Biomedical Research 2017; 28 (14): 6256-6259 *ISSN 0970-938X*
www.biomedres.info

Procalcitonin and C-reactive protein in neonatal infection, a comparison study between intrauterine infection and non-intrauterine infection.

Wei Hao, Jia Song, Gang Li, Bo Han*

Department of Paediatrics, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, PR China

Abstract

Objective: To investigate whether there was difference in levels of procalcitonin (PCT) and C-reactive protein (CRP) in intrauterine infection and non-intrauterine infection and to study the potential of PCT and CRP as for diagnostic markers of intrauterine infection.
Methods: 200 cases were selected, including 98 cases of intrauterine infection and 102 cases of non-intrauterine infection during 2014-16 in Shandong Provincial Hospital Affiliated to Shandong University, China. 50 cases of healthy new-born's was used as a control. The venous blood, cord blood and maternal blood in each group were collected and the levels of PCT and CRP were detected using immunofluorescence assay and immunonephelometric method, respectively. SPSS 18.0 was used to conduct the statistical analysis.
Results: PCT levels in maternal blood of intrauterine infection group were high than the other two groups, but the difference was not significant. However, PCT levels in cord blood of intrauterine infection group were significantly higher than both non intrauterine infection group and the healthy group. PCT levels in the infant's serum of both intrauterine and non-intrauterine infection group were significant higher than the healthy group; but no significant difference was observed in cord blood PCT levels between the non-intrauterine infection group and the healthy control. In intrauterine infection group, CRP levels in both maternal blood and cord blood were significantly higher than the other two groups. However, in infant's serum, no significant different was observed between intrauterine and non-intrauterine infection groups. In both intrauterine and non-intrauterine infection groups, CRP levels were significantly higher in all three blood samples compared with the healthy control.
Conclusion: PCT levels in cord blood could be used as a marker for intrauterine infection and CRP levels in both maternal blood and cord blood could be used as a marker for intrauterine infection.

Keywords: Procalcitonin, C-reactive protein, Neonatal infection, Intrauterine infection.

Accepted on June 13, 2017

Introduction

Though efforts have reduced the neonatal mortality with an average of 2.0% annually since 1990, the rapid is still much slower than corresponding reductions in maternal mortality (2.6%) or mortality in children 1-59 months of age (3.4%) [1]. In the past two decades, almost a half of under-5 child died and about 3 million neonates are still dying every year [2].

Among various causes for neonatal mortality, the neonatal infections are one of the major causes of mortality and morbidity, especially for preterm infants, and represent a heavy burden both for the patient and public health [3]. Untreated infections can not only lead to serious complications such as sepsis which may result in the over prescription of antibiotics, contributing to the antimicrobial resistance and increasing costs and adverse effects, but also can cause death of the neonates [4].

Among the infections, at any time during pregnancy, the intrauterine infection is one of the important risk factors for neonatal sepsis and is a frequent cause of mortality and morbidity in new-born infants [5]. Generally, it is thought that early diagnosis of infection with the use of high sensitivity infection markers with a negative predictive value leads to decreased mortality and morbidity [6]. However, the diagnosis of early onset neonatal infection remains one of the greatest challenges in perinatal medicine, not only because of the quite limited number of tests that obstetrician can rely on, but also because of the possibility of late or absent for positive bacteriological samples, the imprecision of the test and non-specific for traditional markers [7].

Recently, parameters such as Procalcitonin (PCT) and C-reactive protein (CRP) have been considered to be valuable in diagnosis of the infections in new-born's. Several studies have reported that PCT and CAP are potential in diagnosis of the neonatal infection [8,9]. However few of them concern on difference of PCT and CAP in diagnosis between intrauterine infection and non-intrauterine infection.

In the present study, we conducted a comparison study between intrauterine infection and non-intrauterine infection to investigate whether there was difference in levels of PCT and CRP in the two kinds of infections and to study the potential of PCT and CRP as for diagnostic markers of intrauterine infection.

