



Procalcitonin Serum Level in Patients Aged 3-36 Months With Focal Fever Referred to Hospitals in Western Iran in 2020

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Received: 3 Dec. 2020

Accepted: 13 July 2021

ePublished: 29 Sep. 2021

Abstract

Background: Diagnosing viral and bacterial infectious diseases in children is of great importance. The conventional treatment for the given diseases has been proven relatively impractical and, therefore, finding a practical diagnostic method seems necessary. Measuring procalcitonin (PCT) levels in the blood is one of those useful tests which have high sensitivity and specificity compared to other methods. Moreover, many researchers have emphasized that the level of PCT in bacterial infections is significant. Therefore, PCT level measurement can be adopted as a highly effective factor for distinguishing bacterial infections from viral ones. Our study aimed to evaluate the plasma levels of PCT in children aged 3-36 months.

Methods: In this study which was conducted in 2020 in Kermanshah, Iran, 49 children aged 3-36 months having focal fever and referring to the pediatric emergency department of Mohammad Kermanshahi and Imam Reza hospitals in Kermanshah were examined. Distinguishing bacterial infection from viral one was first made by a pediatrician using CBC diff-ESR-CRP tests.

Results: The mean serum level of PCT in bacterial infections was significantly higher than that in viral infections. Furthermore, the mean of white blood cell (WBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) in bacterial infection was significantly higher than that in viral infection.

Conclusions: According to our study findings, plasma levels of PCT could have been considered as a diagnostic indicator of the infection. Therefore, it was recommended that the evaluation of PCT plasma levels in children with infection be performed in early stages of the disease. However, it was also suggested that this evaluation be conducted after performing further investigations in this field.

Keywords: CBC, Procalcitonin, Infection



Background

One of the most important issues in children's infections is to diagnose the type of infection, which is often a difficult and complex issue. Misdiagnosis of the infection type usually leads to unnecessary antibiotic prescriptions. Currently, white blood cell (WBC) and C-reactive protein (CRP) tests are performed to detect the kind of infection when dealing with numerous cases. These diagnostic tests are used in almost 80% of the cases, but sometimes the resulting diagnoses are incorrect (1).

Since 1993, various investigations have revealed that procalcitonin (PCT) is a useful criterion for distinguishing between bacterial and viral infections in infants and adults. Studies from 2008 and 2009 have shown that this substance facilitates the treatment of children afflicted with viral and bacterial infections, reduces the consumption of antibiotics and the drug resistance in these patients, and lowers the cost of treatment (2-4).

PCT is involved in the production of the hormone calcitonin, which regulates calcium levels. It is a peptide precursor synthesized by various cells in the thyroid, nerves, respiratory, and digestive systems (5). PCT levels in

the blood of healthy people are lower than those in people with a bacterial or viral infection. In those with a bacterial or viral infection, PCT increases in response to inflammatory reasons, particularly in response to bacterial agents. PCT in these subjects is mainly produced by lung and intestinal cells (6), and has a high sensitivity (85%) and specificity (91%) compared to other diagnostic methods used for diagnosing some diseases such as systemic inflammatory response syndrome (SIRS) (7). According to the findings from previous studies, the level of PCT in viral or non-viral infections does not increase significantly. Generally, the level of PCT in viral infections and other inflammatory conditions increases slightly and reaches to approximately 15 ng/mL; but in bacterial infections, its level exceeds 100 ng/mL (8). The lifespan of PCT in plasma is approximately one day. High levels of PCT produced during infections do not result in concomitant increases in calcitonin levels or decreased serum calcium levels.

Although the physiological function of the PCT is still unclear, it seems that microbial infections stimulate the expression of the *CALC1* gene, releasing the precursor of calcitonin in the majority of body tissues (9). Given the

importance of PCT discussed above, this study aimed to determine and differentiate the types of infection in children by using PCT analysis.

