

Original Article

Comparison of serum procalcitonin in respiratory infections and bloodstream infections

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Abstract: Purpose: This study observed the relationship between procalcitonin (PCT) and results of sputum culture, the relationship between PCT and results of blood culture to evaluate and compare the value of PCT in respiratory and bloodstream infections. Methods: We analyzed 1616 patients in which PCT and sputum culture were concurrently ordered and analyzed, and 1096 patients in which PCT and blood culture were concurrently ordered and analyzed from January 2014 to May 2015. PCT concentrations were measured by on a Roche Cobas E601 ECL analyzer. Results: The average values of PCT from patients with sputum culture positive and negative were 0.42 (0.17-2.16) and 0.12 (0.06-0.57) ng/ml respectively, and the average values of PCT from patients with blood culture positive and negative were 9.54 (2.10-48.47) and 0.28 (0.10-1.23) ng/ml respectively. In sputum culture, positive rate of PCT in cases with growth of pathogens was 47.1%. In blood culture, positive rate of PCT in cases with growth of pathogens was 89.2%. Conclusions: PCT is useful in early diagnosis of respiratory infections and bloodstream infections, but the specificity of PCT in diagnosing respiratory infections is not as high as it is in bloodstream infections.

Keywords: Procalcitonin, blood culture, sputum culture, respiratory infections, bloodstream infections

Introduction

As a new type of infection indicator, procalcitonin (PCT) has been widely used in clinical testing, most commonly used to in the diagnosis and monitoring of respiratory and bloodstream infections. Sputum culture is an important mean to diagnose respiratory infections, but the process of collection, transportation and inoculation of sputum samples is vulnerable to contamination, the process of culture also costs time, negative result can't completely exclude infection. Similar with sputum culture, blood culture is gold standard to diagnose bloodstream infections, but the process of blood culture costs time, negative result can't completely exclude infection.

PCT, a precursor of calcitonin, is mainly synthesized and released by C-cell of thyroid gland, neuroendocrine cell of lung and intestine can

also secrete a small amount of PCT. Serum PCT is usually very low under normal condition, generally less than 0.05 ng/ml in healthy people. Serum PCT in the elderly, patients with chronic diseases and less than 10% healthy people could be higher than 0.05 ng/ml, but usually no more than 0.3 ng/ml. When under inflammation, in particular bacterial infection or sepsis, various tissues and multiple types of cell would produce PCT and release into blood circulation. PCT may be suitable as an indicator for severity of infection, and also may be used for guiding antibiotic use, assessing effectiveness of antibiotic treatment, judging prognosis [1-6].

In this study, we observed the correlation between PCT and sputum culture results, PCT and blood culture results to evaluate its value in the diagnosis of respiratory and bloodstream infections.

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Table 1. PCT of 1616 cases of sputum culture

Group	Number	PCT [M(P_{25} , P_{75}) ng/ml]	PCT positive [case(%)]
Growth of pathogens	476	0.42 (0.17~2.16)	224 (47.1)
Gram-negative bacteria	384	0.42 (0.18~1.88)	183 (47.7)
Gram-positive bacteria	50	0.30 (0.10~1.24)	17 (34.0)
Mixed bacteria	16	0.88 (0.20~9.18)	10 (62.5)
Fungi	26	2.26 (0.07~11.80)	14 (53.8)
No growth of pathogens	1140	0.12 (0.06~0.57)	300 (26.3)

Table 2. PCT of 1096 cases of blood culture

Group	Number	PCT [M(P_{25} , P_{75}) ng/ml]	PCT positive [case (%)]
Growth of pathogens	102	9.54 (2.10~48.47)	91 (89.2)
Gram-negative bacteria	60	18.29 (2.73~54.43)	56 (93.3)
Gram-positive bacteria	32	5.35 (1.18~13.77)	25 (78.1)
Fungi	10	11.33 (1.60~17.29)	10 (100.0)
No growth of pathogens	994	0.28 (0.10~1.23)	386 (38.8)

Materials and methods

Study population

We selected 1616 patients in which PCT and sputum culture were concurrently requested and 1096 patients in which PCT and blood culture were concurrently requested from January 2014 to May 2015 in The People's Hospital of Guangxi Zhuang Autonomous Region, China. All the patients analyzed were older than 18 years of age; the difference of inspection time between PCT and sputum culture or blood culture was no more than 24 h in all the patients; if repeated inspections occurred on the same patient in one week, only a pair of results was counted; if the difference of repeated inspection time in the same patient was more than one week, then each pair of results were counted.

