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Original Research Article

An observational study to correlate arterial lactate level and peripheral perfusion index in context of tissue perfusion in sepsis

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ABSTRACT

Background: In view of goal directed therapies, the predictive value of the course of peripheral perfusion parameters over time has not been studied. Moreover serial assessment of peripheral perfusion index (PI) can be more predictive for mortality when compared to a single assessment of peripheral perfusion. Successfully normalized PI (≥1.4) during treatment might be an indication to stop the resuscitation, whereas pursuing normalized PI (≥1.4) might not result in better outcomes compared with mild-to moderate PI impairment after a normalized arterial lactate level. Complementing arterial lactate assessment with PI during resuscitation can better identify the endpoint of resuscitation and patients at higher risk of adverse outcomes. By simple clinical assessment of peripheral perfusion immediately during and after resuscitation, clinicians will be able to discriminate patients at high risk for developing severe complications even in the rural setups.
Methods: This prospective study was conducted on 100 patients admitted at Dr. Kiran C. Patel Medical College and Research Institute, over a period of 12months (Janury 2022 to December 2022). Patients of sepsis were selected on the basis of criteria for tissue hypoperfusion and classification of sepsis.
Results: On statistical analysis, PI was found to have significant correlation with arterial lactate levels (P<0.001) in PI <1.4 sub-measurement and not in PI >1.4. SOFA score & metabolic parameters were also found to have statistical significance.
Conclusions: We inferred that peripheral perfusion index monitoring could provide useful information to determine the possibility of hyperlactatemia in critically ill patients thus providing a noninvasive source of tissue-bed perfusion monitoring even in the absence of facilities and infrastructure to measure the lactate levels thereby providing a gross insight in the perfusion haemodynamics of the patients of sepsis even in the primary healthcare setups too.

Keywords: Arterial lactate, Perfusion Index, Sepsis

INTRODUCTION

The presence of poor tissue perfusion in a shocked patient is usually associated with worse outcome. Thus, monitoring of tissue perfusion is an essential step in the management of such patients. It is assumed that peripheral tissue is the first tissue bed to sacrifice in shock and the last to be re-perfused in resuscitation.[1,2] Monitoring of tissue perfusion includes biomarkers of global tissue perfusion and measures for assessment of perfusion in non-vital organs. Many commonly used optical methods for monitoring peripheral perfusion at the bedside include finger photoplethysmography and near-infrared spectroscopy (NIRS). Although these

techniques are particularly promising, as objective numerical information can be obtained within a couple of minutes, the interpretations should be considered in combination with the clinical examination and additional peripheral perfusion measurements.[3] The peripheral perfusion index (PI) is a noninvasive numerical value of peripheral perfusion. The prognostic value of noninvasive monitoring peripheral perfusion to predict outcome remains to be established in septic patients after resuscitation. Lactate level can be used as the diagnostic, therapeutic and prognostic marker of global tissue hypoxia in circulatory shock.[4] A lactate clearance of 10% or more predicts good resuscitation of Sepsis patient and improves survival from septic shock. Two normal lactate levels (<18 mg/dL (2 mmol/L)) at least 2 hours apart is taken as evidence of adequate tissue oxygenation.5 Although the available literature shows clear co-relation between impaired peripheral perfusion and resuscitation, the use of different perfusion indices as a resuscitation target needs more research. Moreover, in many rural areas, due to lack of availability of resources, it's not always possible to check the lactate levels wherein the use of peripheral perfusion index may be beneficial.

METHODS

This prospective study was conducted at Dr. Kiran C. Patel Medical College and Research Institute after approval from Institutional Ethics Committee. A total number of 100 adult patients of sepsis were selected on the basis of criteria for tissue hypoperfusion and classification of sepsis. Study was conducted over a period of 12 months (January 2022 to December 2022).

The study inclusion criteria of the study were patient between age 18 to 65 years, patients fitting in the criteria for tissue hypoperfusion and sepsis.

Exclusion criteria of the study were, patients with absolute contraindication for central venous catheter placement, patients not giving consent for the study, pregnant patients, brain dead patients, patients of cardiogenic/neurogenic/anaphylactic shock.

The patient were investigated for complete blood count, Blood Urea, Serum Creatinine, PT, aPTT, Serum electrolytes, Serum Albumin, Arterial Blood Gas Analysis and Peripheral Perfusion Index using Pulse oximetry.

