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Research Article

Serum Cortisol, Lactate Levels and Correlation with Outcome in Pediatric Shock

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Abstract: Serum cortisol levels rise in response to stress of critical illness but the optimum range of serum cortisol in such settings is not clearly defined. An association of high lactate levels with mortality has been found in adult patients with septic shock. However there is controversial literature regarding the same in children. The aim of this study was to determine the serum cortisol level and lactate level in Pediatric circulatory shock and to correlate their level with mortality. This was a prospective observational study at PICU of tertiary care centre at Indira Gandhi Institute of Child Health. A Total of 50 children admitted to PICU with diagnosis of shock were included in the study. Clinical and demographic characteristics of study patients were recorded. Serum cortisol and lactate levels were measured at 0 and 6 hrs of diagnosis of shock along with other relevant laboratory investigations. The outcome (survival or death) was correlated with cortisol and lactate levels. High mortality was observed in patients with low cortisol level <7mcg/dl and also in patients with high cortisol levels of >46mcg/dl. High mortality was also observed in patients with very high lactate levels. Initial as well as subsequent lactate levels were high in majority of non-survivors. Low cortisol level of <7mcg/dl , high cortisol level >46mcg/dl and very high Lactate levels of >45 mg/dl in circulatory shock is associated with higher mortality and are poor prognostic factors independently.
Keywords: Cortisol level, lactate level, circulatory Shock

INTRODUCTION

Shock is one of the most common Pediatric emergencies with significant mortality if not recognized and treated early. Knowledge of factors which affect the outcome will help in early recognition of children who are at highest risk of death and allow the timely changes in therapy, which may improve the outcome. Serum lactate is a potentially useful biomarker to risk stratify the patients with severe sepsis and septic shock.[1] Lactate is good predictor of death in circulatory shock. Further more Critical illness cause numerous endocrinological alteration that affect a patients Outcome. One of the major stress responses is the activation of hypothalamo – Pituitary adrenal axis which increases cortisol production. Deficiency of cortisol is associated with increased morbidity and mortality during critical illness and complete absence of cortisol production is incompatible with life [2].

Lactate is a by-product of anaerobic metabolism after glycolysis. During global hypoperfusion or shock, when ubiquitous anaerobic metabolism predominates, lactate production exceeds its rate of metabolism in the liver and kidneys, resulting in elevation in blood level. The increase in lactate production in anaerobic setting is the result of an accumulation of pyruvate which is converted into lactate stemming from alterations in the redox potential which occurs during tissue hypoxia, this results in an increase in the lactate/pyruvate ratio. Adequate adrenocortical function is essential to survive critical illness and most critically ill patients display an elevated cortisol level, reflecting activation of pituitary adrenal axis, which is considered to be homeostatic adaption. Glucocorticoids are important for maintenance of vascular tone, endothelial integrity, cardiac contractility and potentiation of catecholamine actions[3]. The present study was conducted with an objective to determine the serum cortisol level and lactate level in shock and to correlate their level with mortality.

MATERIALS AND METHODS

This was a prospective study of 50 children with clinical diagnosis of shock in tertiary care Pediatric intensive care unit of Indira Gandhi Institute of Child Health over a period of two year. Children between the age of 1month to 18years with the clinical evidence of shock were included in the study. Shock was identified

by the presence of tachycardia and/or hypotension along with the signs of systemic hypoperfusion. Demographical and clinical data was taken and then shock was classified functionally into hypovolemic, cardiogenic, distributive and obstructive shock on the basis of history and clinical examination. Serial measurement of serum cortisol , serum lactate level was done at zero hour and 6 hours of admission and also relevant laboratory investigations done. It was not necessary to obtain cortisol levels at a specific time of the day because most critically ill patients lose the diurnal variation in cortisol secretion[4]Study group was divided into 3 different groups based on serum cortisol level and lactate level independently. Group 1-cortisol level < 7 mcg/dl.Group2 –cortisol level >7mcg/dl-46mcg/dl. Group 3-cortisol level >46mcg/dl. First cut off value of cortisol level of < 7mcg/dl was chosen based on that Adrenal insufficiency was defined by baseline cortisol level <7mcg/dl as some studies have shown that low cortisol level is associated with worse outcome in critical illness. 3rd cut off value of cortisol value >46mg/dl was set based on data from literature that very high cortisol levels in ritical illness associated with worse outcome. Both low and very high cortisol level associated with poor outcome. Study group were also specified into another 3 groups based on serum lactate levels. Group A- Lactate value <18 mg/dl. Group B- Lactate value >18mg/dl-45mg/dl. Group C- Lactate value >45 mg/dl. First cut off value of 18mg/dl was taken based on that lactate level upto 18mg/dl(2mmol/l) are usually defined to be normal for critically ill patients.[5] 3rd cut off value of >45 mg/dl was taken based on data from literature that high lactate levels in sepsis, septic shock are associated with high mortality. A lactate value of >45mg/dl is good predictor of death[4,5]. Ultimate outcome measure was survival or death. Serum cortisol and lactate levels including other laboratory parameters were compared between survivors and non survivors.

