Study of C-Reactive Protein Level in Patients with Stable COPD and in Acute Exacerbations

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Abstract

Background: C-Reactive Protein (CRP) is an inflammatory mediator that is increased in patients with Chronic Obstructive Pulmonary Disease (COPD) and can be used as diagnostic and prognostic adjuvant to assess the severity of disease.

Aim of Study: This study was the difference in the CRP level between stable COPD and AECOPD patients.

Subjects and Methods: Sixty COPD patients (30 with stable COPD and 30 with AECOPD) were included in this study and results were compared to those of 10 healthy age/sex-matched controls. Clinical history was taken and full clinical examination was done to assess the patients' conditions and rule out any co-morbidities that could be associated with increased CRP level. Blood samples were drawn to measure the CRP level, ABG and TLC. Pulmonary function test was also done.

Results: CRP level was significantly higher in COPD patients compared to healthy controls (p-value <0.0001). It was also significantly higher in AECOPD patients compared to patients with stable COPD (p-value <0.0001).

Conclusion: CRP level is generally increased in COPD patients, being significantly higher in the AECOPD patients than the stable ones, and thus can be used as a prognostic marker to assess the severity of the disease.

Key Words: COPD – CRP.

Introduction

CHRONIC Obstructive Pulmonary (COPD) has several clinical and pathologic entities, primarily emphysema and chronic bronchitis. Evidence of airflow obstruction is chronic, progressive and almost fixed [1] . CRP is a member of class of defense molecules called acute phase proteins. The levels of acute phase proteins rise rapidly during infection, after injury and in inflammatory condi-

tions [2] . CRP is one of the inflammatory markers which is increasingly evaluated in COPD patients [3] . It is increased in patients with Acute Exacerbations of COPD (AECOPD) and can be used as a prognostic marker to assess the severity of the disease [4] .

Subjects and Methods

This study was performed on seventy subjects: Sixty COPD patients (55 males and 5 females) and ten age/sex matched healthy controls (9 males and 1 female). COPD patients were admitted to the Chest Department at Agouza Police Hospital in the period between June 2016 to August 2017. Thirty patients with stable COPD (28 males and 2 females) and 30 patients with AECOPD (27 males and 3 females) were assessed.

All patients were subjected to the following:

Clinical history (smoking, symptoms: Cough, expectoration, dyspnea and wheezes and other co-morbidities that may raise the CRP level e.g. ischemic heart diseases, hypertension and diabetes mellitus).

General and local clinical examination.

Radiological examination via a plain X-ray (postero-anterior view).

Pulmonary function tests were done, namely FEV_1 and FEV_1/FVC.

Blood samples for Arterial Blood Gases (ABG), CRP level and TLC.

Inclusion criteria include:

Pulmonary functional tests proving the presence of airway obstruction, namely FEV_1/FVC <70%,

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that is irreversible (<10% improvement after use of bronchodilator).

For the stable COPD group: No history of exacerbation for the three months prior to their inclusion in the study.

For the AECOPD group: Symptoms of exacerbation (increased dyspnea, increased amount or purulence of sputum and increased cough) with or without signs of right sided heart failure.

Exclusion criteria include:

Any disease identified by history and clinical examination that may elevate the CRP level as: Pneumonia, bronchial asthma, any cardiopulmonary disease, diabetes mellitus, malignancy, connective tissue disorders or chronic liver disease.

Patient on Non-Steroidal Anti-Inflammatory Drugs (NSAIDS) as these drugs may help to reduce the inflammation, thus reducing CRP level.

Statistical analysis:

Statistical analysis of the present study was conducted, using the mean, standard deviation, analysis of variance [ANOVA] test, chi-square test and independent sample *t*-test by SPSSV.

Results

Table (1): Age and sex distribution among cases.

	Stable COPD No.=30	AECOPD No.=30	Test value	p-value	Sig.
Sex:					
Females	2 (6.7%)	3 (10.0%)	0.218*	0.640	NS
Males	28 (93.3%)	27 (90.0%)			
Age:					
Mean ± SD	52.40±7.52	57.13±9.45	–2.147*	0.036	S
Range	41-68	42-75			

Table (2): Clinical presentation of cases.

