Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/cegh

Original Article

Procalcitonin in pediatric intensive care unit of a tertiary care hospital

A. Achra^a, P. Narsaria^b, R. Lodha^c, S.K. Kabra^d, A. Kapil^{e,*}^a Senior Resident, Department of Microbiology, All India Institute of Medical Sciences, New Delhi 110029, India^b Senior Resident, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi 110029, India^c Additional Professor, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi 110029, India^d Professor, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi 110029, India^e Professor, Department of Microbiology, All India Institute of Medical Sciences, New Delhi 110029, India

ARTICLE INFO

Article history:

Received 23 November 2015

Accepted 6 January 2016

Available online 4 February 2016

Keywords:

Procalcitonin (PCT)

PICU

Sepsis

Mortality

Antimicrobial therapy

ABSTRACT

Objectives: Study was conducted to determine the role of procalcitonin (PCT) in the diagnosis of sepsis and guide antibiotic therapy in pediatric intensive care unit.

Methods: PCT levels were measured from suspected sepsis patients along with a blood culture.

Results: Out of 52 patients, 30 had initial PCT levels ≥ 2.0 ng/ml, 10 (≥ 0.5 – < 2.0 ng/ml) and 12 (< 0.5 ng/ml). Initial PCT values were significantly higher in non-survivors as compared to that of survivors [15.3 (5.3–45.5) vs. 1.8 (0.33–8) ng/ml; $P = 0.006$].

Conclusions: Measurement of serum PCT levels was found to be helpful in diagnosing sepsis in culture negative patients. Lower PCT values can help in ruling out sepsis and limit antimicrobial use. High initial PCT levels can predict severity of sepsis and mortality.

© 2016 INDIACLEN. Published by Elsevier, a division of Reed Elsevier India, Pvt. Ltd. All rights reserved.

1. Introduction

Sepsis is a major cause of death among critically ill patients. Early diagnosis and administration of appropriate antimicrobial treatment have been shown to reduce morbidity and mortality.^{1,2} However, non-infectious conditions may mimic infection in ICU settings and often leads to antibiotic overuse and misuse, this further adds to the ever increasing concern of antimicrobial resistance. There is a growing body of evidence that supports the use of procalcitonin (PCT) to improve diagnosis of sepsis and guide antibiotic therapy in adult

population.^{3,4} However, there are limited data on the general use of PCT in pediatric population. The purpose of this study was to evaluate the utility of PCT to diagnose sepsis and modify antimicrobial therapy in the critically ill patients in pediatric intensive care unit (PICU).

2. Materials and methods

This study was conducted at PICU from September 2013 to June 2014. The ethical approval was taken for the study from the Institutional ethical board. All the patients with clinical signs

* Corresponding author. Tel.: +91 11 26594237; fax: +91 11 26588663.

E-mail address: akapilmicro@gmail.com (A. Kapil).

<http://dx.doi.org/10.1016/j.cegh.2016.01.001>

2213-3984/© 2016 INDIACLEN. Published by Elsevier, a division of Reed Elsevier India, Pvt. Ltd. All rights reserved.

of sepsis, severe sepsis or septic shock at the time of admission to ICU were included in study.⁵ The serum PCT levels were measured along with a blood culture and cultures from other sites at the discretion of the primary critical care team caring for patients in an effort to diagnose sepsis and guide antibiotic therapy. PCT levels were measured at the time of admission and a repeat PCT level was measured based on the decision of the clinician in a patient not responding to therapy or when a patient developed new focus of infection (pneumonia).

PCT concentrations were measured by VIDAS® B-R-A-H-M-S PCT kit using Mini-Vidas instrument (BioMérieux, Marcy-l'Étoile, France) with a measuring range of 0.05–200 ng/L, and blood culture was done by BacT/ALERT 3D system (BioMérieux, Marcy-l'Étoile, France).

As per the manufacturer's instructions, PCT values <0.5 ng/ml were considered as unlikely to suffer from systemic bacterial sepsis, with low risk of progression to severe sepsis. PCT values ≥0.5–<2.0 ng/ml were considered as possibly suffering from systemic bacterial infection and moderate risk of progression to severe sepsis. PCT values ≥2.0 ng/ml were likely to suffer systemic bacterial sepsis with high risk of progression to severe sepsis. To assess effectiveness of PCT measurement, we retrospectively analyzed clinical data of 52 consecutive patients.