Materials and Methods

This study was carried out in 2020 in Kermanshah, Iran. A total of 49 children aged 3-36 months suffering from viral and bacterial infections and referring to the pediatric emergency department of Mohammad Kermanshahi and Imam Reza hospitals in Kermanshah were investigated. The investigation was approved by the Ethics Committee morally University of Medical Sciences, Kermanshah, Iran (IR; KUMS.REC.1398.448). After obtaining voluntary and informed consent from their parents, the children entered the study according to the entry criteria. The inclusion criteria were as follow: children with no immunodeficiency, chronic kidney, and heart diseases; those with previously treated infections; and those with an initial diagnosis of a bacterial or viral infection (by a pediatrician) which was later confirmed by complete blood count (CBC) diff-ESR-CRP laboratory tests. Firstly, blood samples were taken from all patients from their brachial vein and, then, they were examined in order for evaluating erythrocyte sedimentation rate (ESR), CBC, and CRP, as well as for measuring serum PCT. Semi-quantitative measurement of PCT was performed in the immunology-serology laboratory using PCT-Q kits. PCT was determined by immunochromatography using monoclonal antibodies. To this end, the questionnaires including variables of age, sex, weight, type of infection, etc. were prepared. After collecting the data, the final analysis was done using SPSS software version 22.

Results

The average lifespan of the infant was 16.98 ± 9.87 . As for the viral infection, 75.5% of the boys had this infection. In the investigation, 49 children aged 3-36 months with viral and bacterial infections referred to the Pediatric Emergency Department, Mohammad Kermanshahi and Imam Reza hospitals in Kermanshah. The children with the initial diagnosis of bacterial or viral diseases were included in the study. The average plasma levels of PCT, WBC, ESR, and CRP in the bacterial disease type were significantly higher than those found in the viral disease type.

Out of 49 children participating in this study, 37 participants were boys (75.5%) and 12 ones were girls (24.5%). Also, 35 children (71.4%) had a viral infection, whereas 14 ones (28.6%) had a bacterial infection (Tables 1 and 2).

The mean serum level of PCT in bacterial infection was higher than that in viral infection. According to the results from the Mann-Whitney test, there was a significant relationship between the variable and the type of treatment ($P < 0.05$). The average plasma levels of the PCT were not considerably different in terms of sex, and there was no significant association between sex and plasma levels of

PCT ($P > 0.05$) (Table 3).

Mann-Whitney test results also showed that the mean of the variables in the type of bacterial infection was considerably more than that in viral infection. The test results further revealed a significant relationship between the desired variables and the type of infection ($P < 0.05$) (Table 4).

Discussion

Currently, blood culture and other tissue culture tests as well as complementary tests are used to diagnose bacterial infections. If a patient without bacterial infection receives antibiotic treatment, s/he may face some negative consequences such as increased treatment costs, hospital stay, allergy risk, and drug side effects; if the patient with bacterial infection does not receive antibiotic treatment, however, s/he has to accept other negative consequences including death. This situation is more risky and complicated when children are treated since children with the bacterial infection who do not receive antibiotic treatment end up with death in 80% of cases.

PCT was first recommended as a useful criterion for identifying bacterial diseases in patients in 1993. The PCT level for healthy people is extremely low and is normally under 0.1 ng/mL. This level for people afflicted with viral diseases or other infectious conditions reaches to about

Table 1. The Frequency Distribution by Type of Infection and Gender (n = 49)

		No.	Percent
Gender	Boy	37	75.5
	Girl	12	24.5
Type of infection	Viral	35	71.4
	Bacterial	14	28.6

Table 2. The Mean and Standard Deviation of Serum PCT and WBC, ESR, CRP Levels in Individuals

	Mean	Standard Deviation	Min	Max
WBC	12082.86	3350.48	4800	18000
PCT	0.79	1.58	0.20	8.7
ESR	22.06	11.78	5	48
CRP	1.04	0.73	0	3
PMN	0.55	0.12	0.31	0.73
LYM	0.45	0.12	0.27	0.69

WBC, white blood cell; PCT, procalcitonin; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein; PMN, polymorphonuclear; LYM, lymphocyte

Table 3. Serum Levels of PCT in Bacterial and Viral Infections Based on Gender

		Number	Mean	Standard Deviation	P Value
Type of infection	Viral	35	18	630	0.0001
	Bacterial	14	42.5	595	
Gender	Boy	37	24.78	917	0.847
	Girl	12	25.67	308	

