Article N°2 Year 2000

Malaria
AND INFECTIOUS DISEASES IN AFRICA
PALUDISME ET MALADIES INFECTIEUSES EN AFRIQUE

COMPARATIVE STUDY OF ESR AND CRP IN ACUTE MALARIA

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ABSTRACT

The most useful test to evaluate the level of the inflammatory reaction is the erythrocyte sedimentation rate (ESR) and the C reactive protein (CRP). A comparative study between these two tests was carried out in 25 patients infected in Africa with acute malaria due to Plasmodium falciparum. At D1, the mean value of ESR and CRP was respectively 19.8 mm and 94.5 mg/l, and at D7 the mean value was 105 mm and 13.20 mg/l. So, ESR which increased very early, has a better positive predictive value for the diagnosis of malaria than ESR which increase later.

KEY-WORDS

Malaria. C-Reactive Protein. Erythrocyte Sedimentation Rate.

INTRODUCTION

Malaria is a very widespread disease in tropical areas, affecting 400 million people each year. The disease is caused by a Plasmodium and produces an inflammatory reaction in the body. Amongst the investigations widely used to study the inflammatory reaction, we considered it would be useful to compare the role of the erythrocyte sedimentation rate (ESR) and C Reactive Protein (CRP) in the acute attack of malaria.

PATIENTS AND METHODS

This study was conducted in 25 patients suffering from acute malaria (18 men and 7 women), between 17 and 67 years old. The patients had become infected in Africa and presented with fever, often associated with shivering, headaches, weakness or diarrhoea. Plasmodium falciparum infestation was confirmed by a blood film and showed a parasitaemia of between 0.01% and 1% in 20 cases, and between 1% and 8% in 5 cases.

The patients also underwent a full blood count and liver function tests. The erythrocyte sedimentation rate was performed on a venous blood sample withdrawn directly into the vacutainer tube (Becton Dickinson), placed on a specific Seditainer carrier with a 2 mm scale (Figure 1).

Fig 1 : Seditainer carrier (V.S.)

CRP was measured by kinetic nephelometry on a Beckman Array instrument or on a Behring turbidimeter (Figure 2).

Fig 2 : Behring turbidimeter (CRP)

Both tests require approximately the same time, i.e. 1 hour.

RESULTS

Blood counts showed the patients' haemoglobin concentration to be than 11 g/l in 20 cases, a normal leukocyte count in 19 cases and thrombocytopaenia (<100.000 pl./mm^3) in 21 cases. Liver function tests revealed raised transaminases in 20 cases. The average erythrocyte sedimentation rate of the patients was 19.8 mm on D.1 and 39.2 mm on D7. In 5 cases, the erythrocyte sedimentation rate was greater than 105 mm.

Patients	D1		D7	
	ESR	CRP	ESR	CRP
5	9	58	24	16
9	40	107	16	9
10	14	42	44	17
11	18	213	32	10
12	18	85	80	21
14	16	62	28	6
17	13	92	58	7
23	12	78	76	11
25	10	81	63	10

Table I : ESR (mm) and CRP (mg/l), at D1 and D7

The mean CRP was 94.5 mg/l on D1 and 13.20 mg/l on D7. CRP was raised by D2 in all cases (Table I).

DISCUSSION

The increase in erythrocyte sedimentation rate is due to red blood cell agglutination and rouleaux formation due to the presence of positively charged inflammatory proteins in plasma, which neutralise the natural repulsive negative charges on red blood cells [1,2,3]. A large number of factors are involved in changing the erythrocyte sedimentation rate (Table II).

RAISED ESR	DECREASED ESR
Infectious diseases Anaemia Macrocytosis Hyperliproteinaemia Female sex (menstruation) Pregnancy (> 10th week) The elderly Obesity Oestrogen-progestagen therapy Heparin therapy Macromolecular solutions Chronic renal failure Gammopathies Severe injury **Causes of errors:** Knocking the measuring tube High temperature of the measuring tube	Sickle Cell Anaemia Anisocytosis Spherocytosis Microcytosis Haemoglobinopathies Polycythaemia Greatly raised leukocytosis Hyperfibrinogenaemia Liver failure Cachexia High dose corticosteroids Acetyl salicylic acid Nonsteroidal anti-inflammatory agents **Causes of errors:** Coagulated blood sample Delay between blood sampling and starting the test Low temperature of the measurement

Table II :Factors changing the ESR

The normal ESR is 3 to 5 millimetres in men and 7 to 20 millimetres in women.

