Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2015, 7(12):546-550

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Comparison of two biomarkers of inflammation, the erythrocyte sedimentation rate and C-reactive protein measurements: A cross-sectional study

Aissam El Maataoui[1], Ilham Jebrane[2], Naima Khlil[2], Abderrahim Naamane[2] and Nabiha Kamal[2]

[1]*Biochemistry-Chemistry Department, Faculty of Medicine and Pharmacy, Ibn Zohr University Agadir-Morocco*
[2]*Biochemistry-Chemistry Department, Faculty of Medicine and Pharmacy, Hassan II University Casablanca-Morocco*

ABSTRACT

The C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) are commonly used to assess the acute phase response. The purpose of the study is to seek the association between these two parameters. We conducted a cross-sectional retrospective. A total of 76 patients have been selected from a hospitable database. They all had a prescription of CRP and ESR. Another important inclusion criterion is the realization of blood sample for CRP and ESR on the same day and the same hour. ESR and CRP values correlated significantly with each other (Pearson r = 0.516, p < 0.001). Multiple regression analysis was therefore performed to determine the combination of variables that accounted for the greatest proportion of variance in CRP and ESR values. Neutrophils and ESR were related to CRP. Hematocrit, MCV, Albumin concentration and platelets count were significantly related to ESR the prescribers must take into account the concentrations of different parameters that influence the outcome of the CRP and ESR values directly

Key words: C-reactive protein, erythrocyte sedimentation rate, prescription, interpretation

---

INTRODUCTION

C-reactive protein (CRP) is a 224-aminoacid acute phase serum protein and one of the most frequently used markers of inflammation. Rate of CRP increases rapidly in response to inflammation and the release of cytokines IL1β, IL6 [1].It's a parameter that allows direct and quantitative measure of the acute-phase reaction. Another frequently used marker of inflammation but conversely indirectly measures the acute phase reaction is the erythrocyte sedimentation rate (ESR). The ESR is the distance that red blood cells settle in a tube of blood in one hour and reported in mm/h. ESR is often replaced with C-reactive protein measurement by the prescribers because the CRP levels in the blood rise more quickly after the inflammatory process begins and because the ESR is affected by a multitude of factors, such as anaemia, haematocrit and the reference values which differ according to age and sex.

In our medical practice in morocco, we notice there has a prescription of two biomarkers of inflammation namely the ESR and CRP by some doctors. Others prescribe only the ESR or only the CRP. Based on these observations is there a correlation between the two biomarkers? And what are the other biological parameters to prescribe for the right interpretation of the CRP and the ESR?

To answer these questions, we examined retrospectively the laboratory results of patients admitted to the Ibn rushd hospital to seek the association between the CRP and the ESR in patients of different ages. We also sought the association between the CRP and ESR with different biological parameters.

EXPERIMENTAL SECTION

2.1. Subjects

We conducted a cross-sectional retrospective. A total of 76 patients have been selected from a hospitable database. They all had a prescription of CRP and ESR. Another important inclusion criterion is the realization of blood samples for CRP and ESR on the same day and the same hour and for the same patient. All patients had a normal liver and kidney function checked by the values of alkaline phosphatase, transaminases, creatinine and urea levels. All patients were hospitalized in different services of the Ibn Rushd hospital in Casablanca (Morocco) between September 2014 and July 2015 (table1).

2.2. Laboratory evaluation

All blood samples were collected under fasting conditions on the same day between 8 and 10 a.m. The serum concentration of CRP was measured using the immunoturbidimetry method on DIRUI® 1200 cs analyser. The intra and inter-assay variation coefficients in our laboratory were 4.1 % and 6.6 %, respectively. In the present study, reference values were respectively, for CRP was defined as > 10 mg/l and for ESR was defined as > 15 mm/1 hour for males and > 25 mm/1 hour for females. ESR was performed using a standard kit (Sediplast ESR, LP Italiana SpA, Milan, Italy).

2.3. Statistical analysis

Results are presented as means (SD) and categorical variables are expressed as frequencies. To compare ESR and CRP according to variables, t-student test was used. Correlations between continuous variables were calculated using Pearson correlation coefficients. Significant risk factors in the univariate analysis for ESR and CRP were entered to a stepwise conditional binary regression analysis and the resulted odds ratios with 95 % confidence intervals were reported. The level for significance was taken as $p \leq 0.05$. Excel 2010 and SPSS 20.0 were used for statistical analysis.

