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"Role of Serial Estimation of Serum Lactate Levels to Predict the Outcome in Paediatric Shock"

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Abstract:

Background: The severity of the disease can be estimated using many variables measured in seriously ill children, to forecast morbidity and mortality, to determine the cost of treatment,andeventuallyto indicate definite care and to track the effectiveness and timing of t he

treatment. It is doubtful that all of these can be replaced by one indicator, but we will demons trate in this manuscript that lactate levels will come near.

Objectives: The significance of raised levels of lactate is understood by considering both the anaerobic activity along with the aerobic processes and the changes that occur in clearance of lactate from the body. Raised lactate levels typically reflect high morbidity and mortality, despite this complex assessment. Furthermore, two multicenter studies recently indicate that clinical outcomes may be improved by using lactate level assessment in goaldirected therapy. In the early resuscitation of seriously ill children, these re sults certify that controlling lactate level is a valuable parameter. Although tissue hypoxia is strongly connected in our minds, various metabolic processes are followed by the lactate levels that are not associated with tissue hypoxia and are hence subjected to various disorders in different circumstances.

Methodology:Patients will be classified according to the type of shock namely septic shock, cardiac shock, warm shock, obstructive shock and neurogenic shock on the basis of history, examination and investigations. theSerum lactate levels estimation is done routinely while managing cases of shock to guide therapy.

Conclusion: The clinical outcome may be improved by estimating lactate levels in a goal directed therapy. It is confirmed with these findings that monitoring lactate levels is an important parameter in the initial resuscitation of seriously ill children.

Keyword: PICU,Serum lactate, shock

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INTRODUCTION:

The most common life-threatening condition in children worldwide is septic shock [1]. Aerobic metabolism need oxygen as 90% of the energy needs of the body are supplied by it.Anaerobic metabolism takes place and produces lactic acid as a by-product in cases where oxygen is not available readily to the body cells. The lactate levels are raised if cellular metabolism shift from aerobic metabolism to anaerobic metabolism. Although production of ATP generation is less it is an effective method in shock for cellular survival. The lactate level increases with the severity of shock.[2]

As the shock progresses and if not intervened due to delayed recognition of tissue hypoperfusion or lack of any intervention, these sick children land up in refractory shock. The multi organ dysfunction syndrome ensues after few hours for the reaggravating perfusion to kidney and liver. In the late course of illness, neurocardiac dysfunction leads to mortality[3] .if these cases are survive, there is prolonged PICU and hospital stay. There could be persistent neurophysiological deficit. Evidence suggest that elevation of lactate levels precedes clinical development of science[4]. Respiratory or circulatory disorders are referred in tissue hypoxia. Hyperlactatemia is found to be related to bad response in seriously ill children. Not just that, clearance of elevated lactate levels over a period of stay during this treatment may be related with good prognosis[5,6]. The studies are lacking in a population of a rural setup to estimate lactate levels in sick children[7,8]. hence, this study was undertaken to predict outcome in critically ill children by estimation of serum lactate levels.

The evidence suggested by adult studies indicated a role of lactate as an early prognostic marker of mortality while there is some time available for intervention[9,10]. Similar data from paediatric population is inadequate moreover from the developing countries. In the study conducted on neonates, to compare serum lactate levels and PH or base excess. Poor corelation was observed between the two[11]. Raised lactate levels has been associated with the occurence of sepsis in preterm newborns without any estimate on the outcome of the babies. The studies conducted on neonates were lacking in randomisation and stratified sampling[12]. The data was conflicting as reported by Duke et al reporting lactate as a good mortality predictor while Hatherill et al observed no significant difference among discharge cases and death cases[12,13]

In the sense of concrete data role of lactate levels in paediatric and neonatal septic shock remains to be determined. Further studies are needed to confirm the role of lactate. The lactate metabolism clearance occurs in liver. The flow to liver decreased in shock. If the shock persists, anaerobic respiration continues, raising levels of lactate leading to hyperlactatemia. If the lungs are diseased, hypoxia and oxygen deprivation, switches cellular metabolism from aerobic respiration to anaerobic. All the pathologies affecting lung, cardiac diseases and hepatic diseases primarily will lead to raised lactate levels. The signs and symptoms of paediatric shock are subtle by the time they become obvious. Shock can turn into refractory phase hence an objective marker is necessary as a need to identify shock in early phase. Not a single parameter can be relied upon as in this scenario lactate is raised in non-shock conditions. Liver diseases and inborn error of metabolism affecting lactate

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metabolism may alter the serum lactate levels. In last four decades paediatric critical care has come a long way to see consisting improvement in morbidity and mortality. There has been no single biological marker to predict the outcome of mortality in critically ill child[14,15,16,17,18]. The early identification of septic shock in children is of paramount importance as it is the most common life threatening condition in children worldwide[14]. Hyperlactatemia is a primary finding in septic shock which is result of tissue hypoxia[15]. Lactate level between 18-45 mg/dl range is considered hyperlactatemia and lactate range more than 45 mg/dl and PH below 7.35 is considered lactic acidosis[16]. This narrow window of raised lactate levels and PH more than 7.35 may be observed as an early marker for septic shock. In this stage the shock can be reversed with appropriate goal oriented and cause based management[17]. PH level and blood lactate levels have poor corelation in neonates[18].

