EVALUATION OF SERUM LACTATE LEVELS AS A PROGNOSTIC INDICATOR IN VARIOUS TYPES OF SHOCK

Siddaraj Wali[1], Veerabhadra Swamy[2]

[1]Assistant Professor, Department of Emergency Medicine, MR Medical College, Kalaburagi.
[2]Resident, Department of General Medicine, MR Medical College, Kalaburagi.

ABSTRACT

BACKGROUND

Sepsis is a lethal disease that has a complex pathophysiology including a dysregulated inflammatory response, endothelial injury, microvascular thrombosis, vasoplegia and myocardial depression leading to multiorgan failure. Prompt recognition of sepsis, early initiation of antibiotics, source control, optimal fluid and vasopressor therapy are of utmost importance. Early diagnosis of sepsis is very critical for the timely and efficient use of treatment modalities, however, there are no reliable, specific biomarkers that can guide the diagnosis of sepsis. Cardiopulmonary failure, sepsis, trauma, oncologic pathology and so can lead to lactic acidosis.

The aim of the study is to evaluate the serum lactic acid levels as a prognostic marker in various type of shock.

MATERIALS AND METHODS

It is a prospective clinical study with 50 patients studied for 1 year. To study the values of serum lactate levels in shock patients. Statistical analysis- Chi-square test 2. Student's t-test (two tailed, independent).

RESULTS

Out of the 50 patients included in the study, the incidence of shock was found to be high in the 21-30 years age group, 13 (26%). This study of ours revealed the most common focus of sepsis as respiratory tract (60%), followed by urinary tract (25%), skin and soft tissue (15%). Out of the 18 patients who died, it was noted that mortality rates were highest 10 (55.5%) in patients with initial (0 hours) high positive serum lactate levels (>4 mmol/L). Out of the 32 patients who recovered, majority 21 (65.6%) had low positive serum lactate levels (0-2.5 mmol/L) on admission (0 hours). Serum lactate level is significantly reduced in recovered patients.

CONCLUSION

Approximately, 30% to 45% of patients with septic shock and 60% to 90% of patients with cardiogenic shock die within 1 month of presentation. Lactate was chosen because it is used as a prognostic marker of global hypoxia. Serial lactate values followed over a period of time can be used to predict impending complications or grave outcome in patients of shock. Interventions that decrease lactate values to normal may improve chances of survival and can be considered effective therapy.

KEYWORDS

AIDS, HIV, Tuberculosis, Candidiasis, Pneumocystis Carinii, Opportunistic Infections.

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BACKGROUND

In philosophic terms, shock can be viewed as a transition between life and death. Whether shock results from haemorrhage, sepsis or cardiac failure, mortality rates exceed 20%.[1,2,3]

Shock is circulatory insufficiency that creates an imbalance between tissue oxygen supply (delivery) and oxygen demand (consumption). This physiologic state leads to a reduction in effective tissue perfusion with its attendant biochemical, bioenergetics and subcellular sequelae. Reduction in effective perfusion can be global or local and the result is suboptimal substrate use at the cellular or subcellular level.[4]

This leads to a vicious cycle in which impaired perfusion is responsible for cellular injury that causes misdistribution of blood flow, further compromising cellular perfusion; the latter ultimately causes Multiple Organ Failure (MOF) and if the process is not interrupted, leads to death.

When very severe and/or persistent, inadequate oxygen delivery leads to irreversible cell injury; only rapid restoration of oxygen delivery can reverse the progression of the shock state. Lactate, a product of anaerobic glucose metabolism is generated from pyruvate with lactate dehydrogenase as a catalyst. It is cleared from blood, primarily by the liver, by the kidneys (10-20%) and skeletal muscles to a lesser degree.

