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The relationship between PCT and CRP and premature rupture of membranes and intrauterine infection is less than 34 weeks

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Abstract: **To investigate the relationship between PCT (procalcitonin) and C reactive protein (CRP), and to investigate the time of premature rupture of membranes and intrauterine infection less than 34 weeks. 234 cases of <34 weeks preterm infants were collected in the Department of Obstetrics. All patients were divided into group A (52) without premature rupture of fet al membranes, group B of PROM (premature rupture of membranes) <48h premature infant (84), group C of PROM 49-168h (59), and group D of PROM>168h (39), respectively. The infection index of prenatal and postnatal children was collected. The difference of the positive rate of intrauterine infection and the difference of infection index between pregnant women and their pregnant women were compared. The difference of C reactive protein of antenatal infection index of pregnant women was statistically significant (P<0.05). But it did not increase with the prolongation of membrane breaking time. The longer the time of rupture of the membrane, the higher the PCT value of the sick children (P<0.05). The longer fetal membrane breaks, the higher the incidence of CA (chorioamnionitis). There was a significant difference in the incidence of CA between the 4 groups (P<0.05). Prenatal and neonatal blood PCT and CRP are sensitive indicators for early prediction of premature rupture of membranes and placental chorioamnionitis.**

Keywords: Premature rupture of membranes; Procalcitonin; Premature infants; Intrauterine infection; C- reactive protein

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1. Introduction

PROM is the rupture of fetal membranes before labor. It is reported that the incidence of premature rupture of membranes is 2.7%-17%, and the incidence rate is 5%-15%[1]. PROM is one of the common obstetric complications 37 weeks ago. It is characterized by high rate of parturients, high incidence of newborns and high mortality. Studies confirm that chorioamnionitis is a causal relationship with PROM[2]. After intrauterine infection, the perinatal body is easy to invade, and intrauterine infectious diseases, such as neonatal lung disease, NEC, neonatal brain damage and other diseases. As a high-risk factor in perinatal period, PROM plays an important role in the occurrence of infectious diseases in premature infants. Studies have shown that PPROM is closely related to inflammatory reaction and bacterial infection[3,4]. This study found that the longer the time of premature rupture of membranes, the higher the PCT and CRP values, and the higher the incidence of CA as the PROM prolonged. In case of PROM pregnant women or clinical CA related symptoms and signs, the infection index should be monitored in time, and antibiotics and hormones should be used in time to reduce the risk of pulmonary disease in premature infants, and the early detection of infection indicators in the premature infants with PROM can be used to guide the clinical intervention to reduce the damage to the lung disease, and then reduce the incidence of the lung disease. The incidence and mortality of preterm infants with low perinatal stage will further improve the prognosis of premature infants.

2. Research objects

2.1. Research objects

The study selected 234 cases of single preterm infants born in Qingdao Women's and Children's Hospital from October 2016 to February 2018. There were 146 males and 88 females, the average body weight (1797.02 397.25) g and mean gestational age weeks (31.41 1.52). According to whether there is premature rupture of membranes (PROM), all the cases were divided into no PROM (group A), PROM<48h (group B), PROM 49-168h (group C), PROM>168h (group D).

Maternal exclusion criteria: 1) patients with incomplete clinical data; 2) pregnant women with pregnancy complications (pre-eclampsia, gestational diabetes, pregnancy with heart disease and placental abruption, placenta previa, etc.).

Preterm infant exclusion criteria: 1) the clinical data were incomplete; 2) the age of admission was >48h; 3) there were hereditary metabolic diseases, respiratory malformation and other serious malformations.

2.2. Data collection

The data of the child's mother before delivery and the related data after birth were collected. All the selected children had chest X-ray data, parallel cranium, heart and abdomen B ultrasound, partial CT and MRI examination, in order to exclude congenital malformation.

2.3. Placental pathological examination

The placenta and placenta were taken from a special person: (1) a long 2cm membrane was cut from the fetal membrane to the edge of the placenta, and the amniotic membrane was made into a membrane. (2) 2cm placenta tissues were taken at different parts of the placenta, including the fetal surface and the complete maternal surface; (3) the umbilical cord was disconnected from the insertion of the placenta at the placenta. A section of 2-4cm in the middle of the disconnected umbilical cord. All specimens were fixed by 10% formaldehyde, paraffin embedded, sliced, HE stained and made into slices. All pathological sections were diagnosed by doctors with high qualification in pathology department and blinded to the readers.

