

Surfactant Protein D and C-Reactive Protein as serum biomarkers in Chronic Obstructive Pulmonary Disease

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ABSTRACT

Introduction: With the growing awareness of COPD as a systemic disease, there has been a shift in the focus of biomarker discovery away from lung sources and toward blood specimens. **Aim of Work:** The aim of the present work was to evaluate the utility of serum SP-D compared to serum CRP as biomarkers in tracking disease progression of COPD and to assess the effect of smoking and inhaled steroid on their levels. **Subjects and Methods:** Seventy subjects were enrolled in this study divided into 2 main groups: healthy control group (30 subjects) and COPD patients' group (40 subjects). Serum SP-D and serum CRP were measured using enzyme linked immunosorbent assay method (ELISA). **Results:** revealed that COPD is associated with significant higher levels of both serum SP-D and CRP, while smoking is associated with significant higher levels of SP-D only. On the other hand, inhaled steroid is associated with significant lower serum levels of both SP-D and CRP. In addition, serum SP-D levels correlate positively with the severity of COPD disease while CRP levels showed no significant correlation with severity of the disease. **Conclusion:** These results empower the sensitivity of both markers in diagnosis of COPD and in following the response of the patients to steroid therapy. On the other hand, results suggest that SP-D is more accurate than CRP as serum biomarker in tracking disease progression of COPD patients. **Key Words:** COPD, Surfactant protein D, C reactive protein, Biomarker, Inhaled Steroid, Smoking.

INTRODUCTION

COPD is characterized by airflow limitation, chronic lung inflammation, and extrapulmonary systemic effects. In chronic lung inflammation, elevated protease and oxidant levels are believed to contribute to degradation of lung tissue and progression of COPD. When evaluating therapies for COPD or defining different patterns of the

disease, markers that could provide insights into these destructive inflammatory processes would therefore be helpful. New biomarkers for COPD are being explored, including those in exhaled breath, induced sputum, bronchoalveolar lavage fluid, lung biopsy, and serum^(1,2). A biomarker is defined as a biological marker that is objectively measured and evaluated as an indicator of normal biological,

pathogenic processes, or pharmacologic responses to a therapeutic intervention⁽³⁾. Biomarkers can be genetic polymorphisms that contribute new pathogenic insights into COPD⁽⁴⁾ or parameters that may be used for the assessment of disease severity or effects of therapy. Compared with markers measured in other sample material, biomarkers determined in serum are reliably measured using equipment that is cost effective and readily available in clinical settings. However, these markers may be modulated by morbidities other than COPD and thus may, in some circumstances, represent epiphenomena unrelated to the COPD phenotype⁽⁴⁾.

Surfactant protein (SP)-D is a biomarker for COPD. This marker is relatively specific for the lungs and can be measured in serum⁽⁵⁾. SP-D synthesis is mainly restricted to pulmonary tissues. Since SP-D is elevated in the circulation in response to lung pathology⁽⁶⁾, this protein could provide a useful marker of COPD⁽⁵⁾.

C-reactive protein (CRP) is one of the acute phase proteins that increase during systemic inflammation. It is one of the inflammatory markers that increases in COPD patients and relates to the pulmonary function⁽⁷⁾. It has been associated with an increased risk of incident myocardial infarction, stroke, unstable angina, and sudden coronary death⁽⁷⁾. It contributes to the recruitment of circulating leucocytes, the uptake of low density lipoprotein cholesterol by macrophages, and ultimately to a destabilisation of vascular wall atheroma⁽⁸⁾.

The present study aimed to evaluate the utility of, surfactant protein D (SP-D) and CRP as serum biomarkers in COPD and to assess the effect of inhaled corticosteroids and smoking on levels of these biomarkers in COPD.

SUBJECTS & METHODS

The present study was carried out at the outpatient clinic of Chest department at Beni Sueif University hospital during the period between (2009-2010). It included 70 subjects whom were divided into two groups as follows:

Group 1: included 40 patients suffering from varying degree of COPD. Spirometric criteria included FEV1 of less than 80% of predicted with an FEV1 to FVC ratio of less than 0.70 (post-bronchodilator values). Their age varied from 45-65. This group was further classified according to their smoking status and the treatment they receive into:

Group 1a: current-smokers and receiving inhaled steroid (ICS) (fluticasone for at least 2 years) (10 patients).