Statistical analysis was performed using Wilcoxon rank-sum (Mann–Whitney) test.

3. Results

The median age of patients was 1.6 years (range 5 days–13 years) (Table 1). 30 patients had initial PCT levels ≥2.0 ng/ml, and antibiotic therapy was escalated in 19 patients based on high PCT values and worsening clinical symptoms (Table 2). However, empiric antibiotics started before obtaining sample for PCT were continued in 11 patients. 13 (43%) patients in this group died due to septic shock and initial PCT values were high [median 22.59 (range 5.3 to >200) ng/ml].

10 patients had PCT values ≥0.5–<2.0 ng/ml. Empiric antibiotic therapy was continued in 5 patients, while therapy was escalated in 4 patients due to worsening of clinical symptoms. One patient with PCT levels 0.61 ng/ml did not receive any antibiotic. There were three deaths in this group of patients. Persisting high levels and rise in PCT levels 1.1 ng/ml (day1), 1.1 ng/ml (day10) and 6.06 ng/ml (day23) were noted in one of these three patients, and antibiotics were escalated.

12 patients had PCT values <0.5 ng/ml, out of which empiric antibiotic therapy was continued in 6 patients.

Antibiotics were deescalated in 3 patients; however, antibiotics had to be escalated in 3 patients due to worsening clinical symptoms. One patient died in this group, though the cause of death was not sepsis and PCT levels remained <0.5 ng/ml when measured on two occasions.

Overall initial PCT values were significantly higher in non-survivors as compared to that of survivors [15.3 (5.3–45.5) vs. 1.8 (0.33–8) ng/ml; $P = 0.006$].

The blood culture was negative in 49 patients, while in 3 patients where blood culture was positive; PCT values were high, >200 ng/ml (*Enterococcus faecium*), 12.07 ng/ml (*Escherichia coli*) and 3.64 ng/ml (*Salmonella Typhi*).

PCT values were also high in 3 patients with positive bronchoalveolar lavage fluid culture; 5.61 ng/ml (*Pseudomonas aeruginosa*), 2.52 ng/ml (*Klebsiella pneumonia*) and 1.36 ng/ml (*Acinetobacter* spp.).

4. Discussion

Sepsis in most cases is caused by bacterial or fungal infections. Culture and drug sensitivity testing is considered as the gold standard for diagnosis, but culture report becomes available only after 48–72 h. As seen in 3 patients a high PCT value along with positive blood cultures confirms sepsis and rules out possibility of false positive cultures (contamination) and there by guide appropriate antimicrobial therapy.

Also blood culture positivity might be very low in tertiary care ICU settings, as seen in our study, because most of the patients are delayed referrals and on broad spectrum antibiotics prior to admission. Mortality due to septic shock increases significantly (7.6%), with each hour of delay in appropriate antimicrobial chemotherapy.¹ Quantitative PCT measurement, which is available within 30 min can help in timely diagnosing these culture negative sepsis patients and effective management.⁶ Respiratory tract is the one of common sources of sepsis in ICU patients and a positive bronchoalveolar lavage fluid culture along with high serum PCT levels helps distinguish pneumonia from colonization.

PCT measurements (cut off ≥2 ng/ml) helped in identifying these 30 (58%) of suspected sepsis patients and escalation of antibiotic therapy could be done in 19 (36%) patients. In spite of escalated antibiotic therapy 10 out of 19 patients died due to septic shock. Median PCT level was quite high in these patients 34.05 (12.07 to >200). It is documented that a high maximum PCT and an increase for one day are both independent predictors of 90-day mortality.⁷ Another study suggests that a PCT decrease >80% during first 72 h may help to identify individuals at reduced mortality risk, while a non-decrease or increase of PCT within this time frame may help to find patients, who are at high mortality risk.⁸ Increase in PCT (5.3–5.61 ng/ml) was noted at 72 h in one of our nonsurvivors. As repeat PCT measurements were performed on a limited number of patients we could not find such correlation. A recent study from our institute suggested that PCT value ≥7 ng/ml obtained at the time of admission to the adult medical ICU is a predictor of short-term mortality.⁹ High serum PCT levels can help in stratification of patients and to identify patients at higher risk of adverse outcomes. The numbers are small to derive any correlation but a preliminary data suggest that

Table 1 – Baseline clinical information of patients.