Cardiopulmonary failure, sepsis, trauma, oncologic pathology, etc. can lead to lactic acidosis. Lactate levels have been well described to correlate with the presence of tissue

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Corresponding Author:
Dr. Veerabhadra Swamy,
Resident, Department of General Medicine,
MR Medical College, Kalaburagi.
E-mail: drveeruswamyhyb@gmail.com
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hypoperfusion in shock. The primary goal in management of shock is to restore adequate oxygen and substrate delivery to the tissues as quickly as possible and to improve the tissue oxygen utilisation and cellular metabolism. Survival in shock depends on initial resuscitation and the re-establishment of tissue perfusion.

Lactate was chosen, because it is used as a prognostic marker of global hypoxia and because the clearance of circulating lactate is prolonged in patients with shock. Samples of venous blood for lactate can be used as these samples are easily obtained and the results are roughly equivalent to those of assays of arterial samples. Hence, this study is being done to assess the role of serum lactate as a predictor of outcome in patients with shock.

Aims and Objectives

To evaluate the serum lactic acid levels as a prognostic marker in various types of shock.

To study the values of serum lactate levels in shock patients.

1. At admission (0 hour) and at 24 hours.
2. Serum lactate levels will be categorised into-
   - Low positive (0-2.5 mmol/L).
   - Moderate positive (2.5-4 mmol/L).
   - High positive (>4 mmol/L).

Analysis of the outcome (survived or nonsurvived), based on the serum lactate levels.

MATERIALS AND METHODS

Samples are collected in plain tubes with no anticoagulants. The sample is then centrifuged and serum is separated. This is stable for 7 days at 15-25 degrees centigrade, for 4 days at 2-8 degrees centigrade and 6 weeks at -15 degrees. The reagent used contains phosphate, NADH, pyruvate and is at a pH of 7.5.

Source of Data- Patients attending Emergency Medicine Department, Vydehi Hospital, attached to Vydehi Institute of Medical Sciences and Research Centre, Bengaluru.

Method of Collection of Data

Sample Size- 50 patients with diagnosis of shock satisfying inclusion and exclusion criteria are selected.

Inclusion Criteria

- Must be an adult (>18 yrs.).
- Either sex.
- Inclusion Criteria- Patient in shock (systolic blood pressure <90 mmHg), any form of shock (hypovolaemic, haemorrhagic, septic, cardiogenic, neurogenic).

Exclusion Criteria

- Chronic liver disease.
- Malignant disorders.
- Known inborn error of lactate metabolism.
- Alcoholic patients.
- Chronic obstructive pulmonary disease.

Study Design- It is a prospective clinical study.

Serum lactate levels will be collected at 0 hours and 24 hours.

Serum lactate levels will be categorised into-

- Low positive (0-2.5 mmol/L).
- Moderate positive (2.5-4 mmol/L).
- High positive (>4 mmol/L).

Outcome will be based on recovery or death.

Duration of Study- 1 year.

Statistical Methods- Descriptive 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

- This study of ours revealed the most common focus of sepsis as respiratory tract (60%), followed by urinary tract (25%), skin and soft tissue (15%).
- Out of the 18 patients who died, highest deaths- 10 (55.5%) in patients with initial (0 hours) and had a high positive serum lactate levels (>4 mmol/L).
- Out of the 32 patients who recovered, majority-21 (65.6%) had low positive serum lactate levels (0-2.5 mmol/L) on admission (0 hours).
- Serum lactate level is significantly reduced in recovered patients.

Type of Shock	No. of Patients	%
Hypovolaemic shock	10	20.0
Traumatic shock	15	30.0
Septic shock	20	40.0
Cardiogenic shock	5	10.0
	N=50	100

Table 1. Frequency of Cases in Various Types of Shock

Trauma Patients (Age in Years)	No. of Patients	%
18-20	4	26.66
21-30	6	40.00
31-40	1	6.66
41-50	2	13.33
61-70	2	13.33
Total	**15**	**100.0**

