PHYSIOLOGY AND BLOOD BIOCHEMISTRY DURING ACUTE STRESS IN CRITICAL ILLNESS

[SUMMARY]

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CONCISE SUMMARY

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Injury may be defined as an adverse influence, external or internal, on the cell which deranges the cell's ability to maintain a steady normal or adapted homeostasis. The steady state is in fact a fluid range within which the cell oscillates and is capable of optimal functions. The causes of cell injury and death ranges from the gross physical violence of an automobile accident to the subtle genetic lack of vital intracellular enzyme, which impairs normal metabolic functions. Factors that induce injury are; hypoxia, physical injury, chemical injury, biological agents, immune mechanism, genetic defects and malnutrition (Robbins,1989)

When faced with any situation that inflicts harm to the well being of the organism, the body initiates a cascade of physiologic responses designed to maximize the chances of survival. Acute biological stress in critical illnesses like severe infection (sepsis), major surgery and trauma (severe injuries) gives rise to similar physiologic responses to overcome the adverse consequences in these disease states.

Cuthberston *et al.,* (1942) were among the first few to describe the body's response to injury . Since then various authors (Scott *et al.,* 1991 Kinney, 1995) showed an existence of hypermetabolic state in situations like multiple trauma, major surgery

or severe infections. This hypermetabolic state occurs in demands of extra energy to overcome the acute biologic stress of that critical illness. Thus, in spite of the patient being motionless in the bed after severe trauma, the body in fact is in an extremely high energy consumptive state (Scott, 1991). On the other hand, frequently, these patients are kept nil - by - month (fasting) state and hence fed via intravenous route (parenteral nutrition) In these situation it becomes difficult to fulfill the increased caloric requirements occurring due to hypermetabolic states.

The overall manifestation of hypermetabolism which in turn is a complex inter play of various metabolic pathways which is meditated by counter regulatory hormones , central nervous systems and chemical mediators of inflammation.

In spite of decreased caloric input this basic neurohumoral chain of biochemical reactions ultimately derives energy from carbohydrate and protein stores. Thus negative nitrogen balance sets in very commonly in this situations. (Shenkin *et al.,* 1980).

In these circumstances biochemical analysis of blood provides important clue towards diagnosis of existing critical illness, its treatment and subsequent outcome. It is proved beyond doubt that the nutritional status of these critically ill patients is one of the significant parameter that decides the outcome. The early detection of malnutrition helps in replenishing the deficient nutrients by nutritional supplementation. The plasma proteins like albumin, transferrin the albumin have been described as nutritional indicators because they have been thought to reflect

the availability of amino acids for hepatic protein synthesis. The serial measurement of these proteins in blood gives an idea regarding nitrogen balance and indirectly the status of complex metabolism during critical illness and thus helps doctor in deciding

1. Nutritional formula for the patient.
2. The outcome of illness
3. Response to treatment.

Fasting blood sugar levels also showed average rise along with concomitant rise in fasting serum insulin levels, thus manifesting a state of insulin resistance. It gives significant information in diabetic patients as the requirement of insulin dosage increases during the critical illness. Because of insulin resistance insulin mediated glucose disposal is reduced and the patients are frequently less tolerant to exogenous glucose administration.

In patients having complex diseases involving more than one system of body lead to a state of multi-organ system failure (MOSF) where there occurs functional failure of two or more organs of the body. In this situation detailed biochemical analysis of blood gives an idea regarding the functional status of a concerned organ; like, Arterial blood gas analysis represents functional status of respiratory system and acid - base balance of the body, serum electrolytes like Na^+ and K^+ gives an idea about status of body fluids and solutes,blood urea and serum creatinine give an information about kidney function.

The present study was carried out in human beings having acute biological stress due to illness like multiple fractures, major surgery , multi organ system failure .

The patients were selected from Shri Sayajee General Hospital (a government run hospital) and Bhailal Amin General Hospital (a privately run hospital). Details of the clinical data of the patients were noted and the patients were subjected for biochemical tests like serum albumin and serum transferrin, fasting blood sugar and fasting serum insulin levels on 2^{nd} day of illness. Other blood tests done by the hospital authorities were also noted . To show serial changes in serum albumin and serum. Transferrin the same were repeated on 4^{th} and 8^{th} day of beginning of illness. Occurrence of adverse outcome or complications was noted. Total 144 patients were studied out of which 20 were controls (those having minor illnesses and admitted for a week) from each hospital. Twenty having multiple fractures from SSGH and 20 from Bhailal Amin Hospital,.20 patients having undergone major surgery from SSGH and 20 from Bhailal Amin General Hospital. Additionally 24 patients having multiple organ system failure were included in study from Intensive Care Unit of Bhailal Amin General Hospital.

Results were analysed by ANOVA followed by Duncan's Multiple Comparison. It was observed that serum albumin levels were decreased significantly on next day of starting of illness (acute biological stress) in patients undergoing major surgery & those having multiple fractures in SSGH and BAGH compared to control. It was also observed that albumin levels fell significantly over next one week period from the initial levels .The magnitude of albumin fall in both the hospitals with both the

groups of patients was almost similar. We had also estimated serum transferrin levels alongwith serum.albumin. Serum transferrin having a lower molecular weight and shorter plasma half life than serum albumin also showed significant fall in its initial and subsequent measurements. Here the magnitude of fall in serum transferrin levels on the next day of illness was higher compared to albumin fall although a persistent fall was observed over 8 days period. Our observations coincided with the earlier observation Fleck (1988). We did not observe any complications (infections , prolonged recovery) or mortality in patients of major surgery and multiple fractures in both the hospitals despite a significant reduction in serum proteins. Thus it is evident that serum. proteins , neither albumin nor transferrin are the indicators of course and outcome of critical illness. Our observations contrasts the findings of Reinhardt *et al* (1980).