Methods and Materials

Patients

In the present study, a totally of 200 cases were selected, including 98 cases of intrauterine infection and 102 cases of non-intrauterine infection during 2014-2016 in Shandong Provincial Hospital Affiliated to Shandong University, China. 50 cases of healthy new-born's was used as a control. All cases were mothers with singleton pregnancies. In the intrauterine infection group, intrauterine infection symptoms were observed in the late pregnancy of the mothers as follows: premature rupture of membranes>18 h; temperature was >38°C; leukocytosis >15.00 × 10^9/L; maternal (>100 beats/min) and foetal tachycardia (>160 beats/min); meconium stained amniotic fluid [10]. All neonates in the intrauterine infection group were confirmed to be infected during the first 48 h of life by both positive blood culture or clinical symptoms which contained symptoms like pale, grey skin, poor peripheral circulation, respiratory >60/min, apnoea, respiratory insufficiency, muscle tension reduction, lethargy, blood pressure reduction, and CRP>10 mg/L 12~48 h after born but blood culture was negative [11-13]. For the 102 cases of non-intrauterine infection neonates, all cases were diagnosed with no symptoms of infection and were confirmed by blood culture but were infected within 28 d after born. For all cases, the study included pregnancies that ended as premature and term deliveries, pregnancies with congenital foetal malformations and cases that were treated with antibiotic therapy during the past two days were excluded from the study. The study was approved by the ethics committee of Shandong Provincial Hospital Affiliated to Shandong University.

Examination for CRP and PCT

The venous blood was collected from children within 2 h after born and before the use of any antibiotics. Cord blood was collected 10 min after the neonates were born. Maternal blood was collected before childbirth or surgery. Then the levels of PCT and CRP were detected and the blood bacterial culture was performed. The serum PCT concentration was detected by immunofluorescence assay with a Brahms KRYPTOR kit along with the corresponding instruments and reagents. The lowest detection limit of PCT using this method was 0.1 ng/ml. CRP levels were determined by the latex immunonephelometric method (BNA analyser, Behring-Werke AG, Marburg, Germany).

Statistical analysis

The measurement data was expressed by mean ± SD. Independent continuous variables were compared using the t-test and categorical data were compared using the chi square test or Fisher exact test. A P-value was less than 0.05 it was considered to be statistically significant. All analyses were made using SPSS 18.0.

Results

Clinical baseline of the patients

Table 1 demonstrated the clinical baseline of cases in different groups. No significant difference was observed in the mothers age, mean gestational age at delivery and mean birth weight among the 3 groups, P>0.05. However in intrauterine infection group, preterm delivery rate was significant higher than the other two groups, P<0.05.

Table 1. *Clinical baseline of the patients.*

Characteristics	Intrauterine infection group (n=100)	Non-intrauterine infection group (n=100)	Healthy neonates (n=50)
Mean age of mothers	27.42 ± 5.31	26.39 ± 4.68	26.54 ± 5.55
Years	(21~31)	(21~29)	(22~30)
Preterm delivery (%)	25 (25)*#	13 (13)	7 (14)
Mean gestational age at delivery	36.56 ± 7.61	38.42 ± 6.95	37.93 ± 5.86
Weeks	(27~41)	(28~41)	(28~40)
Mean birth weight, kg	3.01 ± 2.15	3.56 ± 3.12	3.17 ± 2.63

*P<0.05, compared with the non-intrauterine infection group; #P<0.05, compared with the healthy neonates.

PCT levels in maternal blood, cord blood and infants' serum of different groups

To investigate the PCT levels in different groups, PCT levels in maternal blood, cord blood and infant's serum were detected respectively. As shown in Table 2, PCT levels in maternal blood of intrauterine infection group were high than the other two groups, but the difference was not significant, P>0.05. However, PCT levels in cord blood of intrauterine infection group were significantly higher than both non-intrauterine

infection group and the healthy group, P<0.05. PCT levels in the infant's serum of both intrauterine and non-intrauterine infection group were significant higher than the healthy group, P<0.05; but no significant difference was observed in cord blood PCT levels between the non-intrauterine infection group and the healthy control, P>0.05. These results suggested that PCT levels in cord blood could be used as a marker for intrauterine infection.

Table 2. *PCT levels in maternal blood, cord blood and infant's serum of different groups (ng/ml).*

PCT levels	Intrauterine infection group (n=100)	Non-intrauterine infection group (n=100)	Healthy neonates (n=50)
Maternal blood	0.93 ± 0.12	0.89 ± 0.11	0.81 ± 0.15
Cord blood	2.98 ± 1.03*#	0.90 ± 0.16	0.85 ± 0.13
Infant's serum	9.11 ± 2.54#	8.94 ± 3.01#	1.13 ± 0.25

*P<0.05, compared with the non-intrauterine infection group; #P<0.05, compared with the healthy neonates.

