ORIGINAL RESEARCH



Clinical application of C-reactive protein, leukocyte and immunoglobulin in the diagnosis and treatment of infantile pneumonia at acute stage

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Abstract

This study aims to explore the clinical significance of C-reactive protein, leukocyte and immunoglobulin in the diagnosis and treatment of infantile pneumonia at acute stage. From January to December 2018, a total of 124 children with pneumonia and healthy children admitted to our hospital were selected as study objects. Among them, 62 children diagnosed with bacterial pneumonia were categorized as the study group, and 62 healthy children who came for physical examination were classified as the control group. The levels of C-reactive protein (CRP), white blood cell (WBC) and immunoglobulin (IgA, IgM and IgG) were observed and compared in the two groups. In this study, higher levels of CRP, IgM, IgG and WBC, along with lower level of IgA were observed in the study group as compared with that in the control group. In the study group, the levels of CRP, IgM, IgG and WBC were lower, but the IgA level was higher in children with mild pneumonia than those with severe pneumonia. After treatment, the levels of CRP, IgM, IgG and WBC were decreased but IgA level was increased after treatment compared with before treatment. In particular, the levels of CRP, WBC, IgA, IgM and IgG in the study group after treatment were restored to comparable levels compared with the control group. Therefore, C-reactive protein, leukocyte and immunoglobulin can be used to determine the diagnosis, condition and outcome of children with pneumonia in the acute stage. This study can provide guidance for clinical diagnosis and treatment of infantile pneumonia based on the alterations of these indicators.

Keywords

C-reactive protein; White blood cells; Immunoglobulin; Acute stage; Infantile pneumonia

1. Introduction

Pneumonia is one of the most common types of disease in pediatric patients, with a high incidence. The proportion of children with pneumonia among pediatric hospitalized patients in China is relatively high, which can be as high as 25–56% [1]. Pediatric patients are young, and various physical functions are not fully developed, and dangerous disease development is common in children at acute stage, with difficulties in clinical response and treatment. Therefore, children with acute pneumonia should be detected, diagnosed, and treated at early stage [2, 3]. There are many relevant indicators used in clinical practice to detect inflammation, and the selection of indicators that can effectively determine the acute stage of infection in children with pneumonia is an important guide to the clinical diagnosis and treatment of children infected with pneumonia [4, 5]. In view of this, this study aims to explore the clinical significance of C-reactive protein, leukocyte and immunoglobulin in the diagnosis and treatment of infantile pneumonia in the acute stage. Children with pneumonia and healthy children admitted to our hospital from January to December 2018 were selected as the study objects for comparative research and the study invalided the important role of C-reactive protein, leukocyte and immunoglobulin in the diagnosis and treatment of infantile pneumonia in the acute stage.

2. Materials and methods

2.1 Clinical information

From January to December 2018, a total of 124 children with pneumonia and healthy children admitted to our hospital were selected for this study. Among them, 62 children diagnosed with bacterial pneumonia were categorized as the study group, while 62 healthy children who came to our hospital for physical examination during the same period were classified as the control group. In the study group, there were 32 males and 30 females, aged 1–11 years with an average age of 5.76 ± 1.02 years. They all met the diagnostic criteria for acute infantile

pneumonia, including 34 severe cases and 28 mild cases. In the control group, there were 33 males and 29 females, aged 1-11 years with an average age of 5.79 ± 1.04 years. There were no significant differences in clinical data such as gender and age between the two groups, and the results of the studies were comparable.

2.2 Sample collection

In the early morning, 3 mL of venous blood of the study objects was drawn on an empty stomach and placed in a centrifuge (Beijing Baiyang Centrifuge, Co., Ltd, Beijing, China) at 2000 r/min for 10 min to separate the serum. The serum was stored in a cryogenic environment at -70 °C. If hemolysis was found in the specimen, the patient's blood sample was recollected and separated as described above.

