

# Clinical significance of serum procalcitonin level monitoring on early diagnosis of severe pneumonia on children

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**Abstract. – OBJECTIVE:** To discuss the method for early diagnosis of severe pneumonia on children.

**PATIENTS AND METHODS:** Fifty-six children with severe pneumonia were enrolled from Department of Pediatrics and Intensive Care Unit (ICU) of our hospital and divided into two groups according to parasitological detection: bacterial pneumonia group consisting of 34 children patients and non-bacterial pneumonia group of 32 children patients. In the meanwhile, 37 healthy children, who were confirmed without infection through physical examination, were also enrolled and grouped in into normal control group. Peripheral venous blood of all children was collected to detect their procalcitonin (PCT).

**RESULTS:** PCT level of patients in bacterial pneumonia group was significantly higher than that in the non-bacterial pneumonia group and control group, and difference had statistical significance ( $p < 0.01$ ); serum PCT level on patients in bacterial pneumonia group before and after treatment had statistical significance ( $p < 0.01$ ); serum PCT level on patients in non-bacterial pneumonia group before and after treatment had no statistical significance ( $p > 0.05$ ).

**CONCLUSIONS:** PCT was a very important biomarker for the diagnosis of bacterial infection and also a sensitive indicator for the distinction of child bacterial pneumonia and non-bacterial pneumonia. It had significant clinical diagnosis and differential diagnosis value.

*Key Words:*

Severe pneumonia, CRP, PCT.

## Introduction

Nowadays, infantile pneumonia, especially severe pneumonia, has become one of the most common diseases and frequently occurring diseases that would seriously threaten children's lives<sup>1-3</sup>. Severe pneumonia is characterized for its acute onset, severe condition, and long course. Any delayed rescue or inappropriate treatment

would result in death<sup>4-6</sup>. From the perspective of etiology, infantile pneumonia is mainly resulted from bacterial infection, virus infection, and *Mycoplasma pneumoniae* infection. Different treatment methods shall be applied corresponding to different pathogen infections<sup>7-10</sup>. In clinic, the most widely used parasitological detection methods include sputum culture, blood culture, etc. But all of them have limitations. So, it is of vital significance for us to choose a quicker, a highly sensitive, and specific laboratory index for the early diagnosis of children severe pneumonia<sup>11</sup>. In recent years, procalcitonin (PCT) has been regarded as a very important biomarker for the diagnosis of systemic bacterial infection. C-reactive protein (CRP), as a kind of acute phase reaction protein, is closely related with inflammatory reaction and tissue injuries<sup>12-14</sup>. In this paper, we aim to discuss the value of serum PCT on the early diagnosis of children severe pneumonia through monitoring the serum PCT concentration on children diagnosed with severe pneumonia.

## Patients and Methods

### Patients

Sixty-five children with severe pneumonia, who were hospitalized in the Department of Pediatrics and ICU of our hospital during January 2010 and January 2014, were enrolled in our study, all of which conformed to the diagnosis criteria formulated mutually by Infectious Diseases Society of America (IDSA) and American Thoracic Society (ATS) in 2007<sup>15</sup> and were divided into two groups according to parasitological detection: bacterial pneumonia group consisting of 34 children patients, of which were 16 cases of male and 18 cases of female, being aged between 10 months and 6 years old and non-bacterial pneumonia group consisting of 32 children patients, of which were 15 cases of male and 17

cases of female, being aged between 11 months and 7 years old. In the meanwhile, 37 healthy children who were confirmed without infection through physical examination were also enrolled and grouped in into normal control group, of which were 17 cases of male and 20 cases of female being aged between 10 months and 6.5 years old.

### Detection Method

Peripheral venous blood of all children was collected and sent to clinical laboratory to detect their PCT, CPR (C reactive protein), and WBC. Roche MODULARE170 electrochemistry luminescence immunity determinator (Roche, Basel, Switzerland) was applied to detect PCT. Reagent came from Roche and testing principle was double antibody sandwich method; immunity transmission turbidity was applied to detect CRP and kit was original reagent provided by Dade Behring Inc., and detection was made through Behring II special protein instrument (Dade Behring, Washington, DC, USA); WBC was detected by Beckman-Coulter LH750 blood analyzer with original kit (Beckman-Coulter, Brea, CA, USA).