PCT assay

PCT was analyzed on a Roche Cobas E601 ECL analyzer. Calibration solution, reagents and quality control materials were provided by Roche. The positive critical value of PCT was 0.5 ng/ml, PCT \geq 0.5 ng/ml was determined to be positive.

Sputum culture and blood culture

Sputum culture was executed under the guideline of common microorganism culture; BacT/

Alert 3D blood culture system and supporting blood culture bottles were used to execute blood culture; pathogenic microorganisms were identified by Bio-Merieux VITEK-2 Compact automated microbial identification analyzer and corresponding reagents.

Statistical analysis

SPSS 18.0 statistical software was used for statistical analysis, overall PCT was expressed by $M(P_{25} \sim P_{75})$, PCT between different groups were compared by Mann-Whitney U test, positive rate of PCT between different groups were compared by Chisquare test,

$P < 0.05$ was considered statistically significant.

Results

PCT of 1616 cases of sputum culture

In the 1616 cases of patients which PCT and sputum culture were concurrently requested, 476 cases resulted in positive sputum culture, among them, 384 were Gram-negative bacteria, 50 were Gram-positive bacteria, 26 were fungi, 16 were mixed bacteria. PCT in group with growth of pathogens and group without growth of pathogens were respectively 0.42 (0.17~2.16) and 0.12 (0.06~0.57) ng/ml, PCT in group with growth of pathogens was significantly higher than group without growth of pathogens ($U=171710.0$, $P=0.000$). Positive rate of PCT in group with growth of pathogens and group without growth of pathogens were respectively 47.1% and 26.3%, there was significant difference between the two groups ($P=0.000$) (**Table 1**).

PCT of 1096 cases of blood culture

In the results of blood culture counted, combined with culture time of positive results, WBC, neutrophil cell ratio and CRP, 18 cases of contaminated bacteria were excluded. In the analyzed 1096 cases of patients which PCT and blood culture were concurrently requested, 102 cases resulted in positive blood culture,

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Table 3. PCT and Species classification of 476 cases of sputum culture with growth of pathogens

Pathogens	Number	PCT [M (P_{25} , P_{75}) ng/ml]	PCT positive [case (%)]
Gram-negative bacteria			
Acinetobacter baumannii	142	0.71 (0.23~2.31)	82 (57.7)
Pseudomonas aeruginosa	139	0.29 (0.14~1.38)	55 (39.6)
Klebsiella pneumoniae	34	0.17 (0.11~1.20)	15 (44.1)
Haemophilus influenzae	22	0.15 (0.06~0.27)	3 (13.6)
Escherchia coli	9	0.30 (0.19~0.88)	3 (33.3)
Enterobacter aerogenes	9	2.73 (0.30~2.96)	5 (55.6)
Stenotrophomonas maltophilia	13	1.88 (1.08~9.13)	11 (84.6)
Branhamella catarrhalis	5	0.06 (0.04~0.15)	0 (0)
Enterobacter cloacae	3	1.41 (1.36~31.19)	3 (100.0)
Pseudomonas alcaligenes	2	2.12 (0.33~3.91)	1 (50.0)
Burkholderia cepacia	2	1.11 (1.09~1.12)	2 (100.0)
Enterobacter gergoviae	1	31.19	1 (100.0)
Elizabethkingia meningosepticum	1	0.33	0 (0)
Serratia liquefaciens	1	3.91	1 (100.0)
Proteus mirabilis	1	4.49	1 (100.0)
Gram-positive bacteria			
Staphylococcus aureus	24	0.36 (0.11~1.32)	10 (41.7)
Streptococcus pneumoniae	22	0.14 (0.07~0.66)	5 (22.7)
Nocardia	2	40.35 (9.32~71.38)	2 (100.0)
Streptococcus pyogenes	2	0.34 (0.30~0.38)	0(0)
Fungi			
Candida albicans	18	2.27 (0.04~14.40)	9 (50.0)
Candida tropicalis	4	2.39 (0.66~4.48)	3 (75.0)
Candida glabrata	2	3.66 (2.15~5.16)	2 (100.0)
Asperillus	2	0.16 (0.03~0.28)	0 (0)
Mixed bacteria	16	0.88 (0.20~9.18)	10 (62.5)
Total	476	0.42 (0.17~2.16)	224 (47.1)

