Application of PCT, CRP and WBC levels in the differential diagnosis of acute bacterial, viral, and mycoplasmal respiratory tract infections

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Abstract

Background

There is a lack of studies comparing PCT, CRP and WBC levels in the differential diagnosis of acute bacterial, viral, and mycoplasmal respiratory infections. It is necessary to explore the correlation between above markers and different types of ARTI.

Methods

108 children with confirmed bacterial infection were regarded as group A, 116 children with virus infection were regarded as group B, and 122 children with mycoplasma infection were regarded as group C. The levels of PCT, CRP and WBC of the three groups were detected and compared.

Results

The levels of PCT, CRP and WBC in group A were significantly higher than those in groups B and C ($P <$ 0.05). The positive rate of combined detection of PCT, CRP and WBC was significantly higher than that of single detection. There was no significant difference of PCT, CRP and WBC levels between the group of Gram-positive bacteria infection and Gram-negative bacteria infection ($P > 0.05$). ROC curve results showed that the AUC of PCT, CRP and WBC for the diagnosis of bacterial respiratory infections were 0.65, 0.55, and 0.58, respectively.

Conclusions

PCT, CRP and WBC can be used as effective indicators for the identification of acute bacterial or no-bacterial infections in children. The levels of PCT and CRP have higher differential diagnostic value than that of WBC in infection, and the combined examination of the three is more valuable in clinic.

Background

Pneumonia caused by the acute respiratory tract infections (ARTI) in children has acute onset, rapid development and high mortality. It is the disease with the highest hospitalization rate and mortality of children under 5 years old[1]. Studies have found that ARTI is related to bacteria, viruses and mycoplasma, among which viral infection is the most common, accounting for about 90%[2]. However, the early symptoms of children with different types of infection were fever, cough, nasal congestion, runny nose and so on. The specificity of these clinical manifestations is low, which is not conducive to clinical differential diagnosis and treatment. Failure to timely and accurately determine the type of infection leads to increased unnecessary antibiotic exposure and possible antibiotic resistance[3]. Therefore, it is

very important to find an accurate and valid method for the differential diagnosis of ARTI. White blood cell (WBC) has been widely used in the diagnosis of infectious diseases. In recent years, inflammatory indicators such as Procalcitonin (PCT) and C-reactive protein (CRP) have received more and more attention in the field of differential diagnosis of ARTI [4–5]. PCT and CRP have a good correlation with disease activity, and can be a good indication of the type of infection[6–8]. Although there are some studies on above indicators as infection markers, the comparative analysis of PCT, CRP and WBC among patients with bacterial, viral and mycoplasma ARTI is rare.

Herein, the levels of PCT, CRP and WBC of children with different types of ARTI in Children's Hospital of Soochow University from February 2020 to March 2021 were detected. This study is to analyze the correlation between the type of ARTI and the level of PCT, CRP and WBC. So as to provide reference for the auxiliary differential diagnosis and accurate medication guidance of children with ARTI.

Methods
General information

358 children with ARTI were included in the study who were hospitalized in the Children's Hospital of Soochow University from March 2020 to February 2021. 108 children of bacterial infection were treated as group A, 61 males and 47 females, age (2.84 ± 3.30) years old. 116 children with viral infection were treated as group B, 54 males and 62 females, age (4.08 ± 3.28) years old. 122 children with mycoplasma infection were treated as group C, 54 males and 68 females, age (4.04 ± 3.14) years old. There was no significant difference between the sex of three groups ($P > 0.05$).

Inclusion criteria

All children with ARTI have typical clinical symptoms, and the diagnostic criteria are mainly based on the 〖practical pediatrics〗[9] by Zhu Futang; The pathogenic virus and IgM antibody of Mycoplasma were detected by peripheral blood, and bacteria were detected by sputum culture; No antibiotics, hormones, etc. were taken before the samples were collected.

Specimen collection and testing

6 mL elbow venous blood was collected and injected into the coagulant tube and the anticoagulant tube containing Ethylene Diamine Tetraacetic Acid. The plasma in the coagulant tube was used to detect PCT, and the whole blood in the anticoagulant tube was used to detect CRP and WBC. The value of PCT above 0.5 ng/mL was considered positive, the value of CRP more than 8 mg/L was determined positive, and the value of WBC above $10*10^9$/L was considered positive.

Statistical analysis

The statistical software of SPSS 20.0 was used for data analysis. The measurement data were expressed by mean and standard deviation($\bar{x} \pm s$), the comparison among groups was tested by t test; The count

data were expressed by rate or composition ratio (%), and the comparison among groups was tested by χ^2 test. Draw Receiver operating characteristic curve (ROC) and calculate the value of area under the curve (AUC). The difference was statistically significant with $P < 0.05$.

