UNIVERSA MEDICINA

January-April, 2010 *Vol.29 - No.1*

Duration of asthma affects pulmonary function in asthmatic children

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ABSTRACT

Asthma is a common chronic disease and information on its management practices at the community level is helpful in identifying problems and improving asthma care. The prevalence of asthma in children below 18 years of age is around 9.3% and is on the increase. The aim of the present study was to determine the relationship between pulmonary function and duration of asthma in children. This was a cross-sectional study conducted at the outpatient clinic of RSUPN dr. Cipto Mangunkusumo in Central Jakarta. The study subjects were children aged 6-18 years with frequent episodic or persistent asthma. Among the 31 subjects there were 28 children with frequent episodic asthma and 3 children with persistent asthma. The duration of frequent episodic asthma ranged from 4 to 84 months, with a mean duration of 28 months. The FEV_1 and V_{50} values decreased in proportion to the duration of asthma (p=0.003 and p=0.012, respectively). Mean FEV_1 in persistent asthma was lower than that in frequent episodic asthma (82.7% vs. 61.2% at p=0.005). Similarly V_{50} and V_{25} were lower in persistent asthma, but the decrease was not statistically significant. The decrease in FEV_1 and V_{50} values was proportional to the duration of asthma. The severity of asthma is indicative of inadequate asthma control, resulting in a proportional decrease in pulmonary function. Therefore prevention of asthmatic attacks is an essential feature of asthma management in children in order to enhance their quality of life.

Keywords: Pulmonary, function, severity, asthma, children

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Univ Med 2010;29:1-7

INTRODUCTION

Asthma is one of the major chronic health problems in children. Worldwide, approximately 40% of all young children have at least one episode of asthmatic symptoms like wheezing, coughing, and dyspnea.[1] Although asthmatic symptoms are common in preschool children, only 30% will have asthma at the age of 6 years and over. The rest of the children with recurrent respiratory symptoms is symptom-free at 6 years and does not have asthma but transient, viral

associated wheeze.[2]

According to the Indonesian National Guidelines for Asthma in Children *(Pedoman Nasional Asma Anak)* the diagnosis of asthma should be based on the presence of wheezing and/or cough, and the following characteristics: episodic and/or chronic; occurring at night or in the early morning hours (nocturnal); seasonal; involvement of precipitating factors such as physical activity; reversible (either spontaneously or upon treatment); positive past history of asthma or other atopic disorders in the patient or the family, after exclusion of other causes.[3]

A common precipitating factor in the development of asthmatic symptoms are housedust mites, animal hair, and pollen. In addition, several pollutants such as cigarette smoke and exhaust gases of automotive vehicles, may also precipitate an attack of asthma, while among asthma precipitating drugs may be mentioned aspirin and non-steroidal anti-inflammatory drugs.[4]

The prevalence of asthma in preschool children may be up to 32% in the United States and Europe, whilst that of children below the age of 18 years is around 9.3% and is still increasing.[5] The prevalence of self-reported wheezing in the previous 12 months in 13 to 14 year old children varied from 1.6% to 36.7% in different centers The corresponding prevalence for parent-reported wheezing for the 6 to 7 year old age group was 0.8% to 32.1%.[6] Within certain regions asthma prevalence is generally lower in developing countries than in more affluent countries. For example, in Southeast Asia, the centers with the lowest prevalence of asthma symptoms were in Indonesia (2.1%) and China (3.3–5.1%), and the centers with the highest rates were in Japan (13.4%), Thailand (12.6–13.5%), and Hong Kong.[7]

Based on the degree of severity, asthma is commonly categorized as infrequent episodic asthma, frequent episodic asthma, and persistent asthma. (Table 1).[8] An asthmatic attack develops upon acute and extensive obstruction of the airways. The degree of asthma is determined by the frequency, duration, and intensity of the asthmatic attack, activity and symptoms outside attacks, and the results of pulmonary function tests.

