

The significance of C-reactive protein in the diagnosis of fetal tachycardia and therapy of chorioamnionitis

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Summary

Background: Pregnant woman with fetal tachycardia have a risk of chorioamnionitis as cause of tachycardia. Different studies have supported or refuted the use of C-reactive protein (CRP) to diagnose chorioamnionitis. The goal of this study was to evaluate serial serum CRP levels for diagnosis of chorioamnionitis.

Methods: The study included 60 woman with chorioamnionitis confirmed after measuring the levels of CRP. Patients were monitored by CRP determination, white blood cell (WBC) count, maternal temperature, maternal and fetal heart rate.

Results: Elevated CRP level was present in 93.33% of cases. Fetal tachycardia was present in 91.67 cases, all associated with elevated CRP level. Increased WBC count was present in 63.33%. A statistically significant difference was found in the level of CRP in pregnant women with increased WBC count compared with those without ($p < 0.01$).

Conclusion: Elevated C-reactive protein levels were more sensitive than other standard laboratory or clinical tests in predicting chorioamnionitis. Also, recent reports indicate that serial CRP levels during this interval may be useful for monitoring antibiotic treatment.

Key words: Chorioamnionitis; Fetal tachycardia; C-reactive protein.

Introduction

Chorioamnionitis is a general term for infections of the chorion, amnion, placenta or even umbilical cord during pregnancy. This infection weakens cell layers causing premature rupture and villi inflammation producing swelling of placental residue which influences decreased blood flow and fetal hypoxia. Moreover, chorioamnionitis may cause different infective diseases of the newborn - these children are at higher risk for septicemia, otitis, meningitis and septic arthritis and newborn pneumonia is almost always preceded by chorioamnionitis. Chorioamnionitis is present in approximately 2% of all pregnancies. Abnormal bacterial colonization of the anus and rectum, and urinary tract infections may create abnormal vaginal and cervical micro flora that penetrates through the cervical canal causing chorioamnionitis. The most common origins are group B streptococcus, *Escherichia coli*, bactericides (*Prevotella* spp), *Ureaplasma* spp, etc.

Symptoms related to chorioamnionitis include: 1. increased temperature; 2. significant maternal tachycardia; 3. fetal tachycardia; 4. purulent amniotic fluid with unpleasant odor; 5. soft uterus; and 6. maternal leukocytosis.

The diagnosis of chorioamnionitis is based on examination of amniotic fluid, maternal blood and/or urine.

Examination of amniotic fluid, urine and genital secretions:

– Screening tests for leucocyte count, pH, glucose level, endotoxins, lactoferrin, and gram positive bacteria.

– Determining the level of cytokines in amniotic fluid (IL_6 , IL_8 , IL_{10} , TNF_0).

– PCR for microorganism identification (cytomegalovirus, bacterial DNA).

– Screening tests of cervicovaginal secretions that use fetal fibronectin and insulin-like growth factor binding protein as markers for cervical or chorion inflammation.

Maternal blood examination:

– Number of leukocytes and level of C-reactive protein (CRP) are usually considered in the diagnosis of chorioamnionitis when there is increased maternal body temperature.

– Recent studies show that α_1 -proteinase inhibitor complex and serum IL_6 are better markers of acute chorioamnionitis than CRP and leukocyte number but their usage is not very diffused yet.

Methods of visualization:

– Ultrasonography.

– Vaginal ultrasonography.

Amniocentesis as a diagnostic procedure presents a risk factor for cell layer damage and intraplacental bleeding, so it is often avoided. Methods of visualization can only add additional information thus putting maternal blood examination in the foreground. CRP is considered a safe marker of infection because if mother used corticosteroids there can be a false increase in the number of leukocytes. CRP is synthesized in the liver; it consists of five identical subunits and presents a non-specific inflammation factor. Its production is urged by IL_1 , IL_6 and TNF -alpha and the level is dramatically increased within six hours after the beginning of an acute inflammation process in the organism. The level of CRP is increased in

Table 1. — Signs of chorioamnionitis.

Signs of chorioamnionitis	Number of women	Percentage of women (%)
Increased CRP level	56	93.33
Fetal tachycardia	55	91.67
Increased number of leucocytes	38	63.33
Maternal tachycardia	17	28.33
Maternal temperature	18	30.00

most inflammatory, infective and malignant diseases including cardiovascular and rheumatic diseases. The velocity of increases and decreases of the CRP level in serum makes it a suitable marker for the diagnosis of acute infective disease with a dramatic course such as appendicitis, pelvic inflammatory disease and sepsis.

