

The value of PCT, IL-6, and CRP in the early diagnosis and evaluation of COVID-19

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Abstract. – OBJECTIVE: The aim of the present study was to assess the value of inflammatory factors procalcitonin (PCT), interleukin 6 (IL-6), and C-reactive protein (CRP) in the early diagnosis and evaluation of novel coronavirus pneumonia (COVID-19).

MATERIALS AND METHODS: The data of 140 patients with pneumonia in our hospital, including 70 who had COVID-19 and 70 who had community-acquired pneumonia (CAP), were statistically analyzed. The levels of PCT, IL-6, and CRP were measured and statistically analyzed to determine the differences between the two groups. The differences in the COVID-19 group were analyzed after subgrouping into the ordinary type, severe type, and critical type.

RESULTS: The PCT and CRP levels in the COVID-19 group were statistically lower than those in the CAP group ($p < 0.05$), but IL-6 was not statistically different between the two groups ($p > 0.05$). Statistically significant differences existed in IL-6 and CRP when comparing the COVID-19 subgroups of the critical type, severe type, and ordinary type ($p < 0.05$). However, there was no clinical meaning in the evaluation of the difference in PCT levels among the three subgroups with COVID-19.

CONCLUSIONS: PCT and CRP could be used as indicators in the differentiation between COVID-19 and CAP, but IL-6 was of little significance in the differentiation. The higher the IL-6 and CRP, the more severe the condition of COVID-19 might be.

Key Words:

Novel coronavirus pneumonia (COVID-19), Pneumonia, CRP, IL-6, PCT.

Introduction

In December 2019, pneumonia of an unknown cause emerged in Wuhan, China. However, after performing an analysis of the viral gene chain,

the pneumonia was clearly caused by coronavirus infection¹. The disease has been officially named “COVID-19” by the World Health Organization (WHO)^{2,3} and it is believed to have originated from the Chinese daisy-headed bat⁴. Subsequently, COVID-19 spread nationally and globally, and the number of infections increased dramatically, resulting in a worldwide pandemic⁵. Therefore, the differential diagnosis of COVID-19 has become particularly important in controlling the pandemic. Traditional inflammatory factors procalcitonin (PCT), interleukin 6 (IL-6), and C-reactive protein (CRP) are commonly used in identifying infectious diseases. They play an important role in the early diagnosis, typing of infection, degree of infection, and prognosis of the disease⁶⁻⁹. The diagnostic value of traditional inflammatory factors for identifying COVID-19 as an emerging infectious disease, and whether these factors are clinically relevant in assessing the disease, remains unclear. In the present study, the data of 140 patients with pneumonia were collected. There were 70 cases of COVID-19 and 70 of community-acquired pneumonia (CAP). The group with COVID-19 included four critical types, 25 severe types, and 41 ordinary types. The data were statistically analyzed to investigate the value of PCT, IL-6, and CRP in the diagnosis and evaluation of COVID-19.

Materials and Methods

General Materials

The data of 140 patients admitted to our hospital between December 2019 and February 2020 were collected. Among them, there were 70 patients with COVID-19 and 70 patients with CAP. COVID-19 was confirmed with nucleic acid testing in accordance with the Seventh Edition of the

Novel Coronavirus Pneumonia Diagnostic and Treatment Standardization¹⁰. The patients with COVID-19 included 41 cases of the ordinary type, 25 cases of the severe type, and four cases of the critical type. The possibility of COVID-19 and other viral infections was excluded in patients with CAP, and all the patients with CAP met the clinical diagnostic criteria for CAP¹¹.

Assay Methods

The venous blood was collected on the morning of the second day after admission under fasting conditions. The anticoagulant was added to the sample and kept frozen. The serum levels of PCT, IL-6, and CRP were detected. The levels of PCT and IL-6 were determined by the ELISA method using the human PCT and IL-6 enzyme immunoassay kit (Shanghai Gaochuang Chemical Technology Co. Ltd., Shanghai, China), respectively. The level of CRP was determined by the immuno-transparency method using reagents produced by DiaSys Diagnostic Systems GmbH (Germany) on the Hitachi Biochemical assembly line.

Statistical Analysis

SPSS 20.0 (IBM Corp., Armonk, NY, USA) and Excel were adopted for data analysis. The data of PCT, IL-6, and CRP of the two groups were expressed as median (lower quartile-upper quartile) [M(25-75)] and tested by the z-test. $p < 0.05$ was considered statistically significant. The rank-sum test (Kruskal-Wallis H method) was adopted for subgroup analysis in the group with COVID-19. $p < 0.05$ was considered statistically significant.

of CRP in the group with COVID-19 was lower than that in the group with CAP ($56.1 > 27.1$, $p = 0.028$), and the level of PCT in the group with COVID-19 was lower than that in the group with CAP ($0.05 > 0.03$, $p = 0.048$). Therefore, PCT and CRP had clinical meaning in the differential diagnosis between COVID-19 and CAP, but IL-6 could not be used for differentiation.