### Statistical Analysis

SSPS10.0 software (IBM, New York, USA) was applied to make statistical analysis, measurement data was presented by mean  $\pm$  standard deviation ( $\pm S$ ), *t*-test was used to make comparisons between groups, chi-square test was adopted to test enumeration data.  $p < 0.05$  was considered with statistical significance.

## Results

PCT level of patients in bacterial pneumonia group was significantly higher than that in the

non-bacterial pneumonia group and control group, and difference had statistical significance ( $p < 0.01$ ); serum PCT level on patients in bacterial pneumonia group before and after treatment had statistical significance ( $p < 0.01$ ); serum PCT level on patients in non-bacterial pneumonia group before and after treatment had no statistical significance ( $p > 0.05$ ) (Table I).

## Discussion

Early diagnosis was of great clinical value in reducing the occurrence of severe pneumonia, and improving the patient children's prognosis. But till now, there is still lack of indicators for the early diagnosis of severe pneumonia. PCT was the precursor substance of calcitonin, which was mainly compounded in thyroid parafollicular cells. It was a kind of hormone-free active glycoproteins, whose molecular weight was 13kU. In recent years, it has become a new biomarker to identify severe bacterial infections<sup>16-20</sup>.

Infectious pneumonia was a common children disease. Its pathogen included bacteria, virus, mycoplasma, fungus, so on and so forth. In clinic, it was hard to judge out its pathogen according to WBC count. WBC count could hint severe bacterial infections, but its diagnostic specificity was very poor. CRP was a kind of acute protein, whose level could be elevated by various infectious and non-infectious factors and which could be detected out only after 12 hours upon the onset of inflammation, so its coincidence rate was not as good as PCT in the diagnosis of adult bacterial infection<sup>21</sup>. PCT, during physiological conditions, was produced by thyroid-C cell and its volume was extremely few and could hardly be detected in the serum of healthy groups. When the patients were suffering from bacterial, fungal, and parasitic diseases and systemic inflammatory

**Table I.** PCT detection results of the three groups before and after treatment ( $X \pm S$ ).

Group	Cases	PCT ( $\mu\text{g/L}$ )	
		Pre-treatment	Post-treatment
Bacterial pneumonia group	36	12.0 $\pm$ 6.7* <sup>#</sup>	2.1 $\pm$ 0.8
Non-bacterial pneumonia group	35	2.8 $\pm$ 1.2 <sup>A</sup>	2.4 $\pm$ 0.7
Control group	37		1.1 $\pm$ 0.2

\*Compared with bacterial pneumonia group after treatment, \* $p < 0.01$ ; <sup>#</sup>Compared with non-bacterial pneumonia group before treatment and the control group, <sup>#</sup> $p < 0.01$ ; <sup>A</sup>Compared with non-bacterial pneumonia group after treatment, difference had no statistical significance,  $p > 0.05$ .

reactions, PCT could be induced by endotoxin of pathogenic bacterium and be produced by thyroid-C cells, and other tissues including macrophage and monocyte in liver, lymphocyte in lung and intestinal tissues as well as neuroendocrine cells and, thus, would lead PCT level to rise or ascend significantly. Moreover, it was also positively related with the degree, development, or recession of infection. However, PCT level on patients suffering virus infection, chronic nonspecific inflammation, tumorous fever, autoimmune diseases, and operative wounds would not increase or increase only slightly<sup>22,23</sup>. Its sensitivity was higher than the detection of traditional C-reactive protein and peripheral blood leucocyte count. It was an important marker for the diagnosis of bacterial infection and a sensitive indicator for the distinction of bacterial pneumonia and non-bacterial pneumonia, and thus was of great clinical diagnosis value and differential diagnosis value. Nowadays, PCT has become a significant biological inflammatory diagnosis biomarker and routine examination<sup>24,25</sup>.