RESULTS AND DISCUSSION

In this study, 76 patients were recruited including 45(59,2%) women and 31(40,8%) men. The distribution of patients by department is shown in the table 1.

Patients with a high level of ESR had significantly high CRP level, low haemoglobin concentration, low haematocrit, high platelets count and a low albumin level (table 2).

Patients who have a high CRP according to the reference values had significantly elevated ESR, low haemoglobin concentration, low haematocrit, high white cells blood count and neutrophils, high platelets count and a low albumin level (table 3).

The values of ESR and CRP correlated significantly with each other (Pearson $r = 0.516$, $p < 0.001$). CRP values was correlated very significantly ($p < 0.001$) and negatively with albumin concentration and positively with neutrophils count. Similarly, the ESR was very significantly and negatively correlated to haematocrit rate, haemoglobin concentration, and red cells count and albumin concentration (Table 4).

Multiple regression analysis was therefore performed to determine the combination of variables that accounted for the greatest proportion of variance in CRP and ESR values. Neutrophils and ESR were related to CRP. Haematocrit, mean corpuscular haemoglobin concentration (MCV), Albumin concentration and platelets count were significantly related to ESR (Table 5,6).

DISCUSSION

This study shows that the ESR and the CRP values correlated significantly with each other (Pearson $r = 0.516$, $p < 0.001$). And according to the results of this study the prescription and the interpretation of the ESR and the CRP must take into account the levels of several parameters. Thus, for the appropriate interpretation of the ESR the parameters are the haematocrit, Mean corpuscular volume, albumin and blood platelet levels. For the CRP single parameters that is the neutrophils count.

We have no data on the exact age of our patients even if several studies have shown that the ESR increases with age which can be explained by the increased prevalence of diseases with age. However in another study there was no significant difference between the results of the younger and elder patients investigated for higher ESRs. In general

in 42.4% of the patients no specific diagnosis could be reached while this was 47.2% in elderly and 37.3% in non-elderly patients (p = 0.24) [2]. Therefore, the relationship of the ESR to age is contentious.

In this study we found that patients who have a level of ESR greater than 59 mm / h have inflammation (CRP above 10 mg / l) regardless of age and sexe. Other result was found by Wyler and al in a study with patients of ESR of 100 mm/h or greater that were retrospectively analysed and infections were found to be the most frequently associated diseases (35%), while malignant disease accounted for only 15% of the patients [3].

Table 1: distribution of patients by department (n=76)

	Number	Percentage (%)
Internal Medicine	15	19,7
Gastroenterology and proctology	11	14,5
Pediatrics	10	13,1
non-hospitalized patients	9	11,8
Infectious diseases	7	9,2
Dermatology	5	6,6
pneumonology	5	6,6
Neurology	4	5,3
rheumatology	4	5,3
Intensive care	2	2,6
Cardiology	2	2,6
emergencies	1	1,3
hematology	1	1,3
Total	76	100,0

Table 2 : Comparison of the different variables with the ESR levels

	ESR<15 Men and ESR<25 women (n=21)	ESR>15 Men and ESR>25 women(n=55)	p
ESR (mm/h) m±SD	10,29±4,54	59,64±37,02	<0,001
CRP (mg/L) m±SD	19,65±42,02	73,99±85,86	<0,001
Hémoglobin (g/L) m±SD	131,2±1,88	110,67±2,34	<0,001
RBC (10^{12}/L) m±SD	4,67±0,47	4,17±0,74	0,001
Hematocrit % m±SD	40,08±4,8	33,99±6,15	<0,001
MCV (fL) m±SD	85,92±7,78	81,8±8,91	NS
MCH (pg) m±SD	28,10±3,07	26,58±3,85	NS
CCMH (g/dL) m±SD	32,65±1,27	32,4±2,14	NS
WBC (10^9/L) m±SD	15,46±22,09	9,45±5,57	NS
neutrophils (10^9/l) m±SD	8,21±9,63	6,23±4,39	NS
eosinophils (10^9/l) m±SD	0,18±0,22	0,30±0,58	NS
basophils (10^9/l) m±SD	0,029±0,027	0,03±0,046	NS
lymphocytes (10^9/l) m±SD	2,7±1,46	2,23±1,59	NS
Monocytes (10^9/l) m±SD	0,88±1,04	0,64±0,35	NS
Platelets (10^9/l) m±SD	231,05±96,25	322,89±21,81	0,006
Cholesterol (g/L) m±SD	1,9±0,39	1,58±0,52	NS
ALP (UI/L) m±SD	84,44±43,46	135,35±9109,786	NS
Albumin (g/L) m±SD	43,73±4,174	33,72±9,57	<0,001
TP (g/L)m±SD	70,33±5,88	64,28±10,15	NS

