

Research Progress of Combined Detection of WBC, CRP and SAA in Early Diagnosis of Respiratory Tract Infection in Children

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Abstract

Objective: To investigate the application of WBC, CRP and SAA combined detection in the early diagnosis of respiratory tract infection in children. **Methods:** Collect the literature reports on the early diagnosis of respiratory tract infection in children by the combined detection of WBC, CRP and SAA in recent years, and follow up the relevant literature reports from the selection of “new three routine” laboratory items for rapid diagnosis in pediatric outpatient department and the application of the combined detection of WBC, CRP and SAA in the early diagnosis of respiratory tract infection in children. **Results:** Many literature studies found that the combined detection of WBC, CRP and SAA has important clinical significance in the early diagnosis of respiratory tract infection in children. **Conclusion:** Through reviewing the relevant literature, we can understand the application of WBC, CRP and SAA combined detection in the early diagnosis of respiratory tract infection in children. To provide more accurate and reliable laboratory data for the early diagnosis and treatment of respiratory tract infection in children in the future.

Keywords

White Blood Cell Count, C-Reactive Protein, Amyloid Protein-A, Children, Respiratory Tract Infection

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1. Background Introduction

Infectious diseases are the main characteristics of outpatients in paediatrics, and virus infection accounts for the majority. Infectious diseases are the most important cause of morbidity and death in children under the age of 5; About 13 million young children die from various infectious diseases every year worldwide, accounting for 63% of all child deaths. Respiratory tract infection is a common and frequently-occurring disease in children; Especially, the immune system of infants and young children is still immature, and the course of disease is fast; If it is not handled correctly in time, it may cause serious consequences. The main diseases in pediatric outpatient department are upper respiratory tract infection, pharyngo-conjunctival fever, bronchitis, bronchopneumonia, etc.; And the occurrence of disease is related to season and age [1]. According to preliminary statistics and survey, the annual distribution of outpatient diseases in paediatrics of a general hospital was: infectious diseases accounted for 80.95%, mainly respiratory infectious diseases; Non infectious diseases accounted for 12.72%, mainly digestive system diseases; Infectious diseases accounted for 8.31%, mainly viral infectious diseases. The top three were diarrhea, chickenpox and herpetic angina. The pathogens causing respiratory tract infection are usually viruses or bacteria, of which viral infection accounts for almost 80% - 90%. The clinical treatment of viral and bacterial infections is completely different, and antibiotic treatment is not recommended for viral infections. Therefore, it is particularly important to quickly and accurately distinguish the two types of infections. The pediatric outpatient department should first do a good job in the diagnosis and treatment of infectious diseases, especially respiratory infectious diseases [2] [3]. To understand the application of WBC, CRP and SAA in the early diagnosis of respiratory tract infection in children; This study collected literature reports on the combined detection of WBC, CRP and SAA in the early diagnosis of children with respiratory tract infection in recent years, and analyzed and summarized the research progress of the combined detection of WBC, CRP and SAA in the early diagnosis of children with respiratory tract infection. The results are summarized as follows.

2. Selection of “New Three Routine” Laboratory Items for Rapid Diagnosis in Pediatric Outpatient Department

In recent years, the combined detection of WBC, CRP and SAA has been emphasized and implemented in the rapid diagnosis of pediatric outpatient department, and the detection results are helpful for the rapid differential diagnosis of infection types in pediatric patients. The combined use of these three routine tests has been called the “new three routine tests” of pediatric tests by well-known professors of pediatrics, which shows its important clinical value [4] [5]. WBC count is a traditional indicator for clinical observation of bacterial infection; However, due to the large individual differences and wide normal reference range, especially the low functional response in infants, there is no signifi-

cant change in WBC count in some children; In addition, the total number of WBC is easily affected by many factors, such as stress reaction, daytime changes, drug treatment, mental state, etc., which lead to certain limitations in the sensitivity of the diagnosis of infectious diseases in infants and young children; Therefore, other indicators are needed for auxiliary monitoring. At present, the commonly used infection detection indicators in outpatient clinics include blood routine and C-reactive protein (CRP). White blood cell count (WBC) in blood routine is one of the traditional indicators for diagnosis of infection; However, due to many physiological and pathological factors, the type and degree of infection cannot be completely identified. According to Evidence-based Guidelines for the Diagnosis and Dealing with Problems of Acute Fever of Unknown Etiology in Chinese Children aged 0 to 5 Years (Standard Edition), CRP testing can be used as an aid to the early diagnosis of infection. The combined detection of blood routine and CRP improves the detection rate of bacterial infection, while the diagnosis of viral infection still depends on the experience of clinicians. The patients with insignificant clinical symptoms or large individual differences are prone to missed diagnosis and misdiagnosis. For example, when children have a viral cold, blood routine and CRP tests are often at the normal level. When the clinical symptoms are not obvious, it is easy to cause clinical missed diagnosis; For some children with CRP slightly higher than the reference range (for example, the concentration is 5.0 - 15.0 mg/L), if antibiotic drugs are used based on experience, the treatment effect will not be good, but also other adverse effects will be caused by antibiotic abuse. SAA is the only indicator that can significantly increase in the early stage of virus infection. For children with bacterial infection, the detection of pathogenic microorganisms is the standard for the diagnosis of infectious diseases, but the detection time is long (2 - 3 days) and the cost is high; Only known common microorganisms can be detected; At the same time, due to the widespread use of antibiotics and the small collection of standardized children's test samples, the positive rate of detection is low, and it is not suitable for rapid diagnosis in outpatient service [6].

