

Procalcitonin Testing reduce Unnecessary Antibiotic Use in Bacterial Infection

Attabak Toofani Milani¹, Mahshid Mohammadian², Sadegh Rostaminasab³, Roghayeh Paribananaem¹, Zohre Ahmadi⁴, Azim Akbarzadeh Khiyavi⁵

¹Department of Biochemistry, Urmia University of Medical Sciences, Urmia 57147, West Azerbaijan, Iran. ²Department of Biochemistry, School of Medicine, Urmia University of Medical Science, Urmia, Iran. ³Department of Biochemistry, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran 1985717443, Tehran, Iran. ⁴MSc student of health education and health promotion, faculty of health, Qom university of medical sciences, Qom, Iran. ⁵Department of Pilot Nanobiotechnology, Pasteur Institute of Iran, Tehran, Iran.

Abstract

Conventional diagnostic test have limitations to deferential diagnosis in clinical suspicion of bacterial infection cases, that in some cases lead to inappropriate antibiotic therapy and increases antibiotic resistance. A new diagnostic insight is procalcitonin (PCT) test to improve diagnosis of bacterial infections and to guide antibiotic therapy. Serum PCT levels are of useful test as a biomarker in patients with bacterial infections for several reasons. Initial rise of PCT levels due to bacterial infection, subsequent sequential PCT levels can be used to assess the effectiveness and duration of antibiotic therapy. Based on clinical researches results, in bacterial infections, promising good results obtained when use of PCT used as differential diagnostic test. But further intervention studies are needed before use of PCT in clinical routine tests. The goal of this review is to study the PCT reliability as infections diagnostic biomarker.

Keywords: Procalcitonin Testing- Bacterial infection- biomarker- antibiotic resistance

Asian Pac J Environment and Cancer; **2 (1)**, 1-3

Submission Date: 12/18/2018 Acceptance Date: 03/01/2019

Introduction

Among all types all diseases, for example [1], cancer than ever much more important [2-3]. Cancer has always been the most important of all diseases. The types of cancers include gastric cancer, brain cancer, breast cancer, ovarian cancer, lung cancer [4-10]. Many studies have shown that there is a relationship between the presence of infectious agents and the incidence of cancers. Many human infections are caused by bacteria. For example, brucellosis in humans is an infectious disease produced by the brucella bacteria. This bacterium causes infectious disease in the heart, brain and bone tissues. Genetic studies of the bacterium in infectious patients have led researchers to focus on cancer humans [11]. Therefore early diagnosis of bacterial infection is appropriate to successful treatment and reduce mortality rate due to it and reducing the risk of cancer. Serious bacterial infections can be treated with antibiotics, which work

by disrupting the bacterium's metabolic processes, but antibiotic-resistant strains are starting to emerge, indeed early identification of bacterial infections, is important because they can be life-threatening. It allows proper prescription of specific treatment for bacterial inflammatory disease and avoid antibiotic resistance phenomena and unnecessary antibiotics administration. On the other hand the inappropriate use of antibiotics in the cases which the illness is not bacterial in origin, may cause delays in proper treatment [12-13]. The conventional diagnostic tests, included inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and leukocyte count, ... helps to solve clinical suspicion of infection, but use these tests have some limitation because of their lack of specificity for infections origins. these tests cant differentiating between bacterial infections, viral infections and systemic inflammation. On the other sides, Microbiologic tests (culture) last where abouts 24-48 hr, and negative results do not show

Corresponding Author:

Dr. Azim Akbarzadeh Khiyavi
Department of Pilot Nanobiotechnology, Pasteur Institute of Iran, Tehran, Iran.
Email: azimakbarzadehkhiyavi21@gmail.com

the definite absence of infection. Moreover, only low percent of blood cultures show microorganisms. So, differentiation between infections origin, infection states and aseptic inflammation is often a challenge in clinical practice. Therefore, there is an obvious need to specific tests to decisive diagnosis [12].