All patients were explained in detail about the purpose of the study and an informed consent was taken. Patient's details were incorporated into a proforma. Biochemical parameters were assessed via arterial and venous blood samples. All patients then underwent all routine investigations as enlisted. Arterial lactate levels were checked on admission. Arterial blood samples were obtained with a heparinized syringe, labeled and analyzed using blood gas analysis machine (ABL 80 FLEX) (available in the ICU) calibrated according to standard quality assurance protocols. Standard haemodynamic monitoring included continuous recording of electrocardiographic data, heart rate (HR), mean arterial pressure (MAP), vasopressor therapy (any dose of norepinephrine), ICU and hospital length of stay, length of ventilator support and 30-day mortality were recorded. We assessed all data needed to calculate the APACHE II score, Sequential Organ Failure Assessment (SOFA) score. All the patients of sepsis were given a fluid bolus of 30ml/kg of crystalloid for hypotension or if lactate>4mmol/L and a vasopressor was added if the patient remained hypotensive during/ after fluid resuscitation to maintain a MAP≥65mmHg. Repeat levels of arterial lactate and peripheral perfusion index were assessed 2 hours after starting of resuscitation of the patient and then at 24 hours and 48 hours of resuscitation.

Study definitions

The tissue hypoperfusion diagnostic criteria was the following: 1) SBP ≤90 mmHg (or a decrease in SBP ≥20 % from baseline); 2) urinary output <0.5 ml/kg/min for more than 2 h; 3) increase in heart rate (HR) ≥10 % from baseline; 4) presence of skin mottling; and 5) hyperlactatemia (>2 mmol/L). If one or more of these criteria were met, clinical tissue hypoperfusion was diagnosed.

Septic shock was defined as severe sepsis with sepsis-induced hypotension persisting despite adequate fluid resuscitation and requiring the administration of vasopressors. The early goals of hemodynamic support were the following: mean arterial pressure >65 mmHg; urine output >0.5 ml/kg of body weight (except in the patients with acute renal failure). The intensivists were blinded to the results of the PI.

Normal arterial lactate was defined as <4, and normal PI was defined as ≥1.4. The critical value of PI was derived from the best cutoff value related to the mortality in the study population. The patients were divided into three categories based on the lactate levels and PI value. PI impairment stratification was done as follows: 1) Normal PI (≥1.4), 2) Mild PI impairment (critical value < PI<1.4) 3) Critical PI impairment (PI ≤ critical value, which will be defined as mentioned above).

Statistical analysis

Data was collected & tabulated. Clinical, hemodynamic, and metabolic variables were compared using ''t'' test. Values were expressed as mean±Standard deviation (SD) and as percentage for categorial parameters. Nominal categorical data between the groups were compared using Chisquare test.

RESULTS

Statistical analysis of PI and blood gas parameters: PI was found to have significant correlation with arterial

lactate levels (P<0.001). In PI <1.4 sub-measurement, P value was found to be extremely significant (<0.001). Although PI >1.4, no statistical significance was obtained (P=0.06) (Figure 1).

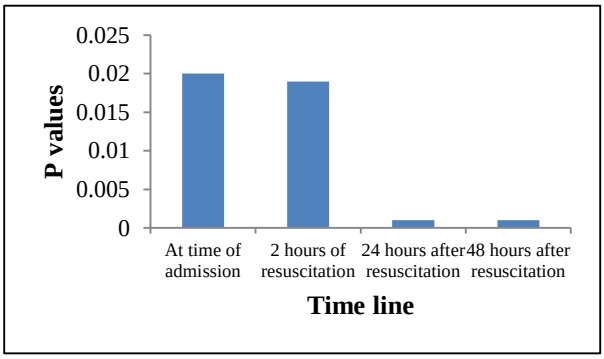

Figure 1: Illustrating peripheral perfusion parameters.

On comparing scoring criteria, SOFA scores were found to have statistical significance when compared to other scoring systems (P=0.043) (Table 1).

On assessing metabolic parameters in the patients with sepsis, mean lactate levels were found to have statistical significance (P=0.01) (Table 2).

Table 1: Characteristic features of patients with sepsis.

Variables	Survivors (n=47)	Non-survivors (n=53)	P values
Age (years)	57±15	69±11	0.07
Gender (female:male)	5:12	4:13	0.56
APACHE II score	17±5	18±4	0.061
SOFA score	9±1	11±2	0.043
Ramsay score	6±0.9	5.9±0.8	0.69
WBC counts	13.1±6.2	8.9±4.2	0.23

Table 2: Metabolic parameters in septic patients as per prognosis.

Parameters	Survivors	Non-survivors	P values
Mean arterial pressure	89±11	88±12	0.52
Mean lactate (mmol/l)	2.2±1.8	6.5±5.1	0.001
pO2	127±44	110±35	0.06
pCO2	0.79±0.12	0.78±0.11	0.54
HCO3-	22±10.1	18±9.1	0.61
pH	7.69±0.6	6.54±0.2	0.52

Table 3: Day-wise hemodynamic and physiological data.