Group 1 b: ex-smokers and receiving inhaled steroid(fluticasone for at least 2 years) (10 patients).

Group 1c: current smokers and not on inhaled steroid (10 patients).

Group 1d: ex-smokers and and not on inhaled steroid (10 patients).

Group 2: included 30 asymptomatic healthy control volunteers who matched with age and sex and were divided according to their smoking status into:

Group 2 a: 10 healthy current smokers.

Group 2 b: 10 healthy ex- smokers.

Group 2 c: 10 healthy non smokers.

Both groups 1 and 2 were subjected to: A detailed medical, tobacco and medication history taking, Physical examination, Chest X ray, Pulmonary function test(Spirometry before and after bronchodilator) and estimation of serum surfactant protein D and serum CRP .

Estimation of SP-D and CRP in serum by ELISA method.

Peripheral venous blood samples were collected from the patients and healthy subjects at the time of registration for the study The samples were collected in plain tubes and were allowed to clot for at least 30 minutes. They were then centrifuged at $1500 \times g$ for 15 minutes at room temperature, divided into aliquots using a sterile plastic transfer pipette and frozen in -80°C conditions until use. The samples were thawed once and SP-D and CRP (Biovendor, Modrice, Czech Republic), were determined using commercially available ELISA kits.

Exclusion criteria: included a history of asthma or alpha-1 antitrypsin deficiency, other chest diseases, infection in the 3 weeks prior to screening, prior lung resection, and ischemic heart disease.

Statistical method:

The data was coded and entered using the statistical package SPSS version 15. The data was summarized using descriptive statistics: mean, standard deviation, minimal and maximum values for quantitative variables. Statistical differences between groups were tested using Independent sample t test and ANOVA (analysis of variance) for quantitative normally distributed variables and Nonparametric Mann Whitney test and Kruskal Wallis test for not normally distributed quantitative variables. Correlations were done to test for linear relations between variables. Linear regression analysis was done to test for significant predictors for surfactant protein in serum. P-values less than or equal to 0.05 were considered statistically significant.

RESULTS

Table (1) Demographic Data of the studied population

GROUPS	N	Age (Mean \pm SD)	Sex	Smoking status	ICS Use	FEV1/FVC	FVC	FEV1
Group 1a	10	55(5)	M	Current	positive	51.8 \pm 9.3	83.9 \pm 16.3	53.7 \pm 3
Group 1b	10	62(8)	M	Ex-Smokers	positive	60.1 \pm 8.1	91 \pm 8.6	69.3 \pm 9.2
Group 1c	10	56(8)	M	Current	None	45.7 \pm 17.7	58 \pm 15.8	29 \pm 4.3
Group 1d	10	69(6)	M	Ex-Smokers	None	48.9 \pm 12.8	68.7 \pm 15.9	40.6 \pm 3
Group 2a	10	56(9)	M	Current	None	83.56 \pm 8.2	91.21 \pm 10.21	88.2 \pm 10.5
Group 2b	10	63(5)	M	Ex-Smokers	None	93.5 \pm 10.5	96.3 \pm 8.56	89.9 \pm 10.5
Group 3c	10	68(6)	M	None	None	93.8 \pm 6.9	96.6 \pm 7.3	92.4 \pm 8.6

Table (2): Statistical analysis of serum SP-D levels (ng/ml) and serum plasma CRP(mg/dl) among COPD patients compared to control

	SP-D in serum(ng/ml)				CRP in serum(mg/dl)		P-value
	N	Mean	S.D	P-value	Mean	S.D	
Control	30	58.3	31.63	<0.001	2.7	1.03	<0.001
Patients	40	319.03	206.29		5.03	1.51	

This table shows that there is a statistically significant difference between COPD patients and control subjects concerning both SP-D level in serum and serum CRP where COPD patients showed significantly higher values of SP-D and CRP when compared to control.

