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Serum CRP in the Diagnosis and Treatment of Pelvic Inflammatory Disease

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Summary. The usefulness of serum C-reactive protein (CRP) measurement was studied in a population of 152 patients admitted to a gynaecological emergency unit. Fifty-one of 55 patients with PID had raised (over 10 mg/l) (13–270 mg/l) CRP levels with a mean of 76.1 mg/l. CRP was elevated (12–40 mg/l) in 2 of 18 patients with threatened abortion with successful outcome, in 8 of 28 patients with incomplete abortion, and in 2 of 16 patients with ectopic pregnancy. Furthermore, 6 of 35 patients with noninfectious disorders (ovarian cyst, uterine fibroid, unexplained pelvic pains) had slightly elevated (12–59 mg/l) CRP levels. Thus, in this series a CRP > 10 mg/l had good sensitivity (93%) and specificity (83%) in the diagnosis of PID. Furthermore, CRP levels became normal much sooner than did erythrocyte sedimentation rate following effective antibiotic therapy, suggesting that it is useful in monitoring therapeutic response.

Key words: CRP – Pelvic inflammatory disease

Introduction

Pelvic inflammatory disease (PID) has many clinical manifestations, including abdominal pain, purulent cervical discharge, cervical excitation pain, adnexal tenderness and masses as well as fever, leucocytosis and an elevated erythrocyte sedimentation rate (ESR) (Sweet and Gibbs 1985). A diagnosis based solely on these observations and findings is, however, uncertain; consequently, some women with PID are misdiagnosed and inappropriately treated. Laparoscopy is the only way to diagnose acute salpingitis with certainty, but it is invasive. Therefore reliable noninvasive measures of pelvic infection are clearly needed. The synthesis and release of C-reactive protein (CRP) in the liver increase

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rapidly in response to interleukins produced by macrophages, monocytes and the reticuloendothelial system in bacterial infections (Pepys 1981; Kaplan 1982). Serum CRP is a good indicator of chorionamnionitis after premature rupture of membranes (Evans et al. 1980; Farb et al. 1983; Hawrylyshyn et al. 1983), but knowledge of the CRP values in PID and other gynaecological conditions is still scanty (Haji et al. 1979; Angerman et al. 1980; Schalla et al. 1984; Sweet and Gibbs 1985; Lehtinen et al. 1986). We therefore assessed the usefulness of CRP measurements in the differential diagnosis of acute gynaecological conditions.

Patients and Methods

One hundred and fifty-two patients with acute gynaecological conditions were studied (Table 1). Fifty-five patients had PID, the diagnosis of which was based on the following criteria: lower-abdominal pain (mostly of postmenstrual onset), cervical excitation pain and bilateral adnexal tenderness as well as at least one of the following: purulent cervical discharge, fever (more than 38°C in the axilla), leucocytosis (more than 10×10^9/l) or elevated erythrocyte sedimentation rate (ESR) (more than 20 mm/h). The diagnosis of PID was confirmed laparoscopically in 1 patient. Pelvic sonography was done in 18 patients, and revealed evidence of tubo-ovarian masses in 11 women. In addition, 8 other women were thought to have uni- or bilateral tubo-ovarian swellings on bimanual examination. Seventeen patients with PID (31%) had been wearing an intrauterine contraception device (IUD), which was removed at admission. *Neisseria gonorrhoea* was isolated from the cervix in 9 patients, and *Clamydia trachomatis* from 8 patients, but bacterial cultures were negative in the remaining patients. All patients were treated with doxicycline plus metronidazole or kefuroxime and metronidazole combinations which were given intravenously for 2–3 days and then orally for 7–10 days. Gynaecological examination was negative in all cases at one month after discharge from hospital.

Sixty-two patients were pregnant (= human chorionic gonadotropin over 5 IU/l l of serum) (Table 1). Eighteen of these had a threatened miscarriage but a live fetus on ultrasound and an ultimately progressive pregnancy. A total of 28 women had an incomplete abortion with scanty retained products of conception on curettage. Sixteen women had a tubal pregnancy confirmed by laparotomy (Table 1).

