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Original Article

Airway reversibility in newly developed asthma in children

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ABSTRACT

Objective To determine factors influencing forced expiratory volume in one second (FEV_1) reversibility in newly developed asthma in children

Methods A cross sectional study was done on 52 patients aged 6-14 years who were recruited from a longitudinal study of 161 newly developed asthmatic children. Pre and post-bronchodilator FEV_1 were obtained to calculate the reversibility. Seven patients had to perform peak expiratory volume (PEV) variability before recruited. Some variables including sex, age, height, onset of asthma, frequency of asthma attacks at the time of the test were analyzed to evaluate their roles in the outcome of FEV_1 reversibility using paired sample t-test, Pearson's correlation coefficient, and multi regression analysis.

Results Mean pre- and post-bronchodilator FEV_1 were 1.14 (SD 0.24) and 1.31 (SD 0.28), respectively. FEV_1 reversibility ranged between 6%-36%. Bivariate analyses demonstrated significant correlation between either cough (p=0.031) or symptom-free (p=0.041) and the airway reversibility. Multivariate analysis showed that cough was an important factor influencing airway reversibility (p=0.0246).

Conclusion Cough is an important influencing factor of the airway reversibility **[Paediatr Indones 2003;43:1-5].**

Keywords: *airway reversibility, asthma, cough, forced expiratory volume in 1 second (FEV_1).*

Asthma is a leading cause of chronic illness in childhood, responsible for significant proportion of lost school days. There is no universally accepted definition of asthma, it may be regarded as a diffuse, obstructive lung disease with (a) hyperreactivity of the airways to a variety of stimuli and (b) a high degree of reversibility of the obstructive process, which may occur either spontaneously or as a result of treatment.[1] The clinical hallmark of asthma is wheezing, a squeaking expiratory sound caused by the partially obstructed larger airways. However, asthma may occur without discernible wheezing and the diagnosis may be missed, especially in children.[2] A patient with asthma may present with a variety of symptoms, which can include wheezing, cough, shortness of breath, and complaints of chest congestion, tight chest, exercise intolerance, and recurrent bronchitis or pneumonia. In many instances, cursory physical examination fails to reveal evidence of pulmonary obstruction, and the disease may be overlooked unless pulmonary function is tested.[3] Tests of lung function most easily conducted are grouped into two broad categories i.e., lung volumes (capacity) and flow rates (volume per unit of time) which include peak expiratory flow rate (PEFR) and forced expiratory volume at 1 second (FEV_1).

In a longitudinal study of newly developed asthma in children at the Department of Child Health, Medical School, Airlangga University, Surabaya during October 1996 to October 1997, patients were asked to perform the FEV_1 test. The purpose of our study was to find possible correlation between patients' condition (dyspnea, cough, rhinitis, and symptom-free) and the FEV_1.

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Methods

This cross sectional study was a part of an observational longitudinal study conducted on 116 children with newly developed asthma (onset of less than 2 years), treated at the Department of Child Health, University of Airlangga. The age ranged from 6-14 years. As part of the longitudinal study, chest x-ray, tuberculin test, peripheral blood, urine and stool examination had been done to exclude other causes of chronic cough. The patients were also skin tested for atopy with caution that they should not take antihistamines, corticosteroids, sympathomimetics, beta-2 agonist, and xanthine 2 days prior to the test. The inclusion criteria included informed consent from the parents or legal guardians and the ability to use turbuhaler correctly as confirmed by a Turbuhaler Usage Trainer (TUT). The diagnosis of asthma was made preferably within one year but not more than 2 years prior to the visit. The diagnosis was verified by symptoms of wheezing, cough, dyspnea, chest tightness, or night awakening at least once a week during 3 months preceding the visit. Reversible airway obstruction was demonstrated as historic data or assessed at the visit (reversibility test only) as increased FEV_1 of more than 12% compared with baseline after the inhalation of a short acting bronchodilator (0.5 mg brycanil turbuhaler) or peak expiratory volume (PEV) variability >15% without bronchodilator, calculated out of 14-day period after discarding the first three day values.