Shock is disproportion between oxygen carriage and oxygen utilisation. Oxygen utilisation is normally three times less than oxygen carriage. Shock is an acute process which is characterised by inability of the body to providesufficient oxygen to cover the metabolic needs of vital organs and tissues. As shock progresses, there will be increase in utilisation of oxygen by the tissues and inability to compensate for this deficit in oxygen carriage, leading to continuous worsening of clinical state and lactic acidosis. lactate is animportant metabolite in 2 energy producing processes of life[19].

(i) glycolysis [19]
(ii) oxidative phosphorylation.

Glycolysis and oxidative phosphorylation metabolise glucose when conditions are stable[20].
2 molecules of pyruvate are produced from glucose and 2 ATP are generated via glycolysis. Excessive pyruvate isslowly accumulated and is converted into lactate[20]. The conversion of lactate and pyruvate is a reversible reaction depending on the condition of the child in stable state lactate is converted to pyruvate when circulation, ventilation and stress is absent. Glucose metabolism produces lactate during tissue hypoxia. In conditionslike sepsis, lactate can be used as trigger for resuscitation and is a marker for hypoperfusion of tissues. The rate of clearance of hyperlactatemia can be used as a marker for improvement in cellular hypoxia.
Children who are Critically ill like those with sepsis and in septic shock are thought to have volume depletion and respond to preload[21,22]

In conditions like sepsis, lactate can be used as trigger for resuscitation and is a marker for hypoperfusion of tissues.[21]. Raised lactate levels are anticipative of outcome in infection and is a reliable tool for risk stratification[23].
This study was undertaken because targeting the normalisation of raised serum lactate levels as a part of management strategy may show improvement in survival in patients with shock.

Importance:-For better management and intervention in critically ill patients in shock estimation of serum lactate levels is needed

Background/rationale: Serum lactate levels are increased not only in anaerobic metabolism but also in critically ill patients

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Objectives: (i) To estimate the serial lactate levels in shock

(ii) Correlation of serial lactate levels to predict the outcome ofchildren in shock.

METHODS:

Study design: Prospective observational cohort study

Setting: AVBRH, Sawangi is a rural medical college located in Maharashtra. This study will be conducted in PICU, Department of Pediatrics, in Jawaharlal Nehru Medical College and AVBRH hospital, Sawangi, Wardha from October 2020 to November2022.

Data collection for the study:

Children found to be eligible after applying the inclusion criteria will be enrolled in the study, demographic essentials like age gender, admission, diagnosis, socioeconomic status, previous illness, associated risk factors like malnutrition will be collected. The cases will be admitted through casualty during emergency hours or through OPD or shifted from general paediatric ward to the paediatric ICU. The clinical history and examination will be again carried out at admission in PICU. A provisional diagnosis will be prepared after the consultation of paediatric intensivist. Routine investigations and if required specific investigations will be sent for the cases. As the evaluation goes on, treatment intervention will be started according to the condition of the child. The severity of the child will be categorised with the use of risk of mortality (PRISM III) score. The course of the patient during the hospitalisation as indicated by the clinical status by the assessment of the vital signs and any other organ manifestations along with presence of any comorbidities will be carried out. All the therapeutic interventions, procedures, medical treatment and surgical interventions if any will be recorded in case record form. If the child lands up in multi organ dysfunction syndrome (MODS) during the treatment, according to criteria from surviving sepsis guidelines, management will be started appropriately [22]. All the evaluation and interventions will be based on institutional protocols for the management of paediatric shock.

Participants:

Inclusion criteria:

Critically ill children in shock in PICU

Exclusion criteria:

1. Suspected or diagnosed cases of inborn errors of metabolism
2. death within 24 hours of admission

Variables:lactate levels, SOFA score

Study size: Precision(%)= 23

Desired confidence level(%)= 90

No. of diseased subjects needed= 144

Sample size- 144

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Quantitative variables:in critical ill children signs of shock like hypotension, decreased urine output, weak pulses, need for inotropes and cold extremities will be observed.

Statistical methods: Statistical analysis id done by entering the data into Microsoft excel sheet. Relationship of various demographic, clinical characteristics and etiology with outcome will be evaluated employing Chi- square test, Fischers exact test for categorical data and student t test for continuous data with normal distribution. p value was considered significant if less than 0.05.