CRP levels in maternal blood, cord blood and infants' serum of different groups

As shown in Table 3, in intrauterine infection group, CRP levels in both maternal blood and cord blood were significantly higher than the other two groups, P<0.05. However, in infant's serum, no significant different was observed between intrauterine and non-intrauterine infection groups, P>0.05. In both intrauterine and non-intrauterine infection groups, CRP levels were significantly higher in all three blood samples compared with the healthy control, P<0.05, indicating that CRP levels in both maternal blood and cord blood could be used as a marker for intrauterine infection.

Table 3. *CRP levels in maternal blood, cord blood and infant's serum of different, (mg/L).*

CRP levels	Intrauterine infection group (n=100)	Non intrauterine infection group (n=100)	Healthy neonates (n=50)
Maternal blood	21.45 ± 5.41*#	1.78 ± 1.03	1.68 ± 0.47
Cord blood	19.24 ± 6.32*#	1.74 ± 1.25	1.65 ± 1.01
Infant's serum	16.31 ± 4.59#	16.24 ± 5.36#	1.79 ± 0.64

*P<0.05, compared with the non-intrauterine infection group; #P<0.05, compared with the healthy neonates.

Discussion

With 3 million neonates still dying every year, nowadays, new-born's death is still a challenge to the whole world. The intrauterine infection is thought to be a common cause of mortality and morbidity in neonates which remains to be a problem in obstetrics. Though it is widely accepted that early diagnosis will significantly reduce the risk of death of infection, the diagnosis of early onset neonatal infection remains one of the greatest challenges in perinatal medicine. Limitations for traditional tests include the low sensitivity and specificity, very limited methods, test not in time and so on. Thus new potent markers for diagnosis of intrauterine infection are still needed.

The diagnostic value of C-reactive protein (CRP) has been recognized for a long time in of lots of infections including intrauterine infection, such as postoperative infections, respiratory tract infection, joint infection [14-17]. Diagnostic value of Procalcitonin (PCT) in new-born's infection was also reported by lots of studies, such as nosocomial infections [18] and sepsis [19]. However diagnostic value of PCT in intrauterine infection was not reported much.

In the present study, we conducted a comparison study between intrauterine infection and non-intrauterine infection to investigate whether there was difference in levels of PCT and CRP in the two kinds of infections and to study the potential of PCT and CRP as for diagnostic markers of intrauterine infection.

To investigate the PCT and CRP levels in different groups, both PCT and CRP levels in maternal blood, cord blood and infant's serum were detected respectively. It was shown that PCT levels in maternal blood had no diagnostic value for intrauterine infection since no significant difference was found between the three groups. However PCT levels in cord blood were significant higher in intrauterine infection group compared with non-intrauterine infection group and healthy neonates, which indicate that PCT levels in cord blood could be used as a marker for intrauterine infection. These results were inconsistent with some other studies. Kordek et al. investigated 15 patients and their infected new-born's and found that maternal PCT concentration during labour did not contribute to early prediction of infection in the neonate, but umbilical cord PCT concentrations, as well as its neonatal venous levels on the second day of life, were related to intrauterine infection [20]. There are also many Chinese studies showing that cord PCT can be used as a potential marker in diagnosis of intrauterine infection which may offer some references [12,21].

For CRP levels, it was found that CRP levels in both maternal blood and cord blood were significantly higher than the other two groups. However, in infant's serum, no significant different was observed between intrauterine and non-intrauterine infection groups, indicating that CRP levels in both maternal blood and cord blood could be used as a marker for intrauterine infection. These results were also in consistent with related studies. Cicarelli et al. reported maternal and cord blood levels of serum CRP during and after delivery and found that CRP were significantly higher in maternal serum than in new-born's at the moment of delivery [22]. Study of Cosickic et al. showed that CRP could be used as a quick and easily available test for the recognition of healthy neonates and for

the choice of neonates who require monitoring and treatment until microbiological results arrive [23].

Conclusion

In summary, we conducted a comparison study between intrauterine infection and non-intrauterine infection to investigate whether there was difference in levels of PCT and CRP in the two kinds of infections and to study the potential of PCT and CRP as for diagnostic markers of intrauterine infection. Results suggested that PCT levels in cord blood could be used as a marker for intrauterine infection and CRP levels in both maternal blood and cord blood could be used as a marker for intrauterine infection.