Table 2. Age Distribution in Patients with Traumatic Shock

Sepsis Patients (Age in Years)	No. of Patients	Percentage
18-20	0	0
21-30	4	20.00
31-40	4	20.00
41-50	2	10.00
51-60	4	20.00
61-70	4	20.00
70-80	2	10.00
Total	**20**	**100.0**

Table 3. Age Distribution in Patients with Septic Shock

Hypovolaemic Patients Age in Years	Number of Patients	Percentage
18-20	3	30.0
21-30	3	30.00
31-40	1	10.00
41-60	2	20.00
90-95	1	10.00
Total	**10**	**100.0**

Table 4. Age Distribution in Patients with Hypovolaemic Shock

Cardiogenic Shock Patients Age in Years	Number of Patients	Percentage
31-40	1	20.00
51-65	4	80.00
Total	**5**	**100.0**

Table 5. Age Distribution in Patients with Cardiogenic Shock

Comorbid Conditions	Number of Patients (n=50)	Percentage
HTN	6	12.0
DM	9	18.0
IHD	1	2.0

Table 6. Comorbidities in the Study Group

Clinical Symptoms	Number of Patients (n=50)	Percentage
Trauma (RTA/fall from height)	15	30.0
Dyspnoea, cough with expectoration	10	20.0
Burning micturition	4	8.0
Cellulitis/abscess	3	6.0
Pain abdomen	3	6.0
Vomiting and loose stools	10	20.0
Chest pain	5	10.0

Table 7. Clinical Symptoms in Study Group

Clinical Signs	No. of Patients (n=50)	%
Pulse Rate (BPM)		
>90	45	90.0
Blood Pressure (mmHg)		
<90/60	50	100.0
MAP <60	38	76.00
Respiratory Rate Cycles /Minute		
12-18	2	4.0
>18	48	96.0
Abnormal CRFT		
>2 seconds	28	56.0
<2 seconds	22	44.0
Temperature		
>99.4 F	24	48.0
<99.4 F	26	52.00
Urine Output	18	36.0
<30 mL in first hour		
>30 mL in first hour	32	64.0
Cellulites/Abscess	3	6.0
Abnormal GCS	14	28.0
Abnormal RS	6	12.0
Abnormal P/A	11	22.0
Abnormal CVS	4	8.0

Table 8. Clinical Signs in Study Group

Organ Dysfunction	Number of Patients (n=50)	Percentage
Renal Function Tests		
Blood urea (mg/dL)		
• <40	23	46.0
• >40	27	54.0
Serum creatinine (mg/dL)		
• <1.3	23	46.0
• >1.3	27	54.0
ARDS	4	8.0
Hepatic dysfunction	2	4.0

Table 9. Organ Dysfunction in Shock Patients

Source of Infection	No. of Patients (n=20)	%
Pneumonia	12	60.0
UTI	5	25.0
Skin and soft tissue infections	3	15.0

Table 10. Source of Infection in Septic Shock Patients

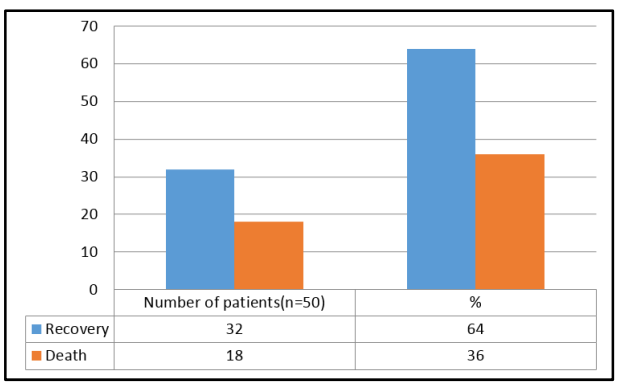

Figure 1. Outcome of the Study

Outcome of Patients Studied

In our study, out of 18 deaths, 9 (50%) were due to traumatic shock, 7 (38.80%) due to septic shock and 2 (11.20%) due to hypovolaemic shock.