	Stable COPD No.	Stable COPD %	AECOPD No.	AECOPD %	Test value	p-value	Sig.
Smoking:							
Negative	3	10.0	0	0.0	3.158	0.076	NS
Positive	27	90.0	30	100.0			
Cough:							
Negative	0	0.0	0	0.0	NA	NA	NA
Positive	30	100.0	30	100.0			
Dyspnea:							
No	5	16.7	0	0.0	60.000	0.000	HS
Mild	25	83.3	0	0.0			
Moderate	0	0.0	20	66.7			
Severe	0	0.0	10	33.3			
Wheezes:							
Negative	18	60.0	13	43.3	1.669	0.196	NS
Positive	12	40.0	17	56.7			
Cyanosis:							
Negative	27	90.0	5	16.7	32.411	0.000	HS
Positive	3	10.0	25	83.3			

Table (3): Pulmonary function in stable COPD and AECOPD.

	Stable COPD No.=30	AECOPD No.=30	Test value	p-value•	Sig.
Range	6.5-14	8-17			
FEV1/FVC:					
Mean ± SD	65.57±3.01	50.57±6.71	11.163	0.000	HS
Range	60-69	36-59			
FEV1 %:					
Mean ± SD	58.13±16.37	45.77±23.93	2.337	0.023	S
Range	22-91	16-94			

Table (4): Arterial blood gases in stable COPD and AECOPD.

	Stable COPD No.=30	AECOPD No.=30	Test value•	p-value	Sig.
PH:					
Mean ± SD	7.39±0.03	7.27±0.11	5.724	0.000	HS
Range	7.32-7.45	7-7.45			
PO2:					
Mean ± SD	82.57±7.83	52.83±15.47	9.393	0.000	HS
Range	70-95	30-80			
PCO2:					
Mean ± SD	41.00±3.07	50.73±6.05	–7.855	0.000	HS
Range	35-45	40-62			
SO2:					
Mean ± SD	92.33±1.77	84.93±2.82	12.191	0.000	HS
Range	89-95	80-91			

Table (5): CRP level in control, stable COPD and AECOPD.

CRP level	Control Volunteers No.=10	Stable COPD No.=30	AECOPD No.=30	Test value•	p-value	Sig.
Mean ± SD	6.10± 2.60	52.47± 19.86	107.63± 16.31	161.34	0.000	HS
Range	2-10	20-90	74-140			

Discussion

Chronic obstructive pulmonary disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients [5].

The chronic airflow limitation that characterizes COPD is caused by a mixture of small airway disease (e.g. obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person. A loss of small airways may contribute to airflow limitation and mucociliary dysfunction, a characteristic feature of the disease. Chronic respiratory symptoms may precede the development of airflow limitation and be associated with acute respiratory events [6].

Several systemic inflammatory mediators such as Tumor necrosis factor alpha, interleukins, acute phase protein (C-Reactive Protein {CRP}, Lipopolysaccharides Binding Protein {LBP}) and leucocytes are increased in COPD [7].

CRP is an acute phase protein synthesized in liver in response to acute inflammation. Non hepatic production of CRP by monocyte and lymphocyte has been demonstrated in inflamed lung [8].

Our study aimed to measure CRP level in stable COPD and Acute Exacerbation COPD (AECOPD). It was done at the Chest Department of Agouza Police Hospital. Sixty patients were included in this study, 30 patients with stable COPD and 30 patients with AECOPD, and the results were compared to 10 age matched healthy controls.

In our study, there was no significant difference between stable COPD and AECOPD regarding sex, however there is a significant difference between the two groups regarding age. The mean age for stable group was 52.40 ± 7.52 and that of AE-COPD was 57.13 ± 9.45 (p=0.036). The stable group include 28 males and 2 females while the AECOPD group included 27 males and 3 females and the control group included 9 males and 1 female.

There was a no significant difference between the stable group and the AECOPD group regarding smoking history. All patients of AECOPD were smokers compared to 27 patients of stable COPD group (p=0.076).

In the current study, the level of CRP was significantly higher in the acute exacerbation cases compared to the stable COPD group and the healthy controls (p-value <0.0001). Moreover, the level of CRP was significantly higher in the stable COPD group compared to the healthy controls (p-value <0.0001). This can be explained as follows: In the stable COPD group the CRP level is high due to the present inflammation while in the acute exacerbation group there is superadded infection which raises the CRP level even more.

This is in agreement with the results of the study performed by Prasad et al., [9] in which 100 COPD patients (80 stable and 20 in acute exacerbation) and 50 age/sex matched controls were studied and analyzed on the basis of clinical history, CRP levels, BMI, obstructive capacity and exercise capacity to assess their functional status and predict their outcome.

On the other hand, their results showed insignificant difference between stable group and AE-

COPD regarding FEV_1% and FEV_1/FVC. These results were not consistent with our study.