Asthma is a chronic inflammatory disease and several studies have suggested that the remodelling process in asthma occurs since its onset and increases in proportion to the frequency of asthmatic attacks.[9,10] The continuing inflammatory process affects the pulmonary function of the asthmatic child and ultimately its quality of life. Atopic sensitization has long been known to be related to childhood asthma.[11] The available evidence suggested that usually only less than half of the asthma cases were attributable to atopic sensitization. In addition, studies showing a strong relation between asthma and atopy come mainly from affluent Western countries.[12] Thus, the link between asthma and atopic sensitization differs between countries.[13,14] Prevention of asthmatic attacks is the goal of long-term management of asthma, which is expected to improve pulmonary function and comprises avoidance of allergens and drug therapy with inhalatory corticosteroids, leukotriene antireceptors, slow-release theophylline, and long-acting beta-2-agonists.[8]

Pulmonary obstruction is a characteristic finding in acute exacerbation of asthma; however, there is a scarcity of data comparing the pulmonary function of children with degree of asthma. The aim of the present study was to compare the pulmonary function of children with degree of asthma and to clarify the relationships between duration of asthma and pulmonary function.

METHODS

Research design

The present study is of cross-sectional design, conducted at RSUPN dr. Cipto Mangunkusumo from Mei-December 2008.

Table 1. Classification of asthma by degree of severity[8]

Parameter	Infrequent episodic asthma	Frequent episodic asthma	Persistent asthma
Frequency of attacks	<1x/month	>1x/months	Frequent
Duration of attacks	< 1x/week	>1x/week	Almost throughout the year
Intensity of attacks	Usually mild	Usually moderate	Usually severe
Between attacks	Symptoms none	Symptoms frequent	Symptoms day and night
Sleep and activities	Not disturbed	Frequently disturbed	Extremely disturbed
Physical examination outside attacks	Normal	Some abnormality may be found	Never normal
Controling drugs	Unnecessary	Necessary	Necessary
Lung function tests (outside attacks)	PEF/FEV_1 >80%	PEF/FEV_1 60-80%	PEF/FEV_1<60%, variability 20-30%
Variability of lung function (during attacks)	> 15%	> 30%	> 50%

Notes: PEF = peak expiratory flow; FEV_1= forced expiratory volume in 1 second

Subjects of study

The study subjects were children with frequent episodic asthma or persistent asthma who were visiting the outpatient allergy or respirology clinics at RSUPN dr. Cipto-mangunkusumo. The children were selected as study subjects when meeting the following inclusion criteria: (i) age between 6-18 years; (ii) diagnosed as mild or severe intermittent or persistent allergic rhinitis with frequent episodic or persistent asthma outside of attacks; (iii) subjects or their parents willing to sign informed consent and agreeing to pulmonary function tests for their children. Exclusion criteria were (i) other pulmonary disorders or abnormalities; (ii) other disorders affecting pulmonary functions; (iii) currently on long-term intranasal, inhalatory, or systemic corticosteroid therapy (>5 consecutive days) by; (iv) unfit for pulmonary function tests.

Data collection and assessment

Data were collected by means of interviews followed by physical examination and pulmonary function tests. The degree of asthma was categorized as infrequent episodic asthma, frequent episodic asthma, and persistent asthma. Pulmonary function tests were performed by means of a spirometer with forced vital capacity maneuver for measuring forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), 50% FVC expiratory flow volume (V_{50}), and 25% FVC expiratory flow volume (V_{25}). These tests were performed outside of asthmatic attacks. The evaluation of spirometric results comprises FEV_1, V_{50}, and V_{25}. Abnormal pulmonary function is designated obstruction if FEV_1/FVC are less than 70%, and FEV_1 is less than 80% of standard value. If FEV_1 is less than 80%, there is borderline obstruction, if FEV_1 is less than 60% there is moderate obstruction, and if FEV_1 is less than 40% there is severe obstruction. The V_{50} and V_{25} values are parameters for determining the presence of an obstruction in the smaller airways.[15]

Ethical clearance

Ethical clearance was issued by the Research Ethics Committee of the Faculty of Medicine, University of Indonesia.

Statistical analysis

All data was analyzed by means of the SPSS 16 software program. Descriptive data

Table 2. Gender, age, and duration of asthma by degree of asthma

Variables	Degree of asthma		p
	Frequent episodic (n=28)	Persistent (n=3)	
Gender			
Male	19 (90.5%)	2 (9.5%)	0.967
Female	9 (90.0%)	1 (10.0%)	
Age group (years)			
6 - 12	24 (88.9%)	3 (11.1%)	0.123
>12	4 (100.0%)	0 (0%)	
Duration of asthma (months) (mean ± SD)	28.3 ± 4.1	44.0 ± 18.3	0.185

were presented in textual and tabular form, and analyzed using the t-test. Analysis of variance was used to assess differences in lung function between children grouped according to the classifications described previously in this paper, with $p< 0.05$ considered as statistically significant.

