Role of Serum Procalcitonin in Sepsis

Haris Alvi, Muhammad Rehan and Abu Talib

ABSTRACT

Objective: Role of serum procalcitonin in sepsis

Study Design: Descriptive / Cross sectional study

Place and Duration of Study: This study was carried out at the Mamji Hospital Karachi from January 2013 to July 2014.

Materials and Methods: The adult patients presented with short duration of fever, altered consciousness, bed sores, cough, increased frequency of urine, diarrhea and vomiting and abdominal pain. ESR, CRP and serum procalcitonin level were sent simultaneously with blood, sputum and urine cultures. The study was conducted in Mamji Hospital F. B. area, data was recorded in a preset proforma. The features like biodata, symptoms/signs, biochemical test and cultures reports were shown in tables. The data was analysed on SPSS version 15.

Results: In this study total cases were 33. Males were 19(55%) and 14(45%)were females. The mean age was 47 $\pm$ 19. With the age range from 28 to 68 years. Males were slightly more than females. The patients were divided into two groups according to the level of procalcitonin. Group I were those with raised procalcitonin level > 0.5 and group II were those with procalcitonin level < 0.5. The ESR and CRP were raised in every case. In Group I total number of cases were 27, pneumonias 06 cases, UTI06 cases, bacterial meningitis 05 cases, bacterial dysentery 05 cases, skin infection 04 cases and septic arthritis 01 cases. In group II total cases were 06, 02 cases were viral one is cytomegalovirus and other is Epstein–Barr virus, 01 cases was connective tissue disease and was diaganosed as systemic lupus erythematosus 01 case was wegner's granulomatosis, 01 case was bronchogenic carcinoma and 01 was peripartum cardiomyopathy. The culture report showed 08 cases were E coli, 6 cases were pseudomonas aeroginosa, 5 cases were staphylococcus aureus, 3 cases Enterobacter 03 cases and streptococcus pneumonia 02 cases.

Conclusion: In cases with fever the early detection of high serum procalcitonin level will clearly differentiate between inflammatory conditions caused by bacterial rather non bacterial conditions.

Key Words: procalcitonin, fever, sepsis, culture

INTRODUCTION

High serum procalcitonin[1] level can differentiate between inflammatory conditions caused by bacterial rather non bacterial. It is a new blood marker and clearly reasonable rather CRP and ESR. Sepsis[2][3][4] can lead to high mortality so early diagnosis and prompt selection of antibiotic is the utmost requirement and so it reduces complications. Procalcitonin is a precursor of calcitonin, is elevated in early sepsis. So is considered as a good early diagnostic marker[5][6][7][8] of sepsis in serious ill patients. It really helps to clearly the bacterial infections and in selection of appropriate antibiotics and shorten the ICU stay and reduced the complication.

Department of Medicine, Civil Hospital, Karachi, Dow Medical College, DUHS, Karachi.

Correspondence: Dr. Haris Alvi, Associate Professor, Department of Medicine, Civil Hospital, Karachi, Dow Medical College, DUHS, Karachi.
Contact No.: 0333-2234706
E-mail: doctorhalvi@gmail.com

Assicot et al in 1993 was the first person who observed that the procalcitonin level was high significantly in bacterial infections. Normally the level of procalcitonin[9] in healthy people were below the detection level that is (0.01 µg/L) it usually rises due to some inflammatory response especially of bacterial origin. It is produced mainly by the cells of the lung and the intestine. It does not rise significantly with viral or non-infectious inflammations. In severe infection the blood levels of procalcitonin may rise to 100 µg/L in vitro its half-life of 25 to 30 hours. Procalcitonin[10][11] has the greatest sensitivity (85%) and specificity (91%) for differentiating patients with systemic inflammatory response syndrome (SIRS) from those with sepsis, when compared with IL-2, IL-6, IL-8, CRP and TNF-alpha. So procalcitonin levels can reduce unnecessary use of antibiotic[12][13]. Clinically the serum procalcitonin level is widely in use.