Thirty-five women with pelvic pain and/or bleeding had no infection or pregnancy (Table 1). The diagnosis in these women was functional bleeding ($n = 10$), functional ovarian cyst ($n = 8$), uterine fibroids ($n = 2$), pelvic endometriosis ($n = 1$), side effects of an IUD ($n = 1$) or unexplained pelvic pain ($n = 13$). Laparoscopy was performed in 6 patients in this subgroup.

Blood samples for CRP were collected from all study subjects within 24 h of admission. Serum was assayed for CRP with radial immunodiffusion (Mancini et al. 1985), and levels exceeding 10 mg/l were regarded as elevated (Pepys 1981). The ESR and leukocytes counts were obtained by routine

Table 1. Some characteristics of the patients studied (mean ± SD)

Diagnosis	Number	Age	Amenorrea (weeks)
Pelvic inflammatory disease	55	29.1 ± 1.3	
Early pregnancy complication			
– threatened abortion	18	30.7 ± 1.1	13.1 ± 1.1
– incomplete abortion	28	31.4 ± 1.2	12.0 ± 0.8
– tubal pregnancy	16	31.3 ± 1.2	5.0 ± 0.5
Noninfectious gynaecological disorder	35	35.6 ± 2.6	

laboratory methods. CRP and ESR measurements in patients with PID were repeated 4–7 days ($n = 42$) and 8–21 days ($n = 21$) after admission.

The sensitivity of the CRP result was defined as True positive (TP)/TP + False negative (FN), the specificity as True negative (TN)/TN + False positive (FP) and the predictive value as TP/TP + FP. The significances of the differences in the mean values were tested with Student's *t*-test.

Results

Of 55 patients with PID, 51 had elevated CRP levels (range 13–270 mg/l) with a mean of 76.1 mg/l (Fig 1). The use of an IUD and the presence of adnexal swelling were accompanied by particularly high CRP levels, but only the IUD/CRP correlation reached statistical significance (Table 2). Four patients in the PID groups had a normal CRP and ESR, and negative cervical swab cultures. None of these 4 patients had a laparoscopy and their symptoms disappeared with antibiotic + metronidazole. The sensitivity of CRP-measurement in the diagnosis of PID was thus 93%.

Twelve of 62 pregnant women (19%) had a raised CRP, but always less than 40 mg/l (Fig. 1). CRP was elevated in 11% of the patients with threatened abortion, 29% of patients with incomplete abortion and 13% of patients with ectopic pregnancy (Fig. 1).

Of 35 patients with noninfectious disorders, six (17%) had a elevated CRP between 12 and 59 mg/l (Fig. 1). These patients had ovarian cysts ($n = 1$), uterine fibroids ($n = 1$) and unexplained pelvic pain ($n = 4$).

Thus, the specificity of CRP in the detection of PID was 81% and the predictive value 74%.

The rises in CRP and ESR correlated closely ($r = 0.408$, $P < 0.001$, $n = 38$), but CRP became normal again sooner than the ESR (Fig. 2).