2.4. Diagnostic criteria for disease

The diagnostic criteria of PROM refer to the eighth edition of Obstetrics and Gynecology[5].

Diagnostic criteria for CA[6]: (1) Clinical CA diagnostic criteria: heating temperature of fever over 37.8℃; (2) mother heart rate more than 100 times; (3) fetal heart rate >160 times or <120 times; (4) blood leukocytes rise to 15>109/L or nuclear left shift, (5) CRP level rise, (6) amniotic fluid has odor, (7) uterus pressure the pain.

Diagnostic criteria for sub-clinical CA: (1) positive placenta and amniotic fluid culture; (2) fetal membranesor placental histopathological examination showed inflammatory manifestations. All the above indicators appear positive, but no clinical symptoms can be diagnosed.

2.5. Statistical analysis

All data were analyzed by SSPS19.0. The normal distribution data were represented by mean number ± standard deviation (± s) or rate (%). Single factor analysis of variance or K-W rank sum test was used in each group. Qualitative data were checked by chi square test, and P<0.05 was statistically significant.

3. Results

3.1. General information

There was no significant difference in gestational age, birth weight, cesarean section, and intrauterine distress in preterm infants (P>0.05). The longer PROM, the higher the use rate of antibiotics and hormones, the incidence of clinical CA, the rate of amniotic fluid pollution and the positive rate of culture in the uterine cavity, the difference was statistically significant (P<0.05), (Table 1).

Table 1. Comparison of general data

	Group A (n=52)	Group B (n=84)	Group C (n=59)	Group D (n=39)	statistics	P
Fetal age (W)	31.41±1.52	31.96±1.56	31.52±1.56	31.45±1.82	1.737	0.160
Birth weight (g)	1797.02±397.249	1823.10±389.84	1769.49±332.97	1742.05±422.48	0.473	0.701
Cesarean section (%)	20.0(38.46)	27.0(32.14)	26.0(44.08)	20.0(51.28)	4.671	0.198
Intrauterine distress (%)	7(13.46)	10.0(11.90)	3.0(5.08)	4.0(10.26)	2.532	0.470
Prenatal use of antibiotics (%)	22(42.31)	58(69.05)*	57(96.61)*#	39(100.00)*#	59.003	0.000
Prenatal hormone use rate (%)	30(57.69)	50(59.52)	56(94.92)*#	38(97.44)*#	41.241	0.000
Clinical type (CA) (%)	10(19.23)	22(26.19)*	19(32.20)*	13(33.33)	17.391	0.001
Amniotic fluid pollution rate (%)	1(1.92)	5(5.95)	6(10.17)	7(17.95)*#	8.570	0.036
Positive rate of culture of uterine cavity secretions (%)	0(0.00)	0(0.00)	5(8.47)*#	6(15.38)*#	18.521	0.000

Note: * compared with A group, P<0.05; # compared with B group, P<0.05.

Table 2.The change of infection index in pregnant women with different time of rupture of membrane ($\bar{x} \pm s$)

	Group A (n=52)	Group B (n=84)	Group C (n=59)	Group D (n=39)	statistics	P
WBC($\times 10^9$/L)	11.54±3.44	12.08±3.81	12.89±3.60	12.26±3.15	1.362	0.255
Neutrophils(N%)	83.00±5.99	81.77±6.87#	82.43±6.13#	79.56±7.03*	99.617	0.000
CRP(mg/dl)	20.0±26.35	13.47±23.07	19.5±26.01	12.56±21.69	1.483	0.231

Note: * compared with group A, #P<0.05 compared with the D group, P<0.05.

3.2. Different time of rupture of membranes and prenatal infection index of pregnant women

There was no significant difference in the number of leukocyte count and CRP (P>0.05). The percentage of neutrophils was statistically significant (P<0.05). The percentage of neutrophils did not increase with the prolongation of PROM.

3.3. Different membrane breaking time and the infection index of preterm infants

The total difference of leukocyte count and CRP in premature infants was not statistically significant (P>0.05). The percentage of neutrophils and PCT has statistically significant (P<0.05). The longer the PROM time, the higher the PCT value, and higher than the percentage of neutrophils, (Table 3).