Results

Comparison of PCT, CRP and WBC levels among the three groups

The levels of PCT, CRP and WBC in group A were significantly higher than those in group B and group C ($P < 0.05$). CRP level of group C is slight higher than group B. There was no significant difference in the levels of PCT, CRP and WBC between group B and group C ($P > 0.05$). See Table 1 for details.

Table 1
Comparison of PCT, CRP and WBC levels [$\bar{x} \pm s$]

Group	n	PCT (ng/mL)	CRP (mg/L)	WBC (10^9/L)
A	108	1.69 ± 3.23	25.66 ± 40.25	10.24 ± 5.38
B	116	0.49 ± 0.86	12.80 ± 22.27	8.83 ± 2.94
C	122	0.55 ± 1.21	14.88 ± 26.04	8.49 ± 3.54
t_{A-B}	-	3.745	2.928	2.408
p_{A-B}	-	< 0.001	0.004	0.017
t_{A-C}	-	3.454	2.378	2.874
p_{A-C}	-	0.001	0.018	0.005
t_{B-C}	-	0.464	0.659	0.810
p_{B-C}	-	0.643	0.510	0.419

Comparison of positive rates of PCT, CRP and WBC among the three groups

The positive rates of PCT and CRP in group A were significantly higher than those in group B and group C. The differences of PCT and CRP levels among the three groups were statistically significant ($P < 0.05$). There was no significant difference in the positive rate of WBC among the three groups ($P > 0.05$). The combined diagnosis of three indicators can significantly improve the positive rate of diagnosis, as shown in Table 2.

Table 2
Comparison of positive rates of PCT, CRP and WBC [n,%]

Group	n	PCT (ng/mL)	CRP (mg/L)	WBC (10^9/L)	Combined diagnosis
A	108	57(52.78)	55(50.93)	42(38.89)	94(87.04)
B	116	25(21.55)	43(37.7.07)	36(31.03)	78(67.24)
C	122	29(23.77)	42(34.43)	34(27.87)	78(63.93)
χ^2	-	31.00	12.07	3.32	17.44
P	-	< 0.001	0.002	0.190	< 0.001

ROC curve analysis of PCT, CRP and WBC in the diagnosis of bacterial ARTI

ROC curve analysis showed that the areas under the curve of PCT, CRP and WBC were 0.65, 0.55 and 0.58 respectively. See Table 3 and Fig. 1 for details.

Table 3
The efficacy of PCT, CRP and WBC in the diagnosis of bacterial ARTI

Index	AUC (95% Confidence interval)	Cut-off	Specificity (%)	Sensitivity (%)	Positive predictive value(%)	Negative predictive value (%)
PCT	0.65 (0.59−0.71)	0.49	74.80	56.5	50.4	79.1
CRP	0.55 (0.48−0.62)	10.63	72.3	46.3	43.1	74.8
WBC	0.58 (0.52−0.65)	11.40	81.1	31.5	43.0	72.3

Distribution of bacterial respiratory tract infection strains

The types of bacteria detected in 108 children of bacterial ARTI were as follows, G$^+$ bacteria were mainly Streptococcus pneumoniae and Staphylococcus aureus, G$^-$ bacteria were mainly Escherichia coli and Haemophilus influenzae. As shown in Table 4.

Table 4
The distribution of bacterial respiratory tract infection strains

Group	Type	n	Ratio (%)	Total	Ratio (%)
G^+ bacteria	Streptococcus pneumoniae	33	30.56	60	55.56
	Staphylococcus aureus	26	24.07		
	Streptococcus agalactiae	1	0.93		
G^- bacteria	Escherichia coli	12	11.11	48	44.44
	Haemophilus influenzae	10	9.26		
	Moraxella catarrhalis	7	6.48		
	Acinetobacter baumannii	6	5.56		
	Pseudomonas aeruginosa	5	4.63		
	klebsiella pneumoniae	4	3.70		
	Burkholderia	2	1.85		
	Enterobacter aerogenes	1	0.93		
	Stenotrophomonas maltophilia	1	0.93		

Comparison of PCT, CRP and WBC levels and diagnostic positive rate between G^+ and G^- bacterial infection group

There were no significant differences in PCT, CRP, WBC levels and diagnostic positive rates between G^+ and G^- bacterial infection groups ($P > 0.05$), as shown in Table 5.