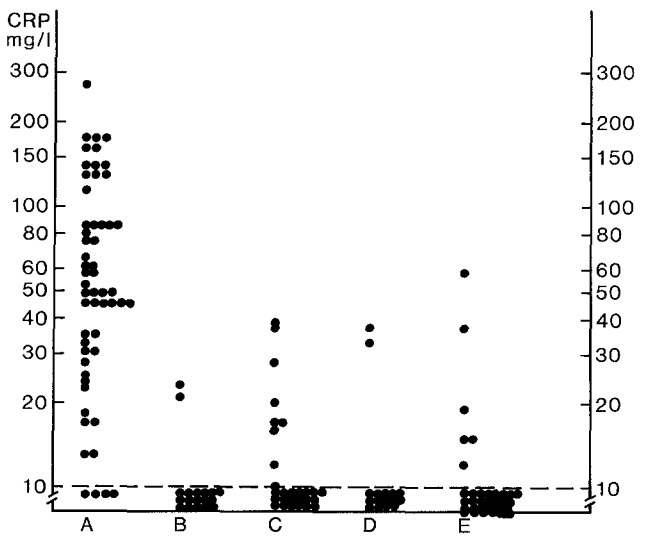

Fig. 1. Concentrations of C-reactive proteins (CRP) in serum within 24 h of admission. A = pelvic inflammatory disease, B = threatened abortion, C = incomplete abortion, D = tubal pregnancy, E = noninfectious disorders. Note the logarithmic scale for CRP

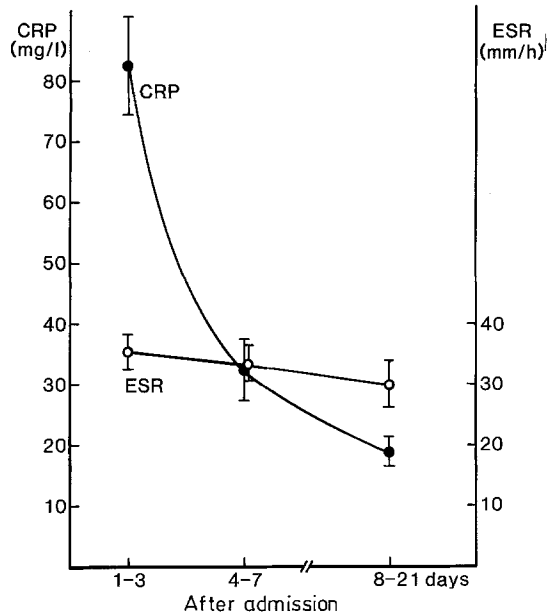

Fig. 2. CRP and ESR values during hospital stay and thereafter (mean ± SE)

Table 2. Maximal CRP and ESR values in patients with pelvic inflammatory disease in relation to the use of intrauterine contraception (IUD) or development of adnexal mass (mean ± SD)

	CRP [mg/l]	ESR [mm/h]
IUD +	100.5 ± 15.9 ($n = 15$)[a]	56.0 ± 4.9 ($n = 12$)
IUD −	65.9 ± 7.9 ($n = 36$)[a]	45.1 ± 3.5 ($n = 27$)
Adnexal swelling +	89.5 ± 13.9 ($n = 19$)	57.9 ± 5.3 ($n = 18$)
Adnexal swelling −	68.1 ± 8.6 ($n = 32$)	40.4 ± 3.8 ($n = 21$)

[a] = $P < 0.05$

Discussion

We assessed the usefulness of CRP assay in the differential diagnosis of gynaecological emergencies. Like Haji et al. (1979), Shalla et al. (1984), Lehtinen et al. (1986) we found CRP very sensitive in the detection of PID. However, 4 patients thought to suffer from PID had normal CRP values. This could suggest that CRP does not always rise in PID. But a more likely explanation could be that since the CRP measurements were done one day after the start of antibiotics, CRP had already become normal in these patients. Furthermore, we should take into account the possibility that these patients, who did not have a laparoscopy, did not have PID. The latter explanation is supported by normal ESR values and negative bacterial cultures in these 4 patients.

We used a raised ESR as a criterion for PID (Sweet and Gibbs 1985), and we cannot, therefore, compare the sensitivities and predictive values of ESR and CRP. However only 71% of our patients with PID had a raised ESR, whereas 93% of them had a raised CRP. This suggests that CRP is more sensitive than ESR in the detection of PID and supports some previous results (Lehtinen et al. 1986). Moreover, the use of an IUD and the presence of adnexal mass in PID patients were both associated with higher CRP levels. This may imply that the magnitude of the CRP rise reflects the severity of PID.