Discussion

Procalcitonin (PCT) engagement etiology in bacterial infection

The initiator element for elevated level of PCT is infection and PCT as component of the complex proinflammatory activity of the innate immune system [14-15]. Different surveys have demonstrated that patients with sepsis have elevated serum PCT levels that this increment is related with the outcome of the disease [16]. Increase in Serum PCT levels have been indicated increasing severity of bacterial infection. So an elevated PCT level might be as an indicator for infectious process [17]. PCT relation with bacterial infection in the pathogenesis of bacterial infection inflammatory. Cytokines have important role. These cytokines initiate the innate immune system's response to the bacterial pathogen (IL)-1 β , tumor necrosis factor (TNF), and IL-6). The role of proinflammatory cytokines during the innate immune activity is a major component of the pathophysiology of bacterial infection [18-19]. In inflammatory condition because of bacterial infection, CALC-1 gene expression increased that leading to release of PCT that related with bacterial infection status [15-20]. New studies identified that PCT is a Promoter agent of inflammatory cascade such as increase in leukocyte secreted inflammatory cytokines, expression of surface markers on leukocyte, increases leukocyte-derived cytokines and also incensement in nitric oxide [15- 21].

Procalcitonin (PCT) as diagnostic test for bacterial infection

Procalcitonin is a peptide precursor of calcitonin composed of 116 amino acids that produced by parafollicular cells of the thyroid and neuroendocrine cells of the lung and the intestine. Calcitonin being involved with calcium homeostasis. In the 1997s, researchers founded that the PCT levels were raised in bacterial infection patients [15-22]. Later in further studies, researchers founds, increased plasma PCT was could be additional and helpful criteria for definition of bacterial infection origin (2003y) [15-23]. Chris et al (2004y) in Cluster-randomized, Single-Blinded Intervention Trial found that the procalcitonin level can help guide antibiotic therapy. In this experiment, based on evaluate serum procalcitonin concentrations, use of antibiotics was more or less discouraged (<0.1 $\mu\text{g/L}$ or <0.25 $\mu\text{g/L}$) or improved (≥ 0.5 $\mu\text{g/L}$ or ≥ 0.25 $\mu\text{g/L}$), respectively [24]. In an earlier survey nonrandomized trial, study results indicated "limited, prognostic value" of procalcitonin measurement [25]. Research Trials from 2009 (Schuetz, et al) and 2008 (Briel, et al) have presented data that shown, procalcitonin test may be useful guide therapy in bacterial infection and

reduce antibiotic use, these ways can help save on cost of antibiotic administration and antibiotic resistance [26-27]. The procalcitonin test is relatively new, but its utilization is increasing. In Differential Diagnosis procedures, Procalcitonin levels may be helpful to distinguish bacterial infections from nonbacterial infections. The procalcitonin test has been approved by the U.S. Food and Drug Administration (FDA) for ordered in along with other laboratory assessments as effective diagnostic criteria in critically ill patients for progression of systemic bacterial infections. For diagnostic purposes, it is best used during the first days of infections. It may be used later on to monitor the response to treatment. Procalcitonin may be ordered, along conventional tests such as a C-reactive protein (CRP), blood culture, complete blood count (CBC),....The procalcitonin level in the healthy individuals blood is low as below the limit of detection (0.01 $\mu\text{g/L}$) of clinical assays [12]. The procalcitonin level rises in a proinflammatory conditions, especially with bacterial provenance. In proinflammatory cases, procalcitonin produced mainly by the cells of the lung and the intestine. Bacterial origin infections with an associated systemic response rises, the blood levels of procalcitonin into 100 $\mu\text{g/L}$ (half-life of 25 to 30 hours in serum). Low levels of procalcitonin in a seriously ill person represent a low risk of sepsis but do not except it. Low concentrations may indicate a localized infection. It may also show another origin such as viral infection, or trauma elevated levels mark a high probability of bacterial sepsis and higher risk of progression to severe state. Moderate increment may be because of non-infectious condition or due to an early infection. The procalcitonin test provides additional data that may help appropriate treatment to be initiated sooner.