Recent clinical practice and related studies have found that [7], the infection marker serum amyloid A (SAA) is significantly increased in viral infection, and SAA is increased earlier and higher than CRP in bacterial infection; If CRP does not rise with SAA at the same time, it is helpful to establish the basis for virus infection. This characteristic of SAA may overcome the difficulty that the early blood routine & CRP can not diagnose virus infection, and help reduce the missed diagnosis, misdiagnosis and abuse of antibiotics in outpatient patients.

3. Application of WBC, CRP and SAA Combined Detection in Early Diagnosis of Respiratory Tract Infection in Children

The combined detection of WBC, CRP and SAA is increasingly used in the early diagnosis of respiratory tract infection in children [8]. The detection results of

WBC, CRP and SAA were different in bacterial infection and viral infection. After viral and bacterial infection, SAA increased earlier than CRP, with a large range. Within 6 hours of infection, CRP may not have increased significantly; Combined with SAA examination can detect infection early and reduce missed diagnosis and misdiagnosis. SAA has good clinical value in the early stage of infection, such as early detection of septicemia, bacterial pneumonia, streptococcal pharyngitis, post-stroke infection, etc. in premature infants. The degree of SAA increase is related to the severity of the disease; The degree of SAA increase is large, the disease is relatively severe, and can be significantly decreased when the treatment is effective. In viral infections, SAA can effectively assist in dynamic monitoring and efficacy evaluation. In the case of bacterial infection, if the disease is relieved and the treatment is effective, which can decrease earlier than CRP. The performance results are shown in **Table 1**. At present, common viral infections in children include influenza virus, cytomegalovirus infection, varicella zoster, infectious mononucleosis, respiratory syncytial herpes virus, enterovirus, adenovirus infection, etc. See **Figure 1** below for relevant research results.

Table 1. Expression of WBC, SAA and CRP in bacteria and viruses.

| Items | Bacteria | Viruses |
|-------|--|---|
| WBC | rise | normal or reduced |
| CRP | increased significantly | without increasing or slightly increasing |
| SAA | It rises earlier and decreases faster than CRP | Increased significantly |

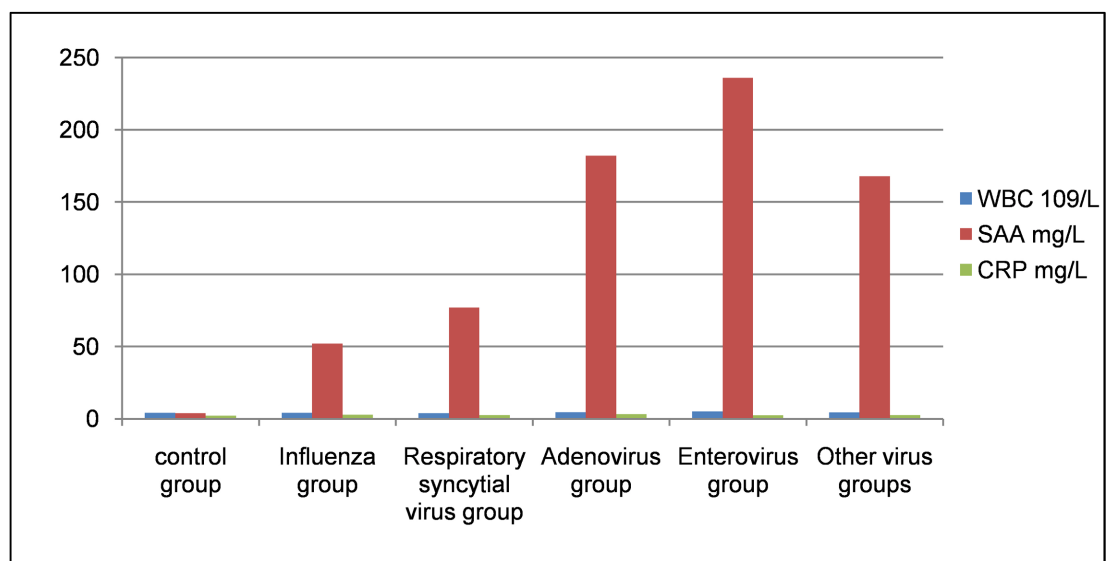


Figure 1. Performance of WBC, SAA and CRP in various viral infection diseases.

