ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 49. 23
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 4, Issue – 1, January - 2019, Page No. : 175 - 178

Cortisol Levels and Mortality in Severe Sepsis at Tertiary Care Center Northern Western, Rajasthan

Monika[1], Preety Kumari[2], Vikas[3], Rajendra Bhati[4], Ritvik Agrawal[5], Kapil Dev Chahar[6], J K Meel[7], R P Agrawal[8]

[1,5] Senior Resident, [2-4] Resident, [6] Assistant Professor, [7]Medical Officer [8] Senior Professor

Department of Medicine, S.P. Medical College & A.G. of Hospitals, Bikaner

Corresponding Author: Preety, Resident, Department of Medicine, S.P. Medical College & A.G. of Hospitals, Bikaner

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Background: Increased cortisol results in increased vascular tone and cardiac output. These effects are necessary for the body to counteract inflammation in situations such as septic shock, where the inflammatory response is activated rapidly.

Methods: Hospital based cross sectional study conducted on 50 cases admitted in medical intensive care unit of SPMC and associated group of hospitals, Bikaner with sepsis and septic shock were taken as per WHO criteria.

Results: Mean serum cortisol level in survivors was 165.37±46.20 and in non survivors it was 489.33±68.79 and on applying student 't' test, the difference was found statistically highly significant ($p<0.001$).

Conclusion: Increased serum free cortisol was associated with high mortality. Keywords- Serum free cortisol, survivors, non survivors.

Introduction

Cortisol is a hormone secreted by the adrenal cortex and is essential for the maintenance of stability of major organs. Increased cortisol results in increased vascular tone and cardiac output. These effects are necessary for the body to counteract inflammation in situations such as septic shock, where the inflammatory response is activated rapidly.[1]

Diagnosing sepsis is not always straightforward, particularly in critically ill patients who often have complex ongoing disease processes. Many of these patients will also recently have received antimicrobial therapy that can render microbial cultures negative; several observational studies have reported negative culture results in as many as 30–40% of ICU patients with severe sepsis[2-4]. Even when cultures are positive, results can take several days to become available, thus slowing the diagnostic process.

The traditional approach to sepsis diagnosis was based on clinical signs and symptoms (or markers) of sepsis such as fever, tachycardia and tachypnea, supported by relevant microbiological data. More recently, biological laboratory markers (biomarkers) have been used, ranging from the relatively simple white blood cell count and C-reactive protein (CRP) to more complex biomarkers, such as procalcitonin (PCT) or cytokine levels and (to some extent) coagulation markers.

Biomarkers of sepsis can potentially be used for prognosis to predict the development of organ dysfunction, to guide antibiotic therapy and to evaluate the response to therapy[5]. Many biomarkers have been proposed over the years, but there is little consensus on which is best and the exact role of individual markers remains uncertain. Biomarker

development represents an important and ongoing area of research within the global sepsis field.

Sam et al[6] studied the relationship between cortisol levels and mortality in severe sepsis and found cortisol levels were elevated in most patients with septic shock. Serum cortisol level > or = 1242 nmol/l were associated with significantly higher mortality. Such types of studies have not been done in our area so to find out any such type of correlation we carried out the study.

Materials And Methods

Place of Study

The Study was carried out in medical intensive care unit, S.P. Medical College & Associated Group of P.B.M. Hospitals, Bikaner.

Duration of study

From April 2015 to 31 March 2016

Design of study

The study was cross sectional study.

Subject selection

50 cases admitted in medical intensive care unit of SPMC and associated group of hospitals, Bikaner with sepsis and septic shock were taken as per WHO criteria.

Inclusion Criteria

Patients admitted in medicine intensive care unit, PBM Hospital, Bikaner with sepsis and septic shock.

Exclusion Criteria

- Age <18 years
- Surgical patients and trauma patients
- Patients who have received glucocorticoid treatment
- Patients receiving etomidate, ketoconazole or any other drug influencing the steroid metabolism.
- Cirrhosis
- Malignancies
- Chronic renal failure

Analysis of Serum Free Cortisol Concentrations

The sample preparation and measurement for serum free cortisol analysis was carried out using HPLC (High Performance Liquid Chromatography)- coupled high resolution MS (mass spectrometry) according to the validated method described by Montskó et al.[7]

Statistical Analysis

Data were assessed using statistical program SPSS version 22.00.

Data was expressed as mean ± SD unpaired student T test was used to compare cases. Correlation between total and free cortisol level and prognosis of critically ill patients was done by correlation coefficient analysis. P value <0.05 will be considered to be significant.

Observations

Table 1

Distribution of cases according to serum free cortisol level in relation to outcome

Serum Free Cortisol (nmol/L)	Survivors		Non Survivors		Total	
	No.	%	No.	%	No.	%
≤200	28	87.5	0	-	28	56.0
201-400	4	12.5	2	11.1	6	12.0
>400	0	-	16	88.9	16	32.0
Total	32	100	18	100	50	100
p-value	0.001					

According to table 1, out of total 50 patients, 32 were survivors and 18 were non survivors. In serum free cortisol level group ≤200, there were total 28 patients and they all were survivors, in serum free cortisol level group 201-400, out of total 6, four and 2 patients were survivors and non survivors respectively while in serum free cortisol level >400 group, total 16 patients were found and they were non survivors. the difference was found statistically highly significant (p<0.001).

