REPORT

Clinical practice of procalcitonin and hypersensitive c-reactive protein test in neonatal infection

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Abstract: To study the clinical practice of procalcitonin and hypersensitive c-reactive protein test in neonatal infection. Two hundred cases of our hospital treatment confirmed infection early newborn children were selected from February 2014 to March 2015. According to the condition, the children were divided into four groups as follows: severe infection group, local infection group, non-infection group and healthy newborns group. At the same time, the new healthy newborns were chosen as control group. The levels of serum procalcitonin and high-sensitivity C-reactive protein were detected in all children and the levels in severe infection group children before and after treatment were also quantitatively detected and the test results were analyzed. There was significant difference in procalcitonin among the four groups ($pS<0.05$). The positive rate of the high-sensitivity C-reactive protein in local infection group has no significant difference compared with the non-infection group ($p>0.05$). But there was significant difference between the local infection group and healthy newborn group. As for the severe infection group, both the levels of procalcitonin and positive rate of high-sensitivity C-reactive protein had significant difference compared with the other groups. The detection of procalcitonin and high-sensitivity C-reactive protein could contribute to the diagnose of the early infection neonatal children and has important values in diagnosis and treatment of infectious diseases in the newborns.

Keywords: Procalcitonin, Hypersensitive c-reactive protein, Pediatrics, Infection, Disease

INTRODUCTION

Newborn was easy to be infected with the bacterial infectious disease owing to the low resistance and immunity (Sanders *et al*., 2008). When the children suffered from the disease, the signs and symptoms are non-specific (Olaciregui *et al*., 2009). Moreover, the development of the disease was quite quick and it had severe damage to the children with the high case fatality rate (Yo *et al*., 2012). Generally, the best treatment time was usually lost due to the lack of reliable early diagnosis index in clinical practice. So, early diagnosis has important clinical value in the diagnosis of pediatric neonatal diseases. At present, the detection of procalcitonin and hypersensitive c-reactive protein were widely used in the clinical diagnose of pediatric examination (Youssef *et al*., 2007). In this paper, we analyzed the application of procalcitonin and hypersensitive c-reactive protein in the clinical diagnosis of neonatal disease. The research was as follows.

MATERIAL AND METHOD

Materials

Two hundred cases of our hospital treatment children were randomly selected from February 2014 to March 2015. According to the condition, the children were divided into four groups as follows: Severe infection group, local infection group, non-infection group and healthy newborns group The new healthy newborns were chosen as control group. In severe infection group, there were male children (26 cases) and female children (24 cases). The born time was 5-20d, average age was (10.5±4.5) d. And there were 31 cases infected with septicemia, 15 cases infected with severe pneumonia and 4 cases with necrotizing enteritis. In local infection group, there were male children (27 cases) and female children (23 cases). The born time was 5-20d, average age was (9.5±5.0) d. There were 25 cases infected with pneumonia, 14 cases infected with enteritis, 5 cases with impetigo and 6 cases infected with omphalitis. As for the non-infection group, there were male children (25 cases) and female children (25 cases). The born time was 6-20 d, average age was (10.8±4.5) d. Among these children, there were jaundice (35 cases), allergic dermatitis (12 cases) and asphyxia (3 cases). For the healthy children, there were male children (26 cases) and female children (24 cases). The born time was 5-20 d, average age was (11.0±4.0) d. There was no significant difference in gender and age of the newborns in each group.

The diagnostic standards of severe infections

The diagnosis of severe infection group was based on the clinical symptoms, imaging findings, laboratory examination results and so on. The children who had

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severe infection and systemic inflammatory response will be diagnosed as severe infection children.

Testing method

The venous blood was collected from children before the use of antibiotics for treatment. Then the levels of procalcitonin and hypersensitive c-reactive protein were detected and the blood bacterial culture were performed. The value of procalcitonin was detected by Chemical luminescence method using the French bioMerieux Mini VIDAS along with the corresponding instruments and reagents. The positive diagnostic criterion was >0.25 ng/ml. Immunofluorescence assay was performed to detect the hypersensitive c-reactive protein. Test instrument is i-CHROMA and the reagent used in the test was produced by South Korea MedInc Boditech company. The positive diagnostic criteria of C reactive protein was >3mg/L. The levels of procalcitonin and hypersensitive c-reactive protein in severe infection group were tested again after the children receiving treatment for 10 d.

STATISTICAL ANALYSIS

All data were assessed by SPSS 16.0 program. The quantitative data was tested by T test and represented by ($x \pm S$). The enumeration data was tested by x^2 test and given by [n (%)]. Differences were considered to be statistically significant at $p<0.05$.

