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TO STUDY SERUM FREE CORTISOL LEVEL IN SEPSIS AT TERTIARY CARE CENTER BIKANER, RAJASTHAN

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Conflicts of Interest: Nil

ABSTRACT:

Background: Cortisol released in response to stress and low blood glucose. It functions to increase blood sugar through gluconeogenesis, to suppress the immune system, and to aid in the metabolism of fat, protein and carbohydrate.

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: On day 1, 3 &7 mean serum cortisol difference between survivors and non survivors was found statistically highly significant ($p<0.001$).

Conclusion: Serum free cortisol is a reliable indicator of the state of severity, mortality and recovery in critically ill patients with sepsis.

Keywords: Serum free cortisol, survivors, non survivors.

Introduction

Cortisol is a steroid hormone, in the glucocorticoid class of hormones, and is produced in humans by the zona fasciculata of the adrenal cortex within the adrenal gland[1].

It is released in response to stress and low blood glucose. It functions to increase blood sugar through gluconeogenesis, to suppress the immune system, and to aid in the metabolism of fat, protein, and carbohydrate[2]. It also decreases bone formation[3].

Cortisol prevents the release of substances in the body that cause inflammation. It is used to treat conditions resulting from over activity of the B-cell-mediated antibody response examples include inflammatory and rheumatoid diseases as well as allergies.

Sam et al[4] 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.

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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[5].

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: Demographic profile of different parameters according to outcome

Parameters	Outcome				t	p
	Survivors (n=32)		Non Survivors (n=18)			
	Mean	SD	Mean	SD		
Age (years)	50.34	9.52	51.11	9.61	0.273	0.786
BMI (kg/m^2)	23.09	3.99	22.69	3.00	0.366	0.716
Respiratory Rate (/min)	26.62	3.05	31.88	2.78	6.031	<0.001
Pulse Rate (/min)	108.46	9.05	123.88	7.11	6.219	<0.001
Temp (°C)	101.46	1.67	101.57	1.19	0.244	0.808
Triglyceride (mg/dl)	110.93	26.87	106.44	35.24	0.507	0.615
Total Cholesterol (mg/dl)	186.84	30.69	181.33	47.10	0.501	0.619
HDL Cholesterol (mg/dl)	47.50	12.72	54.44	14.99	1.734	0.089
LDL Cholesterol (mg/dl)	120.59	26.48	114.00	29.53	0.881	0.421
VLDL Cholesterol (mg/dl)	22.24	5.38	21.05	7.32	0.657	0.514

Table 1 shows demographic profile. All the parameters like age, body mass index, temperature and lipid profile had statistically insignificant difference (p>0.05) except respiratory rate and pulse rate where the difference was found statistically highly significant (p<0.001).

Table 2: Statistical analysis of serum cortisol level on day 1, 3 and 7 according to outcome

Serum Cortisol	Outcome				t	P
	Survivors (n=32)		Non Survivors (n=18)			
	Mean	SD	Mean	SD		
Day 1	165.37	46.20	489.33	68.79	19.894	<0.001
Day 3	246.31	65.43	553.00	67.49	15.731	<0.001
Day 7	315.68	71.84	598.33	20.81	13.330	<0.001

On day 1, mean serum cortisol on day 1 in survivors and non survivors was 165.37±46.20 and 489.33±68.79 respectively and the difference was found statistically highly significant (p<0.001).

On day 3, mean serum cortisol level was 246.31±65.43 and 553.00±67.49 in survivors and non survivors respectively and this difference was also found statistically highly significant (p<0.001).

On day 7, mean serum cortisol level was 315.68±71.84 and 598.33±20.81 in survivors and non survivors respectively and this difference was also 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[6].

Cortisol, a steroid hormone of glucocorticoid class; is released in response of stress and prevents the release of substances in the body that causes inflammation. It plays a protective role by preventing over activation of the inflammatory response but by the same mechanism it also weaken the activity of immune system.

We recruited 50 patients of sepsis of age >18 years, admitted in medical ICU of our hospital after going through detailed history and thorough clinical examination, plasma free cortisol level was measured on day 1,3rd and 7.

On day 1, mean serum cortisol on day 1 in survivors and non survivors was 165.37±46.20µgm/dl and 489.33±68.79µgm/dl respectively and the difference was found statistically highly significant (p<0.001).

On day 3, mean serum cortisol level was 246.31±65.43µgm/dl and 553.00±67.49µgm/dl in survivors and non survivors respectively and this difference was also found statistically highly significant (p<0.001).

On day 7, mean serum cortisol level was 315.68±71.84µgm/dl and 598.33±20.81µgm/dl in survivors and non survivors respectively and this difference was also found statistically highly significant (p<0.001).

Our study is comparable to Tarjányi et al[7], In this prospective, observational study, measurement of total (TC) and free cortisol (FC) levels was made in the serum samples of 69 critically ill patients at admission (0h) and 6, 24, 48, and 96h after admission. The range of TC varied between 49.9 and 8797.8 nmol/l, FC between 0.4 and 759.9nmol/l. The levels of FC at 0, 6, 24, and 48h and TC at 0, 6h were significantly elevated in non-survivors and correlated with the predicted mortality. The prognostic value of these cortisol levels was comparable with the routinely used mortality scores. In predictive models, FC at 6, 24, and 48h proved to be an independent determinant of mortality.

About 80–90% of circulating cortisol is bound to corticosteroid-binding globulin (CBG), but only free cortisol (FC) has biological activity. Albumin binds 10–15% of cortisol with low affinity. The measurement of serum total cortisol (TC) by immunoassay is markedly influenced by the concentrations of the CBG and albumin. In critically ill patients, there is a decrease in CBG concentration due to elevated cytokines or insulin resistance. CBG is saturated at higher cortisol levels. The concentration of FC rises exponentially at higher concentrations due to the release from CBG[8]. The relationship of TC and FC becomes nonlinear in critically ill patients, so FC levels may be more informative[9].

CONCLUSION

Serum free cortisol is a reliable indicator of the state of severity, mortality and recovery in critically ill patients with sepsis.

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