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STUDY ABOUT BIOCHEMICAL AND IMMUNOLOGICAL CHANGES DURING HYPOVOLEMIC SHOCK

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ABSTRACT

Objective: To evaluate biochemical parameters and their clinical implications with their ability to predict the course of shock. **Materials & Methods:** This prospective study evaluate various changes in the biochemical parameters and there clinical relationship in predicating the nature, gravity and possible outcome of the shock. **Results:** Blood sugar, urea levels were found to be raised in severe hypotension in most of patients. Protein levels were in the normal range though on the lower side. Hypokalemia was seen in all the subgroups of shock. Serum lactate continued to remain high in majority of the cases. IgA and IgG levels remained normal throughout the study period whereas lgM levels remained persistently higher in almost all the patients. Complement C_3 was lower than the normal levels in all the groups whereas Complement C_4 was below normal level in only severe case. In severe cases of shock pH ranged above than the normal levels and then tends to recover towards normal range. Saturation of oxygen was below normal levels in severe hypotension patients which recovered with treatment on day five of hospitalization. **Conclusion:** It can be concluded that the clinical monitoring and judgment associated with biochemical monitoring are the best parameters available

KEYWORDS: hypovolemia, biochemical parameters, inadequate perfusion.

INTRODUCTION

Shock is the clinical syndrome that results from inadequate tissue perfusion resulting in cellular injury and inadequate tissue function. Irrespective of its cause, the hypo perfusion induced imbalance between the delivery of and requirement of substrates leads to imbalance which leads to cellular dysfunction.[1] The cellular injury caused by this inadequate perfusion, delivery of oxygen and substrate leads to production and release of inflammatory mediators which further compromise perfusion through functional and structural changes within the microvasculature.

Frequent monitoring is of utmost importance when treating patient suffering from shock. Parameters that must be monitored include heart rate, systolic blood pressure, mean arterial pressure, urine output, central venous pressure, central venous or mixed venous oxygenation saturations, lactate, and measures of cardiac output.[2] There has been substantial attention in developing biomarkers that might be helpful for diagnose, monitor and predict outcome in shock.[3] Biomarkers have been generally defined to have characteristics that can be objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.[4]

Hypovolumic shock is classified as: Mild, Moderate & Severe. Features of mild shock are cold extremities, increased capillary refilling time, and sweating, collapsed veins. In moderate variety of shock in addition to above features, tachycardia, tachypnoea, oliguria and postural changes are present. In severe case addition to about features marked tachycardia, haemodynamic instability, hypotension and finally altered mental state, leading to coma may precipitate.

This study is aimed to evaluate some of the possible parameters that may possibly guide us to the possibility of shock and its gravity; it would further help us to predict the patients who are likely to land in slow process like septicaemia. It would also help us to change treatment towards being more aggressive and much lives. This study has been taken up with this aim to evaluate these parameters and their ability to predict the course of shock.

AIMS AND OBJECTIVES

To correlate the patients admitted with shock on biochemical parameters to evaluate the possibility of prediction of outcome on the basis of biochemical tests like serum sodium and potassium, lactate, protein, albumin, blood urea, blood sugar, immunoglobulins, and blood acid base analysis.

MATERIAL AND METHODS

This prospective study was conducted in the patients with clinical presentation of shock, reported to emergency department of SVBP Hospital attached to L.L.R.M Medical College, Meerut. Patients were included in the study only after taking the informed consent. The period of the study was from 1 January 2005 to 31 December 2006.

Following participants were included:

- Healthy male or female volunteers.
- No history of tubercular, asthma, allergic reaction, renal or bacterial infection in the last 6 month.
- Any severe injury for which hospitalization was required in past 6 months.
- Patients who had not received any I.V supplementation of Fluids to resuscitate patients.

Following group of patients were excluded

- All patients below age of 15 years.
- Patients who had received resuscitation measures in the form of I.V. fluids.
- Patients in whom shock was of cardiogenic in origin.

Study Design

Enrolled patients were subdivided in three subgroups at the time of admission under following criteria. Mild shock (71-90 mmHg), Moderate shock (51-70 mmHg) and Severe shock (≤50 mmHg). Both control group of volunteers and patients were studied on following protocols. Initially sample was taken on day 0 in both volunteers and admitted patients. Then comparisons were made between various parameters on 5th day admission of patients and healthy volunteers. A comparison was made between:

- Control and each subgroup of mild, moderate and severe shock groups.
- Parameters in mild, moderate and severe group patients on day 0 and day 5.