Table (3): Statistical analysis of serum SP-D (ng/ml) and CRP (mg/dl) levels among subjects of the Control group.

	GROUPS	SP-D(ng/ml)				CRP(mg/dl)		
		N	Mean	S.D	P-Value	Mean	S.D	P-Value
Control	Group 1a	10	87.01	14.23	<0.001	2.24	1.04	>0.005
	Group1b	10	29.59	8.88		2.02	1.04	
	Group 1c	10	28.63	8.60	>0.005	2.00	0.86	

As regards **serum levels of SP-D**, this table shows that there is a statistically significant difference between current smokers control subjects (1a) and ex-smokers control subjects (1b) where a higher value was noticed with current smokers, while no statistical significant difference was found between ex-smokers control subjects (1b) and non smokers control subjects (1c). Concerning CRP serum levels, no statistically significant difference was found between these groups.

Table (4): Comparison of serum levels of SP-D (ng/ml) and serum CRP (mg/dl) between current smokers COPD patients and current smokers control subjects, and between ex-smokers COPD patients and ex-smokers control subjects.

GROUPS	N	S P - D	Mean	S.D	P-value	C R P	Mean	S.D	P-value
Current smokers COPD patients	20		439.6	316.7	<0.001		5.07	0.72	<0.001
Current smokers control subjects	10	87.01	14.23	2.24		1.04			
Ex smokers COPD patients	20	198.49	81.4	<0.001	5.00	1.52	<0.001		
Ex smokers control subjects	10	29.59	8.88		2.02	1.04			

This table shows that serum levels of both SP-D and CRP were significantly higher among current smokers COPD patients compared to current smokers control and both SP-D and CRP were significantly higher among ex smokers COPD patients compared to ex smokers control.

Table (5): Comparison of serum levels of SP-D (ng/ml) and CRP between current smokers COPD patients and ex-smokers COPD patients.

GROUPS	N	SP-D	Mean	S.D	P-value	CRP	Mean	S.D	P-value
Current smokers COPD patients	10		439.6	316.7	<0.001		5.07	0.72	0.089
Ex smokers COPD patients	10		198.49	81.4			5.00	1.52	

This table shows that serum levels of SP-D was significantly higher among current smokers COPD patients compared to ex smokers COPD patients ,while serum levels of CRP was insignificantly higher among current smokers COPD patients compared to ex smokers COPD patients.

Table (6): Statistical analysis of serum levels of SP-D (ng/ml) and CRP between current smokers COPD patients not on inhaled steroid and ex-smokers COPD patients not on inhaled steroid.

GROUPS	N	SP-D	Mean	S.D	P-value	CRP	Mean	S.D	P-value
Current smokers COPD patients not on inhaled steroid	10		663.56	19.17	<0.001		5.00	0.84	0.008
Ex smokers COPD patients not on inhaled steroid	10		256.08	14.55			4.92	1.02	

This table shows that serum levels of SP-D was significantly higher among current smokers COPD patients not on inhaled steroid(ICS)compared to ex smokers COPD patients not on ICS, while serum levels of CRP was insignificantly higher among current smokers COPD patients not on inhaled steroid compared to ex smokers COPD patients not on ICS.

Table (7): Statistical analysis of serum levels of SP-D (ng/ml) and CRP between current smokers COPD patients on inhaled steroid (ICS) and current smokers COPD patients not on inhaled steroid.

GROUPS	N	SP-D	Mean	S.D	P-value	CRP	Mean	S.D	P-value
Current smokers COPD patients on ICS	10		215.60	13.80	<0.001		3.1	0.02	<0.001
Current smokers COPD patients not on ICS	10	663.56	19.17	5.00		0.84			

This table shows that serum levels of both SP-D and CRP were significantly lower among current smokers COPD patients on ICS compared to current smokers COPD patients not on ICS .

Table (8): Statistical analysis of serum levels of SP-D (ng/ml) and CRP between ex smokers COPD patients on inhaled steroids and ex-smokers COPD patients not on inhaled steroids

GROUPS	N	SP-D	Mean	S.D	P-value	CRP	Mean	S.D	P-value
Ex- smokers COPD patients on ICS	10		140.91	14.97	<0.001		2.7	0.84	<0.001
Ex- smokers COPD patients not on ICS	10	256.08	14.55	4.92		1.02			

This table shows that serum levels of both SP-D and CRP were significantly lower among ex smokers COPD patients on ICS compared to ex smokers COPD patients not on ICS.