RESULTS

Overall there were 31 subjects participating in the present study, consisting of 21 males and 10 females, with mean age of 9.5 ± 2.3 years and most of them (87.1%) being in the age range of 6-12 years. The youngest study subject was 6 years old and the eldest 15.9 years. A total of 28 (90.3%) subjects had frequent episodic asthma and 3 (9.7%) subjects had persistent asthma. The duration of frequent episodic asthma ranged from 4 to 84 months, with mean duration of 28.3 ± 4.1 months.

There was no significant difference between males and females, age group and degree of asthma. Mean duration of frequent episodic asthma (28.3 ± 4.1 months) was not significantly different from that of persistent asthma (44.0 ± 18.3 months) (p=0.185) (Table 2).

Mean FEV_1 in persistent asthma (61.2 ± 7.3) was significantly lower than that of frequent episodic asthma (82.7 ± 12.2) (p=0.005). This was also the case with the values for V_{50} and V_{25} of respectively 83.2 ± 28.9 in frequent episodic asthma and 54.3 ± 16.3 in persistent asthma (p=0.102), and the values for V_{25} of 85.3 ± 29.4 in frequent episodic asthma and 50.4 ± 21.1 in persistent asthma, respectively (p=0.056) (Table 3).

Duration of frequent episodic asthma in the study subjects ranged from 4 up to 84 months, with mean duration of 28 months. The FEV_1 (p=0.003) and V_{50} values (p=0.012) decreased in proportion to duration of asthma. The V_{25} values decreased also, but the decrease was not statistically significant (p=0.71). Pulmonary function as measured by FEV_1 decreased significantly with duration of asthma (r=-0.522; p=0.003). Similarly V_{50} also decreased significantly with duration of asthma (r=-0.448; p=0.012). However, the decrease in

Table 3. Comparison of pulmonary function by severity of asthma

Pulmonary function	Degree of asthma		p
	Frequent episodic (n=31)	Persistent (n=3)	
FEV_1 (%)	82.7 ± 12.2	61.2 ± 7.3	0.005
V_{50} (%)	83.2 ± 28.9	54.3 ± 16.3	0.102
V_{25} (%)	85.3 ± 29.4	50.4 ± 21.1	0.056

Table 4. Relationship between duration of asthma and pulmonary function

Pulmonary function	Duration of asthma	p
FEV_1	r*=-0.522	0.003
V_{50}	r=-0.448	0.012
V_{25}	r=-0.329	0.071

*r : Pearson correlation

V_{25} values with duration of asthma was not significant (r=-0.329; p=0.071) (Table 4).

Age, duration of asthma, and degree of asthma had a significant influence on pulmonary function as measured by FEV_1. The regression analysis revealed that duration of asthma had the highest impact on FEV_1 in asthmatic children (Table 5). Duration of asthma also affected V_{50} but not V_{25}.

DISCUSSION

In this study the majority of children in the age range of 6-18 years had frequent episodic asthma (90.3%) and only 9.7% had persistent asthma. Similar results were obtained in 10-year old children in Hong Kong and Guang Zou, where 83% of the children had intermittent asthma and 27% persistent asthma (mild and moderate).[16] Asthma is a chronic inflammatory disease that commonly affects pulmonary function tests. A descriptive study in children 10-19 years old, showed that the lung function test in children with asthma can be obstructive, restrictive or combination.[17] The longer the duration of asthma and the more frequent the asthmatic attacks, the greater the decline in pulmonary functions due to remodelling of the bronchial wall.[9,10] This may be seen from the increasingly lower FEV_1 and V_{50} values in proportion to the duration of asthma. The lowered FEV_1 and V_{50} values indicate the presence of obstruction in the large and small airways that may occur in asthma. In addition to asthma, there are several factors influencing the pulmonary functions, namely height, birth weight, and the occurrence of wheezing under the age of one year.[18] However, these data were not collected in the present study and therefore this constitutes one limitation of this study.