Standard chorioamnionitis therapy includes giving clindamicine and aminoglycoside (usually gentamicine) intravenously to the mother and newborn. Cephalosporins of newer generations are used when ampicillin resistant types of *Escherichia coli* are suspected.

The objective of this work was to examine the significance of CRP level as a marker in the diagnosis of chorioamnionitis in mothers with fetal tachycardia, i.e. to show the relation between these two and thus reduce the consequences of tachycardia and complications of chorioamnionitis by timely therapy.

Material and Methods

In the study we used data gained by observing patients in the ward for Pregnancy pathologies at the Institute of Gynecology and Obstetrics in Belgrade. We examined 60 women who delivered between the 32nd and 36th week of gestation and who also had confirmed chorioamnionitis as a cause of premature delivery, established by histological examination after delivery. Indications preceding the diagnosis included: leukocyte number and CRP level in maternal blood, blood pressure and pulse, maternal temperature and fetal pulse (CTG monitor). CRP level was determined by the PCR technique where the level of CRP higher than 10 mg/l was considered pathological. The number of leucocytes was considered increased if it was more than 15,000/mm³ and the temperature was high if it was above 37.8°C. Fetal tachycardia was diagnosed if CTG was above 160 bpm and maternal tachycardia was diagnosed if the pulse was above 120 bpm. Data were processed by statistical methods (simple distribution, X² test, McNemar test, t-test) and were presented in figures.

Results

CRP levels were pathological in most cases, and in 56 patients reaching 93.33%. In all examined patients it ranged between 10 mg/l and 100 mg/l. CRP medium value in the observed group was 50.53 mg/l (Figure 1).

Fetal tachycardia was present in 55 cases, i.e. 91.67%. All pregnant patients with pathological CTG at the same time had increased CRP levels. Fetal tachycardia was in the range of 160 and 200 bpm. If the mothers with tachycardia are divided into two groups, where the ones with CTG between 160 and 180 bpm are in the first group (32

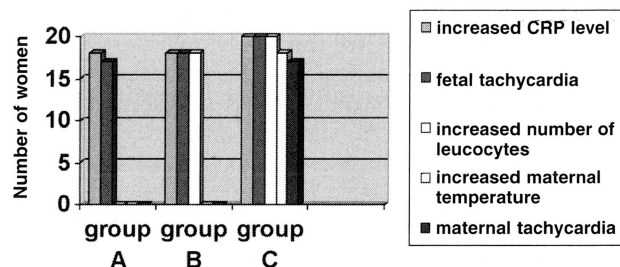


Figure 1. — Division of groups according to chorioamnionitis signs.

patients, 58.18%) and the ones with CTG above 180 bpm are in the second group (23 patients, 41.82%), it can be assumed that in the second group we more frequently find pregnant women with an increased number of leucocytes. This hypothesis was tested by the X² test with $p = 16.86$ (statistically significant) thus demonstrating that CTG level can be a safe index of the severity of chorioamnionitis (Figure 2).

The number of leucocytes was increased in 38 women (63.33%). Increased temperature and maternal tachycardia were associated with each other and other examined parameters in 18 cases of increased temperature and 17 cases of pregnant patients with increased pulse. Increased temperature ranged between 37.8°C and 40.2°C, with a medium value of 38.8°C.

According to the symptoms, the patients were divided into three groups: group A included patients with increased CRP level and fetal tachycardia; group B comprised patients with increased CRP level, tachycardia and also an increased number of leucocytes in the blood; and, group C comprised patients with some or all other parameters increased. Thus, in group A there were 22 women, in group B 18 and in group C 20 women (Figure 3). Measured CRP values in groups A and B were tested by the t-test and it was determined that there was a significant

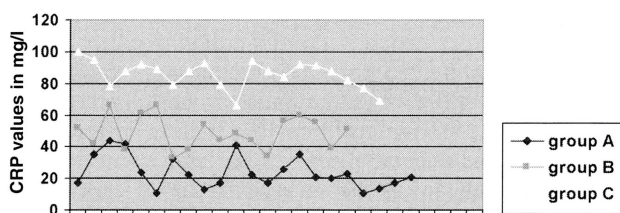


Figure 2. — Level of CRP in groups A, B and C.