Blood infections are very common in our part of the world. Data from US was reported that there were more than half a million cases of blood infections in a calendar year with a high mortality[14]. The key is early

diagnosis and differentiate between infectious to non-infectious conditions. The blood markers like leucocytosis, ESR, CRP have poor sensitivity and specificity. The patients in ER or OPD presented with illness, the early diagnosis and sending different cultures are the gold standard of the management, it helps in identifying definitive organism and antibiotic selection but it needs a delay of 24to 48 hours for first culture and sensitivity report to start the appropriate antibiotics so this delay will create a need to evaluate the early inflammatory marker. So on one hand it cures the patient and on the other hand it reduce the complication. There are chances of false positive results of blood cultures as skin contaminants. Patients with febrile illness and positive blood cultures due to contaminant organisms undergo unnecessary diagnostic measures, hospitalization, and unwarranted antimicrobial therapy, so the prompt checking of serum procalcitonin[15] level can give a logical answer. The procalcitonin level is not elevated in viral infections. Studies in the critical care setting, have clearly proof that the efficacy of serum procalcitonin levels in sepsis. Procalcitonin analysis can be performed in less than 1 hour of reporting in ER, so it is useful for evaluation of febrile patients at risk for bacteremia and sepsis. Early diagnosis of sepsis andprompt start of antibiotics[12] reduces mortality and complications in these patients.

MATERIALS AND METHODS

This is a descriptive / cross sectional study conducted in Mamji Hospital Karachi, a private Hospital. It is a large Hospital and covered a large area of central and north Karachi. The average OPD is more than 450 /day of different specialities and 25-30 admission per day. Emergency room seen more than 350 patients daily. All the patients included were adult and the duration of the study is from Jan 2013 to July 2014.

Basic biodata, detailed history and clinical examination were taken and recorded in preset proforma. The symptoms and sign were recorded and laboratories finding were recorded on the day first and on daily basis. The data were analysed on SPSS version 15.

Inclusion criteria: 1) Adult 18 years and more of age
2) Informed consent
3) Febrile illness
4) Had not received any antibiotic before

Exclusion criteria: 1) Ages less than 18
2) Cultures commonly considers contaminant organism were excluded
3) Patients on antibiotics
4) Cultures that remain negative after fifth day.

RESULTS

Total cases were 33. Males were 19 (55%) and 14(45%) were females. The mean age was 47 ± 19. With the range from 28 to 68 years. Males were slightly more than females as shown in Table No. 1. The patients

were divided into two groups according to the level of procalcitonin. Group I were those with raised procalcitonin level > 0.5 and group II were those with procalcitonin level < 0.5. The ESR and CRP were raised in every case. In Group I total cases were 27, among them pneumonia 06 cases, UTI 06 cases, bacterial meningitis 05 cases, bacterial dysentery 05 cases, skin infection 04 cases and septic arthritis 01 cases. In group II total cases were 06, among them 02 cases were viral one is cytomegalovirus and other is Epstein–Barr virus, 01 case was connective tissue disease and diagnosed as systemic lupus erythematosus 01 case was wegner's granulomatosis, 01 case was bronchogenic carcinoma and 01 case was peripartum cardiomyopathy. The culture report showed 08 cases were E coli, 6 cases were pseudomonas aeroginosa, 5 cases were staphylococcus aureus, 3 cases were Enterobacter, 03 cases were streptococcus pneumonia and 02 cases were klebsella pneumonae. The procalcitonin level, ESR, CRP and total WBC count were shown in Table No. 2 of Group I and of group II in Table No. 3. The Cultures reports of the specimen were shown in Table No. 4.

Table No.1: Biodata

Total Cases	33
Male	19 (55%)
Female	14 (45%)
Mean age	47±19 YEARS
Range of age	28-68 YEARS
Group I	27 (81%)
Group II	06 (19%)

Table No.2: Group I

Infection	No. of Cases	Total Lecocyte Count	C Reactive Protein	Procal-citonin Level	ESR
Pneumonia	06	23000	116	1.5	77
UTI	06	17000	87	1.8	65
Bacterial meningitis	05	15000	145	2.0	45
Bacterial Dysentary	05	14000	57	1.5	55
Soft Tissue Infection	04	22000	66	2.0	63
Septic Arthritis	01	24000	89	3.0	80