The severity of asthma also affects the pulmonary functions. The study conducted by Bacharier et al.[19] demonstrated that FEV_1 did not differ substantially with various degrees of asthma, while apparently FEV_1/FVC was reduced in more severe degrees of asthma. These findings do not support the results of the present study, where the decrease in FEV_1 and V_{50} was greater in persistent asthma than in frequent episodic asthma. The lower values of these parameters indicate a more severe obstruction occurring in the airways. In

Table 5. Multiple linear regression of several main variables by pulmonary function

Variables	Age	Asma duration	Asma severity
FEV_1			
β	2.801	-0.318	-17.706
Beta	0.351	-0.521	-0.400
95% C.I. β	0.411 - 3.751	-30.142 - 5.270	-0.495 - 0.141
V_{50}			
β	3.691	-0.631	-20.883
Beta	0.287	-0.474	-0.218
95% C.I. β	-0.692 - 8.074	-1.096 - -0.166	-53.255 - 11.758
V_{25}			
β	0.347	-0.370	-28.663
Beta	0.026	-0.266	-0.287
95% C.I. β	-4.649 - 5.334	-0.849 - 0.159	-65.838 - 8.512

persistent asthma the FEV_1 and V_{50} values were in the range of 50-60%, even though the children had no asthmatic attacks. This indicates that the obstruction has become permanent and may affect the capacity of the children for activities.

The duration of asthma is inversely and significantly related to pulmonary functions. Consistent findings were obtained in children with mild and moderate asthma. Zeiger and colleagues[20] using the baseline data from the Childhood Asthma Management Program (CAMP) of the National Heart, Lung, and Blood Institute, reported a change in prebronchodilator FEV_1 of almost 1% per year of asthma duration in children with mild to moderate asthma.

The decline in FEV_1 indicates the presence of obstruction in the large airways. whereas V_{25} and V_{50} indicate the presence of obstruction in the smaller airways. In children with asthma there is also obstruction in the smaller airways, which is aggravated by attacks. The occurring inflammation also becomes permanent.[10] The concern in childhood asthma is that the disease adversely impacts the growth of a child's airways such that maximal lung growth is not achieved. Lower lung function in young adults with diagnosed or undiagnosed asthma compared with healthy control subjects is seen in various studies[21] In addition, childhood FEV_1% predicts adult lung function level.[22]

In children with asthma, it turns out that the variable with the greatest influence on FEV_1 and V_{50} is not the degree of frequent episodic asthma and persistent asthma, but the duration of asthma. Thus there is a need for long term drug therapy capable of preventing future attacks. Such a therapy is expected to be able to improve the decreased pulmonary functions. The inflammatory process in asthma may be reduced by long-term administration of inhalatory corticosteroids,[23] as was also demonstrated in the study by Reddel et al.,[24] where inhalatory fluticasone improved FEV_1. Similarly the study conducted by Ramsdell et al.[25] showed significant improvement in FEV_1 through inhalatory administration of methasone furoate dry powder, compared with placebo (20.7% vs 5.1%). Repeated objective measurements of lung function may immediately detect the occurrence of airway obstruction, which may be amenable to adequate treatment.

Another factor capable of affecting the degree of asthma severity and the frequency of asthma attacks is comorbidity, viz. allergic rhinitis and sinusitis. This indicates that with the recovery from sinusitis, waning of asthma symptoms and improvement of pulmonary functions may be expected. In the present study the issue of comorbidity was not evaluated.

CONCLUSIONS

Most children in this study had frequent episodic asthma and the duration of asthma had the most impact on the pulmonary function of asthmatic children, ultimately affecting their quality of life. Prevention of asthmatic attacks is essential, comprising avoidance of allergens and administration of controling drugs in the long term.

ACKNOWLEDGEMENTS

The investigators wish to acknowledge the support of the Dean and Vice-Deans of the Medical Faculty, Trisakti University, for the funding of the present study. We also wish to thank the doctors and staff of RSUPN dr. Cipto Mangunkusumo, and all persons who provided assistance and support until the completion of this study.

REFERENCES

1. Bisgaard H, Szefler S. Prevalence of asthma-like symptoms in young children. Pediatr Pulmonol 2007;42:723-8.
2. Kurukulaaratchy RJ, Fenn MH, Waterhouse LM, Matthews SM, Holgate ST, Arshad SH. Characterization of wheezing phenotypes in the first 10 years of life. Clin Exp Allergy 2003;33: 573-8.