STATISTICAL METHODS

Statistical methods were performed using software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1. Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

RESULTS

Total 50 cases of shock were studied. Most common age group was between 5-10years (48%).Mean age was 2.62+-0.9years with male-female ratio of 1:1.27.There was no significant influence of age(p=0.190) or sex(p=0.525) on outcome in the present study. Nearly 68% of cases were in hypotensive stage of shock which had significant association with non survival (p=0.007). In our study distributive shock patients constituted majority about 72% of Study group, followed by septic shock 24%,and hypovolemic shock by 4%, high percentage of distributive shockis due to the fact that most of the study patients were included during dengue epidemics. Out of 50 cases studied Dengue was the underlying etiology of distributive shock about 36 cases (72%), pneumonia (14%) was the common underlying infection associated with septic shock, followed by meningitis (10%). In our study 3cases (25%) of septic shock had blood culture proven sepsis. We have observed that septic shock had maximum mortality (62.5%), followed by distributive shock (37.5%). In our study adrenal insufficiency as defined by serum cortisol level of <7 mcg/dl was observed in 10% at 0hr and, 6% patients at 6 hrs. This group of patients had high mortality about 66%.Patients with adequate stress response with cortisol level of >7-46mcg/dl(group 2) constituted the majority of study group about 76% 0 hr and 90% at 6 hrs respectively. These group of patients had least mortality about 18%.High cortisol level of >46 mcg/dl(group3) was observed in 14% at 0hr and 4% at 6 hrs respectively .High mortality was observed in this group of patients about 71% . Normal lactate level of <18mg/dl (which is considered to be normal for critical illness.) found in 18% patients at 0 hour and 52% patients at 6 hour. This group of patients had least percentage of mortality. High lactate level in the range of >18-45mg/dl was observed in majority(48%) at 0 hour and 32%of patients at 6 hour, found to have mortality of 21% at 0 hour and 44% at 6 hour. Very high lactate levels of >45mg/dl was found in 34% at 0 and 16% patients6 hours. This group of patients had highest mortality percentage of 64%. Further it was observed that patients who had persistently high lactate value of >45mg/dl even at 6 hours had higher percentage of mortality. Initial as well as at 6 hour median serum lactate level was significantly higher in non-survivor(67.3+-31.49) than survivor (29.44+-15.42) with p value of <0.001. Lactate level of >45mg/dl were significantly associated with non-survivor at both zero hour (p=0.002) and at 6 hour (<0.001). Blood pH was found lower in non-survivors (7.26+-0.14) when compared to survivors (7.41+-0.07) which was statistically significant. No statistically significant difference found in laboratory parameters like creatinine, SGOT, SGPT and serum albumin level between survivors and non-survivors.

Table-1: Comparison of cortisol and lactate level according to outcome.

		Non survivor - n (%)	Survivor- n (%)	Total- n (%)	p-value
Serum cortisol - at 0 hour(mcg/dl)	Group 1 (<7)	4(80%)	1(20%)	5(100%)	< 0.001
	Group 2 (7.1-46)	7(18%)	31(82%)	38(100%)	<0.0001
	Group 3 (>46)	5(71%)	2(29%)	7(100%)	< 0.001
Serum Lactate at 0 hour(mg/dl)	Group A < 18	0(0%)	9(100%)	9(100%)	< 0.001
	Group B 18.1-45	5(21%)	19(79%)	24(100%)	< 0.001
	Group C > 45	11(64%)	6(36%)	17(100%)	0.0069
Serum cortisol - at 6 hour(mcg/dl)	Group 1 (<7)	2(66%)	1(34%)	3(100%)	0.0013
	Group 2 (7.1-46)	12(26%)	33(74%)	45(100%)	< 0.001
	Group 3 (>46)	2(100%)	0(0%)	2(100%)	< 0.001
Serum Lactate - at 6 hour(mg/dl)	Group A < 18	1(4%)	25(96%)	26(100%)	< 0.001
	Group B 18.1-45	7(44%)	9(56%)	16(100%)	<0.2713
	Group C > 45	8(100%)	0(0%)	8(100%)	< 0.001