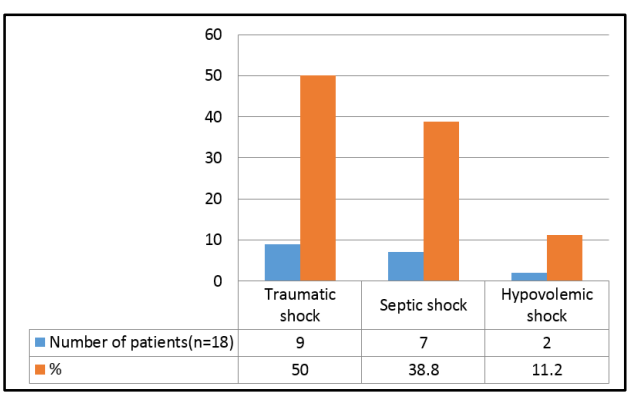

Figure 2. Number of Deaths in the Study Group

	Total Number of Patients	Survivors	Mortality	Mortality rate
Traumatic shock	15	6	9	60.0
Septic shock	20	13	7	35.00
Hypovolaemic shock	10	8	2	20.0
Cardiogenic shock	5	5	0	0
Total	**50**	**32**	**18**	**36.0**

Table 11. Number of Deaths and Survivors in the Study

Serum Lactate Levels (mmol/L) 0 Hour	Serum Lactate Levels (mmol/L) At 24 Hours	Type of Shock
3.2	4.6	Septic shock
4.2	5.8	Traumatic shock
2.1	4.3	Septic shock
2.2	4.6	Traumatic shock
4.6	6.3	Traumatic shock
3.8	5.6	Septic shock
6.4	0	Traumatic shock
3.8	4.9	Hypovolaemic shock
4.3	5.8	Hypovolaemic shock
4.2	6.1	Septic shock
4.2	5.1	Septic shock
2.3	4.8	Septic shock
6.2	0	Traumatic shock
3.7	5.3	Traumatic shock
4.6	5.8	Traumatic shock
3.4	5.1	Septic shock
6.6	0	Traumatic shock
5.3	0	Traumatic shock

Table 12 Serum Lactate Levels MMOL/L in Patients who Died

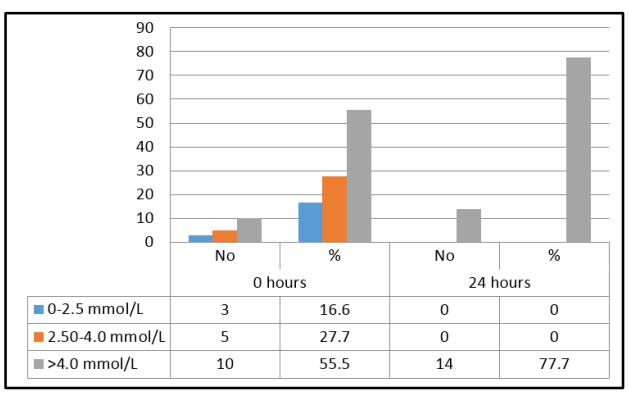

Figure 3. Shows that Out of the 18 Patients who Died

Figure 3 shows that out of the 18 patients who died it was noted that mortality rates were highest 10 (55.5%) in patients with initial (0 hours) high positive serum lactate levels (>4 mmol/L), followed by 5 (27.7%) in the intermediate positive serum lactate levels (2.5-4 mmol/L). Mortality rates were least in the low positive serum lactate levels (0-2.5 mmol/L) being only 3 (16.36). 4 patients (22.22%) died within 24 hours whose lactate levels were high positive (>4 mmol/L). All these deaths were due to traumatic shock. Majority of the patients who died (95.7%) had high serum lactate levels at the end of 24 hours of admission. It remained high positive in 18 (78.3%) and intermediate positive in 4 (17.4%).