Table 2: Distribution of cases according to serum free cortisol level

Serum Free Cortisol (nmol/L)	Survivors	Non Survivors
Mean	165.37	489.33
SD	46.20	68.79
t	19.894	
p	<0.001	

Mean serum cortisol level in survivors was 165.37±46.20 and in non survivors it was 489.33±68.79 and on applying student 't' test, the difference was found statistically Highly Significant (P<0.001).

Discussion

Sepsis is basically the harmful host response to infection; systemic response to proven or suspected infection plus some degree of organ hypofunction. In general, when an infectious etiology is proven or strongly suspected and the response results in hypofunction of uninfected organs, the term sepsis (or severe sepsis) should be used[8].

In our study out of total 50 patients, 32 were survivors and 18 were non survivors. In serum free cortisol level group ≤200, there were total 28 patients and they all were survivors, in serum free cortisol level group 201-400, out of total 6, four and 2 patients were survivors and non survivors respectively while in serum free cortisol level >400 group, total 16 patients were found and they were non survivors.

Our study is also comparable to Venkatesh et al[9] in which two hundred twenty serial measurements of plasma-free cortisol, plasma total cortisol, and interleukin-6 were collected from 80 patients (43 placebo and 37 statins). Data from 10 volunteers were used as controls. Compared with controls, in severe sepsis, baseline plasma total cortisol was elevated two-fold (463 nmol/L [284-742 nmol/L] vs 245 nmol/L [200-299 nmol/L], p < 0.001), plasma-free cortisol 20-fold (75 nmol/L [20-151 nmol/L] vs 5 nmol/L [5-7 nmol/L], p < 0.001), and plasma-free cortisol/plasma total cortisol ratio six-fold (0.15 vs 0.02, p = 0.058). Baseline plasma-free cortisol, plasma total cortisol, and plasma-free cortisol/plasma total cortisol ratios were significantly higher in non survivors as compared with survivors.

Levy-Shraga et al[10] in their study evaluated the cortisol levels at baseline and after adrenocorticotropin (ACTH) stimulation and determined their association to clinical outcome of critically ill children. Ninety-nine patients were enrolled. The mortality rate of children with a baseline cortisol level of 600 nmol/L or greater was 36% (12/33 patients) versus 18% (12/66 patients) for children with a baseline cortisol level of less than 600 nmol/L (odds ratio, 2.6 [95% confidence interval, 1-6.6]; P = 0.05). There was a positive correlation between baseline cortisol and lactate levels (r = 0.40, P < 0.0001), vasoactive-inotropic scores (r = 0.24, P = 0.02), and mortality (P = 0.05). There was no correlation between peak cortisol measured at the ACTH test or the delta increment of cortisol from baseline and mortality.

Conclusion

Increased serum free cortisol was associated with high mortality. Hence, serum free cortisol is a reliable indicator of the state of severity, mortality and recovery in critically ill patients with sepsis and multiple organ dysfunction syndrome (MODS).

References

1. Yang S, Zhang L. Glucocorticoids and vascular reactivity. Curr Vasc Pharmacol 2004;2:1–2.
2. Vincent JL, Sakr Y, Sprung CL. Sepsis Occurrence in Acutely Ill Patients Investigators. Sepsis in European intensive care units: results of the SOAP study. Crit. Care Med. 2006; 34(2):344–353.

3. Blanco J, Muriel-Bombín A, Sagredo V. Grupo de Estudios y Análisis en Cuidados Intensivos. Incidence, organ dysfunction and mortality in severe sepsis: a Spanish multicentre study. Crit Care 2008; 12(6): R158.
4. Vincent JL, Rello J, Marshall J. EPIC II Group of Investigators. International study of the prevalence and outcomes of infection in intensive care units. JAMA 2009; 302(21):2323–2329.
5. Pierrakos C, Vincent JL. Sepsis biomarkers: a review. Crit. Care 14(1), R15. Review demonstrating the large number of biomarkers that have been assessed clinically and experimentally for use in patients with sepsis, yet highlighting that we still have none that are sufficiently specific and sensitive for use in routine practice 2010.
6. Sam S, Corbridge TC, Mokhlesi B, Comellas AP, Molitch ME. Cortisol levels and mortality in severe sepsis. Clin Endocrinol (Oxf). 2004; 60(1):29-35.
7. Montskó G, Tarjányi Z, Mezősi E & Kovács GL. A validated method for measurement of serum total, serum free, and salivary cortisol, using high-performance liquid chromatography coupled with high-resolution ESI-TOF mass spectrometry. Analytical and Bioanalytical Chemistry 2014; 406:2333–2341.
8. Munford RS. Severe Sepsis and Septic Shock. Chapter 325 Harrison's 19th edition.
9. Venkatesh B, Imeson L, Kruger P, Cohen J, Jones M, Bellomo R, et al.. Elevated plasma-free cortisol concentrations and ratios are associated with increased mortality even in the presence of statin therapy in patients with severe sepsis. Crit Care Med. 2015; 43(3):630-5.
10. Levy-Shraga Y, Pinhas-Hamiel O, Molina-Hazan V, Tamir-Hostovsky L, Eini ZM, Lerner-Geva L, Pare G. Elevated Baseline Cortisol Levels Are Predictive of Bad Outcomes in Critically Ill Children. Pediatr Emerg Care 2016.