We excluded patients with asthma for more than 2 years prior to the visit, patients for whom it would be inappropriate to delay treatment with glucocorticoid as judged by the physician at the visit, patients with a history of more than 30 days per year of oral or inhaled glucocorticoid treatment use or one depot injection per year of glucocorticoid irrespective of reason within the last 2 years, with regular at least once daily, antiasthma treatment for more than two years, with pre-bronchodilator FEV_1 <60 % or post-bronchodilator FEV_I <80 % of predicted normal value at the visit, with other affiliated cardiopulmonary diseases such as cystic fibrosis, active untreated tuberculosis, bronchopulmonary dysplasia, severe congenital heart disease, with immunosuppresive therapy, with cancer as past or present diagnosis, and patients with known or suspected difficulty in complying with the study protocol as judged by the investigators.

Data were obtained only from the first visit of the subjects during the period of October 1996 to October 1997. The medical record of each subject was reviewed to confirm the diagnosis including weight, height, BCG, tuberculin test, chest x-ray, atopy status, history of other atopic disease, history of atopy in the family, laboratory data, onset of asthma, and frequency of attack. The subjects' conditions at the time of visit were also recorded (cough, rhinitis, dyspnea, or free of symptom).

During the pulmonary function tests the patients sat and might use a nose clip. The patients should not inhale short and long acting bronchodilator 6 hours and 24 hours respectively prior to these procedures. The largest FEV_1 value and the largest functional vital capacity (FVC) value were recorded out of three forced technically satisfactory expirations, even if the two values did not come from the same curve. The largest FEV_1 and FVC and the second largest FEV_1 and FVC from acceptable curves should preferably not vary by more than 5%. If they differed by more, further measurements would be performed until this condition was met. Pre-bronchodilator FEV_1 was compared with predicted normal value. The pre-bronchodilator value should not be below 60% of predicted normal value. Inhalation of 0.5 mg terbutalin than was initiated. Fifteen minutes after inhalation of terbutalin the procedure was repeated. The post-bronchodilator FEV_1 value should not be below 80% of predicted value. Reversibility in FEV_1 relative to predicted normal should not be less than 13%. If it were less than 13%, PEV variability examination would be performed. The result of PEV variability should not be less than 15%. The most common measurement of flow was prior to allergy skin testing.

All of the data were computerized as a database. Bivariate and multivariate analyses were obtained. Pearson' s correlation coefficient was calculated for quantitative variables (age, weight height onset of attack, frequency of attack, pre- and post-bronchodilator FEV_1, pre- and post- bronchodilator FVC) and the reversibility.

Paired sample t-test was used to compare the variables (cough, rhinitis, dyspnea, symptom-free) to the reversibility. Statistical analysis was performed

using SPSS / PC+, Statistical Package for Social Sciences, Chicago.

Multiple regression analysis was used for the dependent variables including weight, height, age, sex, onset of asthma, frequency of attack, symptom (cough, rhinitis, dyspnea, symptom-free).

Results

From 116 patients only 52 fulfill the inclusion criteria. The age distribution of the patients, which ranged between 6 years and 12 years with the greatest number was 9 years (n=14%), and the mean age was 8.62 (SD 1.6l years).

Examinations prior to the study revealed that 47 patients had BCG scar, and 46 were tuberculin positive. From chest X-rays, 30 patients had normal chest compared to 22 with prominent bronchovascular pattern. Skin test to assess the atopy status was performed. Seven patients had dermographism (13%), 29% showed egg allergy, 25% had rice allergy, overall 45 patients showed positive skin test to a certain allergen. 28 patients had history of other atopic diseases and 23 patients had history of atopy in the family. Laboratory findings revealed 3 patients with eosinophilia; 3 patients had calcium oxalat and 1 patient had uric acid in their urine, while from the stool, we found 1 patient with ascariasis.