Antibiotic therapy must be given before the results of bacterial cultures are available, and quite often cultures from the cervix are negative. The adequacy of antibiotic therapy must be based on therapeutic response (decrease in fever, disappearance of pains etc.). Our data show that raised CRP levels rapidly returned normal with effective treatment. Thus, repeated CRP assays can be used in assessment of therapeutic response. In this regard, CRP is superior to ESR in the monitoring of PID (Fig. 2).

CRP is not specific to bacterial infections, but also rises in inflammation and in conditions involving tissue trauma and/or necrosis (Pepys 1981; Kaplan 1982). In contrast to ESR, the CRP level does not increase during normal pregnancy (Pepys 1981; Kaplan 1982). Our marginally elevated CRP levels in patients with early pregnancy complications suggest that extravascular blood or necrotic pregnancy tissue inside the uterus and/or tubes may trigger the release of CRP. This "necrosis" was evidently greatest in cases of incomplete abortion, these patients showing increased CRP levels most frequently (29%). Perhaps some tissue "necrosis" or extravascular blood was present in the six patients with noninfectious disorders in whom the CRP level has raised. Fortunately, CRP rises in almost all patients with noninfectious disorders were clearly smaller than in patients with PID (Fig. 1). The value of CRP in the differential diagnosis between infections and noninfectious disorders could be significantly improved if only CRP levels higher than 20 mg/l were taken as indicative of infections. If this cut-off limit had been used in the present study, the sensitivity, specificity and predictive value of CRP assay in the detection of PID would have been 84%, 92% and 85%, respectively.

Since the completion of this study, we have measured CRP levels by the turbidimetric method, and the result is obtained within two minutes. Therefore, technical problems no longer inhibit the use of CRP in the acute clinical situation (Sweet and Gibbs 1985). We recommended the routine use of CRP measurements in the diagnosis and treatment of PID.

References

Angerman NS, Evans MI, Morovec WD, Schumacher GFB, Haji SN (1980) C-reactive protein in the evaluation of antibiotic therapy for pelvic infection. J Reprod Med 25:63–66

Evans MI, Haji SN, Devoe LD, Angerman DS, Moawad AH (1980) C-reactive protein as a predictor of infectious morbidity with premature rupture of the membranes. Am J Obstet Gynecol 138:648–651

Farb HF, Arnesen M, Geistler P, Knox GE (1983) C-reactive protein with premature rupture of membranes and premature labor. Obstet Gynecol 62:49–51

Haji SN, Anserman NS, Evans MI, Moravec WD, Schumacher GF (1979) C-reactive protein in the differential diagnosis of gynecological pathology. J Reprod Med 23:284–287

Hawrylyshyn P, Bernstein P, Milligan JE, Milligan JC, Soldin S, Pollard A, Pepsin FR (1983) Premature rupture of membranes: the role of C-reactive protein in the prediction of chorion-amnionitis. Am J Obstet Gynecol 47:240–246

Kaplan M (1982) C-reactive protein. Relation to disease and pathologic significance. Ann NY Acad Sci 389:419–422

Lehtinen M, Laine S, Heinonen P, Teisala K, Miettinen A, Aine R, Punnonen R, Grönroos P, Paavonen J (1986) Serum C-reactive protein in acute pelvic inflammatory disease. Am J Obstet Gynecol 154:158–159

Mancini G, Carbonara AO, Heremans YF (1985) Immunochemical quantitation of antigens by single radial immunodiffusion. Immunochemistry 2:235–254

Pepys MB (1981) C-reactive protein fifty years on. Lancet I:653–657

Shalla WO, Arko RJ, Thompson SE (1984) Evaluation of a C-reactive protein latex agglutination detection test with sera from patients with sexually transmitted diseases. J Clin Microbiol 20:1171–1173

Sweet RL, Gibbs RS (1985) Pelvic inflammatory disease. In: Sweet RL, Gibbs RS (eds) Infectious Diseases of the Female Genital Tract. Williams & Wilkins, Baltimore, pp 53–77

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