2.3 Measurement of indicators

The C-reactive protein (CRP), white blood cell (WBC) and immunoglobulin (IgA, IgM and IgG) were observed and compared in the study and control groups. The levels of CRP and immunoglobulin were determined by immunoturbidimetry (Shenzhen Mindray Bio-Medical Electronics Co., Ltd., Shenzhen, China). Blood routine and WBC count were analyzed by a Mindray Automatic Blood Cell Analyzer (BC-5390CRP). The relevant operations were carried out in strict accordance with the manufacturer's instructions.

2.4 Treatment

The children were administrated with Chinese herbal medicine and Western medicine as an adjuvant therapy. Chinese herbal medicine is prepared in appropriate amounts with various Chinese herbs and taken orally, such as astragalus, platycodon grandiflorum, peppermint, semen brassicae, almonds, gypsum, pinellia ternata, honeysuckle, houttuynia, ephedra, *etc.* To calm the lung asthma, clear heat and resolve phlegm, and supplemented with penicillin or ampicillin dissolved in 5% glucose solution after intravenous drip (skin test qualified) or erythromycin, azithromycin, *etc.*

2.5 Statistics

SPSS (22.0, SPSS Inc., Chicago, IL, USA) software was used for data analyses. The quantitative data were represented as $(\bar{x} \pm s)$, and the categorical data were described as proportion (%). The quantitative data conforming to a normal distribution were analyzed by *t*-test, while χ^2 test was used for the categorical data. A *p* value less than 0.05 was considered as statistically significant.

3. Results

3.1 Comparisons of observational indicators between Study and Control groups

Higher levels of CRP, IgM, IgG and WBC, along with lower level of IgA were observed in the study group as compared with that in the control group. The differences were statistically significant (p < 0.05). As shown in Table 1.

3.2 Comparisons of observational indicators in children with mild or sever pneumonia in the study group

In the study group, the levels of CRP, IgM, IgG, and WBC were lower, but the IgA level was higher in children with mild pneumonia than those with severe pneumonia. The differences were statistically significant (p < 0.05). As shown in Table 2.

3.3 Comparisons of observational indicators before and after treatment in the study group

In the study group, the levels of CRP, IgM, IgG and WBC were decreased but IgA level was increased after treatment compared with before treatment. The differences were statistically significant (p < 0.05). As shown in Table 3. Besides, compared with that in the control group, the levels of CRP, WBC, IgA, IgM and IgG in the study group after treatment were not significantly different (Table 4). To some extent, this result indicated the effective effects of the treatment for children with pneumonia.

4. Discussion

Clinical data have shown that the main pathogen causing pneumonia in children is Mycoplasma pneumoniae [6–8]. Children with Mycoplasma pneumoniae infection account for up to 30% of all children with acquired pneumonia. Moreover, in recent years, this phenomenon has been on the rise, while the age of children has shown a decreasing trend [9]. After the onset of the disease, lung function may be compromised to some extent as the disease progresses, leading to an increased burden on the cardiovascular system, liver and kidney, as well as the blood systems. Since children are at a critical period of growth and development, it thus can be a direct threat to the child's life and health in severe cases [10–12].

The study of infantile pneumonia has become one of the key and topical issues in clinical research [13]. At present, there is no unanimous clinical conclusion on the exact pathogenesis of infantile pneumonia caused by Mycoplasma pneumoniae infection. Some of these beliefs are supported by a proportion of clinicians, including the involvement of both cellular and humoral immune function and the inflammatory response status in children with pneumonia in the progression of this disease [14–16]. Meanwhile, it is generally accepted that how to effectively and scientifically clarify the acute phase of pediatric pneumonia and how to effectively determine the progression of children's disease is of great practical significance for the clinical treatment of infantile pneumonia [17].

According to the above conclusions, our hospital actively summarizes clinical experience and continuously explores clinical practice. In clinical practice, it has been found that CRP, WBC and immunoglobulin are of great significance in determining the acute phase of children with pneumonia and in discriminating the clinical treatment effects [18, 19].