Systemic hemodynamics	At time of admission	2 hours after resuscitation	24 hours after resuscitation	48 hours after resuscitation
(I) Survivors				
Pulse	74.1±52	76±50	80±16	82±19
BP	97±11.2	95±12	96±10.5	97±12.1
pH	7.56±5	7.39±4.9	7.37±3.9	7.42±5.1
Lactate	1.5±0.7	1.49±0.6	1.32±0.51	1.15±0.42
Hb (g/dl)	7.9±0.4	7.91 0.31	7.82±0.62	7.83±0.54
Creatinine	0.9±1.2	0.8±1.1	0.81±1.2	0.79±1.3
PT/aPTT	16±11.1//36.1±12	16.1±10.9//37.2±11	17.2±9.1/37.5±10.1	18.1±10.1/38.1±11.2
Bilirubin	0.7±0.1	0.69±0.2	0.58±0.11	0.42±0.1
Albumin	3.6±0.12	3.67±0.13	3.56±0.14	3.9±0.13
Sodium	145±19.1	146±20.2	149±19.4	147±20
Potassium	4.5±1.39	4.49±1.11	4.45±1.11	4.39±1.19
(II) Non-survivors				
Pulse	76±41	82±49.1	90±50.2	92±48.7
BP	95±12.9	90±10.1	86±9.4	84±8.2
pH	7.49±4.4	7.35±3.9	7.32±2.1	7.29±3.4
Lactate	1.7±0.5	1.65±0.61	1.59±0.42	1.48±0.3
Hb (g/dl)	8.1±0.9	7.9±0.89	7.05±0.91	5.9±0.1
Creatinine	1.1±1.0	1.12±1.1	1.2±1.09	1.3±1.24
PT/aPTT	15.9±10.1/40.9±11.9	15.89±10.11/41.2±10.21	16.9±12.1/40.1±9.8	17.1±13.2//42.3±9.9
Bilirubin	7.3±0.2	6.92±0.4	6.79±0.14	6.92±0.19
Albumin	3.9±0.11	3.91±0.13	4.01±0.5	4.29±0.7
Sodium	149±20.1	149.9±20	148.95±18.9	148.9±17.1
Potassium	4.9±2.45	5.51±1.4	5.53±1.3	5.62±1.4

Table 4: Peripheral perfusion parameters.

Measurement variables	At time of admission	2 hours of resuscitation	24 hours after resuscitation	48 hours after resuscitation
Survivors				
CRT (s)	2.5±0.1	3.5±0.3	3.4±0.2	2.9±0.3
PPI	4.1±0.4	4.2±0.9	3.9±.0.4	4.5±0.4
Non-survivors				
CRT (s)	2.9±0.2	4.9±0.6	5.2±0.4	5.9±0.8
PPI	3.8±0.2	5.1±0.1	3.1±0.2	2.3±0.4

Table 5: Predictive values of peripheral perfusion.

Peripheral perfusion	Odds ratio	(95% CI)	P values
At time of admission	4.51	1.39 to 15.13	0.02 (significant)
2 hours of resuscitation	4.49	1.41 to 12.59	0.019 (significant)
24 hours after resuscitation	5.21	2.89 to 27.98	<0.001 (extremely significant)
48 hours after resuscitation	5.94	2.14 to 20.73	0.001 (highly significant)

On correlating the hemodynamic and physiological parameters among survivors and non survivors, no statistical difference was noted (Figure 4).

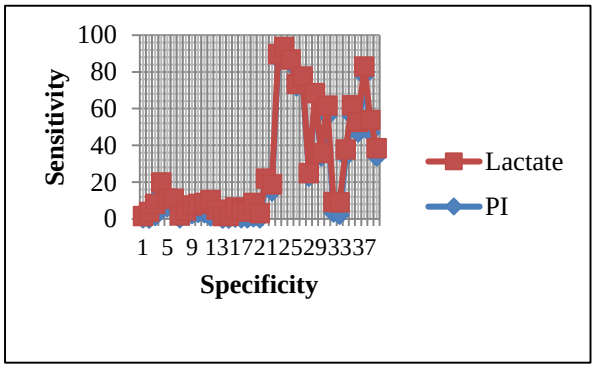

Figure 4: Areas under pi and lactate values.

DISCUSSION

The word 'sepsis' is derived from the Greek word 'sepo' meant decay or putrefaction i.e decomposition of organic matter in a manner that resulted in decay and death.[14] A multicentre, prospective, observational study by Todi S reported 16.45% incidence of severe sepsis in hospital admissions and around 65.2% and 64.6% hospital mortality and 28-day mortality due to severe sepsis.[15]

Monitoring of tissue perfusion is an essential step in the management sepsis, a sequelae of acute circulatory failure. The presence of cellular dysfunction has been a basic component of shock definition even in the absence of hypotension.[16] The ideal parameter for tissue perfusion should be rapid, non-invasive and easily measured without the need of advanced skills wherein the popular biomarkers such as serum lactate and central venous oxygen saturation are used. Assessment of peripheral circulation has become easier after introduction of new non-invasive devices as well as clinical scoring systems.