DISCUSSION

Circulatory shock remains to be an important cause of morbidity and mortality among children and one of the commonest pediatric emergency.[6,7] we have observed the overall mortality due to shock about 32%.Nearly 68% of cases were in hypotensive stage of shock which had significant association with non survival(p=0.007). This is in accordance to the study done by Daljith Singh et al,[8] high mortality in this group of patients can be explained by the fact that in compensated stage, vital organ perfusion is maintained by intrinsic mechanism and early detection and management of shock increase rate of survival before the hypotension develops. [8]Majority (72%) of study group had distributive shock with underlying dengue fever. high percentage of distributive shockis due to the fact that most of the study patients were included during dengue epidemics. In a study done by K R Jat et al[6] septic shock was the most common type of shock comprising about 79.3% of all patients with shock. Pneumonia (14%) was the common underlying infection associated with septic shock, followed by meningitis (10%). In our study 3cases (25%) of septic shock had blood culture proven sepsis. Pneumonia was the most common underlying infection in septic shock as evidenced by other studies .[9] High mortality was observed in septic shock patients can be explained probably due to the fact that majority of the patients were in decompensated stage at admission and also septic shock is difficult to detect in early stages.[10]The optimum range for serum cortisol's in shock remains unclear. This factor , in addition to lack of uniform criteria for diagnosis of adrenal insufficiency in shock has lead to the reported incidence of AI varying from 25-40%.[11]There was a wide range of cortisol levels in our patients, although majority of cortisol were between >7-46mcg/dl. In our study AI as defined by the cortisol level of <7mcg/dl was observed in 10% of patients and they had higher mortality. Higher mortality in this group of patients may be explained by the fact that, increase in corticosteroid levels during acute illness is an important protective response. Adequate adrenocortical function is essential to survive the critical illness, failure to mount adequate cortisol stress response can lead to high chances of mortality. In a study done by Menon et al have found 31% incidence of adrenal insufficiency in pediatric critical illness.[12] Sarthi M, Lodha R ,et al have studied Adrenal status in children with septic shock using low dose ACTH stimulation test and they have found out 30% patients who had relative adrenal insufficiency(increment in cortisol <9mcg/dl) and concluded that relative adrenal insufficiency is common in children with septic shock and is associated with catecholamine refractory shock.[13] Patients with high cortisol levels of >46mcg/dl had high mortality. This is in accordance to study done by Susan S Sam et al , found 81% mortality in patients who had cortisol level >1242nmol/l.[14] Cortisol levels >46mcg/dl was significantly associated with non-survival at both zero hour (p<0.001) and 6 hour (p=0.046). In a study done by Annane and Colleagues about the prognostic value of cortisol level and short corticotrophin stimulation test in patients with septic shock , have found that patients with cortisol level of >34mcg/dl and maximum change of <9mcg/dl after ACTH stimulation test had poor prognosis. [15] This high mortality can be probably explained by the fact that most critically ill patients display an elevated plasma cortisol level, reflecting activation of pituitary adrenal axis, which is considered to be homeostatic adaption. Cortisol level increases with severity of illness. High basal cortisol level have been demonstrated to be correlated with high severity scores and high mortality in various critically ill patients.[16]

This may result from a maximally stimulated HPA axis, a defective cortisol break down or both, association of high cortisol levels with high mortality is probably due to but pejorative value of high cortisol is probably more related to underlying severity of illness than to a direct deleterious effect of this hypercortisolism.[17]Majority of the patients had high lactate levels. Motality was significantly increased in patients who had very high lactate level of >45mg/dl .Initial as well as subsequent levels was significantly higher in non-survivors. Previous study found that initial as well as subsequent lactate levels were significantly higher in non-survivors and also they have found that a lactate value of > 45mg/dl was a good predictor of death at zero hour and 3,12,24 hour .In a study done by Mark E et al,[1] have found that initial median serum lactate level was significantly higher in non-survivor as compared with survivor(30.6 vs 23.4 mg/dl, $p<0.001$). Vincent et al. described that shock patients with the best prognosis were those in whom lactate levels had considerably decreased within 1 hour of resuscitation.[18,19] This high mortality can be explained by the fact that blood lactate level increases during global hypoperfusion due to hypoxia at cellular level resulting in shift from aerobic metabolism to less efficient anaerobic metabolism. Increased blood lactate level is widely believed to be a marker of inadequate perfusion and an anaerobic metabolism.[20] Limitations of our study are, smaller sample size and We have not used ACTH stimulation test to define the adrenal insufficiency as most of the studies have done, however this limitation may be counteracted by the fact that adrenal response to severe endogenous stress has always been a superior test for diagnosis of Adrenal insufficiency compared to the response to exogenous ACTH stimulation.

CONCLUSIONS

This study demonstrated that high mortality was present in patients with either low cortisol level of <7mcg/dl or high cortisol level of >46mcg/dl. Initial as well as subsequent mean cortisol levels were high in non- survivors. High mortality was also present in patients with very high lactate level of >45mg/dl. Initial as well as subsequent lactate levels were high non survivors. Low cortisol level of <7mcg/dl , high cortisol level >46mcg/dl and very high Lactate levels of >45 mg/dl in circulatory shock is associated with higher mortality and are poor prognostic factors independently. Despite the correlation between cortisol level and the severity of illness, it is difficult to estimate usefully what an appropriate response should be in critically ill children like shock. Need for the larger study to demonstrate the cut-off values in pediatric shock patients above which or below which mortality increases significantly. There is also need for larger studies on cut-off value of lactate in pediatric patients above which mortality increases significantly.

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