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COMPARISON OF FIBRINOGEN LEVELS IN SMOKES THAT SUFFER COPD WITH SMOKING THAT DOESN'T SUFFER FROM COPD

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Abstract

Background

Chronic Obstructive Pulmonary Disease (COPD) is a systemic disorder of respiratory disease. Significant complications of COPD can cause hypercoagulable conditions, which can cause life-threatening diseases such as ischemic heart disease, deep vein thrombosis and pulmonary embolism. Therefore, Fibrinogen is a biomarker that is useful for predicting the risk of hypercoagulative conditions in COPD patients..

Methods

Sampling was conducted during July 2019. Total population was 60 people (30 COPD patients and 30 non-COPD patients), the entire population was examined Fibrinogen, Spirometry and Brinkman index, then the results were compared in both populations. The study was conducted after obtaining ethical approval and informed consent.

Results

There was no difference in the Brinkman Index between the COPD and non-COPD groups with p = 0.369 (p> 0.05). There is a difference in FEV between the COPD and non-COPD groups with a value of p = 0,000 (p <0.05), where the COPD group has a lower FEV than the non-COPD group. There is a Fibrinogen difference between the COPD and non-COPD groups with a value of p = 0, 03 (p <0.05). There was a difference in age between the COPD and non-COPD groups with a value of p = 0.001 (p <0.05), where the COPD group had a higher age than the non-COPD group.

Conclusions

Increased fibrinogen levels, in stable COPD patients, can be used to assess a prognosis and as a treatment for determining treatment in hospital.

Keywords: COPD, non-COPD, Fibrinogen.

Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic lung disease that is characterized by the presence of air flow obstructions in the airways that are not completely reversible. The disease is usually progressive and is associated with an abnormal inflammatory response of the lung to harmful particles or toxic gases.[1]

Limited air flow is progressive and is related to the lung's inflammatory reaction to particles or harmful gases, mainly caused by cigarette smoke. Chronic pulmonary obstructive disease (COPD) not only affects the condition of the lungs but also has important systemic consequences. The diagnosis requires a spirometry examination by obtaining the first second forced expiratory volume / forced vital capacitance (VEP_1 / KVP <70%) which shows that there is a restriction of air flow that is not fully reversible.[2]

WHO estimates an increase in mortality due to COPD more than 30% in 10 years, COPD is even estimated to be the third leading cause of death in the world. Seeing the magnitude of the problems posed by COPD, experts continue to strive to perfect understanding of the management of this condition in order to be able to deal with and prevent deterioration. Completion of the paradigm regarding inflammation, exacerbation, and systemic effects.[6]

COPD also has extrapulmomal manifestations. It is stated that persistent pulmonary inflammation can cause the release of chemokines and proinflammatory cytokines into the circulation. This mediator can stimulate the liver, adipose tissue and bone marrow to release a number of leukocytes, CRP, interleukin (IL) -6, IL-8, fibrinogen and TNF-α into the circulation and cause systemic inflammation.[13]

Fibrinogen is an acute phase plasma protein that has emerged as a biomarker in establishing COPD markers. Fibrinogen itself is the most commonly used clinical trial to detect the activation of the coagulation system. Fibrinogen is also an acute phase reactant whose production stimulates high levels of cytokines such as IL-6 and IL-1. So fibrinogen can be used as a marker of inflammation for several diseases.[14]

Material and Methods

Sampling was carried out during July 2019. Total population was 60 people (30 COPD patients and 30 non-COPD patients), the entire population was examined Fibrinogen, Spirometry and Brinkman index, then the results were compared in both populations. The study was conducted after obtaining ethical approval and informed consent.

Results

There was no difference in the Brinkman Index between the COPD and non-COPD groups with a value of p = 0.369 (p> 0.05). There is a difference in FEV between the COPD and non-COPD groups with a value of p = 0,000 (p <0.05), where the COPD group has a lower FEV than the non-COPD group. There is a Fibrinogen difference between the COPD and non-COPD groups with a value of p = 0, 03 (p <0.05). There is a difference in age between the COPD and non-COPD groups with a value of p = 0.001 (p <0.05), where the COPD group has a higher age than the non-COPD group.

Table 1. Characteristics of Research Samples (n = 60)

	Whole subject (n=60)	COPD (n=30)	No COPD (n=30)	*p value*
Gender, n(%) Male	(100%)	(100%)	(100%)	
Age (year)	59 ± 9.47	63.0 ± 10.06	54.9 ± 6.86	<0.001*
FEV_1 (%)	86.3 ± 19.53	69.4 ± 12.79	103.1 ± 5.08	<0.001*
Brinkman Index	351.6 ± 73.5	360.5 ± 78.7	342.8 ± 68.1	0.369

*) significant with the Mann Whitney test

Table 1 shows that all subjects of this study were male. There is a significant difference in age between smokers who have COPD and smokers who do not have COPD. Smokers with COPD are older than 63 years compared to smokers who do not suffer from COPD with an average age of 54 years. In the measurement of FEV levels in COPD patients with an average value of 69.48 ± 12.79, while the FEV levels in non-COPD patients with an average value of 103.16 ± 5.08. There are differences in FEV between the COPD and non-COPD groups with p value = 0,000 (p <0.05), where the COPD group had a FEV lower than the non-COPD group.

In the Brinkman Index measurement in COPD patients with an average value of 360,500 ± 78.76, while the Brinkman Index level in non-COPD patients with an average value of 342,866 ± 68.18. There is no difference in the Brinkman Index between the COPD and non-COPD groups with values p = 0.369 (p> 0.05).

