THE LEVEL OF PLASMINOGEN ACTIVATOR INHIBITORS 1 IN ASTHMA PATIENTS AND CORRELATION WITH LUNG FUNCTION AND DEGREE Of ASTHMA CONTROL

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ABSTRAK

Background
Chronic inflammation in asthma and further occurrence of tissue remodeling would cause airway limitation worse and aggravate the degree of asthma control. Chronic inflammation in asthma may cause damage to the airway and will modulate fibrogenesis. PAI-1 is considered instrumental in the process of fibrosis after inflammation. PAI-1 is a major inhibitor to the tissue-type and urokinase-type plasminogen activators (tPA and uPA) that suppresses fibrinolysis. In prospective studies have reported increased levels of PAI-1 thought to play an important role in the pathogenesis of chronic inflammation and remodeling in asthma.

Objectives
To assess the correlation between levels of PAI-1 and lung function by spirometry. to assess correlation between levels of PAI-1 and the severity of asthma.
Methods
This was a cross sectional study and conducted in the Wahidin Sudirohusodo Hospital and Hasanuddin UniversityHospital, Makassar, from April 2015 to June 2016. The number of samples were 47 asthmatic subjects that meet the inclusion criteria. The asthma subjects was diagnosed by history taking, physical examination, bronchodilator test (using spirometry), x-ray, asthma control test andalsoof PAI-1 levels.This study using cross sectional design (cross-sectional). Data were processed using SPSS version 22.0 for Windows, statistical on Chi-Square test and Mann-Whitney test. The test results significant if $p < 0.05$.

Results: Total 47 patients treated in the outpatient or inpatient clinic Wahidin Sudirohusodo hospital and Hasanuddin University Teaching Hospital and its network during the month of April 2016 until June 2016 that became subject of research. Age range varied subjects 20-74 yearsand FEV1% had a range of 31% -89%. The subject with female sex more than men was 70.2% versus 29.8%. Age range of most research subjects was 56-74 years (38.3%). Body mass index (BMI) research subject mostly in normal BMI (61.7%). Most of the study subjects with a full degree of asthma control (48.9%) with a mild degree of obstruction was found most often (55.3%). Levels of PAI-1 patients with asthma in the study subjects found most frequently in the range of 5.98 to 33.39 and 2.41

to 5.97 as much as 34%. In this study, there was a significant correlation between the levels of PAI-1 with the degree of obstruction (p <0.001), where the percentage of obstruction was significantly increased in accordance with the value tertile 1, 2 and 3 (6.7%, 37.5% and 87.5 %) and there was a significant correlation between the levels of PAI-1 with the degree of control (p <0.001), where a significant percentage of uncontrolled asthma increased with the value tertile 1, 2 and 3 (26.7%, 43.8% and 81, 3%).

Conclusions: There was significant correlation between the levels of PAI-1 and lung function and the degree of control in asthma patients, which the higher levels of PAI-1in severe degree of obstruction and worse degree of asthma control.
Keywords :Asthma, lung function, the degree of asthma control, remodelling, PAI-1

Background

Asthma is a disease that is usually characterized by hyperresponse and inflammation of the chronic airway. Asthma is characterized by a history of symptoms in the airway in the form of wheezing, shortness of breath, chest feeling heavy and coughing which varies in intensity from time to time, accompanied by limitations in expiratory airflow.(1)

Plasminogen Activator Inhibitor-1 is a 50-kDa single-chain glycoprotein. PAI-1 is an inhibitor of the plasminogen activation system (PAS). Plasminogen can be converted to the active enzyme, plasmin. Furthermore, plasmin will degrade fibrin to soluble fibrin. There are two physiological plasminogen activators, namely tissue-type plasminogen activator (tPA) and urokinase-type plasminogen activator (uPA). heavier breathing and worsening asthma. In chronic asthma, irreversible changes in the structure of the airway can occur, characterized by subepithelial fibrosis, deposition of the extracellular matrix, smooth muscle hypertrophy and airway hyperplasia. [13] Inflammatory cells such as T cells, mast cells and eosinophils play a role in chronic inflammation and changes in airway structure by releasing various pro-inflammatory cytokines and growth factors. Chronic inflammation can cause airway damage and modulate fibrogenesis. PAI-1 plays an important role in the fibrosis process after inflammation.1

Method

This was a cross sectional study and conducted in the Wahidin Sudirohusodo Hospital and Hasanuddin UniversityHospital, Makassar, from April 2015 to June 2016. The number of samples were 47 asthmatic subjects that meet the inclusion criteria. The asthma subjects was diagnosed by history taking, physical examination, bronchodilator test (using spirometry), x-ray, asthma control test andalsoof PAI-1 levels

Result

The research subjects were patients diagnosed with asthma based on anamnesis, physical examination and supporting examinations in the form of bronchodilator tests. A total of 47 patients who attended outpatient and inpatient at Wahidin Sudirohusodo Hospital and

Hasanuddin University Hospital and their networks during April 2016 to June 2016 were the research subjects. The ages of the subjects from 20 to 74 years and FEV 1% had a range of 31% -89% table 1.