Table 3. the change of infection index between premature rupture of membranes and premature rupture of membranes

	A group (n=52)	B group (n=84)	C group (n=59)	D group (n=39)	statistics	P
WBC($\times10^9$/L)	10.84±4.51	11.66±6.58	10.41±6.95	10.83±5.77	0.815	0.487
Neutrophils(N%)	49.73±13.98	51.06±13.45*	49.52±13.61*	48.46±15.72*	54.041	0.000
CRP(mg/dl)	0.69±4.14	1.25±6.52	1.51±6.59	1.71±8.98	0.219	0.883
PCT(ng/dl)[a]	5.27(0.20-4.16)	5.74*(0.24-7.96)	11.56*#(0.85-7.85)	19.11*#(0.48-32.36)	16.873	0.001

Note: * compared with group A, P<0.05; # compared with group B, P<0.05.

Table 4. the relationship between the time of different rupture of membranes and the incidence of CA

	A group (n=52)	B group (n=84)	C group (n=59)	Dgroup (n=39)	statistics	χ^2
CA+(%)	30(57.69)	58(69.05)*	49(83.05)	30(76.92)	9.470	0.024

Note: * the expression is compared with the A group, P<0.05.

3.4. The occurrence of different membrane breaking time and CA

The longer the PROM time, the higher the incidence of HCA, the difference in each group was statistically significant (P<0.05). The incidence of CA in A, B and C groups increased gradually, and the incidence of CA in D group was lower than that in C group. They are significant difference between group A and B, (Table 4).

4. Discussion

The incidence of PROM in premature delivery is about 30%-40%[7], and PROM breaks the original inner environment of amniotic cavity and increases the probability of amniotic cavity infection. Many scholars believe that an important reason for PROM is infection[8,9] with PROM. PROM combined with CA is very harmful to perinatal mother and child. Relative to term PROM (PPROM) is also very harmful to mother and child. Early diagnosis of PPROM and intrauterine infection, prevention and treatment of intrauterine infection and CA infection and neonatal infectious diseases have become the research focus. Our study found that the incidence of CA can prolong PROM. PCT and CRP also increased with the prolongation of rupture time.

At present, many indicators for assessment and diagnosis of PROM and CA wasstudied. CRP is an acute phase protein. It occurs when the body is stimulated by inflammatory substances and the inflammatory response. It rises 4-6 hours after the inflammation, reaches a peak of 24-48 hours. The half-life is 6 hours, which decreases rapidly with the decrease of inflammation. Therefore, it is an ideal indicator for the diagnosis of bacterial infection. In recent years, studies have shown that the higher the CRP value suggests, the greater the possibility of intrauterine infection[10] Giuseppina and other[11] studies show that the detection of CRP (less than 12h within the membrane) at admission can help clinicians to manage early PROM. This study found that the incidence of CA was higher with PROM extension. However, in this study, the value of prenatal CRP did not increase with the prolongation of PROM. The CRP partly indicates the occurrence of PROM and intrauterine infection. Gao[12] studies confirmed that CRP is an important marker for the diagnosis of neonatal infection. Its sensitivity is higher than the white cell count. The increase of the value suggests that the bacterial infection may be more likely. This study found that the first day after birth of the premature infants, the WBC number and the CRP level were not statistically significant. It maybe the possibility of premature birth. The time of blood collection after admission must according to

children condition. Therefore, children with high risk factors of PROM and intrauterine infection should be rechecked or monitored continuously for 24 hours after birth.

Calcitonin is a calcitonin propeptide produced by C cells in the thyroid gland. It is rapidly synthesized in the case of inflammatory or severe infectious diseases in the whole body. It increases rapidly within 2-6 hours after infection, and continues to be in high level with the infection progress, and gradually decreases after the infection. The study found that the level of PCT in the first day of premature infants increased gradually with the progress of inflammation, and the difference was statistically significant ($P<0.05$).The sensitivity of PCT to the prediction of intrauterine infection was higher than that of CRP, which could be used as an auxiliary marker to determine the neonate infection without intrauterine infection.

5. Conclusion

The results suggest that the infection index of PROM and pregnant women is increased, and the incidence of chorioamnionitis increases with the prolongation of PROM time. Therefore, in order to reduce the risk of lung injury in preterm infants and reduce the mortality of preterm infants in perinatal period, the risk of infection should be monitored in time. The risk of lung injury in premature infants should also be monitored in time for PROM pregnant women or infection related manifestations.

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