Table 4. Serum Levels of ESR, CRP, WBC, PMN, and LYM by Type of Infection

	Type of Infection	Mean	Standard Deviation	Min	Max	P Value
ESR	Viral	18.70	654.50	5	48	0.0001
	Bacterial	40.75	570.50			
CRP	Viral	21.33	746.50	0	1	0.002
	Bacterial	34.18	478.50			
WBC	Viral	18.80	658.0	5820	18000	0.0001
	Bacterial	40.50	567.0			
PMN	Viral	19.46	681.0	0.31	0.73	0.0001
	Bacterial	38.86	544.0			
LYM	Viral	30.64	1072.50	0.27	0.69	0.0001
	Bacterial	10.89	152.50			

WBC, white blood cell; PCT, procalcitonin; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein; PMN, polymorphonuclear; LYM, lymphocyte

1.5 ng/mL, whereas it exceeds 100 ng/mL for those with bacterial diseases. PCT is one of the major components of the Calcitonin hormone. In microbial infections, it releases PCT precursors by stimulating the expression of the *CALC1* gene in most tissues (10,11).

In the present study, 49 children aged 3-36 months with focal fever were examined. Preclinical findings such as the PCT and WBC, ESR, CRP were investigated. The investigation showed that 71.4% and 28.6% of children had viral and bacterial infections, respectively. The mean serum level of PCT in bacterial infections was significantly higher than that in viral infections. In addition, the mean of WBC, ESR, and CRP in bacterial infection was significantly higher than that in viral infection. Taking into account the results of the present investigation, the application of PCT as a distinguishing indicator for determining bacterial diseases could have been recommended. In a study by Sandri et al, PCT levels were found to increase almost basically in bacteremia diseases, with the highest percentage reported after the first day of fever (12). In another study by Yukioka, PCT plasma statuses were introduced as sensitive criteria for distinguishing between microbial and non-microbial infections, as well as for determining whether or not they were active and able to predict response to the treatment (13). Becker et al identified PCT as an indicative agent in infections; they also discovered that the compound of PCT and C-reactive protein had the most useful information for diagnosing infection (14). Other studies have also shown that assessing the compound of the PCT and the C-reactive protein is the most accurate criterion in diagnosing infection (15). In a research by Carnino et al, it was shown that PCT was significantly increased in bacterial infections compared to fungal infections, but it was not increased in response to other types of inflammation (16). In the study by Hatzistilianou, the PCT was used as a rapid appropriate diagnostic test for daily monitoring of disease progression (17). A study by Gomez et al showed that identifying patients with include bacterial infection (IBI) through PCT in young infants with FWS was better than CRP and that it appeared to be the best indicator of IBI rejection. The PCT has been the most accurate blood

test in patients with normal urinary strip results and fever (18). A study by Gendrel et al showed that the evaluation of plasma PCT could have been used as a diagnostic value in differentiating meningitis caused by bacteria or viruses (4). A study by Schuetz et al on the PCT test for initial detection and dissociation of “non-infectious SIRS, sepsis, severe sepsis, and septic shock” showed that the amount of PCT was highest in patients with the septic disease (19). The results from these studies were in agreement with our study results.

PCT is produced in response to the invasion of inflammatory agents in different parts of the body. Its plasma levels in bacterial diseases increase considerably compared with those in other infections. This can be a useful guide in clinical decisions to start antibiotic treatment (20,21). Due to the small size of and the difference in population investigated in our study, however, it was recommended that further studies be conducted before generalizing about our findings.

Conclusions

According to our study results, it was recommended that PCT be applied as a diagnostic sign for determining inflammatory diseases. Moreover, it was suggested that PCT be considered as a diagnostic test along with other clinical and paraclinical criteria in the early stages of the disease, which could have facilitated diagnosing and treating the disease in earlier stages.

Ethical Approval

Ethical approval of this research was granted by the Ethics Committee of Kermanshah University of Medical Sciences, Iran (IR; KUMS. REC.1398.448).

Conflict of Interests

The authors declare that they have no conflict of interests.

Funding

This research was financially supported by Kermanshah University of Medical Sciences, Iran.

Acknowledgments

The authors gratefully acknowledge the financial support of Kermanshah University of Medical Sciences, Kermanshah, Iran.

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