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The Role of Serum Lactate as a Prognostic Biomarker in Major Burn Patients: A Prospective Study

SHERIEN METWALLY SALAMA, M.D; AHMED GADALLAH, M.Sc. and MOHAMED FATHY FEKRY, M.Sc.

The Department of Plastic, Burn and Maxillofacial Surgery, Faculty of Medicine, Ain Shams University

Abstract

Background: Severe burn results in a devastating and unique derangement called burn shock. Fluid resuscitation is the foundation of immediate burn care, and the primary goal of resuscitation is to restore and preserve tissue perfusion. Historically, resuscitation has been guided by a combination of basic laboratory values, invasive maneuvers, and clinical data, but the optimal guide to the end point of resuscitation remains controversial.

Objective: The aim of this study is: To investigate the diagnostic and prognostic validity of serum lactate in major burn patients and to determine the utility of an initial and serial serum lactate measurement during the first 36 hours for identifying substantial risk of death and adequacy of fluid resuscitation.

Patients and Methods: 40 individuals who had significant burns (greater than 20% of TBSA). Both operated and non-operated patients are included. Twenty were female and twenty were male of the forty cases. The research covered all adult burn patients hospitalized during the first twenty-four hours following their injury. Individuals who were released or died 48 hours after admission, or who were hospitalized after 24 hours following a thermal injury, were not included.

Results: As a prognostic tool, serial blood lactate measurements performed better than solitary measurements. 24 hours after admission, lactate levels that were reduced or returned to normal were linked to a better chance of survival. Since serial blood lactate measurements predict death in patients with significant burns, this study validates the predictive utility of serum lactate for mortality in these patients.

Conclusion: Our study demonstrated that lactate level in major burn patients is a promising prognostic biomarker, that could facilitate ideal management and initiate proper antimicrobial therapy and good prognostic value as an early predictor of mortality.

Key Words: *Serum lactate – Sepsis – Major Burn Patients – Diagnosis – Intensive Care Unit.*

Correspondence to: Dr. Ahmed Gadallah,
E-Mail: ahmed.gadallah93@gmail.com

Ethical Committee: The Ethical Committee of the College of Medicine at Ain Shams University had approved the study. All patients received written informed consent detailing the methodology used in this study, particularly care and attention to the confidentiality of patient identities and addresses.

Disclosure: No conflict of interest.

Introduction

Burn injuries continue to be a major global source of morbidity in the population **[1]**.

As per the WHO data dated March 6, 2018, burns result in over 18,000 fatalities per year, with most of these instances happening in middle- and low-income nations, with two-thirds of them occurring in the African and Southeast Asian region **[2]**.

Research from both clinical and experimental settings has shown that within hours of damage, a severely dysregulated inflammatory host response develops in response to severe burns, regardless of the etiology **[2]**.

Large burn injuries produce a necrotic zone, which is followed by a stasis zone and the production of inflammatory mediators such as histamine, prostaglandins, thromboxane, and nitric oxide. These mediators enhance capillary permeability and cause localized edema in the burn site **[3]**. This happens minutes to hours after the damage, and when the ischemic tissues are re perfused, highly reactive oxygen species (ROS) are produced **[4]**.

Adequate fluid resuscitation is especially crucial in burn treatment **[5]**. Maintaining circulation, replacing circulating volume, and preventing or treating hypovolemic shock are the objectives. Fluid resuscitation is our most crucial aid in keeping the circulation going, even if infusions could make the edema worse **[6]**. The goal of sufficient fluid resuscitation is to continue oxygen supply while limiting the development of interstitial edema **[7]**.

Lactate has been shown to be a strong predictor of outcome. Studies have shown that baseline lactate level is a useful parameter in distinguishing survivors from non-survivors. Smoke inhalation victims are especially at risk for lactate elevation due to inhalation of cyanide or carbon monoxide **[8]**.

The larger the burned surface area and the greater the depth of burned tissue, the greater the fluid leakage, leading to hypovolemic shock and tissue hypoperfusion in the patient, which is accurately reflected in the patient's serum lactate concentration. Similarly, a delay in initiating fluid resuscitation leads to failure to replace fluids for longer periods of time, which also leads to reduced blood flow to tissues, leading to elevated lactate concentrations **[9]**.

Aim of study:

To determine lactate's predictive value in major burn patients and to assess its efficacy as a diagnostic and prognostic tool.

Patients and Methods

The study was conducted at the burn intensive care unit (ICU) of Ain Shams University Hospital.

Patient details: 40 individuals who had significant burns (greater than 20% of total body surface area (TBSA)). Both operated and non-operated patients are included. Twenty were female and twenty were male of the forty cases.

Type of study: Prospective study.

Inclusion criteria: Both sexes, ages 18 to 65, arrived at the emergency room with burns that covered at least 20% of their TBSA.

Exclusion criteria: Extremes of Age, electric burn, inhalational Injury based on bronchoscopy evaluation, and medical Comorbidities, for example, hypertension, diabetes mellitus, liver, and kidney illnesses.