In conclusion, Recent studies have shown that it has promise in helping to evaluate the seriously ill person situation is with systemic bacterial infection. Elevated serum PCT show the severity of the inflammation, and a reduced level is a indicator of improvement, indeed reducing procalcitonin levels in a person being treated for a severe bacterial infection indicate a response to therapy during bacterial treatment. PCT evaluating test offer important procedure in early diagnosis in during antimicrobial treatment in bacterial infections.

In fact, PCT can be useful for antimicrobial treatment and its utilization may safely cause decrease in unnecessary antimicrobial therapy [15-28]. Research show that, treatment based on PCT-test protocols is effective guide for antibiotic treatment in bacterial infections [29]. Occasionally, a procalcitonin test may be ordered at intervals to monitor the effectiveness of antimicrobial treatment.

References

1. Ebrahimi Far M, MazdapourM, Kaki A, Mohammadi P, et al (2015). Comparison of Biochemical Factors and Liver Enzymes in type 2 Diabetes Patients and Healthy Individuals. Bull. Env. Pharmacol. Life Sci, 4, 1-4.
2. Ebrahimi Far M, Nili-Ahmadabadi A, Akbarzadeh A, et al

- (2017). Preparation, Characterization and Cytotoxic Effects of Pegylated Nanoliposomal Containing Carboplatin on Ovarian Cancer Cell Lines. *Ind J Clin Biochem*, 32, 230-234.
3. Arshad Z, Rezapour-Firouzi S, Mohammadian M, et al (2018). The Sources of Essential Fatty Acids for Allergic and Cancer Patients; a Connection with Insight into Mammalian Target of Rapamycin: A Narrative Review. *Asian Pac J Cancer Prev*, 19, 2391-2401.
 4. Ebrahimi Far M, Hasanzade Ganroudsari M, Kazemi M, et al (2017). Enhancing Effects of Curcumin on Cytotoxicity of Paclitaxel, Methotrexate and Vincristine in Gastric Cancer Cells. *Asian Pac J Cancer Prev*, 18, 65-68.
 5. Izadi M, Ebrahimi Shahemabadi H, Kanaani L, et al (2016). Investigation of characteristics of loaded carboplatin on the liposomal nanoparticles on the cell carcinoma of the human brain c6. *Adv. Biores*, 7, 113-118.
 6. Kanaani L, Ebrahimi Far M, Kazemi M, et al (2017). General Characteristics and Cytotoxic Effects of Nano-Poly (Butyl Cyanoacrylate) Containing Carboplatin on Ovarian Cancer Cells. *Asian Pac J Cancer Prev*, 18, 87-91.
 7. Kanaani L, Javadi I, Ebrahimi Far M, Ebrahimishahmabadi H, et al (2017). Effects of cisplatin-loaded niosomal nanoparticles on BT-20 human breast carcinoma cells. *Asian Pac J Cancer Prev*, 18, 365-368.
 8. Poy D, Ebrahimi Shahemabadi H, Akbarzadeh A, et al (2017). Carboplatin liposomal nanoparticles: preparation, characterization and cytotoxicity effects on lung cancer in vitro environment. *International Journal of Polymeric Materials and Polymeric Biomaterials*, 67, 367-370.
 9. Poy D, Akbarzadeh A, Ebrahimi Shahmabadi H, et al (2016). Preparation, Characterization and Cytotoxic Effects of Liposomal Nanoparticles Containing Cisplatin: An in Vitro Study. *Chemical Biology & Drug Design*, 88, 568-573.
 10. Mohamadi N, Mohammadian M, Toofani Milani A, et al . Toxicity of cisplatin-loaded poly butyl cyanoacrylate nanoparticles in a brain cancer cell line: Anionic polymerization results. *Asian Pac J Cancer Prev*, 2017, 18, 629-32.
 11. Naser P. brucellosis: generates infections and cancer in humans. *Journal of arak university of medical sciences*, 2011;14(6):95-99.