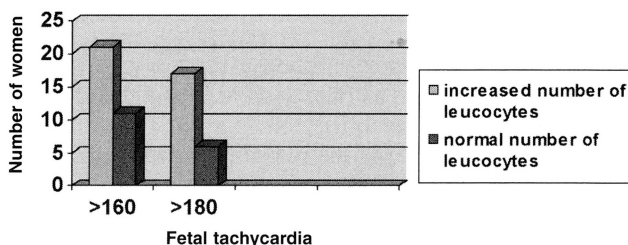


Figure 3. — Relation between fetal tachycardia and number of leucocytes.

difference between the groups, i.e. group B had a significantly higher level of CRP ($p < 0.01$).

Also, by the t-test, we determined a statistically significant difference in the distribution of CRP levels in groups B and C ($p < 0.01$). Based on this, we can say that CRP level increases are in line with the severity of the clinical picture.

In group A, after two days without antibiotic therapy, there was an increase in leucocyte number above normal in 15 women (68.18%). If we again compare groups A and B, it can be concluded that out of the total number of women in these two groups (40), 18 patients had increased leucocyte number on the first day, and after two days that number was 33. The significance of this increase was tested by the McNemar method and a statistical significance was found ($p < 0.05$) - enough for preventive usage of antibiotics, i.e. CRP increase was a sufficient index of possible chorioamnionitis.

Moreover, we observed the condition and length of hospital treatment of newborns. They all received antibiotics according to the antibiograms: one antibiotic (children that had no increased level of CRP, leucocytes or temperature); two antibiotics (increased temperature and number of leucocytes); and three antibiotics (increased level of CRP, increased number of leucocytes and temperature). There were 21 children in the first group, 24 in the second and 15 in the third group. We assumed the hypothesis that the children in the first group were from mothers in group A, in the second, children from mothers in group B and in the third children from mothers in group C, respectively. All hypotheses were tested by the X^2 test and the relations in all three cases were statistically significant ($p_1 < 0.01$, $p_2 < 0.01$ and $p_3 < 0.01$).

Discussion

We have determined in this study not only that the significance of CRP level is higher but also that CRP itself is a sufficient index for diagnosis. If we assume that in the mothers from group A chorioamnionitis was timely established and treated, then the previous hypothesis that mothers from group A (early stage of chorioamnionitis) most frequently have children that belong in the first group confirms that the level of CRP along with tachycardia is significant as the earliest marker of chorioamnionitis, because all other signs are not present in that stage. Thus the usage of antibiotics is justified if increased CRP is the only index of chorioamnionitis.

Because of its short half-life (19 hours), it is expected that the CRP level will decrease quickly after successful elimination of the cause [2]. Therefore CRP can serve in following the effects of antibiotic therapy and in our study it also served as a criterion for canceling therapy in the third group of newborns.

Causes of fetal tachycardia can be fetal hypoxia, maternal increased temperature, hyperthyroidism, maternal or fetal anemia, chorioamnionitis, fetal tachyarrhythmia, etc. According to some studies, persistent tachycardia of more than 180 bpm, especially when associated with increased maternal temperature, points to chorioamni-

onitis as a cause [5]. Our study showed that fetal tachycardia is a good index of infection because it appears to be associated with increased CRP level. It also showed that the level of tachycardia correlates well with the level of CRP and the increase in number of leucocytes.

We did not observe increased temperature or pulse rate of pregnant patients unless CRP, leucocytes or CTG were increased. Increased temperature cannot be considered a sign of chorioamnionitis because in some studies it appears in the greatest percentage after epidural anesthesia [6].

Moreover, all obtained data were compared with data in published studies of chorioamnionitis with rupture of membranes in the 37th week of gestation; increased maternal temperature was present in 99.2% of the cases, pathological CTG was present in 82% of the cases and maternal tachycardia in 19.4% of the cases [5]. We found significant differences in the incidence of increased temperature in the observed group with advanced chorioamnionitis that led to rupture, thus we can conclude that increased body temperature is not an early index of chorioamnionitis. However, if we compare the incidence of pathological CTG in Hanth *et al.* and Lieberman *et al.* [5, 6] studies, it is present in a high percentage, thus according to our findings it correlates significantly with the increase of CRP level.

Our study showed that fetal tachycardia and the incidence of CRP in maternal blood are significantly present in early stages of chorioamnionitis, pointing to a possibility of timely initiation of antibiotic therapy and prevention of the consequences of chorioamnionitis to the mother and fetus. Moreover, the correlation between the level of CRP and severity of the clinical picture and the usage of CRP in observing therapeutic effects are also confirmed, thus increasing the significance of CRP in the diagnosis and therapy of chorioamnionitis.

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