In the collected references, in order to explore the diagnostic value of the combined detection of SAA, CRP and WBC in children with acute respiratory infection, Qin Wenzhen [9] [10] [11] tested three indicators. The results showed that the detection levels of CRP and WBC in the bacterial group were higher than those in the viral group and mycoplasma group ($P < 0.05$), and the difference was statistically significant. The detection level of SAA in bacteria group was slightly higher than that in virus group ($P < 0.05$), and the difference was statistically significant; Virus group and bacteria group were higher than mycoplasma group ($P < 0.05$), and the difference was statistically significant. The positive rate of the three combined tests was higher than that of the single tests of SAA, CRP and WBC ($P < 0.05$), and the difference was statistically significant. The researchers believe that there are significant differences in the detection levels of various indicators among the three groups of subjects, and the combined detection of SAA, CRP and WBC is more accurate; For the clinical diagnosis of children with acute respiratory tract infection, the combined detection of SAA, CRP and WBC should be adopted, which has higher application value. In order to explore the clinical diagnostic value of serum amyloid A (SAA), whole-course C-reactive protein (CRP) and white blood cell (WBC) in children with acute upper respiratory tract infection, Zhong Hongwen *et al.* [12] [13] [14] measured serum SAA, whole-course CRP, WBC and other indicators in children with acute upper respiratory tract infection and healthy children respectively, and observed the differences of serum SAA, whole-course CRP, WBC and other indicators between the two groups; Then the results showed that the levels of serum SAA and whole-course CRP in children with acute upper respiratory tract infection were significantly increased, WBC and neutrophil% (N%) were slightly increased, and lymphocyte% (L%) was slightly decreased; The difference between the two was statistically significant ($P < 0.05$). It is believed that the combined detection of serum SAA, whole-course CRP, WBC and other indicators has important clinical significance for the early diagnosis, treatment and prognosis of acute upper respiratory tract infection in children. In order to explore the value of the combined detection of serum amyloid protein (SAA), C-reactive protein (CRP) and white blood cell count (WBC) in the differential diagnosis of acute respiratory tract bacterial infection and *Mycoplasma pneumoniae* infection in children, Cha Wei [15] [16] and others tested three indicators; And the results showed that CRP and WBC in the bacterial infection group were higher than those in the *Mycoplasma pneumoniae* infection group; SAA was lower than that of *Mycoplasma pneumoniae* infection group, and the difference was statistically significant ($P < 0.05$). When SAA, CRP and WBC were used to diagnose bacterial infection, the area under the curve (AUC) of SAA, CRP and WBC were 0.874, 0.967 and 0.708, respectively, and the AUC of the combined detection of the three indexes was 0.993, among which SAA and CRP combined with WBC showed the highest sensitivity in the diagnosis of bacterial infection. When SAA, CRP and WBC were used to diagnose *Mycoplasma pneumoniae* infection, the

AUC of SAA and CRP were 0.924 and 0.846, respectively, and the AUC of combined index detection was 0.946 ($P < 0.05$). It is concluded that SAA and CRP combined with WBC have the highest sensitivity in the diagnosis of bacterial infection, and SAA combined with CRP has the highest sensitivity in the diagnosis of *Mycoplasma pneumoniae* infection, which has high clinical application value.

4. Outlook and Summary

Infectious diseases are common types of diseases in children. Because children's immune function is not fully developed, they are easy to be invaded by bacteria and viruses, leading to various infectious diseases in children. With the occurrence and development of infection, it is easy to bring multiple hazards to children and threaten their life safety. Therefore, early diagnosis and treatment is the key [17]. Previous studies have found that when children are infected, their serum C-reactive protein (CRP) will increase significantly; CRP is an acute phase reactive protein produced by the liver; When infected by pathogens, there will be an acute phase response, which will lead to a significant increase in CRP levels; However, CRP has a low specificity in the diagnosis of some children with infectious diseases. How to diagnose children more accurately is the key [18]. Both SAA and CRP are acute phase response proteins synthesized by the liver. SAA is a relatively sensitive acute phase response protein, and its concentration can reach more than 1000 times of the normal value in acute or chronic inflammation. SAA reacts very quickly under weak inflammatory stimulation, and the time of exceeding the upper limit of the reference range is earlier than CRP, and the half-life is also shorter than CRP. Especially when the virus is infected, SAA increases and CRP is basically normal [19]. Serum amyloid A (SAA) is one of the important serological indicators discovered in recent years, and it is an acute phase protein secreted by liver cells, the same as CRP [20]. Among many references, most scholars believe that simultaneous detection of SAA, CRP and WBC can provide more useful reference value for clinicians to diagnose acute respiratory infection in children.

5. Conclusion

In conclusion, the combined detection of WBC, CRP and SAA has good application value in the early diagnosis of respiratory tract infection in children, which can provide more accurate and reliable laboratory data for the early diagnosis and treatment of respiratory tract infection in children in the future, and is worthy of popularization and application.

6. Limitations of the Study

Since the reference documents collected in this paper belong to the "three new conventional" items used by pediatric outpatient departments for early diagnosis and examination in recent years, the research documents are relatively few, and the newly discovered diagnosis and treatment application points are also not

many, which require further research by the majority of clinical medical workers to obtain more comprehensive research results, so this paper has certain limitations in material collection.

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Conflicts of Interest

For the publication of this paper, all members of the research group hereby declare that there is no conflict of interest in the ranking order of the authors.

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