paed/BabyBody Option Squeeze version 8.0 was used in this study (See figure 1). V'maxFRC was determined pre and post bronchodilator challenge test. It was reported as the absolute value in mL/s. The best value which is the highest flow from a technically acceptable curve (See figure 2) was reported, provided it is within 10% or 10mL/S (whichever is greater) of the next highest value. The mean of the three to five technically satisfactory curves was also made available as a measure of the intra-subject variability.

Criteria for acceptability of the flow volume curve were as follows: there should be no evidence of leak during data collection; the rapid rise time at start of forced expiration with the peak forced expiratory flow being attained before 30% of tidal volume has been expired; length of the jacket compression time sufficiently long enough to fully complete forced expiration; forced expiration should have a smooth curve and continue beyond FRC (See Figure 2). Three technically acceptable maneuvres were required (25).

Plan for Data Processing and Analysis

ANOVA was used to determine whether there was a significant difference in the values of V'maxFRC pre and post bronchodilator challenge among groups. Pearson Chi-square was also used to compare if there was a significant difference in the percent change pre and post bronchodilator challenge.

Ethical Considerations

Since infants were sedated in this study, careful assessment and monitoring were done for their safety. Pre sedation assessment included physical examination, observation of vital signs and any other physical findings. Resuscitation equipment such as bag with oxygen, suction apparatus, catheters and emergency kit were also made available. Subjects were also monitored continually with pulse oximetry until they were fully awake. Infants were only released home following sedation until they were fully arousable and capable of swallowing. In addition, parents were also advised that the infant maybe drowsy and unsteady for several hours and should not be left unattended.

IV. Results:

There were 114 infants recruited, but only 84 were initially enrolled (had no parental consent (n=19), history of recent respiratory tract infection (n =8), prematurity (n=1), cleft lip and palate (n=1) and gastroesophageal reflux disease (n=1)). Among 84 infants, 10 infants did not complete the study due to failed sedation and 5 who completed the study did not produce acceptable flow-volume loops. A total of 69 infants completed the study and were included in the final statistical analysis. They were then divided into three groups: Group 1 were infants with recurrent wheezing who had a positive API (n=23) ; Group 2 were infants with recurrent wheezing who did not fulfill the API (n=23), and Group 3 were normal healthy infants who never had an episode of wheezing and did not also fulfill the API (n=23).

The demographics are shown in Table 1. There were no significant difference among groups in terms of their age, gender, length and weight.

Table 1. Demographic Profile

		Group 1[a] n = 23	Group 2[a] n = 23	Group 3[a] n = 23	p-value
Age (mo)		16.83 ± 6.38	17.83 ± 4.68	14.96 ± 5.46	0.213 (NS)[b]
Gender	Female	14 (60.9%)	11 (47.8%)	16 (69.6%)	0.319 (NS)[c]
	Male	9 (39.1%)	12 (52.2%)	7(30.4%)	
Length (cm)		77.46 ± 9.52	78.24 ± 6.92	78.59 ± 7.88	0.891 (NS)[b]
Weight (kg)		12.14 ± 14.23	9.70 ± 1.11	9.17 ± 1.67	0.437 (NS)[b]

a – Mean ± sd or count (%)
b – using ANOVA F-test
c – using Pearson Chi-square

Table 2 shows the comparison of the pre-bronchodilator challenge and post bronchodilator challenge test determination of V'max FRC among groups. There was no significant difference in the pre-bronchodilator challenge determination of V'maxFRC in terms of its best, mean and median values. The V'maxFRC post bronchodilator challenge test was also significantly higher in infants with recurrent wheezing fulfilling the API compared to those without API and normal infants with values of 164.3, 142.61 and 123.87 respectively. On further analysis, there was a significant difference between infants with recurrent wheezing fulfilling the API when compared to a group of normal infants.