Reference

1. Lawn JE, Blencowe H, Pattinson R. Stillbirths: Where? When? Why? How to make the data count? Lancet 2011; 377: 1448.
2. Lawn JE, Blencowe H, Oza S. Every new-born: progress, priorities, and potential beyond survival. Lancet 2014; 384: 189-205.
3. Khorvash F, Abdi F, Dialami K. Serum procalcitonin and C-reactive protein as nosocomial infection markers in hospitalized patients without localizing signs. J Res Med Sci 2011; 16: 1280-1285.
4. Limper M, Kruif MDD, Ajubi NE. Procalcitonin as a potent marker of bacterial infection in febrile Afro-Caribbean patients at the emergency department. Eur J Clin Microbiol Infec Dis 2011; 30: 831-836.
5. Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. New Engl J Med 2000; 342: 1500.
6. Santos RP, Tristram D. A practical guide to the diagnosis, treatment, and prevention of neonatal infections. Paediatr Clin North Am 2015; 62: 491-508.
7. Bhutta ZA, Das JK, Bahl R. Can available interventions end preventable deaths in mothers, new-born babies, stillbirths and at what cost? Lancet 2014; 384: 347.
8. Kordek A, Torbe A, Tousty J. The determination of procalcitonin concentration in early-onset neonatal infection: a valuable test regardless of prenatal antibiotic therapy. Clin Paediatr 2016.
9. Yao A, Liu J, Jing C. Report-clinical practice of procalcitonin and hypersensitive C-reactive protein test in neonatal infection. Pak J Pharm Sci 2016; 753-756.
10. Mostaghel N, Nahid A, Azar Z. Meconium-stained amniotic fluid and puerperal infection. Marine Biol Res 2008; 1: 375-387.
11. Ibrahim KA, Abdel-WAA, Ibrahim AS. Diagnostic value of serum procalcitonin levels in children with meningitis: a comparison with blood leukocyte count and C-reactive protein. J Pak Med Assoc 2011; 61: 346.
12. Lin YY, Lin XZ, Ya-DLI. Cord blood procalcitonin, interleukin-6 and C-reactive protein as aids in the diagnosis of neonatal intrauterine bacterial infection. Chinese J Neonatol 2014.
13. Elvedi-GV, Peter B. Maternal group B streptococcus infection, neonatal outcome and the role of preventive strategies. Coll Antropol 2008; 32: 147-151.
14. Nowak M, Oszukowski P, Szpakowski M. Intrauterine infections: The role of C-reactive protein, white blood cell count and erythrocyte sedimentation rate in pregnant women in the detection of intrauterine infection after preliminary rupture of membranes. Ginekol Pol 1998; 69: 615.
15. Verkkala K, Valtonen V, Jarvinen A. Fever, leucocytosis and C-reactive protein after open-heart surgery and their value in the diagnosis of postoperative infections. Thorac Cardiovasc Surg 1987; 35: 78-82.
16. Cals JWL, Bock LD, Beckers PJHW. Enhanced communication skills and c-reactive protein point-of-care testing for respiratory tract infection: 3.5-year follow-up of a cluster randomized trial. Ann Fam Med 2013; 11: 157.
17. Parvizi J, Jacovides C, Adeli B, Mark B. Coventry award: synovial C-reactive protein: a prospective evaluation of a molecular marker for periprosthetic knee joint infection. Clin Orthop Relat Res 2012; 470: 54-60.
18. Chiesa C, Pacifico L, Rossi N. Procalcitonin as a marker of nosocomial infections in the neonatal intensive care unit. Intensive Care Med 2000; 26: 175-177.
19. Sastre JBL, Solis DP, Serradilla VR. Evaluation of procalcitonin for diagnosis of neonatal sepsis of vertical transmission. BMC Pediatr 2007; 7: 9.
20. Kordek A, Torbe A, Czajka R. Maternal venous procalcitonin levels do not correlate with umbilical cord blood and venous blood concentrations in the neonate. J Perinat Med 2006; 34: 462-465.
21. Chen YT, Xiong Y, Xue-Tang SU. The clinical significance of procalcitonin for diagnosis of the pregnant women with intrauterine infection. J Int Obstet Gynecol 2012.
22. Cicarelli LM, Perroni AG, Zugaib M. Maternal and cord blood levels of serum amyloid a, C-reactive protein, tumour necrosis factor-α, interleukin-1β and interleukin-8, during and after delivery. Mediators Inflamm 2005; 2005: 96-100.
23. Cosickic A, Skokic F. Evaluation of diagnostic values of C-reactive protein in neonatal infections. Materials Lett 2013; 12: 424-428.

*Correspondence to

Bo Han

Department of Paediatrics

Shandong Provincial Hospital Affiliated to Shandong University

Jinan

PR China