Statistical analysis

- Mean of a particular parameter followed by standard deviation was calculated. Comparison of parameter in two groups by applying 'T' test and calculation of 't' values were done. 'p' value was obtained and its significance was evaluated.

The patients and volunteers were clinically examined and investigations were carried out as per protocol. 10 ml of blood was taken out from each patients and control, then the serum was separated by centrifugation and stored at 4˚C to 8˚C till the estimation of various parameters.

OBSERVATION

During the study period, out of total 3, 20105 patients, 1048 patients were admitted with various causes of shock and out of these 148 patients were enrolled for the study.50 healthy control cases who volunteered for the study were included in the study for evaluation after obtaining their consent for the study. The study was conducted as per protocol and results were evaluated and compared with other studies.

In control group, maximum number of healthy volunteers were from 21-30 years, followed by 31-40 years. In the patients with mild shock group (71-90 mmHg) patients were almost equally distributed in 21-30, 31-40 and 51-60 years of age group (12 each approximately). In moderate group 12 patients were of 21-30 age groups whereas 13 each in 31-40 yrs and 41-50 years age group. However it can be clearly observed that in each category, affected patients were of most productive years both socially or economically. (Table - 1) Males predominated over female in each subgroup – mild (34:16), moderate (34:14) and severe (38:12) One of the main reasons of male preponderance was that males are more commonly involved in road side accidents leading to poly trauma and shock.

Blood sugar levels increased significantly as the levels of stress increased in proportion to duration on level of stress. There was no significant difference in blood sugar levels in the patients of same category (in mild, moderate or severe) on day of admission and on 5th day amongst survivors. (Table 2)

Blood urea levels, its level were significantly raised on day 5 of hospitalization also due to continued stress and catabolic activities. (Table 3) In all the cases albumin levels were below normal range. It was observed that control group was from middle class while most of the patients were from poor strata. Total protein was within normal range though on lower side of the range. The deviation from the control group was on the lower side significantly.

Deviation on sodium level was significantly on the lower side between control and various subgroups- the mild, moderate and severe group. The adequate replacement therapy resulted in improvement in sodium levels on day 5 in all the groups. In severe group the correlation was not effective due to continued severe stress. Deviations in the potassium levels are insignificantly on lower side in all the groups and they tend to recover with treatment adequately on day 5 of admission.

lgM levels were significantly on the higher side during day 0 of study and remained on significantly higher side on day 5 also. There was no significant deviation among the lgM levels in same subgroups on day zero and day five.(Table 4) lgG and lgA levels were within normal range in this study in all subgroups of study.

Serum lactate deviation was quite significant in all the subgroups under study. The variations were also seen to be significant on day 5 from day 0 (Table 5).

Complement C_3 levels were of severe shock day 0 vs day 5 was significant. In all the subgroups of the study and

returned towards normal range significantly in subsequent study on day 5.Complement C_4 levels were significantly on the lower side in almost all the cases and tended to return towards normal side as seen in complement C_3.

The variations in pH level in moderate and severe group were significant on day of admission and on day five. pH variation were seen altered in moderate and severe group of patients both on the day of admission and on day 5 of admission. PaO_2 levels were also seen to be significantly altered in all subgroups under study due to stress and subsequently due to corrective measures. The variations were statistically significant on day of admission in moderate and severe groups. It was insignificant in mild group and tends to return towards normal side with treatment in moderate and severe group significantly. The deviation in oxygen saturation in mild, moderate and severe groups was significant in all the groups on the day of admission and on 5^{th} day of admission.

Table 1: Age Distribution of patients.

Age Groups (Years)	Control	Patients		
		Mild (71-90 mmHg)	Moderate (51-70 mmHg)	Severe (≤50 mmHg)
15-20	2	4	1	4
21-30	30	12	12	20
31-40	18	12	13	8
41-50	-	8	13	10
51-60	-	10	7	6
>61	-	4	2	2
Total	50	50	48	50

Table 2: Comparison of mean blood sugar level.