RBC : Red blood cells, ALP: Alkaline phosphatase, TP: Total protein, MCV : Mean corpuscular volume? MCHC: mean corpuscular haemoglobin concentration, MCH: mean corpuscular haemoglobin, WBC: White blood cells

Patients with a high level of ESR had significantly high CRP levels, low haemoglobin concentration, low haematocrit, high platelet counts and a low albumin levels. So for the interpretation of the results of the ESR we must take into account the concentrations of different parameters that influence its outcome directly. Paulus and al have found almost the same result, the ESR is affected by red blood cell size, shape, and haematocrit, sex and age [4]. So following the results of this study we added two parameters to take into account for the interpretation of the ESR namely the concentration of albumin and platelet count. Thus, low albumin can be used as a marker of increased circulating acute phase reactants.

We found that the ESR and the CRP values correlated significantly with each other (Pearson r = 0.516, p < 0.001). CRP is one of the most frequently used biomarkers of inflammation. It's a direct and quantitative measure of the acute-phase reaction that responds very quickly to inflammatory stimuli. The recommended reference range for serum CRP concentrations is usually not adjusted for age and sex. Even if the CRP value as the ESR value depend of the demographic factors, including age, sex, and race, should be used to adjust the upper reference limit for CRP [5]. Ford and al describe the distribution of CRP concentrations among children and young adults in the US. CRP concentrations increased with age. Females 16-19 years of age had higher concentrations than males in this age

range (P = 0.003). Mexican Americans had the highest CRP concentrations among the three major race or ethnic groups (P <0.001) [6].

Table 3 : Comparison of the different variables with the CRP levels

	CRP<10 mg/l (n=34)	CRP>10 mg/l (n=42)	p
ESR (mm/h) m±SD	29,14±25,61	59,64±42	<0,001
CRP (mg/L) m±SD	3,97±2,91	103,50±84,38	<0,001
Hémoglobin (g/L) m±SD	124,5±1,82	110±2,62	0,006
RBC (10^{12}/L) m±SD	4,49±0,51	4,17±0,812	0,044
Hematocrit % m±SD	37,81±4,67	34,03±7,10	0,007
MCV (fL) m±SD	84,49±8,01	81,8±9,22	NS
MCH (pg) m±SD	27,80±3,25	26,38±3,93	NS
CCMH (g/dL) m±SD	32,86±1,62	32,15±2,12	NS
WBC (10^9/L) m±SD	7,54±3,31	13,95±16,26	0,017
neutrophils (10^9/l) m±SD	4,58±2,94	8,51±7,61	0,003
eosinophils (10^9/l) m±SD	0,15±0,21	0,36±0,64	NS
basophils (10^9/l) m±SD	0,026±0,019	0,04±0,05	NS
lymphocytes (10^9/l) m±SD	2,21±1,35	2,47±1,730	NS
Monocytes (10^9/l) m±SD	0,57±0,26	0,82±0,79	NS
Platelets (10^9/l) m±SD	245,6±64,41	337,69±207,24	0,009
Cholesterol (g/L) m±SD	1,93±0,35	1,43±0,49	0,047
ALP (UI/L) m±SD	100,71±98,7	136,83±97,01	NS
Albumin (g/L) m±SD	43,87±4,63	32,03±8,98	<0,001
TP (g/L)m±SD	70,33±5,69	61,25±10,61	0,018

RBC : Red blood cells, ALP: Alkaline phosphatase, TP: Total protein, MCV : Mean corpuscular volume MCHC: mean corpuscular hemoglobin concentration, MCH: mean corpuscular hemoglobin, WBC: White blood cells

Table 4: Correlation between C-reactive protein, ESR and different biological parameters (n=76)