RESULTS

The comparison of the serum concentrations of procalcitonin and hypersensitive c-reactive protein in each group

There were significant differences in serum concentrations of procalcitonin and hypersensitive c-reactive protein for each group ($p<0.05$). Compared with other groups, the testing results of severe group had significant differences. While for the hypersensitive c-reactive protein detection, the results showed that there was no significant difference between local infection group and non-infection group with the $p>0.05$. But compared with the healthy children group, the results had significant difference. All the data were shown in table 1. Studies have shown that the results of the detection of hypersensitive c-reactive protein in bacterial infection is significantly higher than that of non-bacterial infection. Under normal circumstances, the content of hypersensitive c-reactive protein in serum is very low, when the bacteria invade the body by stimulating the production of inflammatory, the peak concentration tens to hundreds times of basic value.

The positive rate of the procalcitonin and hypersensitive c-reactive protein in each group

The results showed that the positive rate of the hypersensitive c-reactive protein had no significant difference between local infection group and non-infection group ($p>0.05$). But there was significant difference compared with the healthy children group with the $p<0.05$. As for the severe infection group, both the positive rate of procalcitonin and hypersensitive c-reactive protein had significant difference compared with the other groups ($p<0.05$). The results were revealed in table 2.

Comparison of the levels of procalcitonin and hypersensitive c-reactive protein in severe infection group before and after treatment

The results revealed that the levels of procalcitonin and hypersensitive c-reactive protein in severe infection group had significant difference before and after treatment. The results were shown in table 3. Procalcitonin levels were significantly elevated when there were severe bacterial infections and systemic manifestations. The procalcitonin decreased after infection being controlled and it was only slightly increased in viral infection and local bacterial infection. It demonstrated that most of the calcitonin was combined with the thyroid and other organs, which indicated that it had better specificity and sensitivity to bacterial pneumonia and mycoplasma pneumonia.

DISCUSSION

Infectious diseases seriously affect the health and safety of newborn in pediatric clinical treatment and the mortality rate caused by infectious diseases was especially high (Zhang *et al*., 2014). Bacteria could survive and multiply in the blood of newborns and produce toxin constantly which would affect the safety of newborns (O'Donnell, 2011). In pediatric clinical treatment of neonatal infection, it was difficult to diagnosis the disease because the children just suffer from fever, poor response and other clinical manifestations, which were not obvious (Yo *et al*., 2012). Therefore, it is important to make the diagnosis and efficacy assessment of neonatal infection disease to enhance the clinical treatment.

Newborn was easy to be infected with the bacterial infectious disease owing to the low resistance and immunity (Gilsdorf, 2012). Based on the previous study, the incidence of infectious diseases was 0.1-1%, but the mortality rate was up to 15%-50% (Sachdev, 2004). In the current clinical diagnosis, procalcitonin and hypersensitive c-reactive protein were valued as the observation index for the early diagnosis of newborn infectious disease. Procalcitonin was mainly produced by thyroid cells and it had no biological activity (Riedel, 2012). However, the children's lung, liver, endocrine cells would also produce procalcitonin when the newborn was infected. Hypersensitive c-reactive protein is synthesized by liver and is thought to be the inflammatory index due to the higher sensitivity in the clinical diagnosis (Sanders *et al*., 2008).

Table 1: The comparison of the serum concentrations of procalcitonin and hypersensitive c-reactive protein in each group

Groups	Procalcitonin (ng/ml)	Hypersensitive c-reactive protein(ng/ml)
Severe infection group	8.5±7.1*&#	37.5±15.6*&#
Local infection group	2.3±1.0*&	18.5±6.2*
Non-infection group	0.7±0.4*	17.1±15.9*
Healthy group	0.3±0.2	3.5± 0.8

Table 2: The positive rate of the procalcitonin and hypersensitive c-reactive protein in each group [n (%)]

Groups	Cases	Procalcitonin (ng/ml)	Hypersensitive c-reactive protein (ng/ml)
Severe infection group	50	45(90.00)	31(62.00)
Local infection group	50	34(68.00)	22(44.00)
Non-infection group	50	6(12.00)	20(40.00)
Healthy group	50	3(6.00)	2(4.00)

Note: Compared with control group, *p<0.05; Compared with non-infection group, & p<0.05;compared with local infection group, #p<0.05

Table 3: Comparison of the levels of procalcitonin and hypersensitive c-reactive protein in severe infection group before and after treatment

	Procalcitonin (ng/ml)	Hypersensitive c-reactive protein (ng/ml)
Before the treatment	8.5±7.1	37.5±15.6
After the treatment	1.1±0.4	9.5±3.1
T	7.3582	12.4483
P	0.0000	0.0000

In this study, we analyzed the levels of procalcitonin and hypersensitive c-reactive protein in the blood of severe infection, local infection, non-infection and normal healthy children. The number of positive cases in each group was 45,34,6 and 3 cases for procalcitonin and 31, 22, 20, 2 cases for hypersensitive c-reactive protein, respectively. The results showed that the levels of procalcitonin and hypersensitive c-reactive protein in the blood of severe infection group were even up to (37.5), (8.5) before the treatment. However, the data were separately after treatment which indicated that the content of procalciton in the serum of severe infection group was relatively high and it also demonstrated the sharp increase of the procalciton in the serum was closely related to the infection. In this study, the content of procalcitonin and hypersensitive c-reactive protein in the serum of newborns were as follows: Severe infection group > local infection group > non-infection group > healthy group.