Table 5
Comparison of PCT, CRP and WBC levels and diagnostic positive rate between G^+ and G^- bacterial infection group [$\bar{x} \pm s$]/[n, %]

Group	n	PCT (ng/mL)		CRP (mg/L)		WBC (10^9/L)		Combined diagnosis
G^+bacteria	60	1.66 ± 3.19	34(56.67)	22.37 ± 36.86	31(51.67)	9.82 ± 4.00	21(35.00)	52(86.67)
G^- bacteria	48	1.74 ± 3.31	23(47.92)	29.76 ± 44.18	24(50.00)	10.77 ± 6.74	21(43.75)	40(83.33)
t/χ^2	-	0.13	0.82	0.95	0.03	0.91	0.86	0.24
p	-	0.90	0.37	0.35	0.86	0.34	0.35	0.63

Discussions

ARTI is the most common infectious disease in children, and has a significant impact on children's health[10]. The diagnosis and differential diagnosis of infection types need the support of bacterial culture and serological diagnosis. The process is time-consuming and tedious, and the results can not be fed back to the clinic in time. Experiential medication is a common clinical treatment, and it is also one of the causes of antimicrobial drug abuse and bacterial resistance[11]. It is an urgent problem to quickly distinguish the types of infection and guide clinical accurate drug use. WBC count in blood routine is a common method in clinical diagnosis of infection[12]. It is easy to operate and the result is fast. However, it is easy to be interfered by external factors, which affects the choice of clinical medication. Both PCT and CRP are acute phase reaction proteins, which can change according to the level of inflammatory factors. The level of PCT in serum increases significantly, when the body is infected with pathogens. The degree of increase is related to the degree of infection[13-14]. CRP is a non-specific acute phase reaction protein synthesized by hepatocytes. As an inflammatory marker, it is easy to detect and has high accuracy. It is widely used in the diagnosis of acute infection and the prognosis of patients[15-16]. Therefore, on the basis of bacterial culture and serological identification, combined with other inflammatory factors, it is expected to quickly distinguish the types of acute respiratory infection, and provide meaningful data for clinical reference.

The results of this study show that the levels of PCT, CRP and WBC in group A were significantly higher than those in group B and group C($P < 0.05$). It's clear that bacterial infections can lead to elevated levels of above indicators. It is consistent with the relevant research results [17-18]. This may be related to the failure of PCT to break down into calcitonin under the action of cytokines during bacterial infection, resulting in the increase of PCT level in blood[19]. There was no significant difference in the levels of PCT, CRP and WBC between group B and group C ($P > 0.05$). And these are similar to the normal value. It further suggests the value in the differential diagnosis of bacterial infection. When PCT, CRP or WBC remarkably increased, the possibility of bacterial infection increased significantly. It can guide the clinical early use of broad-spectrum cephalosporins or aminoglycoside antibiotics for treatment, and can achieve ideal therapeutic effect. Then the positive rates of PCT, CRP and WBC among the three groups were compared. The positive rates of PCT and CRP in group A were significantly higher than those in group B and group C ($P < 0.05$). This result is consistent with the above. There was no significant difference in the positive rate of WBC among the three groups ($P > 0.05$). More importantly, the combined diagnosis of three indicators can significantly improve the positive rate of diagnosis. In agreement with the findings of the present study, a large number of studies showed that combined detection is conducive to the diagnosis of the disease[20-21]. This suggests that clinical multi-index joint detection is very important for the diagnosis of disease.

To further analyze the diagnostic efficacy of PCT, CRP and WBC using ROC curve for bacterial ARTI. The result showed that the AUC of PCT, CRP and WBC were 0.65, 0.55 and 0.58 respectively. The sensitivity and AUC of PCT were higher than those of CRP and WBC. It suggested that the diagnostic value of PCT

and CRP was better than that of WBC in bacterial infection, and WBC is not useful at all. It was consistent with the relevant research studies[22−23]. Because the preferred antibiotics for different bacterial infections are not the same, single broad-spectrum antibiotic treatment is difficult to continuously control the development of the disease, so it is necessary to further explore the types of bacterial infections. Among 108 children with bacterial ARTI, there were 60 cases of G^+ bacteria and 48 cases of G^- bacteria.. As shown in Table 4, G^+ bacteria were mainly *Streptococcus pneumoniae* and *Staphylococcus aureus*, G^- bacteria were mainly Escherichia coli and *Haemophilus influenzae*. As we all know, these bacteria are common pathogens of respiratory tract. Children are very vulnerable to infection due to their poor development and low immunity. Next, the levels and diagnostic positive rate of PCT, CRP and WBC between G^+ and G^- bacterial infection group were depth comparative analyzed. As shown in Table 5, the overall levels of G^- bacterial group are slightly higher than that of G^+ bacterial group. However, there were no significant differences in PCT, CRP, WBC levels and diagnostic positive rates between G^+ and G^- bacterial infection groups ($P > 0.05$). This result is a little different from that of Tang et al [6], which may be due to insufficient cases included in this study. In the follow-up work, more cases will be considered in order to get more accurate results for clinic.