	CRP (mg/L)	ESR (mm/h)
ESR (mm/h)	0,516**	
Hémoglobin (g/L)	-0,378*	-0,596**
RBC (10^{12}/L)	-0,207	-0,564**
Hematocrit %	-0,368*	-0,633**
MCH (pg)	-0,249*	-0,208
WBC (10^9/L)	0,372*	0,030
neutrophils (10^9/l) m±SD	0,407**	0,147
Platelets (10^9/l)	0,343*	0,385*
Cholesterol (g/L)	-0,627*	-0,464
ALP (UI/L)	0,386*	0,354
TP (g/L)	-0,527*	-0,472*
Albumin (g/L)	-0,578**	-0,628**

<0,05* *<0,001*

Table 5: Multiple linear regression analysis with CRP as dependent variable (n=76)

	Non-standardized coefficients		standardized coefficients	t	p	95% confidence intervals for B	
	A	Erreur standard	Bêta			Minimum	Maximum
Neutrophils (10^3/µl)	9,813	3,291	0,488	2,982	0,007	2,949	16,678
ESR (mm/h)	0,736	0,300	0,402	2,454	0,023	0,110	1,361

Table 6: Multiple linear regression analysis with ESR as dependent variable (n=76)

	Non-standardized coefficients		standardized coefficients	t	p	95% confidence intervals for B	
	A	Erreur standard	Bêta			Minumum	Maximum
Hématocrit %	-4,459	0,951	-0,642	-4,690	<0,001	-6,457	-2,462
MCV (fL)	1,465	0,524	0,280	2,796	0,012	0,364	2,565
Albumin (g/L)	-1,511	0,496	-0,331	-3,048	0,007	-2,552	-0,469
Platelet (10^3/µl)	0,091	0,036	0,273	2,493	0,023	0,014	0,167

MCV : Mean corpuscular volume

The variables that accounted for the greatest proportions of variance in the CRP value in this study were the neutrophils and the ESR. So neutrophils can provide a practical strategy for monitoring inflammatory response, especially those with liver impairment. Because of CRP is produced by the liver in response to interleukin-6, interleukin-1, and tumor necrosis factor α. Buoro and al found that Median value of all-leukocyte parameters was different in ICU patients compared to healthy subjects. Leukocytes, neutrophils and immature granulocytes in sepsis and septic shock were higher than no sepsis, with an area under the curve: 0.81, 0.82 and 0.78 respectively [7].

Our study has strengths and limitations. All measurements were performed in the same laboratory with the same technique. All samples were requests for the same patient on the same day and even in the same time of blood collection. There were some limitations of this study. First of all this was a retrospective study and the population size, the lack of information about age and the clinical diagnosis of each patient.

CONCLUSION

Finally we must recognize that the ESR is affected by multiple factors, and for a good interpretation of this parameter we must have a minimum the haematocrit rate, whereas CRP is only affected by the presence and degree of inflammation. The professors in medicine should educate their medical students on the preference for ordering CRP instead of the ESR as the general inflammatory marker of choice.

REFERENCES

[1]L Marnell; C Mold; TW Du Clos. *Clinical immunology*., **2005**,117(2):104-11. PubMed PMID: 16214080.
[2]M Cankurtaran; Z Ulger ; M Halil ;BB Yavuz ; IK Onal; S Unal; Ariogul S. How to assess high erythrocyte sedimentation rate (ESR) in elderly? Arch Gerontol Geriatr., **2010**, 50(3):323-6. doi: 10.1016/j.archger.**2009**.05.008. Epub **2009** Jun 23. PubMed PMID: 19552971.
[3]DJ Wyler. *South Med J.*, **1977**,70(12):1428-30. PubMed PMID: 594794..
[4]HE Paulus; E Brahn . *J Rheumatol*., **2004**, 31(5):838-40. Review. PubMed PMID: 15124238.
[5]MH Wener; PR Daum; GM McQuillan. *J Rheumatol*. **2000**, 27(10):2351-9. PubMed PMID: 11036829.
[6]ES Ford; WH Giles; GL Myers; N Rifai; PM Ridker; DM Mannino. C-reactive protein concentration distribution among US children and young adults: findings from the National Health and Nutrition Examination Survey, **1999**-**2000**. *Clin Chem*., **2003**, 49(8):1353-7. PubMed PMID: 12881452..
[7]S Buoro; T Mecca; G Azzarà; S Apassiti Esposito; M Seghezzi; M Vavassori; A Crippa; G Marchesi; E Castellucci; C Ottomano; G Lippi. *Ann Transl Med*., **2015**, 3(17):244. doi: 10.3978/j.issn.2305-5839.2015.09.41. PubMed PMID: 26605290; PubMed Central PMCID: PMC4620099.