Table 2. Pre-bronchodilator Challenge and Post Bronchodilator Challenge Test V'max FRC determination

	Group 1[a] n = 23	Group 2[a] n = 23	Group 3[a] n = 23	p-value
Pre-bronchodilator Challenge				
Best V'maxFRC	152.30 ± 61.43	149.13 ± 55.34	127.13 ± 49.91	0.256 (NS)[b]
Mean V'maxFRC	137.02 ± 53.59	132.24 ± 49.32	113.51 ± 48.85	0.258 (NS)[b]
Median V'maxFRC	138.24 ± 55.16	133.33 ± 47.30	115.80 ± 49.33	0.295 (NS)[b]
Post Bronchodilator Challenge Test				
V'maxFRC	164.30 ± 59.65	142.61 ± 54.38	123.87 ± 48.05	0.047*[b]

a – Mean ± sd or count (%)
b – using ANOVA F-test
c – using Pearson Chi-square
* – significant at the 0.05 level of significance

Table 3 shows the comparison of the percent change in V'max FRC post bronchodilator challenge test among groups. Percent change was the difference between the best V'maxFRC value pre-bronchodilator and post bronchodilator challenge. The difference was then divided by the baseline (pre-bronchodilator) V'maxFRC value and multiplied by 100. Group 1 had a mean percent change of 13.44 $\pm$ 38.62 while groups 2 and 3 had -2.41 $\pm$ 22.43, -1.64 $\pm$ 11.86 respectively. Using the anova test, there was no significant difference in the mean percent change in V'max FRC when compared among groups (p= 0.083).

Table 3. Percent Change in V'max FRC Post Bronchodilator Challenge Test

	Group 1 n = 23	Group 2 n = 23	Group 3 n = 23	p-value
Post Bronchodilator Challenge Test				
Mean absolute values of V'max FRC Change from baseline	12.00 ± 45.80	-6.52 ± 35.53	-3.26 ± 15.64	0.162 (NS)
V'max FRC Change 95% CI	(-7.80, 31.80)	(-21.89, 8.84)	(-10.02, 3.50)	
% Change from Best V'maxFRC	13.44 $\pm$ 38.62	-2.41 $\pm$ 22.43	-1.64 $\pm$ 11.86	0.083 (NS)
% Positive responders	13 (56.5%)	9 (39.1%)	9 (39.1%)	0.392 (NS)

* – significant at the 0.05 level of significance

DISCUSSION:

Maximum flow at functional residual capacity (V'max FRC) has been used as an index of intrathoracic airway function (26). Using the rapid thoracoabdominal compression technique, bronchodilator responsiveness can now be demonstrated in asymptomatic infants as it can reproduce a flow-volume curve like in older children and adults. Physiologically, a decrease in airway calibre brought about by bronchodilation should decrease airway resistance thus producing higher flows.

To achieve a successful measurement using the tidal rapid thoracoabdominal compression technique, generally, a sedation is required. Sedation does not affect the phlethysmographic result measurements of infants but in fact facilitates the child to be in a quiet sleep essential for a reproducible measure of V'maxFRC. Out of the 84 infants who were included in this study, there were 10 infants who were not able to complete the test due to failed sedation. The onset of action of chloral hydrate and the duration of sleep were unpredictable (between 15-90 minutes) (27). The time required to obtain an informed consent, assessment of the infant, time for the infant to fall asleep and duration of the test may require a parent to spend around 3 - 4 hours at the pulmonary laboratory. It actually limited their willingness to stay and some refused to have their child be given an additonal second dose or come back to have the test repeated. Due to the bitter taste of chloral hydrate, infants had a tendency to cry or spit out which probably was also one reason why other infants had failed sedation. Others had a light sleep prior to the study conduct making them less susceptible to sedation. No other adverse events were noted upon sedation of these infants. To facilitate sedation, parents should be reminded and advised that infants should be sleep deprived.

Morever, there were 5 infants who were excluded due to unacceptability of the loops due to the following reasons: early inspiratory effort during the forced expiratory phase, flow distortion due to narrowing or closure of the glottis or larynx during forced expirations and fluctuations in the expiratory signal which may reflect presence of secretions mobilized during the maneuvers. Considerable caution has been required to interpret such loops due to a marked natural physiologic variability between infants. Proper positioning and handling of secretions must then be observed.

In a previous study by Shavit et. al. they have found out that bronchodilator responsiveness can help predict early childhood respiratory morbidity. In this study, there was a significant difference in the V'maxFRC values between infants with recurrent wheezing fulfilling the API compared to normal infants (164.30 ± 59.65 vs 123.87 ± 48.05). This only implies that these values may be used to identify the wheezy infant suffering from asthma at an early age.

The recurrent wheezy infants were group into two groups, those fulfilling and not fulfilling the API. As mentioned in the previous literature, infants not having the API have a less than 3% chance of developing asthma at the age of 3. This study aimed to identify current asthma in this small number of infants. However, there was no significant difference found between infants with recurrent wheezing not fulfilling the API when compared to normal infants. This finding suggests that the API still has a value to predict asthma in the young age group. Also, since there was no positive response in this group of infants (Group 2), it was assumed that the cause of the recurrent wheezing was not due to bronchial hypereactivity but to other more common causes such as in viral infections. The pre-bronchodilator values of V'max FRC among groups were also not statistically significant as infants, irregardless of the API, has a comparable baseline smooth muscle tone.