Our study showed that (1) Serum proteins changes are not solely dependent on nutritional support. (2). Serum proteins show significant serial fall in acute illness even in absence of complications. (3). Serum albumin and transferrin are almost equal indicators of serum. protein changes during first 8 days of acute illness. This findings can be explained by following facts :

(1) The acute illness increases the transcapillary escape of proteins and hence it has a much more profound effect on the concentration of these proteins in plasma than does malnutrition.

(2) In acute illness the circulating concentration of these proteins is also affected by large fluid shift associated with shock and resuscitation.

(3) The synthesis of acute phase reactant (fibrinogen , C- reactive protein) occurs preferentially over the visceral proteins (albumin, transferrin, prealbumin) regardless of nutritional status, Shaw *et al.*, (1987).

Thus the study indicated that although measurement of plasma albumin and transferrin may be of little value in initial nutritional assessment of the critically ill patients but, serial assessment of these proteins may be useful in monitoring the response to nutritional support.

The fasting plasma glucose and insulin levels showed significant rise in both the groups of patients in both the hospitals. .Here in-spite of the rise in blood. glucose level serum insulin levels increased disproportionately. This manifests the state of *Insulin Resistance* as observed by Kinney (1995). This represents a complex interplay of stress- hormones like Epinephrine, nor epinephrine growth hormone, Glucagon , Glucocorticoids and their effect at the site of insulin actions mediating a state of insulin resistance. The significance of insulin resistance is observed in patients of diabetic mellites having critical illness in whom the requirement of insulin would increase and the chances of acquiring infection become high.

In 24 patients with multi organ failure (MOF) at BAGH , 9 patients had MOF sepsis , 6 had malaria with other infestation (parasitic infection), 5 had cardiac and respiratory failure , 4 had acute pancreatitis.

Serum albumin and transferrin levels showed significant fall since onset of critical illness, both the protein continued to fall till 8 days of observations. The initial transferrin fall in these patients was more drastic compared to serum albumin. This could be because of transcapillary escape of transferrin in shock like state of these illnesses . Transferrin being a smaller molecule compared to albumin would shift into extra capillary space faster than albumin.

Fasting blood glucose level was raised in all patients of MOF, out of which 3 had pre-existing diabetes mellitus , thus in all other patients fasting hyperglycemia was a striking feature. Serum insulin was also high in these patients having high glucose, thus disproportionately raised blood glucose level with hyperinsulinemia represents a state of *Insulin Resistance* .In critical illness interplay of stress hormones is said to cause decreased peripheral effect of insulin in lowering blood glucose levels thereby causing hyperglycemia (Porte and Woods, 1990).

Hemoglobin levels were significantly decreased in all groups of MOF, in patients with malaria and leptospirosis the severe anemia observed could be because of hemolysis. Whereas total white blood cell (WBC) count showed significantly high count in 3 out of 4 subgroups of MOF, but same showed fall in total WBC count in repeat estimation of WBC count on 8^{th} day.

Renal infection tests like blood Urea and serum Creatinine were also done . Blood urea was raised significantly in all 4 sub groups. This could be due to kidney failure as a part of MOF either because of low blood perfusion to kidneys due to septic

shock or direct toxic or hypoxic injury to kidney tubules. Serum creatinine was raised in all 4 sub groups and remained persisting till 8th day of illness . Here either toxin by pathogens damages glomerulus and tubules or microvascular blockade because of sludgging of RBC in capillaries causes reduced renal perfusion causing decreased excretion of metabolic toxic products. Patients with pancreatitis showed normal renal parameters.

Serum electrolytes like Na^+ and K^+ were also studied, they were altered variably in different patients. Their levels in serum were dependent on Acid - base balance in the body, kidney function, transcapillary escape of salt and water etc. Those who had acidosis had high serum K^+ because K^+ comes out of cell during the state of acidosis. Decreased urine output due to decreased renal function causes Na^+ retention in blood.

Arterial Blood Gas Analysis (ABG) is a basic investigation of MOF patients , and is carried out frequently . We have noted ABG in starting period of multi organ dysfunction Arterial pH was towards acidosis zone in 2 out of 4 sub groups.(Sepsis with MOF and cardiac and respiratory. Failure) and the same being normal in other two sub groups. In sepsis the patients had circulatory shock which decreases peripheral perfusion thereby causing tissue hypoxemia leading to anaerobic metabolism and production of lactic acid causing acidosis (metabolic acidosis).In cardiac and respiratory failure hypoxemia because of decreased blood oxygenation or decreased acid excretion in kidney because of poor blood circulation causes acidosis and fall in blood pH.

Arterial carbon dioxide was lower significantly in all 4 sub groups of MOF that is a manifestation of respiratory compensation of metabolic acidosis Arterial oxygen showed significantly lower levels (hypoxemia) in 3/4 sub groups of MOF only patients with malaria and other infestations had normal P_aO_2 . This is because of affection of lungs in infection or pulmonary edema. Serum bicarbonate levels were significantly lower in all 4 sub groups of patients which is the manifestation of metabolic acidosis, percentage of oxygen in Arterial blood co-relates with oxygenation of hemoglobin that showed parallel fall a P_aO_2 in all 4 sub groups.

Thus overall Arterial Blood Biochemistry, which is a basic and essential blood test showed an association of acidosis hypoxemia and hypocapnia in majority of patients.

This information helps the treating Doctors in deciding the line of treatment and also the repeated testing gives an idea regarding prognosis of the illness and evaluating the response to the treatment.