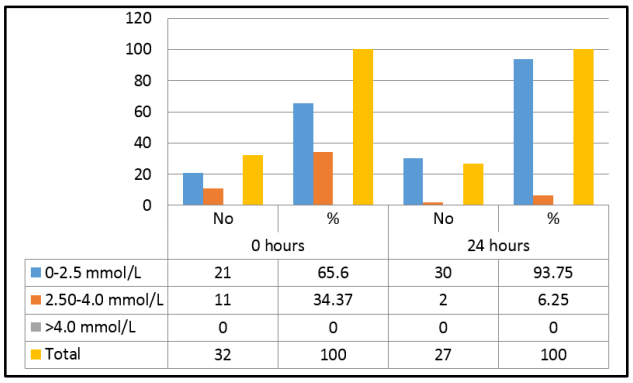

Figure 4. Serum Lactate Levels MMOL/L in Patients who Recovered

Figure 4 shows that out of the 32 patients who recovered, majority 21 (65.6%) had low positive serum lactate levels (0-2.5 mmol/L) on admission (0 hours), 11 (34.37%) had intermediate lactate levels.

It was noted that none had high positive serum lactate levels (>4 mmol/L) at admission. Serum lactate level is significantly reduced in recovered patients.

Majority of the patients who recovered had low positive 30 (93.75%) and intermediate positive 2 (6.25%) serum lactate levels at the end of 24 hours of admission.

Serum Lactate	Outcome		P value
	Recovery (n=32)	Death (n=18)	
Serum lactate mmol/L at admission	3.60 ± 0.80	4.33 ± 1.30	0.018*
Serum lactate mmol/L at 24 hours	2.89 ± 1.08	4.95 ± 1.32	<0.001**

Table 13. Correlation of Serum Lactate with Outcome

Table 13 shows that there was moderately significant correlation of outcome with serum lactate levels at 0 hours after admission (P value 0.018).

There was strongly significant correlation of outcome with serum lactate levels at 24 hours after admission (P value <0.001).

Mortality increases with high positive and intermediate positive serum lactate levels.

DISCUSSION

Type	Comment
Hypovolaemic	Caused by inadequate circulating volume
Cardiogenic	Caused by inadequate cardiac pump function
Obstructive	Caused by extracardiac obstruction to blood flow
Distributive	Metabolic derangements that impair cellular respiration such as cyanide toxicity, sepsis

Table 14. Classification of Shock

Empirical Criteria for Diagnosis of Circulatory Shock[5]
(Regardless of cause four criteria should be met)-

1. Ill appearance or altered mental status.
2. Heart rate >100 beats/min.
3. Respiratory rate >20 breaths/min. or PaCo2 <32 mmHg.
4. Arterial base deficit <-4 mEq/L or lactate >4 mm/L.
5. Urine output <0.5 mL/kg/hr.
6. Arterial hypotension >20 minutes duration.

Complications

1. Acute Lung Injury (ALI) leading to ARDS is a major complication of severe sepsis, septic shock and traumatic shock. The incidence of ARDS is approximately 18% in patients with septic shock and mortality rates approach 50%.[6]
2. Acute Renal Failure (ARF) occurs in 40-50% of patients with septic shock.
3. Disseminated Intravascular Coagulation (DIC) occurs in 40% of patients with septic shock.7
4. Other complications of shock include chronic renal dysfunction, mesenteric ischaemia, myocardial ischaemia and dysfunction, liver failure and other complications related to prolonged hypotension and organ dysfunction.

Management

1. The ABCDE tenets of shock resuscitation are establishing airway, controlling the work of breathing, optimising the circulation, assuring adequate oxygen delivery and achieving endpoints of resuscitation.
2. Arterial oxygen saturation should be restored to >93% and ventilation controlled to maintain a $PaCO_2$ of 35 to 40 mmHg.