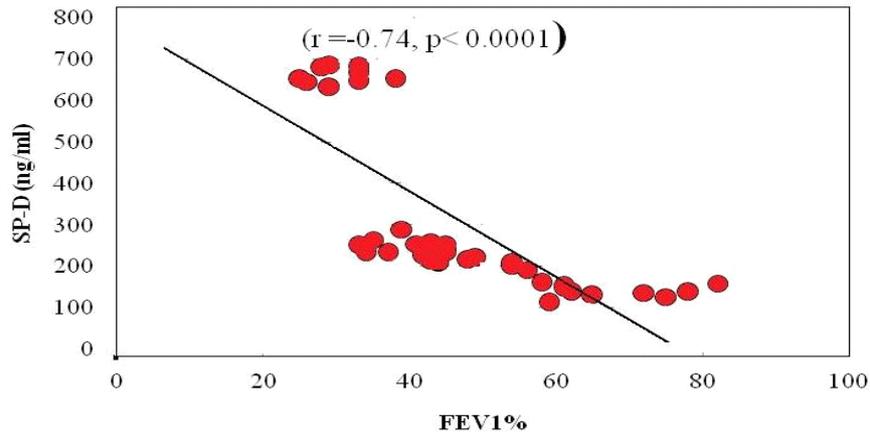


Figure (1): Scatter plot showing the negative correlation between SP-D in serum and FEV1 in COPD patients.
 A negative correlation was found between SP-D serum level and FEV1 with P-Value= <0.0001 and r-value = -0.74 .

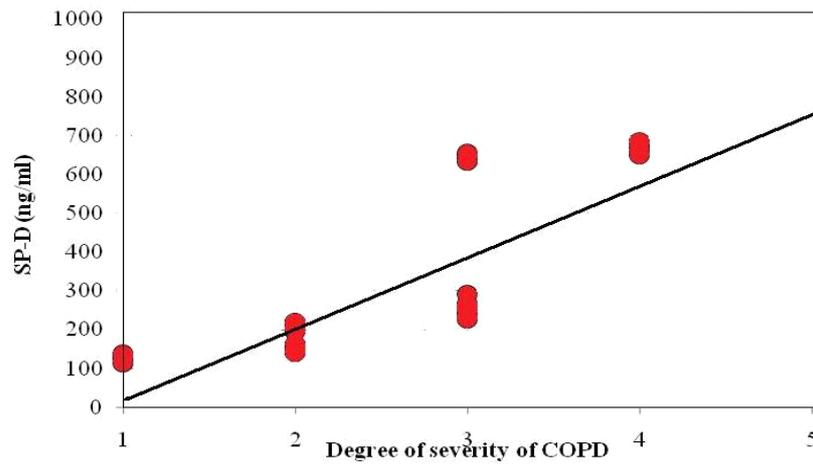


Figure (2): Scatter plot showing the positive correlation between SP-D serum level (ng/ml) and severity of disease
 A positive correlation was found between SP-D serum level and severity of disease with P-Value= <0.217 and r-value = 0.335

DISCUSSION

COPD is a growing epidemic in the world. Despite its huge burden, currently, there are very few COPD-specific drug therapies that can significantly improve health outcomes of COPD patients. There is a pressing need to develop novel drug targets to curb the global epidemic of COPD. SP-D is produced exclusively by type 2 pneumocytes and non-ciliated bronchioloveolar cells. Its presence in the blood is largely determined by the leakiness of the pulmonary epithelium. SP-D has many functional properties including its anti-inflammatory and anti-oxidant capacities, and protection against respiratory infections. Collectively, these properties may make it an attractive molecule for further evaluation as a biomarker for epithelial integrity, or a drug target in COPD⁽¹⁾.