	Mean+SD	t Value	p value
Control	**86.56±10.24**		
Control Vs Mild Do	86.56±10.24Vs89.86±84.20	0.225	>0.70
Control Vs Mild D5	86.56±10.24 Vs 92.64±35.34	2.94	<0.01
Control Vs Moderate Do	86.56±10.24 Vs 98.43±35.34	2.274	<0.01
Control Vs Moderate D5	86.56±10.24 Vs 97.44±8.313	5.594	<0.001
Control Vs Severe DO	86.56±10.24 Vs 118.18±30.88	6.874	<0.001
Control Vs Servere D5	86.56±10.24 Vs125.48 ±27.81	1.195	>0.2
Mild DO Vs D5	89.86±84.20 VS 92.64 ±35.34	0.221	>0.8
Moderate DO Vs D5	98.43±35.34 Vs 97.44±8.33	0.179	>0.8
Severe Do Vs D5	118.18±30.88 Vs 125.48±27.81	1.193	>0.2

*p < 0.01 significant, ** p < 0.001 highly significant, (normal range 75-115 mg/dl)

Table 3: Comparison of mean blood urea level.

	Mean+SD	t value	p value
Control	2O.19±4.64		
Control VS Mild Do	20.19±4.64 Vs 33.27±26.82	0.305	> 0.7
Control VS Mild D5	20.19±4.64 Vs 31.27±8.006	6.322	< 0.001**
Control VS Moderate Do	20.19±4.64 Vs 48.37±44.30	4.465	<0.001**
Control VS ModerateD5	20.19±4.64 Vs 50.92±45.96	4.641	<0.001**
Control VS Severe DO	20.19±4.64 Vs 55.4±12.341	12.341	<0.001**
Control VS Severe D5	20.19±4.64 Vs 45.45±12.46	2.872	<0.001**
Mild Do VS D5	33.27±44.30 Vs 50.42±45.96	8.974	<0.001**
Moderate D0 Vs D5	48.37±44.30 Vs 50.42±45 .96	0.217	>0.8
Severe D0 Vs D 5	55.4±12.34 Vs 45.45 ±12.46	3.872	<0.001**

**p < 0.001 highly significant (normal range 20-40 mg/dl)

Table 4: Comparison of mean blood IgM level.

	Mean±SD	t value	P value
Control	**120.6 13.85**		
Control VS Mild Do	120.6 ±13.85 vs 177.56 ±20.53	16.264	<0.001**
Control VS Mild D5	120.6 ± 13.85 vs 177.24 ±10.639	22.226	<0.001**
Control VS Moderate Do	120.6 ±13.85 vs 170.77 ± 15.84	16.679	<0.001**
Control VS ModerateD5	120.6 ± 13.85 vs 160.65 ±11.52	15.056	<0.001**
Control VS Severe DO	120.6 ± 13.85 vs 182.86 ± 13.37	22.873	<0.001**
Control VS Severe D5	120.6 ±13.85 vs 177.83 ±26.18	1.213	>0.2
Mild Do VS D5	177.56 ± 20.53 vs 177.24 ± 10.639	0.094	>0.9
Moderate D0 Vs D5	170.77 ±15.84 vs 160.65 ±11.52	3.454	<0.01**
Secere D0 Vs D 5	182.86 ±13.37 vs 177.83 ± 26..18	1.194	>0.2

*p < 0.01 significant, **p < 0.001 highly significant, (normal range 45-150 mg/dl)

Table 5: Comparison of mean blood lactate level.

	Mean+SD	t value	p value
Control	10.75 ± 1.28		
Control VS Mild Do	10.75 ± 1.28 vs 19.62 ± 2.34	23.528	<0.001**
Control VS Mild D5	10.75 ± 1.28 vs 19.07 ± 3.26	16.726	<0.001**
Control VS Moderate Do	10.75 ± 1.28 vs 18.39± 4.42	11.7	<0.001**
Control VS ModerateD5	10.75 ± 1.28 vs 15.47 ± 3.26	12.654	<0.001**
Control VS Severe DO	10.75 ± 1.28 vs 21.17± 1.34	35.442	<0.001**
Control VS Severe D5	10.75 ± 1.28 vs 16.78 ± 3.36	8.206	<0.001**
Mild Do VS D5	19.62 ± 2.34 vs 19.07 ± 3.26	0.955	>0.3
Moderate D0 Vs D5	19.07 ± 3.26 vs 15.47 ± 2.26	6.02	<0.001**
Secere D0 Vs D 5	21.17 ± 1.64 Vs 16.78 ± 3.36	8.206	<0.001**

* p < 0.01 significant, ** p < 0.001 highly significant, (normal range 5-15 mg/dl)

DISCUSSION

This study was carried to evaluate the various changes in the biochemical parameters and there clinical relationship and value in predicating the nature, gravity and possible outcome of the shock. Controls were selected from the healthy volunteers after their consent and 148 patients were taken up for the study that fulfilled the criteria as laid in the protocol.