Conclusions

According to the above results, PCT, CRP and WBC are helpful to distinguish acute bacterial or no-bacterial infections in children to a certain extent, and their levels can prompt clinicians about infection and try to avoid the abuse of antibiotics. The differential diagnosis effect of PCT and CRP is better than that of WBC. The combined diagnosis of PCT, CRP and WBC can significantly improve the positive rate of diagnosis. It is of great significance for the diagnosis and differential diagnosis of infection.

Abbreviations

Procalcitonin (PCT), C-reactive protein (CRP), White blood cell (WBC), Acute respiratory tract infections (ARTI), Receiver operating characteristic curve (ROC), Area under the curve (AUC).

Declarations

Authors' contributions

YL: Funding acquisition (lead); Methodology (equal); writing—original draft (equal). L-F M: Data curation (equal); Formal analysis (equal); Methodology (equal). XZ: Conceptualization (lead); data curation

(equal); data curation (equal); formal analysis (equal); validation (equal); writing—original draft (equal); writing—review and editing (lead).

Availability of data and materials

The data are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This research has been approved by the ethics committee of *Children's Hospital of Soochow University*. Ethics number is 2021CS158.

Consent for publication

The ethical approval and patient information include consent to publish collected data.

Competing interests

The authors declare that there is no conflct of interest.

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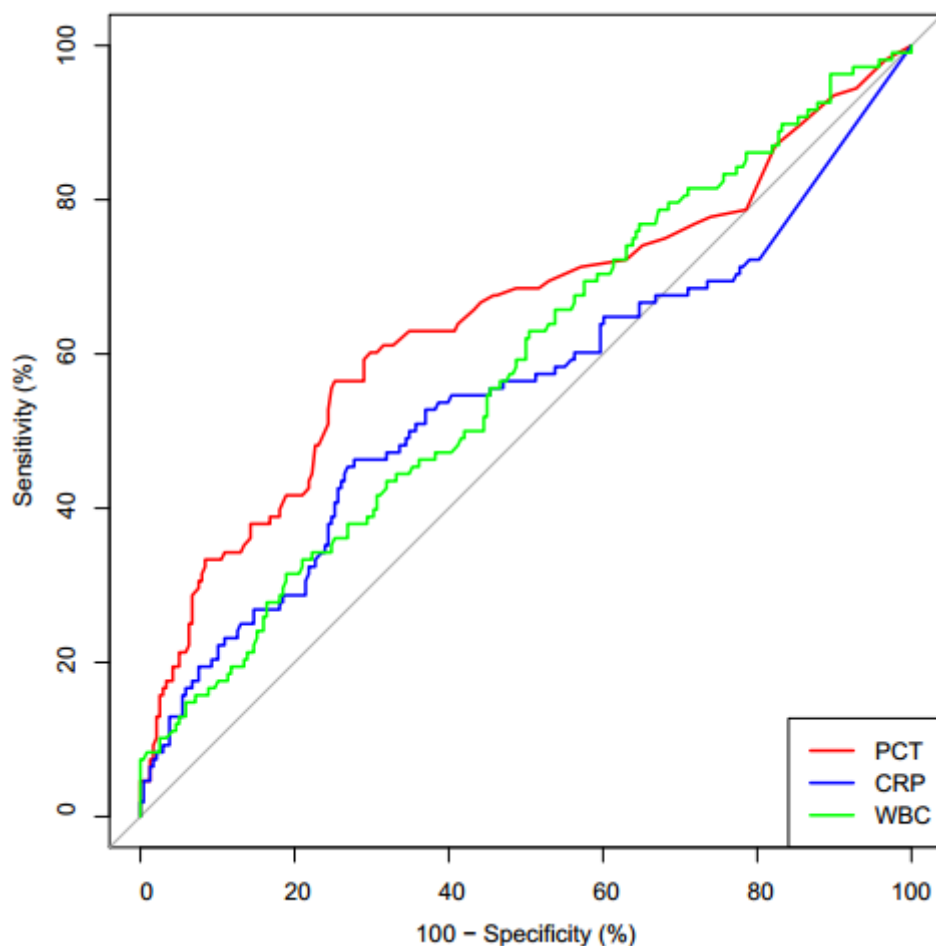
Figures

Figure 1

ROC curve of PCT, CRP and WBC in diagnosis of bacterial ARTI