Severe pneumonia was characterized for its serious infection, rapid onset, and high mortality. If infection could be effectively controlled in the early period of severe pneumonia, the prognosis of patients could be greatly improved. So, an appropriate antibiotic therapy was important. Although bacterial culture could precisely instruct the application of clinical antibiotic, its culture period was too long, thus, making little sense in early therapy<sup>26,27</sup>.

## Conclusions

The result of our study showed that PCT level of patients in bacterial pneumonia group was significantly higher than that in the non-bacterial pneumonia group and control group, and difference had statistical significance ( $p < 0.01$ ); serum PCT level on patients in bacterial pneumonia group before and after treatment had statistical significance ( $p < 0.01$ ); serum PCT level on patients in non-bacterial pneumonia group before and after treatment had no statistical significance ( $p > 0.05$ ), all of which indicated that the rise of PCT level could be used as a marker protein in acute phase after bacterial infection and had great guiding significance in the early diagnosis and identification of infection as well as evaluation of disease severity and instruction of proper use of antibiotics.

## Conflict of Interest

The Authors declare that there are no conflicts of interest.

## References

- 1) XIAOMENG Z, JIARUI W, BING Z, LING D. Potassium dehydro and rographolide succinate injection for treatment of infantile pneumonia: a systematic review and meta-analysis. *J Tradit Chin Med* 2015; 35: 125-133.
- 2) AL J, WANG SC, DAI M, CHEN S, YI ZX, DAI QG, XU S. Relevant pathogenesis of heat and phlegm in infantile viral pneumonia: an analysis by association rules. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2013; 33: 1485-1488.
- 3) CHEN CH, WEN HJ, CHEN PC, LIN SJ, CHIANG TL, HSIEH IC, GUO YL. Prenatal and postnatal risk factors for infantile pneumonia in a representative birth cohort. *Epidemiol Infect* 2012; 140: 1277-1285.
- 4) KURVERS RA, WESTRA D, VAN HEIJST AF, WALK TL, WARRIS A, VAN DE KAR NC. Severe infantile Bordetella pertussis pneumonia in monozygotic twins with a congenital C3 deficiency. *Eur J Pediatr* 2014; 173: 1591-1594.
- 5) ZHU R, LUO L, ZHAO L, DENG J, WANG F, SUN Y, SONG Q, DING Y, QIAN Y. Characteristics of the mosaic genome of a human parechovirus type 1 strain isolated from an infant with pneumonia in China. *Infect Genet Evol* 2015; 29: 91-98.
- 6) YAN Y, YUE GL. Effect of auxiliary Chinese medicine drug therapy via percutaneous medication in treating 78 patients with infantile pneumonia. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2010; 30: 772-773.
- 7) BIN GADEEM H, BARNA M, TÓTH A, JANÁKÓ M. Cryptosporidium as a co-pathogen in infantile diarrhea and pneumonia. *Orv Hetil* 1990; 131: 1423-1425.
- 8) HYVÄRINEN M, PIIPPO-SAVOLAINEN E, KORHONEN K, KORPPI M. Teenage asthma after severe infantile bronchiolitis or pneumonia. *Acta Paediatr* 2005; 94: 1378-1383.
- 9) SCHAAD UB, ROSSI E. Infantile chlamydial pneumonia-a review based on 115 cases. *Eur J Pediatr* 1982; 138: 105-109.
- 10) ONO M, TAKEDA K, OKUDA Y, NAKAMURA K, YAMAGUCHI N. Chest X-ray findings in infantile Chlamydia trachomatis pneumonia; report of two cases. *Rinsho Hoshasen* 1989; 34: 173-176.
- 11) CANTANI A, ARCESE G, SERRA A, LUCENTI P. Effectiveness of a test for verification of the presence of acari in house dust for the prevention of respiratory allergies in children. *Riv Eur Sci Med Pharmacol Sci* 1995; 17: 3-9.
- 12) LIU YJ, DU P, RAO J. Procalcitonin as a diagnostic and prognostic marker for sepsis caused by intestinal infection: a case report. *Eur Rev Med Pharmacol Sci* 2013; 17: 1311-1313.