The main reason for the increase of the procalcitonin was that the patient's thyroid system will occur lesions when the patients were infected with the bacteria and viruses. It would result in the release of thyroid cells to increase the amount of procalcitonin, thereby increasing the concentration of the procalcitonin in the patients' blood.

Hypersensitive c-reactive protein is an acute phase protein synthesized by the liver. It is found in the serum of patients with acute inflammation and secreted by the liver in the inflammatory stimulation. It is regulated and induced by many cytokines, such as IL-I, IL-6, TNF-, etc. which were also the nonspecific markers of inflammation. Hypersensitive c-reactive protein was generated by the liver which was stimulated by the activation of neutrophils and macrophages such as leukocyte interleukin -6 in the acute stage of inflammatory cytokines. The levels of hypersensitive c-reactive protein began to rise in several hours and reach peak during 48 hours. It returned to normal with the lesions subsided.

Hypersensitive c-reactive protein was not affected by the factors of age, sex, body temperature and anemia, so it is considered to be a preferred index for the distinguish of bacterial infection and viral infection. The hypersensitive c-reactive protein can activate the complement system of the organism after binding to the protein on the cell wall of the pneumococcal cell, and promote the process of humoral immune cell immunity and other immune regulation. But the increasing trend of hypersensitive c-reactive protein in the virus infection is usually not significant. Compared with the children who had mycoplasma pneumonia, viral pneumonia and healthy children, the levels of hypersensitive c-reactive protein were significantly increased in the children who had bacterial pneumonia. In all, the levels of hypersensitive c-reactive protein were respectively bacterial pneumonia in children > mycoplasma pneumonia in children > virus pneumonia in children> healthy children. Therefore, the hypersensitive c-reactive protein is one of the important

indicators for the differential diagnosis of early infection in children with pneumonia.

Related studies have shown that the levels of procalcitonin would increase when the patients suffer from the systemic infection. It might be explained by the reason that the patients' other organs also released the procalcitonin expect the thyroid cells (Tay *et al*., 2006). It had been confirmed that stem cells would produce a large number of procalcitonin in the induction of tumor necrosis (Smith *et al*., 2006). However, the peripheral blood mononuclear cells are the main sites of the production of calcitonin and the content of procalcitonin would increase significantly in the stimulation of lipopolysaccharide.

The procalcitonin is a glycoprotein consisting of 116 amino acids and precursor peptide of calcitonin without the active hormone calcitonin. It was found that the selective induction of elevated procalcitonin was associated with high sensitivity and specificity for bacterial infections and was proportional to the severity of the disease. In chronic renal failure (CRF), inhalation injury, acute bacterial infections, and other non-thyroid injury, serum procalcitonin level has increased to a certain degree, some even increased exponentially which indicated that there are still other cells secreting and storaging procalcitonin except for medullary thyroid cells. Related research found that the increasing of the original value of procalcitonin is usually not obvious. But when the body suffered from severe infection (such as bacteria, fungi or parasites infection) and had systemic manifestations, calcitonin hormone levels will be increased significantly. The study showed that the main cause of the induced procalcitonin was the response of the organism to the bacterial endotoxin.

Generally speaking, the content of hypersensitive c-reactive protein in the blood of healthy people was relatively low, but in this study we found that the level was especially high in the serum of the severe infection, local infection and non-infection patients. The results revealed that the concentration of hypersensitive c-reactive protein would increase dramatically as soon as the patients were infected with bacteria or within 6-12h. After being infected for 24-28h, the levels would reach the maximum which were even hundreds of times or thousands of times of the normal person. And the concentration would decrease as soon as the infection or inflammation alleviate. Compared with the other related studies, our results about the content of hypersensitive c-reactive protein in the serum of patients had no significant difference. It proved that our study is of great significance and the level of hypersensitive c-reactive protein could be used as an early diagnostic index for the diagnosis of pediatric infections.

In this paper, our results showed that the levels of procalcitonin and hypersensitive c-reactive protein were of great importance for the clinical diagnosis. It could help to diagnose, monitor the disease and enhance the accuracy of diagnosis, so the detection of procalcitonin and hypersensitive c-reactive protein could be widely applied to the clinical diagnosis of pediatric patients.

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