Males predominated over female in each subgroup .One of the main reasons of male preponderance was that males are more commonly involved in road side accidents leading to polytrauma and shock.

Blood sugar levels persistently remained high during the phase of hypovolemic shock (stressful condition) and were found to be on higher side on the day of admission to fifth day. This is attributed to impairment of effective insulin action or in the circulating glucose due to increased catabolic activities. As shock continues the levels of both insulin and glucose decline. An infusion of glucose after prolonged hypovolemia, when metabolic and physiologic functions of the organism have started to deteriorate, elicits another rise in plasma insulin.[5] This fact is supported by Mandache[6], Tegtmeyer[7] and Burl[8], who observed blood sugar levels increased with severity of stress due to less effective insulin in blood. Lair[9] observed that if the plasma sugar levels were more than 200mgm/dl then the mortality and morbidity rates were very high. Udeani[10] also observed that hyperglycemia was a persistent feature in critically ill patients. Similar observation were made by Hucker.[11]

Albumin levels in serum were found to be lower than the normal range in this study. It was due to increased uptake by organs to repair the damaged system. Some amount of lower values of albumin can be explained by the poor economic status of the patient also. The lower levels of albumin have been explained by leakage of proteins into extravascular space also. Similar observation have been made by Fleck and Myers,[12] and Sharma.[13] Fenel observed that hypo-albuminia was an ubiquitous abnormality in all patents.[14]

Total protein levels in hypovolumic shock were noted to be within normal range although on the lower side in the study and it might be to the ongoing repair process. Different electrophoretic studies of serum, by Singer[15], in the patients of trauma and in acute phase response had shown decrease in albumin band and increase in α1 and α2 globulin bands resulting in net proteins to be within normal limits. Increased protein catabolism and conservation of water was observed by Landry[16] and Singer.[15]

During this study sodium value was found to be on the lower side in moderate and severe shock. Hyponatremia occurred more so after day 5 of illness although it occurred only in 25% of cases approximately. Similar observations were made by Tegtmeyer.[7] Potassium levels were also found to be on the lower side. In case of

hypovolemia there is an effort by kidney to conserve water resulting in hyponatremia or it may be a part of syndrome of inappropriate anti-diuretic hormone secretion. Similarly hypokalemia was observed by Agarwal[17] in approximately 30% of the cases.

Lactate levels were found on higher side in almost all the cases. Lactic acid is produced due to tissue hypoxia due to hypovolemia. Similar observations were found by Fiddian Green[18] with patients with trauma, sepsis and other shock states in which he observed that lactic acid portends poor prognosis in such patients.

It was also observed that there was no effect on IgA and IgG levels. However IgM levels were found to be elevated in majority of cases. Possible it can be explained by the fact that IgM is the first immunoglobulin to be raised in response to antigens. Similar observations were reported during American College of Chest Physician and Society of Critical Care Consensus Conference in 1992.[19]

Complement C_3 andC_4 were found of is below normal levels in all types of shock- mild, moderate or severe cases in this study. Complements tend to return towards normal range as the shock is combated by replacement therapy. Lower complement levels were reported by Fleck and Myers[12] and Muller–Eberhard.[20] In their studies, similar sequential changes in serum complement level were observed after injury similar to present study.

During this study pH was found to be on lower slide on the day of admission and persisted on day 5 also in most of the cases. Similar observation was also made by singer.[15] $PaCO_2$ and HCO_3 levels were also seen to be on the lower side in cases of shock during this study and tend to return towards normal limits with treatment.

Hypovolumic shock remains a challenge to be treated. It requires extensive evaluation of patients. Clinical judgment supported by invasive monitoring make the diagnosis of hypovolumic shock possible.

CONCLUSIONS

It can be concluded that the clinical monitoring and judgment associated with biochemical monitoring are the best parameters available. The severity of insult can be adequately assessed by derangements in the biochemical parameters like blood sugar, blood urea, lactate levels, complement levels, and blood gas analysis.

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