Moore et al. suggested that the concept of early goal-directed therapy should be revised, and the inclusion of the restoration of peripheral circulation perfusion in the early resuscitation would be meaningful.[6] In a multicentre, prospective, observational study by Todi S, it was reported that there was 16.45% incidence of severe sepsis in hospital admissions and around 65.2% and 64.6% hospital mortality and 28-day mortality due to severe sepsis.[7,8]

In a study done In a large population of healthy volunteers, the median PPI value was 1.4%.9 In critically ill patients, the same value was found to represent a very sensitive cutoff point for determining abnormal peripheral perfusion, as defined by a prolonged CRT and an increased skin temperature difference.[9-11]

He et al. reported that the lactate levels correlated strongly with a lower PI (PI <1.4) in the subset measurements.[12] However, the relationship was lacking for normal PI (PI ≥1.4). While the presentation of normal PI might suggest sufficient perfusion, hyperlactatemia may not result from tissue hypoperfusion. Therefore, the relationship between lactate and PI was weak for normal PI (PI ≥1.4).

He et al. also reported that PI is an independent risk factor for 30-day mortality following resuscitation.[12] Successfully normalized PI (≥1.4) during treatment might be an indication to stop the resuscitation, whereas pursuing normalized PI (≥1.4) might not result in better outcomes.

Lactate is the end product of anerobic glycolysis.[17] Serum lactate level increases in states of cellular hypoxia or low peripheral perfusion; thus, serum lactate level is considered a surrogate of cellular perfusion.[17] Lactate is

the most frequently used marker of tissue perfusion.18 Lactic acidosis is a predictor of in-hospital mortality in septic shock.[19,20] Increased lactate clearance during resuscitation of septic shock was associated with improved outcomes.[21] Peripheral perfusion index (PPI) represents "the ratio between the pulsatile and non-pulsatile component of the light reaching the pulse oximeter".[22] As the pulsatile (arterial) flow is the only portion affected with vasoconstriction and vasodilatation, PPI has been considered as a numerical non-invasive measure for peripheral perfusion. In states of tissue hypoperfusion, PPI reduces due to decreased pulsatile component but the non-pulsatile component of blood flow remains constant. The sacrifice of peripheral tissue is a self-protecting mechanism for the vital organs during shock. The peripheral tissue is the first tissue-bed to be sacrificed during shock and the last to be re-perfused in resuscitation. Therefore, we speculated that there would be a critical PI value related to mortality, which works as the safe limit. In critically ill patients, PPI less than 1.4 is a marker of hypoperfusion; also, PPI less than 0.6 is an independent factor for 30-day mortality.[22,23] In an observational study, Hernandez and colleagues reported that early recovery of peripheral perfusion indices (such CRT, Tc-toe, and P (v-a) CO2) is a marker of successful resuscitation of septic shock patients.[24] A randomized controlled trial (RCT) investigated the perfusion-based approach during resuscitation of 30 septic shock patients was conducted by the same group of authors.[24] The aforementioned study reported that the perfusion-based approach resulted in lower fluid replacement, less organ dysfunction, and shorter length of stay.[24] In a large population of healthy volunteers, the median PPI value was 1.4%.[25] In critically ill patients, the same value was found to represent a very sensitive cutoff point for determining abnormal peripheral perfusion, as defined by a prolonged CRT and an increased skin temperature difference.[25]

In our study, we found that the patients with a normal PI (>1.4) did not have a better outcome as compared to the patients with mild PI impairment (0.6-1.4) after resuscitation and these findings very well correlated with many of the studies done in this regard. Therefore, it is possible to predict that ensuring total normalization of peripheral perfusion might lead to over-resuscitation, without improving the overall outcome after achieving the target lactate levels. In other words, pursuing a better physiological status is not always associated with a better outcome. We suggest that mild PI (0.6-1.4) impairment might be "permissive impaired peripheral perfusion" which does not call for immediate and aggressive resuscitative efforts by the treating doctor.

Limitations

More such studies should be done to compare the efficacy of our study as very limited data is available in this regard. The study population was only 100 in our case and such trials on a bigger set of patients would be more valuable.

CONCLUSION

To the best of our knowledge, no one has quantified peripheral perfusion index to the outcome in patients with septic shock. The noninvasive peripheral perfusion potential value to predict outcome remains to be established in septic patients. This study was conducted as a prospective evaluation of the predictive value of the noninvasive peripheral perfusion indicators, traditional metabolic variables, and global hemodynamic parameters in septic patients after resuscitation. This could provide valuable insights about perfusion monitoring in septic patients and help to delineate the potential role and limitations of noninvasive peripheral perfusion as a target for resuscitation.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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