In this study, higher levels of CRP, IgM, IgG and WBC, along with lower level of IgA were observed in the study group as compared with that in the control group. In the study group, the levels of CRP, IgM, IgG and WBC were lower, but the

TABLE 1. Comparisons of observational indicators between study and control groups $(x \pm s)$.								
Group	Ν	CRP (g/L)	IgA (g/L)	IgM (g/L)	IgG (g/L)	WBC (×10 ⁹ /L)		
Study group	62	38.61 ± 16.14	0.86 ± 0.20	1.62 ± 0.31	9.63 ± 1.83	20.76 ± 5.47		
Control group	62	1.64 ± 0.23	1.42 ± 0.34	0.98 ± 0.11	4.39 ± 0.42	6.21 ± 0.45		
<i>t</i> value		18.0342	11.1784	15.3201	21.9750	20.8741		
<i>p</i> value	—	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001		

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CRP: C-reactive protein; WBC: white blood cell; IgA, IgM and IgG: immunoglobulin.

TABLE 2. Comparisons of observational indicators in children with mild or sever pneumonia in the study group

$(\bar{x} \pm s).$								
Group	Ν	CRP (g/L)	IgA (g/L)	IgM (g/L)	IgG (g/L)	WBC (×10 ⁹ /L)		
Severe	34	52.68 ± 5.15	0.71 ± 0.10	1.87 ± 0.15	10.98 ± 1.24	25.31 ± 2.51		
Mild	28	21.53 ± 2.11	1.05 ± 0.11	1.31 ± 0.06	8.00 ± 0.81	15.24 ± 1.54		
t value		44.0708	18.0085	27.2938	15.8425	27.7283		
<i>p</i> value		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001		

CRP: C-reactive protein; WBC: white blood cell; IgA, IgM and IgG: immunoglobulin.

TABLE 3. Comparisons of observational indicators before and after treatment in the study group ($ar{x}~\pm~s$).								
Group	Ν	CRP (g/L)	IgA (g/L)	IgM (g/L)	IgG (g/L)	WBC (×10 ⁹ /L)		
Before treatment	62	38.61 ± 16.14	0.86 ± 0.20	1.62 ± 0.31	9.63 ± 1.83	20.76 ± 5.47		
After treatment	62	1.71 ± 0.21	1.35 ± 0.23	1.01 ± 0.08	4.41 ± 0.69	6.33 ± 0.40		
t value		18.0004	12.6586	15.0025	21.0160	20.7165		
<i>p</i> value	—	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001		

CRP: C-reactive protein; WBC: white blood cell; IgA, IgM and IgG: immunoglobulin.

TABLE 4. Comparisons of observational indicators between the study group after treatment and the control group

			$(x \pm s)$.			
Group	Ν	CRP (g/L)	IgA (g/L)	IgM (g/L)	IgG (g/L)	WBC (×10 ⁹ /L)
Study group after treatment	62	1.71 ± 0.21	1.35 ± 0.23	1.01 ± 0.08	4.41 ± 0.69	6.33 ± 0.40
Control group	62	1.64 ± 0.23	1.42 ± 0.34	0.98 ± 0.11	4.39 ± 0.42	6.21 ± 0.45
<i>t</i> value		1.7697	1.3427	1.7367	0.1950	1.5694
<i>p</i> value	—	0.0793	0.1818	0.0850	0.8458	0.1192

CRP: *C*-reactive protein; *WBC*: white blood cell; *IgA*, *IgM* and *IgG*: immunoglobulin.

IgA level was higher in children with mild pneumonia than those with severe pneumonia. After treatment, the levels of CRP, IgM, IgG and WBC were decreased but IgA level was increased after treatment compared with before treatment. In particular, the levels of CRP, WBC, IgA, IgM and IgG in the study group after treatment were restored to comparable levels compared with the control group. These results were consistent with investigations in the previous reports [20-22].

After further investigation, CRP, as a commonly used indicator in clinical tests, can exclude the influences of individual differences in patients, such as age, gender, and even anemia [23–25]. CRP is expressed at high levels when the body is infected or has accumulated immune complex for other causes. Increased levels of CRP can effectively activate the relevant complement locally in patients and can effectively promote

the function of phagocytes. In turn, it can fight pathogenic bacteria and microorganisms that invade the human body, and also effectively remove damaged necrotic cells caused by infection and inflammation. It is clinically sensitive compared to other indicators, especially in distinguishing bacterial from nonbacterial infections and in determining the status and extent of the inflammatory response [26, 27].