3. Kling S, Gie R, Goussard P. Inhaled corticosteroids in childhood asthma. Curr Allergy Clin Immunol 2003;16:8-10.
4. Terr AI. The atopic diseases. In: Parslow TG, Stites DP, Terr AI, Imboden JB, editors. Medical immunology. 10th ed. Boston: McGraw Hill;2003. p.349-69.
5. Savichi G, Dovey M. Chronic childhood asthma: definition, epidemiology, and pathophysiology. Available at : http://www.uptodate.com. Accessed November 11,2009.
6. Beasley R, Keil U, von Mutius E on behalf of the ISAAC Steering Committee. Worldwide variation in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema: the international study of asthma and allergies in childhood (ISAAC). Lancet 1998;351:1225–32.
7. Beasley R, Ellwood P, Asher I. International patterns of the prevalence of pediatric asthma: The ISAAC program. Pediatr Clin N Am 2003; 50:539–53.
8. UKK Pulmonologi. Pedoman nasional asma anak. Dalam: Rahajoe N, Supriyatno B, Setyanto DB, penyunting. Jakarta: PP IDAI;2004.h.1-44.
9. Bousquet J, Jeffery PK, Busse WW, Johnson M, Vignola AM. Asthma, from bronchoconstriction to airways inflammation and remodeling. Am J Respir Cri Care Med 2000;161:1720-45.
10. Payne DNR, Rogers AV, Adelroth E, Bandi V, Guntupalli KK, Bush A, et al. Early thickening of the reticular membrane in children with difficult asthma. Am J Respir Crit Care Med 2003;167: 78-82.
11. von Mutius E. Environmental factors influencing the development and progression of pediatric asthma. J Allergy Clin Immunol 2002;109:S525–32.
12. Weinmay G, Weiland SK, Bjo¨rkste´n B, Brunekreef B, Bu¨chele G, Cookson WOC, et al. Atopic sensitization and the international variation of asthma symptom prevalence in children. Am J Respir Crit Care Med 2007; 176:565–74.
13. Scrivener S, Yemaneberhan H, Zebenigus M, Tilahun D, Girma S, Ali S, et al. Independent effects of intestinal parasite infection and domestic allergen exposure on risk of wheeze in Ethiopia: a nested case-control study. Lancet 2001;358:1493–9.
14. Palmer LJ, Celedon JC, Weiss ST, Wang B, Fang Z, Xu X. Ascaris lumbricoides infection is associated with increased risk of childhood asthma and atopy in rural China. Am J Respir Crit Care Med 2002;165:1489–93.
15. Kaswandani N. Uji fungsi paru pada batuk kronik. Dalam: Trihono PP, Kurniati N, penyunting. Strategi pendekatan klinis secara professional batuk pada anak. Jakarta: Departemen Ilmu Kesehatan Anak FKUI-RSCM;2006. h.26-39.
16. Ko FWS, Wang HY, Wong GW, Leungz TF, Hui DSC, Chan DPS, et al. Wheezing in Chinese schoolchildren: disease severity distribution and management practices, a community-based study in Hong Kong and Guangzhou. Clin Exp Allergy 2005;35:1449–56.
17. Tehuteru ES. Profile of lung function test in pediatric asthma patients. Univ Med 2003;22:1-4.
18. Joseph-Bowen J, de Klerk NH, Firth MJ, Kendall GE, Holt PG, Sly PD. Lung function, bronchial responsiveness, and asthma in a community cohort of 6-year-old children. Am J Respir Crit Care 2004;169:850-4.
19. Bacharier LB, Strunk RC, Mauger D, White D, Lemanske RF, Sorkness CA. Classifying asthma severity in children. Am J Respir Crit Care Med 2004;170:426-32.
20. Zeiger RS, Dawson C, Weiss S. Relationships between duration of asthma and asthma severity among children in the Childhood Asthma Management Program (CAMP). J Allergy Clin Immuno 1999;103:376-87.
21. Apostol GG, Jacobs DR, Tsai AW, Crow RS, Williams OD, Townsend MD, et al. Early life factors contribute to the decrease in lung function between ages 18 and 40: the coronary artery risk development in young dults study. Am J Respir Crit Care Med 2002;166:166–72.
22. Covar RA, Spahn JD, Murphy JR, Szefler SJ, for the Childhood Asthma Management Program Research Group. Progression of asthma measured by lung function in the childhood asthma management program. Am J Respir Crit Care Med 2004;170:234–41.
23. Mauad T, Bel EH, Sterk PJ. Asthma therapy and airway remodeling. J Allergy Clin Immunol 2007;120:997-1009.
24. Reddel HK, Belousova EG, Marks GB, Jenkins C. Does continuous use of inhaled corticosteroids improve outcomes in mild asthma? A double-blind randomized controlled trial. Primary Care Respiratory J 2008;17:39-45.
25. Ramsdell JQ, Nayak AS, Bensch GW. Efficacy of treatment with once-daily evening dosing of mometasone furoate dry powder inhaler 200 micrograms in asthma stratified by baseline severity. Am J Respir Crit Care Med 2009;179: 19-24.