Table 1. Frequency Distribution Characteristics of Subjects (n = 47)

Variable		n	%
Age[a]	20-44	15	31.9
	45-55	14	29.8
	56-74	18	38.3
Gender	Male	14	29.8
	Female	33	70.2
Nutritional Status	Normal weight	29	61.7
	Over weight	18	38.3
Degree of obstruction	Mild	26	55.3
	Moderate	21	44.7
Degree of control	Complete control	23	48.9
	Uncontrolled	24	51.1
Levels of PAI-1[a]	0,95-2,40	15	31.9
	2,41-5,97	16	34.0
	5,98-33,39	16	34.0

In this study, a comparative analysis of levels of PAI-1 according to degrees was performed. Obstruction where the results of PAI-1 levels were significantly higher in moderate obstruction than mild obstruction, namely 2.62 to 1.54 , p <0.001. (table 2)

Table 2. Comparison of levels of PAI-1 by the degree of obstruction

Degree of obstruction	n	Levels of PAI-1			P
		Median	Mean	SD	
Mild	26	1.00	1.54	0.647	**0.001**
Moderate	21	3.00	2.62	0.590	

Mann-Whitney test

comparison of PAI-1 levels according to the degree of control was also carried out where

the PAI-1 levels were significantly higher in uncontrolled asthma than in controlled ones, namely 2.38 to 1.65 ($p < 0.01$) (Table 3). These results can be interpreted as a significant relationship between PAI-1 levels and the degree of control

In this study, there was a significant correlation between the levels of PAI-1 with the degree of obstruction ($p < 0.001$), where the percentage of obstruction was significantly increased in accordance with the value tertile 1, 2 and 3 (6.7%, 37.5% and 87.5 %) see Table 4. A significant correlation between the levels of PAI-1 with the degree of control ($p < 0.001$), where a significant percentage of uncontrolled asthma increased with the value tertile 1, 2 and 3 (26.7%, 43.8% and 81, 3%) see table 5.

Table 3. Comparison of levels of PAI-1 according to level of control

Derajat Kontrol	N	Kadar PAI-1			P
		Median	Mean	SD	
Controlled	23	2.00	1,65	0.714	**0.001**
Uncontrolled	24	3.00	2,38	0.770	

Mann-Whitney test

Table 4. Correlation PAI-1 with degree of obstruction

PAI-1 Levels		Degree of Obstruction		Total	
		Mild	Moderate		
0.95-2.40	N	14	1	15	**p=0.000**
	%	93.3%	6.7%	100.0%	
2.41-5.97	N	10	6	16	
	%	62.5%	37.5%	100.0%	
5.98-33.39	N	2	14	16	
	%	12.5%	87.5%	100.0%	
Total	N	26	21	47	
	%	55.3%	44.7%	100.0%	

Chi Square

Table 5. Correlation PAI-1 with degree of control

PAI-1 Levels		Degree of Control		Total	
		Controlled	Uncontrolled		
0.95-2.40	N	11	4	15	
	%	73.3%	26.7%	100.0%	
2.41-5.97	N	9	7	16	
	%	56.3%	43.8%	100.0%	
5.98-33.39	N	3	13	16	**p=0.008**
	%	18.8%	81.3%	100.0%	
Total	N	23	24	47	
	%	48.9%	51.1%	100.0%	

Chi Square

Discussion

In this study, there was a significant relationship between the PAI 1 level and the degree of obstruction ($p < 0.001$), where the percentage of moderate obstruction significantly increased according to the calculated value

Oh et al in 2002 found that PAI-1 increased extracellular matrix deposition which suppressed matrix metalloproteinase-9 (MMP-9) activity in the airways of experimental animals with asthma.2,3 Wenzel et al 2003, proved that increased levels of MMP-9 in the sputum of asthmatics were correlated with decreased FEV1 (lung function) values and the degree of asthma severity. 4,5

this study, there was also a significant relationship between the level of PAI-1 and the degree of control ($p < 0.001$), where the percentage of uncontrolled asthma significantly increased in accordance with the statistical values 1, 2 and 3 (26.7%, 43.8% and 81 , 3%). Hashimoto et al. have shown that there is an increase in vascularity (angiogenesis) in the airways of asthma patients which correlates with the degree of asthma control. As previously explained, the role of PAI-1 in the angiogenesis process is also responsible for the remodeling process.(7)

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