The highest proportion of immunoglobulin indicators is IgG, which is produced in the spleen and lymphatic system and accounts for approximately 75% of all immunoglobulins. It has a relatively long half-life and is the basis for the body's defence against external infections and internal inflammatory responses. IgG is most persistent in the body's primary immune response. IgA, which is second only to IgG, accounting for about 10-20% of immunoglobulins, acts mainly on the

mucosal tissues of the respiratory tract and digestive tracts of the human body, producing a targeted immune response to these systems and defending them against interfering factors. Compared to immunoglobulins such as IgG and IgA, IgM is relatively small in quantity, but has the largest molecular weight. Like IgG, it is produced in the body's spleen and lymphatic system. IgM has a pronounced bactericidal effect on bacteria and, similar to CRP, it activates relevant complement locally and can exert immunomodulatory effects and promote phagocytosis. As one of the important components of immunoglobulins, IgM has the same characteristics as CRP to exclude the influences of individual differences, shows a high sensitivity and is often used for clinical differential diagnosis [28, 29]. Other clinical studies have shown that ABC count is also an important indicator commonly used to determine bacterial infection in patients, but it is susceptible to a number of factors that can lead to a lower percentage of positivity compared to indicators such as CRP and IgM [30, 31]. However, this phenomenon was not reflected in the data from this study, which may be related to the small sample size of this study and the exclusion of differences in age, gender and other factors [32, 33].

5. Conclusions

In conclusion, C-reactive protein, leukocytes and immunoglobulins can be used to determine the diagnosis, condition and outcome of children with pneumonia in the acute phase, and changes in these indicators can be used to provide guidance for the clinical diagnosis and treatment of infantile pneumonia.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

JXC, WL and CBY—designed the research study. JXC, WL and CBY—performed the research. JXC, WL and CBY analyzed the data. JXC, WL and CBY—wrote the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Beijing Luhe Hospital, Capital Medical University (Approval no. 2018018). Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