Although primarily affecting the lungs, the chronic inflammatory process of COPD does have systemic repercussions. Inflammatory markers, including C reactive protein (CRP), lipopolysaccharide binding protein, the soluble TNF transmembrane receptor 75 (sTNF-R75), and soluble adhesion molecules are increased in the systemic circulation of patients with COPD^(2,3,4). The impact of the systemic manifestations of COPD on prediction of mortality using a multidimensional index have recently been reported⁽⁵⁾. Of these blood-based biomarkers, CRP has shown the greatest promise.

The aim of the present study was the evaluation of the utility of serum

SP-D and CRP as biomarkers for COPD and assessing the effect of inhaled corticosteroids and smoking on their levels.

The results of the current study showed that serum SP-D level was significantly higher in COPD patients when compared to healthy control subjects matching with age and sex (table 2).

By comparing current smokers COPD patients and current smokers control subjects another statistical higher value of SP-D was found with current smokers COPD patients. Once more, a significant higher SP-D serum levels was observed with ex smokers COPD patients when compared with ex smokers control subjects (table 4). These results reveal that COPD is independently associated with increase in SP-D serum levels.

The results of the present work agreed also with **Mutti et al.**⁽⁹⁾ study which included 50 healthy subjects, 30 healthy smokers, 30 asthmatics, and 50 patients with stable COPD. The serum pneumoproteins were immunoassayed and results revealed that serum SP-D concentrations were higher in both smokers and COPD patients than in normal control subjects.

Another study performed by **Sims et al.**⁽¹⁰⁾ showed that COPD is independently associated with a significant lower level of SP-D in **bronchoalveolar lavage (BAL)**. In the latter study ,BAL was collected from 20 subjects with varying degrees of COPD (8 ex- smokers and 12 current smokers) and 15 asymptomatic healthy control subjects

(5 non smokers, 3 remote ex-smokers, and 7 current smokers).

The possible explanation of all the previous results is that about 75% of SP-D is found in bronchoalveolar lavage fluid **Kishore et al.**,⁽¹¹⁾ and its production in BAL increases as certain inflammatory cytokines such as interleukin (IL)-4, IL-6, and IL-13 are potent inducers of its production in the airways **Haczku et al.**,⁽¹²⁾ and **Kierstein et al.**,⁽¹³⁾ and it is likely that this hydrophilic protein, or its degradation products, leak from the lung as a consequence of increased vascular permeability associated with inflammation. They are then detected within the circulation.

The present study showed that there was a significant difference in mean serum CRP level between COPD patients and healthy subjects as CRP serum concentration was higher in patients with COPD (table 2).

Yende et al.,⁽¹⁴⁾ also reported a higher level of serum CRP in cases with an obstructive pattern in their spirometry (3.5 mg/L) in comparison to normal population (2.5 mg/L) ($p < 0.0001$).

In a study conducted by **Broekhuizen et al.**,⁽¹⁵⁾ stable COPD patients had increased levels of inflammatory markers like CRP ($p = 0.03$).

Pinto-Plata et al.⁽¹⁶⁾ showed that there was a significant higher level of CRP in COPD patients (5.03 ± 1.51 mg/L) rather than smoking (2.02 ± 1.04 mg/L) and non smoking control groups (2.24 ± 1.04 mg/L) ($P < 0.001$).

CRP increases in COPD patients may be due to the inflammatory process itself or related factors such as ischaemic heart disease or

smoking⁽¹⁷⁾. In our study IHD patients were excluded and COPD effect on CRP was evaluated as independent factor, so our results further supports the concept that the increase in the CRP level in patients with severe COPD cannot be attributed only to concomitant IHD. As suggested by others,⁽¹⁸⁾ it is possible that the persistent systemic inflammation in patients with COPD may contribute to the pathogenesis of atherosclerosis and cardiovascular disease and explain a high risk of cardiovascular mortality in patients with mild and moderate COPD.