TBSA was calculated based on the Lund and Browder chart. Resuscitation fluid was calculated using the Parkland equation. Half of this amount was administered during the first 8 hours and the remainder during the additional 16 hours. Lactated Ringer's was a resuscitation fluid.

Study procedures:

I- *Assessment of the patient:*

Clinically: Generally: Vital signs and full level of consciousness, burn: Cause, extent, distribution, depth, and time of presentation and burn wound infection and sepsis: According to American Burn Association guidelines.

Initial Plasma Lactate measurements were obtained within the first 36 hours of admission to hospital. The time of admission to ICU was considered zero hour (within 4 hours of burn time), the second measurement was performed at 12th hour, the third at 24th hour, and the fourth at 36th hour.

The standard lactate level was set as 1.4–2.3 mmol/L **[10]**.

Sample collection:

For each sample, 5ml venous blood was settled in a grey top tube (sodium fluoride). (Fig. 1-B).

Specimen type: Whole blood (Venous) (Fig. 1-A).

Transport: Transport immediately.

Plasma specimen was analyzed by Beckman Coulter AU480 Chemistry Analyzer (Fig. 2).

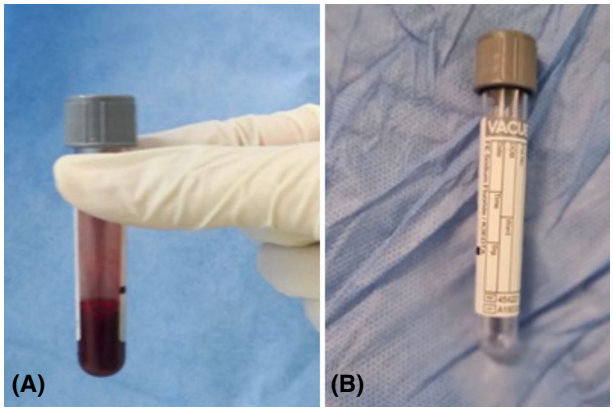

Fig. (1): (A): Grey top tube (sodium fluoride), (B): Blood sample collected.

Fig. (2): Beckman Coulter AU480 Chemistry Analyzer.

Regimen of fluids resuscitation of admitted patients:

Resuscitation of these patients was performed according to the Parkland formula based on the size of the burn and the patient's body weight and was applied as a first estimate of the required rate of fluid administration. Fluid resuscitation was then adjusted to achieve a target urine output of 0.5 to 1ml/Kg/h and a target mean blood pressure >65mm (about 2.56 in) Hg.

DAY 1: Started from the time of burn till the same hour of the next day.

- Type: Isotonic crystalloids (lactated ringer).
- Total per 24h: 4ml/kg/%TBSA (max TBSA 60%).
- Rate: ½ the amount in 1st 8hr and ½ the amount over the next 16 hrs.
- Other measures were taken as standard treatment.

DAY 2: +

- 2 ml/kg/%TBSA.
- 2/3 ringer lactate at a rate of (…ml/h).
- Albumin 5% according to serum albumin level (100ml albumin 20% (20mg) + 300ml Ringer lactate). Serum albumin level of 2.5g/dl is a reasonable goal.

Results

The mean age was 36.02±10.89 years. And the mean TBSA burn injury of the study population was 32.17±11.06 Table (1).

The previous table shows that initial serum lactate value was proportional to total body surface area burned (TBSA).

Total body surface area burned was found to be associated with mortality with highly significant statistical value.

As shown in Table (3) serum lactate at zero hour (p=0.001), 12th hour (p=0.000), 24th hour (p=0.000) and 36th hour (p=0.000) was statistically more accurate in predicting the outcome.

An association was noted in the differences between the admission time and the 24h and between the admission time and 36h was found, but not between admission and the first 12h.

Table (1): Characteristics of the patients.

		No. = 30
Age	Mean ± SD	36.02±10.89
	Range	18-65
Gender	Female	20 (50%)
	Male	20 (50%)
% TBSA	Mean ± SD	32.17±11.06
	Range	21-60

Table (2): Age, sex, and TBSA% in relation to Mortality.

Variable	Outcome		Test value	p-value	Sig.
	Live No. = 28	Died No. = 12			
Age:					
Mean ± SD	31.23±10.13	41.63±8.67	–2.574•	0.016	S
Range	25-55	26-48			
Sex:					
Female	10 (35.7%)	4 (33.3%)	0.085*	0.770	NS
Male	18 (64.3%)	8 (66.7%)			
TBSA%:					
Mean ± SD	32.45±8.33	46.38±7.05	–4.201•	0.000	HS
Range	21-60	38-60			

S = Significant.
NS = Non-significant.
HS = Highly significant.

Table (3): Shows comparison between different serum lactate measurements and the outcome of each.