Expected Outcomes/Results:

The common cause for PICU admission and mortality is septic shock. In this study we are expected to have higher blood lactate levels in children who died. Thevariables of death in septic shock will be raised serum lactate levels at zero and sixth hour i.e more than 5mmol/l and PRISM III score of more than 10[24]. Persistently raised lactate levelsare expected to have high mortality. Hence it is animportant prognostic marker in cases of risk of death[24].

DISCUSSION:

Though few studies were published which explain the relationship between hyperlactatemia on admission and death in children[25,26], the knowledge of it's significance is linited in children[27,28].In a population of severely ill children the lactate levels estimated once at admission rather than serial estimation of lactate is controversial[29].In one study where lactate levels were estimated after 24 hours of admission in 75 children admitted in PICU, was found to be corelated better with the outcome. When the lactate was sent at 6 hours of admission even if lactate levels were raised, was not as significant as 24 hours of admission. It showed a high sensitivity and specificity[29]. In a study done in 50 patients with initial hyperlactatemiai.e more than 2mmol/l within 6 hours of admission, continued hyperlactatemia for 24 hours after admission in PICU is associated with detorioration and death. In the same study, the lactate levels was not found to be corelated with the rate of survivors than those non survivors. This study was recent but retrospective in nature suggested that concentration of lactate may not be associated with poor outcome of all the causes of paediatric shock the most common one is paediatric septic shock. Hypovolemic shock often does not need PICU admission as it can be managed easily by giving fluid boluses[30-34].

Usually, in critically ill patients we take many variables likes blood pressure, heart rate, saturation and other blood investigations to estimate severity of the disease and condition of the patient, to anticipate the morbidity and mortality, for evaluation of cost and specified treatment regimens. It is usually questionable that only one parameter can diagnose and predict the outcome, but in this study we willassessifthe measured lactate level could surface or not[35].

The normal serum lactate levels range from 9-10 mg/dl (0.5 – 1 mmol/L) .hyperlactatemia occurs in tissue hypoxia due to shock[36,37].The rate of production of lactic acid in the body is 0.8mmol/kg/hour that amounts to 1300mmol/day. The production rate exceeds as the shock deepens. Due to inadequate treatment, further levels of lactate increase which may lead to

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irreversible cellular damage. The lactic acidosis is the condition where the serum lactate levels are more than 45mg/dl associated with metabolic acidosis i.e PH less than 7.35. patients admitted in PICU who had elevated levels of serum lactate levels initially and the cases with persistent elevation of serum lactate levels are found to be associated with poor outcome[38]. Paediatric shock is not just one condition where the lactate levels are elevated, there are many conditions of hyperlactatemia. Severe hepatic damage, renal failure, inborn error of metabolism and ingestion of toxins can lead to raised lactate levels. In cases of sepsis, production ofcatecholamine increases which results in induced glucose flux besides tissue hypoxia and hypoperfusionfollowed byraised serum lactate levels.[39]

Severe sepsis and septic shock have a remarkable effect on public health and are hence considered as medical emergencies. It is agreed by the intensivists that traditional markers likeBPand urine output, are not enough indicators of adequate global perfusion.[40]It is found through many studies that serum lactate level is afunctional parameter denoting hypoperfusion induced by sepsis.[41-42] in adults the rule of lactate in serum is established for diagnosis and treatment of sepsis and septic shock, however in paediatrics conflicting data is reported by Koliski et al. they concluded the estimation of serum lactate levels after 12 hours of admission and treatment in PICU not able to efficiently prevent the mortality. The lactate level when estimated after 24 hours of admission and appropriate treatment can predict the survival and the risk of death. The sensitivity in this study was found to be 55.6% and a specificity of 97.2%. similar data was demonstrated by Balasubramanian et al[43]. on comparison of lactate with other parameters, no corelation was obtained with the estimation of lactate levels[29,42,43]. A number of related studies were reported[44-46]. Related studies by Girish et. al. [47], Nitnawareet. al.[48] and Reddy et. al. [49]were reviewed.

LIMITATION

Our centre scatters to a rural population which included more cases of cardiogenic shock and septic shock. So the other types of shock may not be observed in this study. Medications like epinephrine known to affect the lactate level is wildly used in paediatric shock as the first line inotropic agent of choice. The centre has no infrastructure facilities for the evaluation of inborn metabolism which will overestimate the serum lactate levels.

CONCLUSION:

The study expects elevated serum lactate levels in paediatric shock. There may be a pattern of a serum lactate level applicable to etiology, types of shock and the outcome. The rate of clearance and its association with outcome may have potential therapeutic effect on the critically ill children.

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