among them, 60 were Gram-negative bacteria, 32 were Gram-positive bacteria, 10 were fungi. PCT in group with growth of pathogens and group without growth of pathogens were respectively 9.54 (2.10~48.47) and 0.28 (0.10~1.23) ng/ml, PCT in group with growth of pathogens was significantly higher than group without growth of pathogens ($U=14138.0$, $P=0.000$). Positive rate of PCT in group with growth of pathogens and group without growth of pathogens were respectively 89.2% and 38.8%, there was significant difference between the two groups ($P=0.000$) (**Table 2**).

PCT of 476 cases of sputum culture with growth of pathogens

PCT in Gram-negative bacteria, Gram-positive bacteria, fungi and mixed bacteria were respectively 0.42 (0.18~1.88), 0.30 (0.10~1.24),

2.26 (0.07~11.80) and 0.88 (0.20~9.18) ng/ml, there was no significant difference in the four groups ($P=0.092$). Positive rate of PCT in Gram-negative bacteria, Gram-positive bacteria, fungi and mixed bacteria were respectively 47.7%, 34.0%, 53.8% and 62.5%, there was no significant difference in the four groups ($P=0.139$) (**Table 3**).

PCT of 102 cases of blood culture with growth of pathogens

PCT in Gram-negative bacteria, Gram-positive bacteria and fungi were respectively 18.29 (2.73~54.43), 5.35 (1.18~13.77) and 11.33 (1.60~17.29) ng/ml. PCT in Gram-negative bacteria was significantly higher than that in Gram-positive bacteria ($U=634.0$, $P=0.008$), but there was no significant difference between Gram-negative bacteria and fungi ($U=223.0$,

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Table 4. PCT and Species classification of 102 cases of blood culture with growth of pathogens

Pathogens	Number	PCT [M (P_{25} , P_{75}) ng/ml]	PCT positive [case(%)]
Gram-negative bacteria			
Escherchia coli	23	54.43 (6.13~100.00)	23 (100.0)
Acinetobacter baumannii	9	9.70 (0.68~49.93)	7 (77.8)
Klebsiella pneumoniae	9	5.40 (3.45~35.76)	9 (100.0)
Pseudomonas aeruginosaa	6	20.01 (2.73~48.70)	6 (100.0)
Salmonella	4	3.00 (0.60~11.22)	3 (75.0)
Serratia marcescens	3	23.08 (8.36~52.33)	3 (100.0)
Proteus mirabilis	2	55.08 (42.68~67.48)	2 (100.0)
Enterobacter cloacae	1	100.00	1 (100.0)
Alcaligenes xylosoxidans	1	5.45	1 (100.0)
Pseudomonas stutzeri	1	0.17	0 (0)
Brucella melitensis	1	0.59	1 (100.0)
Gram-positive bacteria			
Staphylococcus aureus	14	9.38 (2.05~14.16)	12 (85.7)
Coagulase-negative Staphylococcus	8	1.20 (0.21~10.94)	5 (62.5)
Enterococcus Faecium	6	5.35 (3.75~10.97)	5 (83.3)
Streptococcus pneumoniae	2	1.27 (0.28~2.26)	1 (50.0)
Group B streptococcus	1	56.82	1 (100.0)
Streptococcus galloyticus	1	97.45	1 (100.0)

Table 5. PCT distribution in positive sputum culture and positive blood culture

Group	Number						Total	
	PCT (ng/ml)	<0.05 (n)	0.05~0.1 (n)	0.1~0.5 (n)	0.5~2.0 (n)	2.0~10.0 (n)		>10.0 (n)
Positive sputum culture (n=476)		25	45	182	102	75	47	476
Positive blood culture (n=102)		0	0	11	12	30	49	102

P=0.196), no significant difference between Gram-positive bacteria and fungi (U=128.0, P=0.344). Positive rate of PCT in Gram-negative bacteria, Gram-positive bacteria and fungi were respectively 93.3%, 78.1% and 100.0%, there was significant difference between Gram-negative bacteria and Gram-positive bacteria (P=0.032) (**Table 4**).