Comparison of Levels of PCT, IL-6, and CRP Among COVID-19 Subgroups (Ordinary Type, Severe Type, and Critical Type)

The levels of PCT, IL-6, and CRP in each patient with COVID-19 were detected and compared. The results indicated a statistical difference in the level of IL-1 among different subgroups in the group with COVID-19 ($p < 0.001$). Further comparisons revealed that the level of IL-6 was higher in the severe type group than in the ordinary type group ($43.7 > 16.8$, $p < 0.05$) and higher in the critical type group than in the ordinary type group ($209.6 > 43.7$, $p < 0.05$). Moreover, further comparisons revealed that the level of CRP in the severe type group was higher than that in the ordinary type group ($58.3 > 10.9$, $p < 0.05$). There was no statistical difference in the levels of PCT among different subgroups ($p = 0.940$). These results suggested that the more severe COVID-19 was, the higher the IL-6 and CRP levels were, while the levels of PCT were similar among the various types. Therefore, IL-6 and CRP could be used in the typing and severity assessment of the disease, but PCT was of little significance in the severity assessment (as shown in Table II).

Results

Comparison of Levels of PCT, IL-6, and CRP Between the COVID-19 and CAP Groups

As shown in Table I, the results indicated that there was no statistical difference in IL-6 between the two groups ($p > 0.05$). The level

Discussion

COVID-19 is an emerging acute infectious disease, whose diagnosis relies on the detection of nucleic acids in respiratory secretions. In the section of laboratory tests in the Novel Coronavirus Pneumonia Protocol, Seventh Edition, it is

Table I. Analysis of PCT, IL-6, and CRP between COVID-19 and CAP groups.

	IL-6 (pg/ml) 0-7	CRP (mg/l) 0-6	PCT (ng/ml) 0-0.5
COVID-19 group	25.7 (12.1-54.6)	27.1 (7.6-69.5)	0.03 (0.02-0.09)
CAP group	19.5 (4.8-53.2)	56.1 (10.4-115.9)	0.05 (0.02-0.32)
z	-1.478	-2.203	-1.979
p	0.14	$p < 0.05$	$p < 0.05$

Table II. The analysis of three indicators in different sub-groups with COVID-19.

	IL-6 (pg/ml) 0-7	CRP (mg/l) 0-6	PCT (ng/ml) 0-0.5
The ordinary type	16.8 (5.9-27.7)	10.9 (4.3-36.3)	0.04 (0.02-0.10)
The severe type	43.7 (27.3-75.8) ^a	58.3 (26.5-97.6) ^a	0.03 (0.02-0.09)
The critical type	209.6 (50.1-515.3) ^b	68.1 (20.5-170.5) ^b	0.04 (0.01-0.16)
χ^2	22.23	16.595	0.124
<i>p</i>	<0.001	<0.001	0.940

Note: ^aIndicates a statistically significant difference ($p < 0.05$) when compared to normal; ^bIndicates a statistically significant difference ($p < 0.05$) when compared to heavy.

clearly indicated that most patients have normal PCT and elevated CRP, with no elaboration on IL-6; however, it clearly indicates that patients with the severe type and critical type often have elevated inflammatory factors^[10].

PCT has been widely used in identifying infectious diseases in recent years and is now recognized as a validated serological marker for the identification of microbial infections. This is of great significance in the diagnosis of early infection and in the assessment of the extent of early infection⁶. PCT is present at minimal but stable levels in healthy populations. The levels of PCT increase significantly when a patient develops an infectious disease. The more severe the infection, the higher the level of increase, and vice versa. In the present study, the level of PCT was significantly higher in patients with CAP than in those with COVID-19. However, PCT was of limited value in the typing and severity assessment of COVID-19. The limitation in the sample size means that the present result requires further verification.

IL-6 is a cytokine that stimulates the proliferation, differentiation, and enhanced function of cells involved in immune responses and is involved in the inflammatory response. Viral infection may induce healthy cells to produce IL-6^[12]. IL-6 can induce B-cell differentiation, the proliferation of plasmacytoma and myeloma, and expression of IL-2 and its receptor, thereby inducing the differentiation of monocytes, further induction of cytotoxic T lymphocytes, and enhanced NK cell activity. Therefore, IL-6 plays an important role during an inflammatory reaction. IL-6 is significantly elevated in the serum of patients with COPD^{13,14} and is associated with a long-term chronic inflammatory response, with further elevation in the acute phase¹⁵. In the present study, there was no statistical difference in the level of IL-6 between patients with COVID-19

and those with CAP, which suggested that IL-6 was meaningless in the determination of infected pathogens. However, there were statistically significant differences in the typing and severity assessment of COVID-19, suggesting that the more severe the disease, the more significant the IL-6 elevation, which was of concern to clinicians.

Compared with PCT and IL-6, CRP is the most common and widely used inflammatory factor in clinical practice and is the best-known one for identifying infections. CRP is one of the cytokines released by injured tissues and cells, which can induce a series of acute-phase responses. It is now recognized that CRP has fairly high specificity for identifying bacterial or viral infections¹⁶. Therefore, CRP can be used as one of the main indicators to differentiate COVID-19 from CAP. In the present study, the level of CRP in patients with COVID-19 was noticeably lower than for those patients with CAP. If there is an early elevation of CRP, there is a possibility that it could result in more occurrences of bacterial infection. Moreover, it was suggested that in COVID-19 cases, there was a statistically significant difference in CRP in the differentiation of the critical type, the severe type, and the ordinary type, indicating that the more severe the disease, the more pronounced was the elevation of CRP. Therefore, the presence of a clinically significant or even persistent elevation of CRP in patients diagnosed with COVID-19 indicated a greater likelihood of the severe type and critical type.

Conclusions

The present study suggested that PCT, IL-6, and CRP might be valuable in the diagnosis and evaluation of COVID-19. However, as an emerging infectious disease, COVID-19 is still being explored, and further research is needed.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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