 12. Dandona P, Nix D, Wilson MF, Aljada A, Love J, Assicot M, et al. Procalcitonin increase after endotoxin injection in normal subjects. *The Journal of Clinical Endocrinology & Metabolism*. 1994;79(6):1605-8.
 13. Shaikh MM, Hermans LE, Van Laar JM. Is serum procalcitonin measurement a useful addition to a rheumatologist's repertoire? A review of its diagnostic role in systemic inflammatory diseases and joint infections. *Rheumatology*. 2015;54(2):231-40.
 14. Gilbert DN. Procalcitonin as a biomarker in respiratory tract infection. *Clinical infectious diseases*. 2011;52(suppl 4):S346-S50.
 15. Shiferaw B, Bekele E, Kumar K, Boutin A, Frieri M. The Role of Procalcitonin as a Biomarker in Sepsis. *J Infect Dis Epidemiol*. 2016;2(006).
 16. Afsar I, Sener AG. Is procalcitonin a diagnostic and/or prognostic marker in sepsis? *Infectious Diseases in Clinical Practice*. 2015;23(1):3-6.
 17. Kibe S, Adams K, Barlow G. Diagnostic and prognostic biomarkers of sepsis in critical care. *Journal of antimicrobial chemotherapy*. 2011;66(suppl 2):ii33-ii40.
 18. Stearns-Kurosawa DJ, Osuchowski MF, Valentine C, Kurosawa S, Remick DG. The pathogenesis of sepsis. *Annual review of pathology*. 2011;6:19.
 19. Faix JD. Biomarkers of sepsis. *Critical reviews in clinical laboratory sciences*. 2013;50(1):23-36.
 20. Tavares E, Miñano FJ. Immunoneutralization of the aminoprocalcitonin peptide of procalcitonin protects rats from lethal endotoxaemia: neuroendocrine and systemic studies. *Clinical Science*. 2010;119(12):519-34.
 21. Assicot M, Bohuon C, Gendrel D, Raymond J, Carsin H, Guilbaud J. High serum procalcitonin concentrations in patients with sepsis and infection. *The Lancet*. 1993;341(8844):515-8.
 22. Karzai W, Oberhoffer M, Meier-Hellmann A, Reinhart K. Procalcitonin—a new indicator of the systemic response to severe infections. *Infection*. 1997;25(6):329-34.
 23. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 secm/esicm/accp/ats/sis international sepsis definitions conference. *Intensive care medicine*. 2003;29(4):530-8.
 24. Christ-Crain M, Jaccard-Stolz D, Bingisser R, Gencay MM, Huber PR, Tamm M, et al. Effect of procalcitonin-guided treatment on antibiotic use and outcome in lower respiratory tract infections: cluster-randomised, single-blinded intervention trial. *Lancet*. 2004;363(9409):600-7.
 25. Brunkhorst F, Al-Nawas B, Krummenauer F, Forycki Z, Shah P. Procalcitonin, C-reactive protein and APACHE II score for risk evaluation in patients with severe pneumonia. *Clinical microbiology and infection*. 2002;8(2):93-100.
 26. Schuetz P, Christ-Crain M, Thomann R, Falconnier C, Wolbers M, Widmer I, et al. Effect of procalcitonin-based guidelines vs standard guidelines on antibiotic use in lower respiratory tract infections: the ProHOSP randomized controlled trial. *Jama*. 2009;302(10):1059-66.
 27. Briel M, Schuetz P, Mueller B, Young J, Schild U, Nusbaumer C, et al. Procalcitonin-guided antibiotic use vs a standard approach for acute respiratory tract infections in primary care. *Archives of internal medicine*. 2008;168(18):2000-7.
 28. Riedel S. Procalcitonin and the role of biomarkers in the diagnosis and management of sepsis. *Diagnostic microbiology and infectious disease*. 2012;73(3):221-7.
 29. Hohn A, Schroeder S, Gehrt A, Bernhardt K, Bein B, Wegscheider K, et al. Procalcitonin-guided algorithm to reduce length of antibiotic therapy in patients with severe sepsis and septic shock. *BMC infectious diseases*. 2013;13(1):1.



This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License.