As regards the effect of smoking on the SP-D, in the present study we found that current smokers COPD patients showed significant higher SP-D serum levels compared to ex-smokers COPD patients (table 5). Also, there was a statistical significant difference in serum SP-D between current smokers control subjects and ex-smokers control subjects where a higher SP-D level is noticed with current smokers control subjects (table 4). On the other hand, no statistical difference was found between ex-smokers control subjects and non smokers control subjects (table 3). Also serum level of SP-D (ng/ml) was significantly higher in current smokers COPD patients not receiving ICS than those Ex-smokers COPD patients not receiving ICS (table 6), and also serum level of SP-D (ng/ml) is significantly higher in current smokers COPD patients receiving ICS than those Ex-smokers COPD patients receiving ICS (table 7).

These results reveal that current smoking status is independently

associated with significant higher serum SP-D.

The same results were also reported by **Mutti et al.**⁽⁹⁾ in his previously mentioned study found the same positive correlation between current smoking status and serum SP-D.

Fernandez-Real et al.⁽¹⁹⁾ in his trial to investigate the role of SP-D as a potentially novel risk factor for glucose intolerance and insulin resistance, reported that smokers with normal glucose tolerance showed significantly higher serum SP-D concentration than non smokers.

By measuring SP-D level in bronchoalveolar lavage, **Sims et al.**⁽¹⁰⁾ found that SP-D concentrations were lower in current smoker patients than in ex- and non smoker patients.

Thus, smoking is associated with elevation in serum level of SP-D. Several mechanisms may explain this and among them are: (1) smoking may reduce the production of SP-D by type 2 pneumocytes; or (2) smoking may increase the alveolar-capillary permeability causing SP-D to leak from the lung compartments into the systemic circulation. To test the first mechanism, **Hirama et al.**⁽²⁰⁾ exposed 8-week old B6C3F1 mice to daily cigarette smoke (2 cigarettes per day) for 6 months and compared SP-D expression in the lungs of mice exposed to cigarette smoke with the control. The mice exposed to cigarette smoke developed mild emphysema and airway inflammation characterized by increased expression of metalloproteinase (MMP)-9, 12, tumor necrosis factor (TNF)- α , and granulocyte macrophage-colony stimulating factor (GM-CSF) in the

lungs. They also found increased expression of SP-D in the lungs at both the mRNA and protein level. These data indicate that cigarette smoke up-regulates SP-D expression in the lungs.

There is a large body of evidence indicating that smoking perturbs the integrity of the alveolar capillary interface, leading to increased diffusion of hydrophilic solutes across this barrier **Mason et al.**⁽²¹⁾

In our study, no difference was observed in the mean CRP level between control smokers and non smokers (table 3). Similarly, there was no difference among the patients with COPD who were current smokers and those who were ex smokers (table 5). These findings may be due to the absence of an inflammatory response in the smokers, or persistent inflammation in COPD patients even after smoking cessation as seen in human lung samples. The observation that CRP levels did not differ between smoker and non-smoker controls, and between smoker and ex-smoker patients with COPD, also suggests that the increase in CRP levels may represent a phenotype of CRP responders. Little is known about the reason why some persons exposed to cigarette smoke develop clinically important COPD whereas others do not. We speculate that there may be individuals with an "inherited" inflammatory genetic profile. If they are "exposed" to environmental factors (such as smoking or pollution), they have a higher risk of developing COPD.

Concerning the effect of inhaled steroid on SP-D level in serum, a significant difference was found

between patients receiving inhaled steroid when compared to those receiving bronchodilator only. Serum level of SP-D was significantly lower in current smokers COPD patients receiving ICS than those current smokers COPD patients not receiving ICS (table 7). Also serum level of SP-D was significantly lower in ex-smokers COPD patients receiving ICS than those ex-smokers COPD patients not receiving ICS (table 8), suggesting that SP-D may be a biomarker for response to steroid therapy.

A biomarker that reflects the intrapulmonary inflammation of COPD should respond to the administration of a potent anti-inflammatory agent. This is what **Sin et al.**⁽⁵⁾ succeeded in demonstrating by examining 289 patients with COPD in a randomized controlled trial, as they found that serum SP-D levels increased during the 4 weeks when inhaled corticosteroids and long-acting β_2 -agonists were withdrawn. In contrast, 4 weeks of treatment with either fluticasone or fluticasone/salmeterol was associated with reduced serum SP-D, indicating that an inhaled corticosteroid in conjunction with a long-acting β_2 -agonist can decrease circulating levels of SP-D.