Haemorrhagic Shock

1. Ensure adequate ventilation/oxygenation provide immediate control of haemorrhage, when possible (e.g., traction for long bone fractures, direct pressure), initiate judicious infusion of isotonic crystalloid solution (10-20 mL/kg).
2. With evidence of poor organ perfusion and 30-minute anticipated delay to haemorrhage control, begin Packed Red Blood Cell (PRBC) infusion (5-10 mL/kg).
3. With suspected central nervous system trauma or Glasgow coma scale score <9, immediate PRBC transfusion maybe preferable as initial resuscitation fluid.
4. Treat coincident dysrhythmias (e.g., atrial fibrillation with synchronised cardioversion).

Cardiogenic Shock

1. Ameliorate increased work of breathing provide oxygen and Positive End-Expiratory Pressure (PEEP) for pulmonary oedema.
2. Begin vasopressor or inotropic support, norepinephrine (0.5 mcg/min.) and dobutamine (5 mcg/kg/min.) are common empirical agents.
3. Seek to reverse the insult (e.g., initiate thrombolysis, arrange percutaneous transluminal angioplasty).
4. Consider intraaortic balloon pump counter pulsation for refractory shock.

Septic Shock

1. Ensure adequate oxygenation; remove work of breathing.
2. Administer 20 mL/kg of crystalloid or 5 mL/kg of colloid and titrate infusion to adequate central venous pressure and urine output.
3. Begin antimicrobial therapy, attempt surgical drainage or debridement.
4. Begin PRBC infusion for haemoglobin <8 g/dL.
5. If volume restoration fails to improve organ perfusion, begin vasopressor support, initial choice includes dopamine, infused at 5-15 mcg/kg/min. or norepinephrine infused at 0.5 mcg/min.