Table No.3: Group II

Diseases	No. of cases	Total Leucocyte Count	C Reactive Protein	Proca-lcitonin Level	ESR
Viral infection	02	9000	54	0.2	26
Connective tissue disease	01	6600	23	0.3	100
Vasculitis	01	7000	55	0.2	95
Carcinoma	01	5400	66	0.1	100
Peripartum Cardiomyopathy	01	7600	52	0.3	67

Table No. 4: Culture Report

Organism	No. of Cases
E coli	08
Pseudomonas aueregenosa	06
Staphlococcus aureus	05
Enterobacter	03
Streptococcus pneumonae	03
Klebsella pneumonia	02

DISCUSSION

The health structure of Pakistan is not so developed nor it covers its citizens and the people of this country are poor and uneducated so they cannot understand and maintain their health status. There are climate extremes and resources are insufficient to cope with the situation. I mean to state that the health issues are great and they are difficult to cope. When in emergency if some patients report with the feature of febrile illness and with some comorbid then it is our responsibility to counter the response and manage the patient requirement. In this situation it is pertinent to identify infectious diseases with non infectious febrile illness. The old markers[16] like raised ESR, CRP and raised WBC would not enough to predicts. It been shown that serum procalcitonin level [10] has a good specificity and a good positive predictive value for systemic bacterial infection. With a cut off level for PCT of >0.5 ng/ml for diagnosis of bacterial infection. PCT[17] levels only rose significantly during systemic bacterial or fungal infection. In patients with fever or inflammatory syndrome who have PCT levels >1.2 ng/ml, we consider that bacterial infection. In this study we studied 33 patients they were 47 ± 19 years and the age has same worldwide distribution shown in other studies[18,19,20] males were little bit more than females. In other studies the ratio of males were also higher, all the patient were presented with fever and they were toxic in look and very much sick and it was a sign to set that all the investigation like blood complete picture , renal profile, liver profile, random blood sugar level, urine detailed report, ECG, X-ray chest PA view, abdominal ultrasound and the possible sample of culture from the sites of involvement together with ESR, CRP and serum procalcitonin levels[21,22] were sent and convectional antibiotic was started according to the available culture sensitivity report of the hospital and related co-morbids. Patients were admitted in intensive care unit and follow and up them daily. Among the patients 27 were in group I which had high serum procalcitonin level and the infections were lobar pneumonia and bronchopneumonia, UTI, bed sores, meningitis and arthritis. The commonest organism was E-coli. While in other group there were only six cases and they were two viral, one is SLE, one is bronchogenic carcinoma, one is vasculitis and one is peripartum cardiomyopathy. The duration of the stay in ICU, selection of the antibiotics[23], other treatments modalities were very much influenced by the serum procalcitonin level and because of the perfect timing and early diagnosis we saved all the patients for that hospital stay.

The patients in group I were all serious and they appeared to be very toxic but with the help of serum procalcitonin level and prompt antibiotic they all saved and it is highly recommended that the PCT level is very effective. Other[15,18,20,21] studies on the same issue were also have promising result. In group II the case of peripartum cardiomyopathy was very challenging as she had a C- section 20 days back and had no known co-morbid, her antenatal care was also uneventful and it was her third child, and patient was breathlessness, fever with no pedal edema or raised JVP but the normal serum procalcitonin level easily gave a clue to think for else and her ejection fraction on ECHO was 30 %. Our study showed a 100 % result while in other studies there were nearly 97 % were reported. The main reason of such high sensitivity is the less number of cases and early and prompt timing of the test.

CONCLUSION

In cases with fever the early detection of high serum procalcitonin level will clearly differentiate between inflammatory conditions caused by bacterial rather non bacterial conditions. Further studies were required to set the format but it is an early and quick way to differentiate the issue.

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Castelli GP, Pognani C, Meisner M, Stuani A, Bellomi D, Sgarbi L. Procalcitonin and C reactive protein during systemic inflammatory response syndrome, sepsis and organ dysfunction. Critical Care 2004;8:R234.

2. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology in the united states from 1979 through 2000. N Engl J Med 2003;348:1546-54.

3. Angus DC, Linde Zwirbe WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe infection in United States: analysis of incidence, outcome and associated costs of care. Crit Care Med 2001;29:1303-10.