- [1] Marzollo A, Conti F, Rossini L, Rivalta B, Leonardi L, Tretti C, et al. Neonatal manifestations of chronic granulomatous disease: MAS/HLH and necrotizing pneumonia as unusual phenotypes and review of the literature. Journal of Clinical Immunology. 2022; 42: 299–311.
- [2] Nenna R, Iovine E, Laudisa M, Bloise S, La Regina DP, Midulla F. Comment on Jaworska, J. *et al.* Consensus on the application of lung ultrasound in pneumonia and bronchiolitis in children. *Diagnostics 2020*, *10*, 935. Diagnostics. 2021; 11: 55.
- [3] Lee J, Lin J, Chen H, Wang C, Lu C, Chang L, et al. Impact of pneumococcal conjugate vaccination on hospitalized childhood pneumonia in Taiwan. Pediatric Research. 2022; 92: 1161–1167.
- [4] Luo Z, Wei H, Li X. Granulocyte-macrophage colony-stimulating factor suppresses induction of type I interferon in infants with severe pneumonia. To be published in Pediatric Research. 2022. [Preprint].
- [5] Roncin C, Vanel N, Morand A, Belghiti Alaoui M, Michel F. Systematic endotracheal aspiration in the pediatric intensive care unit reduces broadspectrum antibiotic use for ventilator-associated pneumonia. Pediatric Infectious Disease Journal. 2022; 41: 544–548.
- [6] Ding N, Liu D, Duan X, Zhang J, Ma S, Chen Y. Twist2 reduced NLRP3-induced inflammation of infantile pneumonia *via* regulation of mitochondrial permeability transition by FOXO1. International Archives of Allergy and Immunology. 2022; 183: 1098–1113.
- [7] Dudognon D, Levy C, Chalumeau M, Biscardi S, Dommergues MA, Dubos F, *et al.* Diagnostic accuracy of routinely available biomarkers to predict bacteremia in children with community-acquired pneumonia: a secondary analysis of the GPIP/ACTIV pneumonia study in France, 2009–2018. Frontiers in Pediatrics. 2021; 9: 684628.
- [8] Maggio M, Cimaz R, Failla M, Dones P, Corsello G. Typical Kawasaki disease with atypical pneumonia: a paediatric case report. Scandinavian Journal of Rheumatology. 2021; 50: 248–249.
- [9] Chen L, Chen Y, Huang J, Zhang J. LncRNA LINC00707 serves as a sponge of miR-382-5p to alleviate lipopolysaccharide (LPS)-induced WI-38 cell injury through upregulating NKAP in infantile pneumonia. Autoimmunity. 2022; 55: 328–338.
- Yu Y, Yang T, Ding Z, Cao Y. Circ_0026579 alleviates LPS-induced WI-38 cells inflammation injury in infantile pneumonia. Innate Immunity. 2022; 28: 37–48.
- [11] Cui J, Wang J, Lv Y, Xu D. LncRNA NEAT1 regulates infantile pneumonia by sponging miR-146b. Molecular Biotechnology. 2021; 63: 694–701.
- [12] Zhang J, Wang CH, Liu XJ, Cheng SF, Han LH, Lv CL. Efficacy and safety analysis of dopamine combined with creatine phosphate sodium in the treatment of infantile pneumonia combined with heart failure. Journal of Biological Regulators and Homeostatic Agents. 2020; 34: 2103–2108.
- [13] Iovine E, Petrarca L, Regina DP, Matera L, Mancino E, Di Mattia G, *et al.* The key role of lung ultrasound in the diagnosis of a mature cystic teratoma in a child with suspected difficult to treat pneumonia: a case report. Children. 2022; 9: 555.
- [14] Xie F, Chen R, Zhao J, Xu C, Zan C, Yue B, *et al.* Cell cycle kinase CHEK2 in macrophages alleviates the inflammatory response to *staphylococcus aureus*-induced pneumonia. To be published in Experimental Lung Research. 2022. [Preprint].
- [15] Ding N, Meng Y, Liu L, Ma S, Chen Y. Sphingosine Kinase-1 (SPHK1) promotes inflammation in infantile pneumonia by regulating NLRP3 inflammasome and SIRT1 expression. To be published in Histology and Histopathology. 2022. [Preprint].
- [16] Albrijawy R, Alomar K, Aldeen RS, Sharief FAL, Saleh IEA, Hamdan O. Case report: a rare case of congenital non-metastatic low-grade

fibrosarcoma of the pleura in a 6-month-old infant manifested as pneumonia. International Journal of Surgery Case Reports. 2022; 99: 107714.