Diagnosis at admission	Number (%)
Pneumonia	12 (23)
Sepsis	10 (19)
Congenital heart disease	7 (13)
Lymphoreticular malignancy	4 (8)
Dengue shock syndrome	4 (8)
Central nervous system disease	3 (6)
Others	12 (23)

Table 2 – Correlation of PCT values with antibiotic change and final outcome.

PCT values (ng/ml)	No. of patients	Antibiotics deescalated	No change in antibiotics	Antibiotics escalated	Recovered	Death
<0.5	12	3	6	3	11	1
≥0.5–<2.0	10	1	5	4	8	2
>2.0	30	0	11	19	17	13

aggressive supportive care along with escalated antibiotic therapy can help in reducing mortality in these patients.

As documented previously PCT measurements assisted in identifying patients without sepsis and limit antimicrobial use.³ Antibiotics could be deescalated in 4 (7.7%) and 11 (21%) did not require escalation on the bases of single PCT measurement (cut off <2 ng/ml). In a patient of autoimmune encephalitis, repeat PCT levels on two occasions (<0.5 ng/ml) were helpful in ruling out sepsis in spite of worsening clinical symptoms. However in spite of low PCT values in 4 patient's (PCT ≥0.5–<2.0 ng/ml) and 3 patients (PCT <0.5 ng/ml), antibiotics were escalated due to worsening of clinical symptoms. This could be due to low PCT values early in the course of infection and a repeat PCT test showing higher values, performed after 6–12 h could have helped in diagnosing sepsis in these patients.³ The number of specimen that could be tested in all patients was not possible in this pilot study due to financial constraints in doing the tests in all patients at different intervals. This was the major limitation of our study, but that could have been helpful in monitoring and antibiotic deescalate decisions in these patients. As the study was conducted on patients admitted from single unit, it was not possible to recruit enough number of patients during the study period. Also as this was a retrospective study, it has all the limitations associated with retrospective studies, as such.

5. Conclusions

Our study shows that PCT measurement can assist management of culture negative sepsis and compliment clinical signs to guide antimicrobial therapy in pediatric population. However a larger prospective study needs to be carried out to assess PCT based algorithms for antibiotic therapy decisions in pediatric population.

Author's contributions

A. Achra: Conceptualized the study, collected the data, reviewed the literature and drafted manuscript.

P. Narsaria, R. Lodha and S.K. Kabra: Conceptualized the study and involved in management of the patients.

A. Kapil: Conceptualized the study, reviewed the literature and revised manuscript for important intellectual content.

All authors critically reviewed the manuscript and approved the final version of the manuscript.

Conflicts of interest

The authors have none to declare.

Acknowledgment

We thank Dr. Navjeet Singh, head medical affairs, BioMerieux India for his technical support.

REFERENCES

- Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med.* 2006;34:1589–1596.
- Becker JU, Theodosios C, Jacob ST, Wira CR, Groce NE. Surviving sepsis in low income and middle-income countries: new directions for care and research. *Lancet Infect Dis.* 2009;9:577–582.
- Kibe S, Adams K, Barlow G. Diagnostic and prognostic biomarkers of sepsis in critical care. *J Antimicrob Chemother.* 2011;66(suppl 2):ii33–ii40.
- 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.
- Goldstein B, Giroir B, Randolph A. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med.* 2005;6(1):2–8.
- Anand D, Das S, Bhargava S, et al. Procalcitonin as a rapid diagnostic biomarker to differentiate between culture-negative bacterial sepsis and systemic inflammatory response syndrome: a prospective, observational, cohort study. *J Crit Care.* 2015;30(1):218.
- Jensen JU, Heslet L, Jensen TH, Espersen K, Steffensen P, Tvede M. Procalcitonin increase in early identification of critically ill patients at high risk of mortality. *Crit Care Med.* 2006;34:2596–2602.
- Schuetz P, Maurer P, Punjabi V, Desai A, Amin D, Gluck E. Procalcitonin decrease over 72 hours in US critical care units predicts fatal outcome in sepsis patients. *Crit Care.* 2013;17: R115.
- Jain S, Sinha S, Sharma SK, et al. Procalcitonin as a prognostic marker for sepsis: a prospective observational study. *BMC Res Notes.* 2014;7:458.