However, the absolute values obtained postbronchodilator challenge also has a wide range making it as one limitation of the study. There was actually an overlap of values between infants with recurrent wheezing and normal infants. Infants who will be identified to have a positive bronchodilator response can actually be just normal infants and vice versa. The mean percent change post bronchodilator challenge between groups was also not statistically significant ($p = 0.083$) probably because of this wide range of values (*Group 1= 13.44 ± 38.62; Group 2= -2.41 ± 22.43; Group 3 = -1.64 ± 11.86)*. It was noted in the previous studies that infants less than 1 year of age actually has a wider range of responses with mean percent changes in their spirometric values significantly higher compared with those infants older than 1 year of age (28). In this study, no subgroup of infants in terms of their age was made.

Furthermore, there was also a large intra subject variability in the determined V'maxFRC values. In this study, there was only one determination made of the V'maxFRC post bronchodilator challenge. To

minimize the observed variability, three determinations should also have been made.

It should also be taken into consideration that infants both in the wheezy and normal groups have varied responses to a bronchodilator challenge test. There were only 13 (56.5%) infants who had a positive response in group 1 and there were 9 (39.1%) in groups 2 and 3. Although there were more infants with a positive API who had bronchodilator responsiveness, it was not still statistically significant. It is also important to note that a normal infant can still have some degree of responsiveness. This can be supported by previous study where normal infants were responders with their spirometric measurements significantly increased after an inhalation of a beta 2 agonist (28). However, it was noted in their study that in those responders, they had a signifi2acantly higher percentage of mothers who smoked during pregnancy compared with the non responders. However, in this study, history of maternal smoking was not accounted for to those infants who had a positive response.

Aside from the positive responses elicited in the different groups, there were also a number of infants with a decline in forced expiratory flow rate after salbutamol inhalations. This finding has been similiar to a study by Prendeville et. al. where there were infants with paradoxical response to salbutamol inhalations which can be explained by the relative effect of bronchodilator drugs on airway compliance (by altering smooth muscle tone) and on airway calibre. An increase in airway compliance due to a decrease in airway smooth muscle tone will tend to diminish maximum flow rates at low lung volumes. If the intrathoracic airway calibre did not improve by bronchodilator treatment, then the net effect of these drugs would be little or no improvement in overall airway resistance or lung volume during quiet breathing but a decline in end expiratory flow rates during forced expirations (26).

The action of salbutamol actually has adverse effect in most of the infants . Clinical success in bronchodilator treatment may be explained by reversal of airway narrowing due to an excessive smooth muscle tone (26). If the cause of the airway narrowing is due to inflammation or edema such as in a viral infection which is common is this age group, then any reduction in airway smooth muscle tone may have an adverse effect of increasing airway compliance and hence cause a decrease in flow.

Careful monitoring should be done in infants when therapies such as giving salbutamol inhalations can have varied responses. Using the tidal rapid thoracoabdominal compression technique, bronchodilator responsiveness can be assessed. Asthma therapies can be initiated for the secondary prevention of respiratory morbidity to those who have a positive response. It can also help in monitoring the response to asthma therapies and aid in the plan for management in infants with recurrent wheezing. For infants who may have a paradoxical response to salbutamol, careful monitoring is essential. Parents can be educated that one common cause of recurrent wheezing in infancy can be still viral infections which may not benefit with asthma therapies.

CONCLUSION AND RECOMMENDATION:

There was a significant increase in the values of V'max FRC post bronchodilator challenge in infants with recurrent wheezing who fulfills the asthma predictive index compared to normal infants. Since there was no statistical difference in the mean percent change postbronchodilator challenge test from the baseline, it is recommended that only the absolute values in the post bronchodilator challenge can be used to identify asthma in infancy. However, due to the wide range of absolute values, accurate identification of asthmatics from those who are not is limited. The large variability of values should also be minimized probably by doing at least three technicaly acceptable determination of V'maxFRC post bronchodilator challenge. This study recommends to make a subgroup analysis among infants younger and older than 1 year of age. Maternal smoking as a risk factor should also be taken into consideration.

To further assess response to treatment, further studies to be made should also include a follow-up for patients who were initiated with asthma therapies.

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