CRP is the most widely used of the acute phase inflammatory proteins because of its early rise and rapid kinetics [4]. It has a half life is 5 to 6 hours. CRP is concentrated in tissues involved in the inflammation where it exerts its biological properties: activation of complement, indirect bacteriostatic activity by facilitating ingestion of micro-organisms, facilitating resorption of damaged tissue by phagocytosis and activating platelet aggregation. In addition, CRP is believed to prevent entry of the sporozoite into the hepatocyte [5]. Normal CRP concentrations are 0 to 8 mg/l and do not differ according to sex or age [6]. CRP is raised in certain disorders (Table III).

DISEASES	Raised CRP	CRP little or not raised
Rheumatological	Rheumatoid arthritis Horton's disease Ankylosing spondylitis Behcet's disease Vasculitides....	Systemic lupus erythematosis Dermatomyositis Scleroderma Gougerot-Sjogren's Syndrome
Gastro-intestinal	Crohn's Disease Acute appendicitis Acute peritonitis Acute Pancreatitis	Haemorrhagic Ulcerative colitis
Malignancies	Lymphomas Certain solid tumours	Leukaemia
Ischaemic	Myocardial infarction	Coronary artery disease
Traumatic	Head injury with fracture Burns Surgery	Uncomplicated head injury
Infectious	Bacterial infections Pneumonia, meningitis, septicaemia Upper urogenital tract infections Acute prostatitis	Viral infections Lower urogenital tract infections Chronic prostatitis

Table III : Variation de la Protéine-C-réactive (CRP)

Mononuclear cells, which are activated by the plasmodium during a malarial attack, produce inflammatory cytokines such as Tumor Necrosis Factor (TNF) interleukin 1 (IL1) or interleukin 6 (IL 6) [7, 8]. These cytokines stimulate the hepatic synthesis of acute phase inflammatory proteins including CRP [9], orosomucoid and haptoglobin, which all rise in malaria [10].

In contrast, a fall in haptoglobin reflects the presence of haemolysis [11]. More red blood cells are destroyed than are infected with the *Plasmodium* because of immune complexes which bind to the non-parasite infected erythrocytes and which are then destroyed by macrophages from the reticulo-histocyte system [8]. In addition, TNF inhibits erythropoiesis in the bone marrow. Haemolysis leads to the release of haemoglobin which binds to haptoglobin, reducing serum haptoglobin concentrations [12].

The rise in CRP in malaria has already been reported by other authors [13, 14]. In contrast to other authors, our study has not found any relationship with the severity of the parasitaemia [15]. CRP was greatly elevated (from 42 to 231 mg/l) in 17 cases. CRP has also been used as a good positive predictive indicator for the diagnosis of malaria in febrile people returning from a tropical area [13], and is a marker for malaria in epidemiological studies [16].

The rise in plasma immunoglobulin concentrations in patients suffering from malaria explains why the erythrocyte sedimentation rate increases. The sedimentation rate, however, remained normal in 50% of our patients [14]. Other studies have failed to find any significant differences between patients suffering from malaria and those suffering from other febrile conditions [17]. The rise in erythrocyte sedimentation rate is also influenced by anaemia, as was the case in 2 of our patients [1].
Twelve of the patients in our study had a normal sedimentation rate, whereas the CRP was raised in all of these cases. Dissociation between a normal sedimentation rate and raised CRP has already been reported for other inflammatory diseases [18], including those in children [19].
The changes in these two parameters were extremely interesting. The CRP fell significantly ($p = 0.004$) between day 1 (mean 95 mg/l) and day 7 (mean: 13 mg/), corroborating results from other studies on this subject [20]. The CRP increased from the first hours of inflammation and fell between D.1 (mean: 20 mm) and D.7 (mean 39 mm); difference not significant ($p = 0.01$). It required 3 to 6 weeks to return to normal.

In conclusion, the erythrocyte sedimentation rate appears to be inadequate to make a rapid diagnosis of the acute phase inflammatory reaction, whereas CRP offers excellent predictive value. In addition, the early rise in CRP as soon as the inflammatory reaction develops, makes it a distinctly preferable investigation to the sedimentation rate amongst the diagnostic factors used for malaria. It is, of course, the blood film which remains the fundamental investigation to confirm this diagnosis, allowing both the causative species and parasitaemia to be established. These are essential factors in the therapeutic management of the disease.

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