4. Choi SW, Kim H, Kim KH, Shin DW, Park JS, Roh JY, et al. Procalcitonin as a prognosis marker for the severe sepsis and septic shock patients in Emergency Department. Korean J Critical Care Med 2011;26:250.

5. Meisner M, Tschaikowsky K, Palmaers T, Schmidt J. Comparison of procalcitonin(PCT) and C-reactive protein (CRP) plasma concentration at different SOFA scores during the course of sepsis and MODS. Critical Care 1999;3:45.

6. Roxen C, Stephanie V, Herbert S, Kristein VE, et al Plasma procalcitonin and C reactive protein in acute septic shock. Clinical and biological correlates. Critical Care. Med 2002;30(4):757-762

7. Simon L, Gauvin F, Devendra K, Amre, Louis PS, Lacroix J. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: A systematic review and meta analysis. Clin Infect Dis 2004;39(2):206-17.

8. Louis VJ. Procalcitonin The marker of sepsis? Critical Care Med 2000;28(4):1226-28.

9. KennethL B, Richard S, Eric N. Procalcitonin assay in systemic inflammatory infection and sepsis: Clinical utility and limitations. Critical Care Med 2008;36(3): 941-952.

10. Yuan GS, Yin Z, Feng Q, Jiong Y, Wang Hong M. Procalcitonin is a Marker of Gram negative Bacteremia in Patients with sepsis. Am J Med Sci 2015;349(6):499-504.

11. Akiko N, Hideo W, Makoto I, Tsuyoshi H, Hiroyuki S, et al. Efficacy of procalcitonin in early diagnosis of bacterial infections in a critical care unit. Shock 2009;31(6): 587-592.

12. Jensen Jens U, Lara H, Bettina L, Bestle Mortem H, Mohr Thomas T, et al. Procalcitonin guided intenvention against infections to increase early appropriate antibiotics and improve survival in the intensive care unit. A randomized trial. Critical Care Med 2011;39(9):2048-2058.

13. Schuetz P, Chiappa V, Briel M, Greenwald JL. Procalcitonin Algorithms for Antibiotic therapy decisions. A systematic review of randomized controlled trials and recommendations for clinical Algorithms. Arch intern Med 2011;171(15): 1322-1331.

14. Ulrik JJ, Lars H, Hartvig JT, Kurt E, Peter S, Michael T. Procalcitonin increased in early identification of critically ill patients at high risk of mortality. Cri Care Med 2006;34(10):2596-2602

15. Abderrahim O, Janina F, Pierre FT, Nejla, Isabelle AG, et al. Diagnostic Accuracy of procalcitonin for predicting blood culture results in patients with suspected bloodstream infection: An observation study of 35343 consecutive patients. Medicine 2015;94(44):1774.

16. Schuetz P, Christ Crain M, Muller B. Procalcitonin and other biomarkers to improve assessment and antibiotics steward ship in infections:hope for hype? Swiss Med Wkly 2009;139(23-24):318-326.

17. Michael D, Stephen P, Natalie K, Hao Z, Neil H. Procalcitonin correlates with severity of sepsis and mortality in cancer patients. Cri Care Med 2013: 10:1097/01.

18. Pedro FG, Luiz MF, Isabel DP. Procalcitonin as biomarker of infection: implication for evaluation and treatment. Post Author Corrections 2015:10: 1097.

19. Sullivan Shannon M, Rueden V, Kathryn T. Using Procalcitonin in septic shock to guide antibacterial therapy. Dimensions of critical Care Nursing 2016; 23(1):1-2.

20. Ilhan A, Gamze SA. Is procalcitonin a diagnostic and /or prognostic marker in sepsis? Infectious Diseases in Clinical Practice 2015;23(1):3-6.

21. Rafal S. C-reative protein and procalcitonin as markers of infection inflammatory response, and sepsis Clinical Pulmonary Medicine 2007;14(3): 127-139.

22. Phillip S, Issam R, Amin Devendra N. Using procalcitonin-guided algorithms to improve antimicrobial therapy in ICU patients with respiratory infections and sepsis Current Opinion in Critical Care 2013;19(5):453-460.

23. Trienski Tamara L, Thomas M. Implementation of a procalcitonin assay requires appropriate stewardship to result in improved antimicrobial use. Infectious Diseases in Clinical Practice Jan 2015;23(1):1-2.