Sex distribution was not equal, there were 62% (n=32) males compared to 38 % (n= 20) females. The ratio was 1.6: 1. The other variables were listed in **Table 1**.

Paired sample t-test showed that cough and symptom-free had significant correlation to the reversibility (**Table 2**).

Pearson's correlation coefficient was calculated on those variables and revealed significant correlation (p=0.019) between pre bronchodilator FEV_1 and reversibility. The correlation of the other variables was not significant (**Table 3**).

Comparative analysis pre and post bronchodilator was done using paired samples t-test for pre- and post-bronchodilator FEV_1 and pre- and post-bronchodilator FVC, and both revealed significant correlation (p = 0.000) (**Table 4**).

Table 1. Mean and standard deviation of the other variables

Variable	Mean	SD	Min	Max
Age	8.62	1.61	6	12
Weight	25.31	6.65	15	46
Height	126.20	9.54	110	157
Onset	10.35	6.65	1.0	24
Freq. Attack	4.81	3.36	1	12
FEV_1-pre	1.14	0.24	0.74	2.22
FEV_1-post	1.31	0.28	0.86	2.51
FVC- pre	1.35	0.26	0.94	2.35
FVC-post	1.48	0.30	1.06	2.63

Table 2. Results of t-test for each variable

Variable	t-value	DF	p
Sex	.32	50	.752 (NS)
Cough	-2.21	50	.031 (S)
Rhinitis	- .61	50	.534 (NS)
Dyspnea	-1.22	50	.227 (NS)
Symptom-free	- 2.35	50	.023 (S)

S = significant, NS = not significant

Table 3. Pearson's correlation for each variable

Variable	t- value	Approximate significance
Age	-.56611	.57395 (NS)
Onset attack	- .07535	.94024 (NS)
Freq. Attack	-.87794	.38418 (NS)
FEV_1 pre-	- 2.41808	.01929 (S)
FEV_1 post-	-.15980	.81368 (NS)
FVC pre-	-1.81727	.07517 (NS)
FVC post-	-.33976	.73546 (NS)
Weight	- .30172	.76414 (NS)
Height	-.36684	.71532 (NS)

S = significant, NS = not significant

Table 4. Comparison analysis of FEV1 and FVC pre- and post-bronchodilator

Variable	Mean	SD	Difference		t-value	DF	p
			Mean	SD			
FEV1 pre-	1.1448	0.241	- 0.2705	0.104	-14.38	51	.000 (S)
FEV1 post-	1.3523	0.256					
FVC pre-	1.3506	0.284	-0.1763	0.118	-10.76	51	.000 (S)
FVC post-	1.4919	0.296					

Multiple regression analysis for the dependent variables including weight, height, age, sex, onset of asthma, frequency of symptom (cough, rhinitis, dyspnea, free of symptom) was done and only the symptom of cough had significant correlation with the reversibility (p = 0.0246) (**Table 5**).

Most of the patients were symptom-free (30 cases), 14 of them had reversibility below 20% and 5 had to perform PEV variability examination at home before the inclusion criteria was met. Only 7 patients suffered from rhinitis and none of them had to perform PEV variability examination. The next symptom found was cough in 16 patients while 7 of them had reversibility below 20% and 1 of them had to perform PEV variability examination. Eleven patients had dyspnea during the test and only 1 of them had to perform PEV variability examination (**Table 6**).