The changes observed in serum SP-D with withdrawal and institution of therapy could be due to (1) changes in SP-D leakage from the lungs into the circulation, (2) changes in extrapulmonary SP-D production, or (3) changes in SP-D clearance from the circulation. Although none of these can be totally excluded, the first hypothesis seems the most likely as SP-D is primarily produced in the lungs,

corticosteroids in this trial were delivered in lung, and other lung pathologies also are associated with elevated serum SP-D **Hartl and Griese,**⁽⁶⁾ and **Sørensen et al.**⁽²²⁾.

Corticosteroids have been shown to induce expression of SP-D in the fetal lung tissue of both rats and humans (**Dulkerian et al.**⁽²³⁾ and **Wang et al.**⁽²⁴⁾).

The study performed by **Sims et al.**⁽¹⁰⁾ showed that inhaled corticosteroid use is associated with higher levels of SP-D in the lung. Also their study investigated adult type II alveolar epithelial cells isolated from rat lungs and found that similarly to fetal cells, SP-D synthesis depended on constitutive presence of dexamethasone. Given that there are several high potency inhaled steroids widely used to treat COPD and that these steroids are deposited directly on the epithelium, the site of SP-D production. So **Sims et al.**⁽¹⁰⁾ suspected that these medications may have effects on local SP-D gene expression. Given the high level of evolutionary conservation of the SP-D gene promoter sequence between rats and humans, they speculate that inhaled corticosteroids induce expression of SP-D in the adult human lung. Further, this mechanism may enhance the anti-inflammatory effects of inhaled corticosteroids in COPD.

The CRP level in patients with COPD was lower in ICS users than in non users. These results are in agreement with **Sin et al.**⁽⁵⁾ study in which they showed that withdrawal of ICS from patients with mild and moderate disease was associated with a 71% increase in the baseline CRP

level. It would be interesting to study larger groups of patients with COPD treated with ICS or withdrawn from ICS to determine if the changes in the number of COPD exacerbations and quality of life observed in those studies correlate with changes in the CRP level.

The current study showed a significant increase in SP-D serum levels with increasing severity of disease (as assessed by GOLD score) (figure 2).

Similarly, **Sin et al.**⁽¹⁷⁾ reported a significant inverse relationship between FEV1 and SP-D level in serum among 23 patients of variable degrees of obstruction.

Krane and Griese⁽¹⁸⁾ reported also the previous correlation but among patients with cystic fibrosis. 22 patients with CF and 19 control patients without a pulmonary disease were enrolled in their study and results revealed a clear negative correlation between SP-D concentration and overall lung function, i.e. forced expiratory volume in one second.

Lomas et al.⁽⁸⁾ reported no significant correlation between severity of COPD (as assessed by GOLD score) and serum SP-D.

Supporting the results of the previous study **Sims et al.**⁽¹⁰⁾ though reported that subjects with very severe COPD (GOLD 4) had lower levels of SP-D in BAL compared with subjects with GOLD stage 2 or 3 diseases, yet it showed that this difference was not statistically significant. Clearly, further studies with larger numbers of subjects are required to ultimately prove or disprove this correlation.

Regarding the severity of disease based on GOLD criteria, the mean serum CRP level was increased in severe cases but this correlation was not statistically significant.

Pinto-Plata et al.⁽¹⁶⁾ showed that there was no significant difference between the severity of disease and serum CRP level but **de Torees and co-workers**⁽²⁵⁾ indicated that serum CRP level was significantly increased by aggravation of disease. Although we expect the inflammatory process to be worse and the inflammatory markers to be increased by increasing the severity of disease, more studies are required in this regard.

In conclusion, we have confirmed that serum CRP and SP-D levels are significantly raised in patients with COPD and this increase is not related to smoking. Also our study revealed that both markers are lowered by inhaled steroid which empower the sensitivity of both markers in diagnosis of COPD and following the response of the patients to steroid therapy. On the other hand, SP-D levels increased significantly with increasing severity of COPD disease, while CRP did not. This reflects that only SP-D but not CRP could be used as a serum marker to track disease progression in COPD patients.