- 13) NIU WY, WAN YG, LI MY, WU ZX, ZHANG LG, WANG JX. The diagnostic value of serum procalcitonin, IL-10 and C-reactive protein in community acquired pneumonia and tuberculosis. *Eur Rev Med Pharmacol Sci* 2013; 17: 3329-3333.
- 14) MAGRINI L, TRAVAGLINO F, MARINO R, FERRI E, DE BERNARDINI B, CARDELLI P, SALERNO G, DI SOMMA S. Procalcitonin variations after Emergency Department admission are highly predictive of hospital mortality in patients with acute infectious diseases. *Eur Rev Med Pharmacol Sci* 2013; 17 (Suppl 1): 133-142.
- 15) MANDELL LA, WUNDERINK RC, ANZUETO A, BARTLETT JG, CAMPBELL GD, DEAN NC, DOWELL SF, FILE TM JR, MUSER DM, NIEDERMAN MS, TORRES A, WHITNEY CG; INFECTIOUS DISEASES SOCIETY OF AMERICA; AMERICAN THORACIC SOCIETY. Infectious Disease Society of America/ American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. *Clin Infect Dis* 2007; 44: S27-72.
- 16) LIDAN C, QUNSI W, HONG X. Dynamic change and value of serum procalcitonin level on children with systemic inflammatory response syndrome. *Chin Pediatr Emerg Med* 2008; 15: 113-115.
- 17) PAOSONG S, NARONGROEKNAWIN P, PAKCHOTANON R, ASAVATANABODEE P, CHAIAMNUAY S. Serum procalcitonin as a diagnostic aid in patients with acute bacterial septic arthritis. *Int J Rheum Dis* 2015; 18: 352-359.
- 18) KIM SY, JEONG TD, LEE W, CHUN S, MIN WK. Procalcitonin in the assessment of bacteraemia in emergency department patients: results of a large retrospective study. *Ann Clin Biochem* 2015; 52: 654-659.
- 19) ANAND D, DAS S, BHARGAVA S, SRIVASTAVA LM, GARG A, TYAGI N, TANEJA S, RAY S. Procalcitonin as a rapid diagnostic biomarker to differentiate between culture-negative bacterial sepsis and systemic inflammatory response syndrome: a prospective, observational, cohort study. *J Crit Care* 2015; 30: 218.e7-12.
- 20) FRIEND KE, BURGESS JN, BRITT RC, COLLINS JN, WEIRETER LN, NOVOSSEL TJ, BRITT LD. Procalcitonin elevation suggests a septic source. *Am Surg* 2014; 80: 906-909.
- 21) ZHUING L, YAJING Z, XIN W. Measurement of children with severe pneumonia PCT resulted from different infectious agents and the change of C-reactive protein and white blood cell count and its clinical significance. *Chin J Heal Bir Child Care* 2009; 15: 19-21.
- 22) QIAOLIAN X, HAN L, YING L. Monitor serum procalcitonin level to optimize the anti-infectious treatment strategy of severe pneumonia. *J Molec Biol* 2013; 12: 348-350.
- 23) LEI Z, AIQUN X, HEXIANG N. Diagnostic significance of serum procalcitonin in severe pneumonia. *Acad J Chin PLA Med School* 2013; 34: 112-114.
- 24) WENBIN C, XIANGLIN P. *Diagnostics*. The 7th edition. Beijing: People's Medical Publishing House 2010; pp. 439-440.
- 25) WANG Y, JI W, CHEN Z, YAN YD, SHAO X, XU J. Comparison of severe pneumonia caused by Human metapneumovirus and respiratory syncytial virus in hospitalized children. *Indian J Pathol Microbiol* 2014; 57: 413-417.
- 26) FISCHER N, ROHDE H, INDENBIRKEN D, GÜNTHER T, REUMANN K, LÜTGEHETMANN M, MEYER T, KLUGE S, AEPFELBACHER M, ALAWI M, GRUNDHOFF A. Rapid metagenomic diagnostics for suspected outbreak of severe pneumonia. *Emerg Infect Dis* 2014; 20: 1072-1075.
- 27) HUONGPLE T, HIEN PT, LAN NT, BINH TQ, TUAN DM, ANH DD. First report on prevalence and risk factors of severe atypical pneumonia in Vietnamese children aged 1-15 years. *BMC Public Health* 2014; 14:1304.