TABLE 5. RESULTS OF MULTIPLE REGRESSION ANALYSIS

Variable	t	Sig t (p)
Cough	2.319	.0246 (S)
Rhinitis	-.110	.9125 (NS)
Dyspnea	.655	.5158 (NS)
Symptom-free	-703	.4854 (NS)
Sex	-.093	.9261(NS)
Age	-.159	.8743 (NS)
Onset	-.038	.9699 (NS)
Frequency	-1.052	.2982 (NS)
Weight	-.463	.6453 (NS)
Height	.488	.6279 (NS)

S = significant, NS = not significant

TABLE 6. RESULTS OF THE REVERSIBILITY

Symptom	n	reversibility (%)	N	PEF variab. (n)
Cough	16	<20	7	1
		20-29	2	0
		>30	6	0
Rhinitis	7	<20	3	0
		20-29	3	0
		>30	1	0
Dyspnea	11	<20	4	1
		20-29	3	0
		>30	3	0
Symptom-free	30	<20	14	1
		20-29	13	2
		>30	3	2

Discussion

Out of 52 recruited patients, 45 showed positive skin test including 15 patients with egg allergy (29%) and 13 with rice allergy. The strong association between these two groups was striking and it was estimated that two third to three fourth of all children with asthma are allergic.[2,4] The number of male patients was high (62%) compared to female (38%) which was 1.6:1. The overall ratio is 2:1 with a higher ratio of males as disease severity increases. In chronic asthma, the ratio of boys to girls varies from 2:1 in the first 2 years of life to 1.5:1 at age 7 and reaches 1:1 at adolescence.[5]

We limited the youngest patients at 6 years because of special considerations in their ability to understand and use the turbuhaler correctly since it might influence pulmonary function tests. Most children learn to perform the maximal vital capacity maneuver reliably after 4 to 5 minutes of practice but some may require longer periods.[6] Age and height seemed to have superlative correlation with the result of FEV1 and FVC.

Spirometry was used here to assess the degree of reversibility of airflow obstruction in response to a bronchodilator. Baseline spirometry gives a highly accurate 'snapshot' of asthma severity and the degree of airway obstruction. FEV_1 in spirometry is the most reproducible pulmonary function parameter and is linearly related to the seventy of airways obstruction, besides having no contraindication. Spirometry is widely available at reasonable cost and methods and result interpretation are comprehensively standardized. Post-bronchodilator FEV_1 measured the best lung function that could be achieved by bronchodilator therapy on the day of the visit.[7,8]

In children, asthma is frequently a completely reversible obstructive airway disease and indeed no abnormality in pulmonary functions was found in many asthmatic patients when they become symptom-free.[9-12] Fourteen of 30 symptom-free patients had reversibility below 20 % and 5 of them had to perform PEV variability examination because the FEV_1 result could not reach 13%. This shows only a little difference in the airway caliber before and post bronchodilator, maybe because airway in symptom-free patients was almost normal (no obvious bronchoconstriction).[13,14] Bivariate and multivariate analyses proved that symptom-free was one of significant factor of reversibility (p=0.041).

From the statistical analysis we found that cough could significantly influence the reversibility (p=0.031

). There were 16 patients with cough, and 7 showed reversibility below 20%, including one who performed PEV variability examination. These data support the result of our clinical observations. Coughing patients had difficulties making smooth expected spirogram and often had to repeat the blow because of the presence of artifact in the spirogram. In these patients the difference between pre- and post-bronchodilator FEV_1 was not so wide which maybe caused by airway secretion preventing bronchodilator contact with airway mucosa,[15,16]. The presence of cough during pulmonary function test does not always indicate the presence of bronchoconstriction so that the difference of pre- and post-bronchodilator reversibility is not always reached.[17-19] Multiple regression analysis showed that cough was indeed a significant factor of reversibility ($p=0.0246$). Formerly we thought that dyspnea might be an important factor. From 11 dyspneic patients, 6 had more than 20% reversibility but then statistical analysis proved dyspnea did not significantly influence the airway reversibility ($p>0.5$).

In conclusion, a significant correlation to the airway reversibility was found with cough ($p=0.031$) and symptom-free patients ($p=0.041$). Cough was proven to be the only significant factor of airway reversibility ($p=0.0246$).

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