Table 15. Clinical Guidelines for Management of Shock

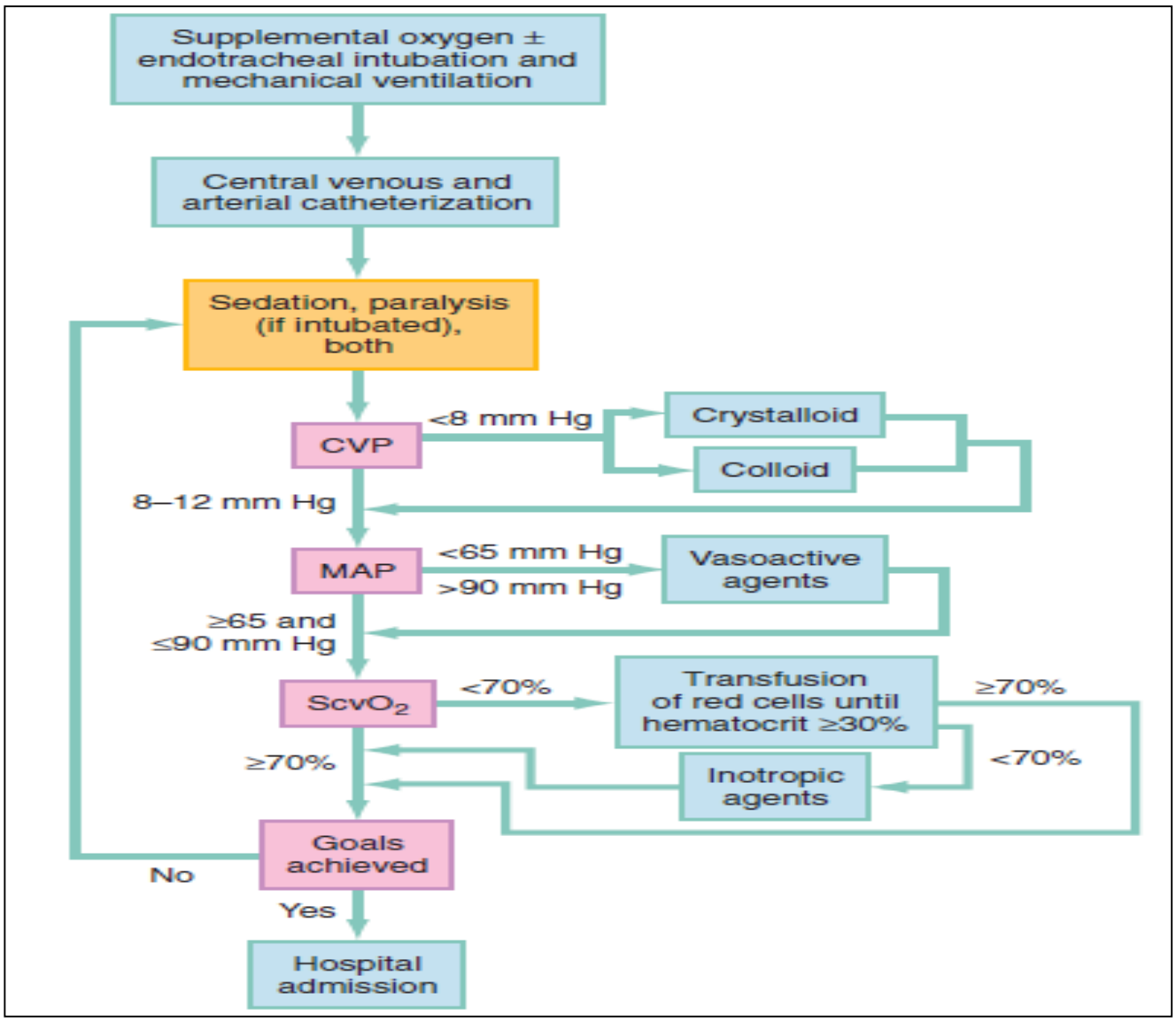

Figure 5. Early Goal Directed Therapy

An analysis of the lactate values as a quantum in the survivors and nonsurvivors of trauma and sepsis shows a higher set of values in nonsurvivors. Patients of trauma had higher values than patients of sepsis/hypovolaemia.

As evident from the study data, the mean lactate values clearly showed a decreasing trend to normal in trauma survivors as compared with the nonsurvivors. The trauma survivors not only had an obviously lower set of mean lactate values as compared with nonsurvivors, but also reached normal levels within 24 hrs. in our study. Serum lactate level is significantly reduced in recovered patients with P=0.013.

Lavery et al[8] measured venous lactate within 10 mins. following admission to the ED in 375 trauma patients. This study showed that an increased lactate level (> 2.0 mmol/L) was a better predictor of morbidity and mortality than physiological triage criteria (composed of heart rate, blood pressure, Glasgow coma scale and respiratory rate).

In patients with normal blood pressure, increased blood lactate levels (>4.0 mmol/L) were associated with a 10 times higher mortality rate than normal lactate levels (mortality 26.5%).

In our study, out of 15 trauma patients who presented in shock (SBP <90), 9 (60%) patients did not survive, whose initial serum lactate levels (in ED-0 hour) were more than 4 mmol/L. Out of 9 deaths, 4 died within 24 hrs. whose serum lactate levels were more than 6 mmol/L.

Out of 6 patients who survived, 4 patients had low positive serum lactate levels (0-2.5 mmol/L) and 2 patients had intermediate positive serum lactate levels (2.5-4 mmol/L) on admission and reached normal levels within 24 hrs. However, the sepsis survivors did show a lower range of mean lactate values and the lactate values reached normal levels within 24 hrs. Sepsis nonsurvivors did not ever reach a normal lactate value during the course of follow-up in the study.

These findings correlated with studies undertaken by Meregalli et al.[9] These observations underline the importance of following the trend of lactate levels in critically ill patients. In patients with septic shock, serial determinations of blood lactate levels are good predictors of the development of MODS and death. In this respect, the duration of lactic acidosis is more important than the initial lactate value.