Table 2. Comparison of Fibrinogen in Smokers with Chronic Obstructive Pulmonary Disease with Smokers who Don't Have Chronic Obstructive Pulmonary Disease (n = 60)

	Fibrinogen (mg/ml)		p value
	Mean ± SD	Median (Min - Max)	
COPD	357.9 ± 104.9	350 (59 - 574)	
No COPD	312.6 ± 50.04	299 (184 - 433)	0.03*

*) significant with the Independent T Test

Table 2 shows that there are significant differences in fibrinogen levels between smokers who suffer from COPD and smokers who do not suffer from COPD (p <0.05). Smokers who suffer from COPD have higher fibrinogen levels compared to smokers who do not suffer from COPD (357.9 vs 312.6 mg / ml).

Table 3. Relationship of Age, Forced Expiratory Volume Values, and Brinkman Index with Fibrinogen Levels in Smokers

		Fibrinogen (mg/ml)	Median (Min-Max)	p value
Age	<50 year	327.6 ± 75.7	317.5 (244-493)	0.8[a]
	50-59 year	341.3 ± 91.5	347 (184-574)	
	≥ 60 year	337.1 ± 88.4	331 (59-561)	
FEV_1 (%)	≥ 100	312.5 ± 46.0	297 (244-433)	0.06[a]
	80-99	324.7 ± 62.3	343.5 (184-448)	
	50-79	365.7 ± 130.9	356 (59-574)	
	30-49	389.7 ± 43.2	381 (348-449)	
Brinkman Index	Light (0-299)	316.6 ± 114.1	296.5 (59-497)	0.32[b]
	Medium (300-599)	343.2 ± 71.9	357 (238-574)	

a) Kruskal Wallis Test
b) Mann Whitney Test

Table 3 shows that the lower the FEV1 value of smokers, then the fibrinogen levels will get higher. Smokers who have value Normal FEV1 (≥ 100%) has a fibrinogen level of 312 mg / ml, vice versa smokers who have decreased FEV1 values below 30%, levels the fibrinogen increased to reach 389.7 mg / ml, albeit in a manner not statistically significant enough. Table 3 also shows that there is no relationship between the age of the smoker and the amount of cigarette consumption (Brinkman Index) by levels blood fibrinogen.

Discussion

There are several risk factors for COPD, namely smoking, age, sex, respiratory hyper responsiveness, airway infection, occupational exposure, air pollution, social status and genetic factors. A study conducted from 1990 to

2004 in 28 countries found a higher prevalence of COPD in smokers compared to nonsmokers.[8] According to WHO data in 2008, smoking was a major cause of COPD. Smoking is said to be a major risk factor for COPD.[6,7]

There is an age difference between the COPD and non-COPD groups with a value of p = 0.034 (p <0.05), where the COPD group has a higher age than the non-COPD group.[7]

In a study conducted by Yudika et al 2012 obtained a mean VEP1 of 1238.14 ± 381.5 ml with the highest VEP1 value of 1910 ml and the lowest of 630 ml. The mean predicted VEP1 value was 54.30 ± 13.90% with the highest value being 74% and the lowest 28%. The results of this study indicate that there is a significant relationship between fibrinogen levels with predictive VEP1 (Pearson test p = 0.04).

In a study conducted by Yudika et al 2012 obtained subjects of smokers in this study had higher levels of fibrinogen compared with subjects who were former smokers. The average fibrinogen level in smokers was 435.0 ± 46.7 mg / dl while the mean fibrinogen in former smokers was 361.1 ± 69.6 mg / dl.[12]

Chronic Obstructive Pulmonary Disease not only causes an abnormal inflammatory response to the lung but also causes systemic inflammation including systemic oxidative stress, activation of inflammatory cells in the systemic circulation and an increase in proinflammatory cytokines. This inflammatory process stimulates the hematopoietic system, especially the bone marrow to release leukocytes. and platelets and stimulate the liver to produce acute phase proteins such as CRP and fibrinogen.[7]

T-independent test on fibrinogen of COPD patients with non-COPD patients, based on the analysis obtained comparison of fibrinogen in smokers suffering from chronic obstructive pulmonary disease with smokers who do not suffer from chronic obstructive pulmonary disease obtained by comparison with a value of p = 0.037 (p <0.05). where the COPD group had higher Fibrinogen than the non-COPD group.

In this study, an increase in fibrinogen in smokers suffering from COPD, but there are several factors that are thought to cause COPD in smokers are caused by several gene factors including CHRNA3 / 5 (cholinergic nicotine allotin receptor 3/5), IREB2 (iron binding protein) 2), HHIP (protein that interacts with porcupines), FAM13A, AGER (receptors for end glycosylation products specifically) .[19]

This result is in accordance with Pujari's study, 2018 found a significant relationship between fibrinogen levels in 50 stable COPD patients with a control group of 50 healthy people, where p <0,0001. COPD patients are associated with higher fibrinogen levels than control subjects. This shows that fibinogen levels correlate with COPD severity.

Conclusion

- Age differences were found between the COPD and non-COPD groups, where the COPD group had a higher age than the non-COPD group.
- There were differences in FEV between the COPD and non-COPD groups, where the COPD group had a lower FEV than the non-COPD group.
- There is no difference in the Brinkman Index between the COPD and non-COPD groups.
- There are differences in fibrinogen in smokers who suffer from COPD and there is no increase in fibrinogen in patientsnon COPD smokers.

Increased fibrinogen levels, in stable COPD patients, can be used to assess a prognosis and as a treatment to determine treatment in the hospital.

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