Discussion

PCT is a polypeptide consists of 116 amino acids, which coding gene is CALC-I on chromosome 11 [7]. Now PCT is most commonly used to diagnose and monitor respiratory infections and bloodstream infections, many literature have respectively reported its value in respiratory infections and bloodstream infections. In our study, we observed the relationship of PCT and results of sputum culture, PCT and results of blood culture to compare its value in respiratory infections and bloodstream infections.

Pathogenic microorganisms which cause respiratory infections were diverse, including viruses, bacteria, fungi and atypical pathogens. Therefore PCT displayed diversity in patients with respiratory infections, mainly related with the type of pathogens, severity of infection and systemic inflammatory response. PCT in patients with bacterial pneumonia was higher than that of virus, atypical pathogens and mycobacterium tuberculosis [8-12]. But PCT wouldn't increase in all patients with bacterial pneumonia, it is reported that, PCT was less than 0.5 ng/ml in nearly 50% patients with bacterial pneumonia and was less than 0.1 ng/ml in 28% patients with bacterial pneumonia. In our study, PCT was less than 0.5 ng/ml in 52.9% patients whose sputum culture resulted in positive, and was less than 0.1 ng/ml in 31.3% patients whose sputum culture resulted in positive, which was consistent with the report. So normal or slightly elevated PCT can't exclude bacterial pneumonia [13-17].

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Level of PCT was related with the severity of respiratory infections, low level of PCT (<0.1 ng/ml) suggested mild infection or a better prognosis, which was a reference index for no or stop use of antibiotic. PCT monitor could be a mean to assess the effect of antibiotic treatment, continued increase or no decrease of PCT was an ineffective performance of treatment. It was reported that the time of antibiotic use with guide of PCT was shorter than that without guide of PCT in patients with bacterial pneumonia, the amount of antibiotic use was also reduced under guide of PCT [18-24]. As showed in **Table 5**, PCT distributed in each numerical value range in patients with positive sputum culture, mostly distributed in the range of 0.1~0.5 ng/ml, the specificity of PCT for diagnosis of respiratory infections was not high.

In our study, PCT was higher than 0.5 ng/ml in 89.2% patients whose blood culture resulted in positive, compared to respiratory infections, the specificity of PCT for diagnosis of bloodstream infections was high. Research showed that it was unlikely to happen highly risky bacterial infection and hardly to occur bloodstream infections on patients whose PCT was less than 0.05 ng/ml [25-28]. As showed in **Table 5**, none PCT was less than 0.05 ng/ml in patients whose blood culture resulted in positive, which was consistent with the research. Compared to the diversity of PCT in respiratory infections, PCT in bloodstream infections mostly presented high level.

In the 102 cases of patients whose blood culture resulted in positive, in addition to *Acinetobacter baumannii*, *Salmonella* and a case of *Pseudomonas stutzeri*, positive rate of PCT was all 100% in other Gram-negative bacteria. Positive rate and level of PCT in Gram-negative bacteria were both higher than in Gram-positive bacteria, but there was no significant difference between the positive rate and level of PCT in Gram-negative bacteria and that in fungi. In the 476 cases of patients whose sputum culture resulted in positive, no significant difference existed in the positive rate and level of PCT in Gram-negative bacteria, Gram-positive bacteria and fungi. It was thought that endotoxin made the positive rate and level of PCT in Gram-negative bacteria higher than that in Gram-positive bacteria in bloodstream infections [29, 30]. Endotoxin is an ingredient of cell

wall in Gram-negative bacteria, when Gram-negative bacteria appear in blood, thalli crack, endotoxin is released into blood, then the organism is stimulated and lead to significant increase of PCT. Respiratory infection is local infection, no or only a small amount of endotoxin is released into blood, which wouldn't lead to significant increase of PCT.

In summary, PCT is useful in early diagnosis of respiratory infections and bloodstream infections, but the specificity of PCT in diagnosing respiratory infections is not as high as it is in bloodstream infections.

Disclosure of conflict of interest

None.

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