- [17] AlShamrani AS, Alzaid MA, Fadl SM, AlFaki MA. A case of infantile exogenous lipoid pneumonia with an unusual complication managed by modified whole lung lavage. Sudanese Journal of Paediatrics. 2021; 21: 82–88.
- [18] Naraoka T, Sumi T, Keira Y, Nakata H, Chiba H. Epirubicin and cyclophosphamide-induced acute fibrinous and organizing pneumonia. American Journal of Respiratory and Critical Care Medicine. 2021; 204: e92–e93.
- [19] Wu Z, Liu Y, Xu J, Xie J, Zhang S, Huang L, *et al.* A ventilator-associated pneumonia prediction model in patients with acute respiratory distress syndrome. Clinical Infectious Diseases. 2020; 71: S400–S408.
- [20] Cornely OA, File TM, Garrity-Ryan L, Chitra S, Noble R, McGovern PC. Safety and efficacy of omadacycline for treatment of community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections in patients with mild-to-moderate renal impairment. International Journal of Antimicrobial Agents. 2021; 57: 106263.
- [21] Liang J, Yin Z, Li Z, Gu H, Yang K, Xiong Y, et al. Predictors of dysphagia screening and pneumonia among patients with acute ischaemic stroke in China: findings from the Chinese Stroke Center Alliance (CSCA). Stroke and Vascular Neurology. 2022; 7: 294–301.
- [22] Ma Q, Yao C, Shi H, Xu J, Dai H, Fei Z, et al. Targeted delivery of dexamethasone in acute pneumonia. Biomaterials Science. 2021; 9: 5569–5576.
- ^[23] Simoni C, Camozzi P, Faré PB, Bianchetti MG, Kottanattu L, Lava SAG, et al. Myositis and acute kidney injury in bacterial atypical pneumonia: systematic literature review. Journal of Infection and Public Health. 2020; 13: 2020–2024.
- Guo J, Cheng Y. Retraction notice to "MicroRNA-1247 inhibits lipopolysaccharides-induced acute pneumonia in a549 cells *via* targeting CC chemokine ligand 16" [Biomed. Pharmacother. 104 (2018) 60–68]. Biomedicine & Pharmacotherapy. 2021; 142: 111597.
- [25] Lee JH, Yum H, Jamous F, Santos C, Campisi A, Surani S, et al. Diagnostic procedures and clinico-radiological findings of acute fibrinous and organizing pneumonia: a systematic review and pooled analysis. European Radiology. 2021; 31: 7283–7294.
- [26] Klompas M, Branson R, Cawcutt K, Crist M, Eichenwald EC, Greene LR, et al. Strategies to prevent ventilator-associated pneumonia, ventilator-

associated events, and nonventilator hospital-acquired pneumonia in acute-care hospitals: 2022 update. Infection Control & Hospital Epidemiology. 2022; 43: 687–713.

- [27] Hermes Z, Joynt Maddox KE, Yeh RW, Zhao Y, Shen C, Wadhera RK. Neighborhood socioeconomic disadvantage and mortality among medicare beneficiaries hospitalized for acute myocardial infarction, heart failure, and pneumonia. Journal of General Internal Medicine. 2022; 37: 1894–1901.
- [28] Leroy AG, Caillon J, Caroff N, Broquet A, Corvec S, Asehnoune K, et al. Could azithromycin be part of *pseudomonas aeruginosa* acute pneumonia treatment? Frontiers in Microbiology. 2021; 12: 642541.
- ^[29] Wang Z, Cai R, Wang G, et al. Combination therapy of phage vB_KpnM_P-KP2 and gentamicin combats acute pneumonia caused by K47 serotype *klebsiella pneumoniae*. Frontiers in Microbiology. 2021; 12: 674068.
- [30] Siegel ER, Croze RH, Fang X, Matthay MA, Gotts JE. Inhibition of the lipoxin A4 and resolvin D1 receptor impairs host response to acute lung injury caused by pneumococcal pneumonia in mice. American Journal of Physiology-Lung Cellular and Molecular Physiology. 2021; 320: L1085– L1092.
- [31] Mazzola M, Pugliese NR, Zavagli M, De Biase N, Bandini G, Barbarisi G, et al. Diagnostic and prognostic value of lung ultrasound b-lines in acute heart failure with concomitant pneumonia. Frontiers in Cardiovascular Medicine. 2021; 8: 693912.
- [32] Guo Z, Hou J, Yu S, Zhang H, Yu S, Wang H, et al. Eosinophils, strokeassociated pneumonia, and outcome after mechanical thrombectomy for acute ischemic stroke. Frontiers in Aging Neuroscience. 2022; 14: 830858.
- [33] Dai Y, Liu Z, Zhan H, Zhang G, Wang P, Zhang S, et al. Reduced inspiratory muscle strength increases pneumonia in patients with acute myocardial infarction. Annals of Physical and Rehabilitation Medicine. 2022; 65: 101511.

How to cite this article: Junxia Chang, Wei Liu, Changbin Yin. Clinical application of C-reactive protein, leukocyte and immunoglobulin in the diagnosis and treatment of infantile pneumonia at acute stage. Signa Vitae. 2023; 19(5): 225-229. doi: 10.22514/sv.2023.089.