Meregalli et al[9]	Our study
N=44 patients	N=50 patients
Mortality - 15	Mortality - 18
Mortality due to septic shock-4 (26.66%)	Mortality due to septic shock - 7 (38.88%)
Serum lactate level at admission- P value not significant	Serum lactate level at admission - P value 0.018. moderately significant
Serum lactate level at 24 hours after admission- P = 0.012, significant	Serum lactate levels at 24 hours after admission P value <0.001

Table 16. Comparison with Other Studies

- Lavery et al[8] measured venous lactate within 10 mins. following admission to the ED in 375 trauma patients. This study showed that an increased lactate level (> 2.0 mmol/L) was a better predictor of morbidity and mortality than physiological triage criteria (composed of heart rate, blood pressure, Glasgow coma scale and respiratory rate).
- Howell et al[9] evaluated the prognostic value of one single venous lactate measurement shortly after admission to the ED in patients with clinically suspected infection/sepsis.
- Henning et al[10] observed that in patients with AMI persistent hyperlactatemia was associated with an ominous prognosis; no patients whose arterial blood lactate was greater than 4 mmol/L for more than 12 hours survived regardless of the magnitude of the stroke volume, the left ventricular filling pressure or the cardiac work.
- The trauma survivors not only had an obviously lower set of mean lactate values as compared with nonsurvivors, but also reached normal levels within 24 hrs. in our study.
- In patients with septic shock, serial determinations of blood lactate levels are good predictors of the development of MODS and death. In patients with normal blood pressure, increased blood lactate levels (>4.0 mmol/L) were associated with a 10 times higher mortality rate than normal lactate levels (mortality 26.5%).
- There is increasing evidence supporting the use of lactate as a diagnostic, therapeutic and prognostic marker of global tissue hypoxia in cases of cardiogenic shock.
- When very severe and/or persistent, inadequate oxygen delivery leads to irreversible cell injury; only rapid restoration of oxygen delivery can reverse the progression of the shock state.
- To conclude, serial lactate values followed over a period of time can be used to predict impending complications or grave outcome in patients of shock. Interventions that decrease lactate values to normal early may improve chances of survival and can be considered effective therapy. Lactate values need to be followed for a longer period of time in critical patients.

REFERENCES

[1] Angus DC, Linde-Zwirble WT, Lidicker J, et al. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome and associated costs of care. Crit Care Med 2001;29(7):1303-1310.
[2] Topalian S, Ginsberg F, Parrillo JE. Cardiogenic shock. Crit Care Med 2008;36(Suppl 1):S66-S74.
[3] Williams RS. Canaries in the coal mine: mitochondrial DNA and vascular injury from reactive oxygen species. Circ Res 2000;86(9):915-916.
[4] Kumar A, Parillo JE. Shock: classification, pathophysiology, and approach to management in critical care medicine: principles of diagnosis and management in the adult. 3rd edn. Philadelphia, PA: Mosby Inc., 2008: p. 379.
[5] Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368-1377.
[6] Sebat F, Musthafa AA, Johnson D, et al. Effect of a rapid response system for patients in shock on time to treatment and mortality during 5 years. Crit Care Med 2007;35(11):2568-2575.
[7] Jones AE, Focht A, Horton JM, et al. Prospective external validation of the clinical effectiveness of an emergency department-based early goal directed therapy protocol for severe sepsis and septic shock. Chest 2007;132(2):425-432.
[8] Lavery RF, Livingston DH, Tortella BJ, et al. The utility of venous lactate to triage injured patients in the trauma center. J Am Coll Surg 2000;190(6):656-664.
[9] Meregalli A, Oliveira RP, Friedman G. Occult hypoperfusion is associated with increased mortality in hemodynamically stable, high-risk, surgical patients. Crit Care 2004;8(2):R60-R65.
[10] Henning RJ, Weil MH, Weiner F. Blood lactate as prognostic indicator of survival in patients with acute myocardial infarction. Circ Shock 1982;9(3):307-315.