In the study performed by Kaparianos et al., [10], which compared 162 consecutive male smokers (80 non-COPD smokers marked as controls and 82 COPD smokers) regarding: Age, ABG and pulmonary function test; they found no significant difference between the two groups regarding age, PH & PCO_2. This is in agreement with our study.

Additionally, they found significant difference between the two groups regarding the CRP level and FEV_1% and that was also in agreement with our results.

Moreover, they found no significant difference between the two groups regarding the PO_2 and FEV_1/FVC. This was not the case in our study where there was a significant difference regarding the PO_2 and the FEV_1/FVC between the stable COPD group and the healthy controls with a p-value of <0.0001. In our opinion, this can be explained by the fact that the control subjects in the Kaparianos et al., study were all smokers, while those included in ours were non-smokers.

Our study is in agreement with that of Al-Aarag et al., [11] who also found a significant difference between the control group and the COPD group regarding the CRP level.

In a case-control study conducted by Silva et al., [12], CRP levels were determined and pulmonary function tests were performed in a total of 60 stable COPD patients and 30 controls. They found no significant difference between the two groups regarding the CRP level and smoking. This was not the case in our study. These differences can be explained by the fact that they only included patients who had quit smoking in their study.

Regarding the FEV_1% and the FEV_1/FVC, they found a significant difference between the two studied groups, being in agreement with our results.

In a study performed by (Xiong et al., [13], 368 stable COPD patients ≥40 years old and 296 control subjects >40 years old with or without smoking history were enrolled and the results of their routine blood tests were studied to assess their role in predicting the prognosis of COPD. They found no significant difference between the two studied groups in relation to their leucocytic count. This was comparable to the findings of Zhang et al., [14] who enrolled 90 patients with AECOPD who were investigated in the acute phase and reassessed when convalescent (stable COPD), and 90 matched

controls. Routine blood tests and pulmonary function were assessed. they also found no significant difference between the stable COPD and the control groups in relation to their leucocytic count. This was not the case in our study where we found the leucocytic count to be significantly higher in the stable COPD than the healthy controls with a p-value of 0.003. This difference can be attributed to the comparably small number of subjects in our study.

Zhang et al., [14] also found a significant difference between the stable group and the control group in relation to the CRP level. That is in agreement with our study.

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دراسة مستوى البروتين التفاعلى فى المرضى الذين يعانون
من مرض الإنسداد الرئوى المزمن المستقر وفى التفاقم الحاد

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الخلفية: البروتين سى التفاعلى (CRP) هو وسيط إلتهابى يزيد فى المرضى الذين يعانون من مرض الإنسداد الرئوى المزمن (COPD) ويمكن إستخدامه كمساعد تشخيصى ولتقييم شدة المرض.

الهدف: دراسة الفرق فى مستوى البروتين سى التفاعلى CRP بين مرضى الإنسداد الرئوى المزمن المستقر وفى التفاقم الحاد.

المواضيع والآساليب: تم تضمين ستين مرضى مرض الإنسداد الرئوى المزمن (٣٠ مع مرض الإنسداد الرئوى المزمن المستقر و٣٠ فى التفاقم الحاد) فى هذه الدراسة وتمت مقارنة النتائج مع النتائج من ١٠ متطوعين. تم آخذ التاريخ السريرى وتم إجراء فحص سريرى كامل لتقييم حالات المرضى وإستبعاد آى حالات مرضية قد تترافق مع زيادة مستوى CRP. تم سحب عينات الدم لقياس مستوى البروتين سى التفاعلى CRP، غازات الدم الشريانية ABG وعد خلايا الدم الآبيض TLC.إختبار وظائف الرئة كما تم.

النتائج: كان مستوى البروتين سى التفاعلى CRP آعلى بكثير فى المرضى الذين يعانون من مرض الإنسداد الرئوى المزمن مقارنة مع الضوابط الصحية (قيمة $p<0.0001$). كان آيضاً آعلى بكثير فى مرضى مرض الإنسداد الرئوى المزمن آثناء التفاقم الحاد مقارنة بالمرضى الذين يعانون من مرض الإنسداد الرئوى المزمن المستقر (قيمة $p<0.0001$) ومع الضوابط الصحية.

الخلاصة: يتم زيادة مستوى البروتين سى التفاعلى CRP بشكل عام فى مرضى الإنسداد الرئوى المزمن، وآعلى بشكل ملحوظ فى مرضى مرض الإنسداد الرئوى المزمن آثناء التفاقم الحاد مقارنة بالمستقر، وبالتالى يمكن إستخدامه كعلامة تشخيصية لتقييم شدة المرض.