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البروتين المتفاعل سي وبروتين السيرفاكتنت د كدالاتين حيوييتين في الدم في مرض السدة الرئوية المزمنة

يعد مرض السدة الرئوية المزمنة أحد الأمراض التي تزداد خطورتها في العالم. وبالرغم من فداحة الخسائر التي يسببها إلا أن هناك نقص واضح في العقاقير التي لها تأثير فعال في علاج هذا المرض. وتعتبر العقبة الرئيسية في اكتشاف عقاقير فعالة هو قلة الدلالات الحيوية في الدم التي يمكن استخدامها لتقييم فاعلية تلك العقاقير.

ان بروتين السيرفاكتنت(د) - (أحد البروتينات المستمدة من الرئة) له دور كبير في الوقاية من امراض الجهاز التنفسي. كما ان البروتين المتفاعل سي يعد من بروتينات الطور الحاد الذي يسجل مستواه زيادة في حالات الالتهابات الحادة.

تهدف هذه الدراسة الى تقييم استخدام البروتين المتفاعل (سي) و بروتين السيرفاكتنت(د) كدالاتين حيوييتين في الدم في مرض السدة الرئوية المزمنة وتوضيح تأثير كل من التدخين والكورتيزون المستنشق على مستويهما في الدم.

وقد تضمنت الدراسة 70 حالة تم تقسيمهم الى مجموعتين رئيسيتين:
مجموعة ١) : (وتشمل 40 حالة من مرضى السدة الرئوية المزمنة وقد تم اعادة تقسيمهم) وفقا لحالة التدخين وللعلاج الذي يتعاطونه (الى :

- مجموعة ١١ مدخنين حاليين ومستنشقي الكورتيزون (١٠ حالات).
- مجموعة ١٢ مدخنين سابقين ومستنشقي الكورتيزون (١٠ حالات).
- مجموعة ١٣ مدخنين حاليين وغير مستنشقي الكورتيزون (١٠ حالات).
- مجموعة ١٤ مدخنين سابقين وغير مستنشقي الكورتيزون (١٠ حالات).

مجموعة ٢) : وتشمل 30 حالة من الاصحاء كمجموعة ضابطة وقد تم اعادة تقسيمهم الى:-

- مجموعة ١٢ :مدخنين حاليين (١٠ حالات)
 - مجموعة ٢٢ :مدخنين سابقين (١٠ حالات)
 - مجموعة ٢٣ :الغير مدخنين (١٠ حالات)
- وقد خضعت جميع حالات الدراسة الى:

- اخذ تاريخ مرضى كامل.
- فحص اكلينيكي شامل.
- عمل اشعة سينية على الصدر.
- تقدير للبروتين المتفاعل (سي) في الدم
- تقدير لبروتين السيرفاكتنت (د) في الدم.

كما خضعت حالات السدة الرئوية المزمنة، بالإضافة الى ذلك، الى عمل وظائف للرئة .

وقد اظهرت النتائج ان كلا من بروتين السيرفاكتنت (د) والبروتين المتفاعل(سي) قد ازدادا ازديادا ذي دلالة احصائية في مرضى السدة الرئوية المزمنة وان هذه الزيادة ليست مرتبطة بكون المرضى من المدخنين كما اوضحت النتائج ايضا ان كلا من الدالاتين محل الدراسة قد انخفضا انخفاضاً ذي دلالة احصائية بفعل استنشاق الكورتيزون. على الجانب الاخر ازداد بروتين السيرفاكتنت (د) (وحده دون البروتين المتفاعل سي) زيادة ذي دلالة احصائية مع ازدياد حدة مرض السدة الرئوية المزمنة .

ويستخلص من هذه النتائج حساسية كل من الدالاتين محل الدراسة في تشخيص مرض السدة الرئوية المزمنة وفي استخدامها لمتابعة مدى استجابة المرضى للعلاج با لكورتيزون المستنشق بينما توضح النتائج حساسية بروتين السيرفاكتنت (د) وحده في متابعة الحالة الصحية لمرضى السدة الرئوية المزمنة.