Serum Lactate	Outcome		Test value	*p*-value	Sig.
	Live No. = 28	Died No. = 12			
At zero hour:					
Median (IQR)	3.5 (2.1-6.1)	11.55 (9.3-13.15)	–3.355	0.001	HS
Range	1-13.4	3.7-18			
12hr:					
Median (IQR)	2.6 (2-3.7)	10.65 (9.6-12.5)	–3.873	0.000	HS
Range	1-10.3	5.2-15			
24hr:					
Median (IQR)	2.95 (1.7-3.4)	11.85 (8.55-14)	–4.083	0.000	HS
Range	1-7.9	7.8-18			
36hr:					
Median (IQR)	1.95 (1.6-2.9)	15.5 (12.15-17.2)	–4.129	0.000	HS
Range	0.9-4	7.7-18.5			

Table (4): Comparison between changes in serum lactate measurements and throughout the different intervals.

% Changes	Outcome		Test value	*p*-value	Sig.
	Live No. = 28	Died No. = 12			
Zero to 12hr:					
Median (IQR)	-16.07 (-33.33 – 5.41)	7.29 (-13.17 – 14.43)	–1.829	0.067	NS
Range	-67.5 – 16.67	-38.89 – 40.54			
Zero to 24hr:					
Median (IQR)	-21.29 (-49.12 – -7.50)	19.09 (-19.29 – 26.27)	–2.298	0.022	S
Range	-62.5 – 66.67	-35.00 – 127.03			
Zero to 36hr:					
Median (IQR)	-46.18 (-60.40 – -22.86)	37.63 (-0.59 – 47.73)	–2.673	0.008	HS
Range	-82.5 – 80	-37.40 – 397.30			

Discussion

Severe burns require appropriate fluid management during the acute phase to ensure adequate perfusion of target organs. However, increased capillary permeability allows intravascular fluid and proteins to escape into the interstitium. Reactive oxygen species help increase endothelial permeability (Nakajima et al., 2019).

The larger the burned surface area and the greater the depth of burned tissue, the greater the fluid leakage, leading to hypovolemic shock and tissue hypoperfusion in the patient, which is accurately reflected in the patient's serum concentration.

Similarly, a delay in initiating fluid resuscitation leads to failure to replace fluids for longer periods of time, which also leads to reduced blood flow to tissues, leading to elevated lactate concentrations (Mokline et al., 2017).

The main findings of our study are that we have shown that high serum lactate concentrations can categorize patients with severe burns into survivors (live) and non-survivors (died). Dead patients had higher blood lactate concentrations than survivors. Another finding is that we used serial serum lactate measurements to predict patient mortality, and this was clearly better than using a single measurement. Although blood lactate concentration on admission has neither sensitivity nor specificity as a predictor of mortality, reduction, or normalization of lactate concentration within the 24-hour period (p=0.022) after admission is associated with significantly higher survival rates. As a predictor of mortality,

blood lactate concentration showed higher sensitivity and specificity after 36 hours of ICU admission (p=0.08).

Lactate levels are known to predict survival or death in shocked patients. Vincent et al., 2003 reported that shock patients with the best prognosis were those whose lactate levels decreased significantly within 1 hour of resuscitation. In 2001, Smith et al., suggested that hyperlactatemia could identify patients at risk of death and could also be used as an indicator of intensive care admission. Additionally, Husain et al., in 2003 confirmed that increased lactate levels on admission and after 24 hours of admission were associated with mortality. This study supports the role of serum lactate as a predictor of mortality in patients with severe burns, as it showed that most patients who died had higher blood lactate concentrations than those who did not.

In 2009, Mikkelsen et al., showed that elevated blood lactate levels were strongly correlated with mortality in patients with severe sepsis. Additionally, Cochran et al., in 2007 examined 128 patients with a mean TBSA rate of 41.7% and measured baseline deficit and lactate levels over a 6-hour period. They found that Non survivors had higher lactate levels at admission, 12, 18, and 24 hours compared with the survivor group. These results matched our results as high serum lactate levels can predict mortality in burned patients.

In this study, patients with major burns and frank shock clearly need urgent resuscitation with fluids and should be monitored in the intensive care unit. Hourly heart rate, blood pressure, and urine output were monitored to ensure the patient remained adequately resuscitated, with serum lactate levels measured at 0-hour, 12-hour, 24-hour, and 36-hour intervals.

Some authors have used a single assessment of blood lactate as a predictive value for mortality in a large retrospective study conducted by Khosravani et al., in 2009. The odds ratio (OR) of death increased from 1.94 to 10.89 depending on lactate concentration, compared with hospitalized patients' lactate <2mmol. The studies by Smith et al.in 2001 and Nichol et al., in 2010 also demonstrated an incredibly significant impact of increased lactate on admission, greater than 2.0mmol/L or 1.5mmol/L, on mortality in hospitalized patients.

In our study most of the dead patients had higher blood lactate levels than the survivors and that their serial monitoring for predicting death is better than their single measurement.

In our study we demonstrated that higher blood lactate values can be utilized to mark patients at substantial risk of developing organ dysfunction after severe burns. Mortality after burns was clearly predicted from serum lactate over a 24-hour follow-up period. The cut-off serum lactate for prediction of mortality was 4mmol/L with a good sensitivity and specificity. Therefore, when there is a severe or persistent elevation in serum lactate levels, the clinician will be advised to supervise patient care as much as possible or, alternatively, acknowledge the potential futility of clinical intervention.

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