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The Journal of Critical Care Medicine 2020;6(1):59-64

RESEARCH ARTICLE

DOI: 10.2478/jccm-2020-0005

Prognostic Value of Serum Lactate Levels in Critically Ill Patients in an Intensive Care Unit

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Abstract

Introduction: The patient in critical condition, regardless of the cause of admission, continues to be a challenge for health systems due to the high mortality that it reports. There is a need to identify some marker of early obtaining, easy to interpret and with high relevance in the prognosis of these patients. **Objective**: To determine the prognostic value of serum lactate in an Intensive Care Unit (ICU). **Method**: One hundred and forty-five patients admitted to an ICU were enrolled in the study. The Acute Physiology and Chronic Health Evaluation II (APACHE) prognosis score, Sequential Organ Failure Assessment, hemodynamic support need, mechanical ventilation, cause of admission, stay in ICU, analytical and physiological variables were determined. The probability of survival of patients who had elevated and normal serum lactate levels was calculated. The risk of dying was determined using the Cox regression model. **Results**: Twenty-eight patients died (19%) in the ICU. The serum lactate value was higher in the group of patients with trauma, infections, APACHE II and high creatinine levels; as well as with decreased mean arterial blood pressure, need for hemodynamic support and mechanical ventilation. The survival capacity was higher in patients who had normal serum lactate. Serum lactate was the sole independent predictor of mortality (AHR 1.28 [1.07-1.53], p = 0.008). **Conclusions**: Patient assessment through the determination of serum lactate levels provides useful information in the initial evaluation of the critical patient.

Keywords: serum lactate, prognosis, intensive care unit, hyperlactatemia, APACHE

Received: 18 November 2019 / Accepted: 29 January 2020

Introduction

The seriously ill patient is currently a challenge for both the medical staff and the health system, given its complexity and variability. New strategies and therapies to reduce mortality, hospitalization time, sequelae and costs are required [1].

Severity indexes or prognostic scales are necessary methods to estimate the severity of anatomical lesions, physiological alterations and the probability of survival of the patients. Validation of these indices has allowed their widespread use and the adoption of a universal language on the subject [2].

There are different scales to assess the clinical status of a patient, which allow a diagnosis of the existing severity and which help anticipate possible imminent and late complications, including death [3].

For several years the use of a predictor of organic dysfunction in critically ill patients (CIP) has been proposed, recommending that the ideal should meet the criteria in the context of critical care, be simple, routinely reproducible and promptly evaluable [3].

Serum lactate levels can be a useful tool in confirming tissue hypoperfusion and organic dysfunction. Knowledge of this marker allows the establishment of values that allow an early indication of the severity of the patient's clinical condition and the ability to monitor the progression of the critical situation, thus impacting on the patient's prognosis and possibly reducing mortality [4,5].

According to the published literature, multiple studies relate the serum lactate levels in patients with septic [6] and polytraumatized states [7], but data concerning the general context of intensive care remain scarce.

The objective of this study is to determine the prognostic value of serum lactate in patients admitted to the ICU.

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Materials and methods

Design

A cohort, observational, prospective study was carried out in the Intensive Care Unit (ICU) of the General Hospital, Havana, Cuba between October 1, 2016, and October 1, 2017. The study was approved by the hospital's Scientific Council and the Ethics Committee. Prior to data collection, written informed consent was obtained from patients and family members.

Patients

All patients older than 18 years who presented with manifestations of tissue hypoperfusion, such as arterial hypotension, oliguria, sensory abnormalities, skin temperature gradient and delayed capillary filling time, were included. Complementary studies were performed and different physiological variables were recorded within the first 6 hours after admission to the ICU. Two samples were taken, one at admission to the ICU and another at 6 hours after the initial resuscitation, the averages of serum lactate and all the analytical values and physiological variables that were measured during the study were calculated. Patients with incomplete medical records in the database and those subjects who did not undergo serum lactate determination within the established time period were excluded.

Data collection

From the ICU database, the following variables were taken at admission: age, sex, prognostic score Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA), need for hemodynamic support, mechanical ventilation, cause of admission, stay in the ICU, analytical values and physiological variables. The analytical values evaluated were: Leukocytes, hematocrit, platelet count, serum creatinine, arterial blood gas, sodium and potassium. While the physiological variables measured were: Heart rate, respiratory rate and medium arterial tension. The response variable was global mortality in ICU.

The population was divided into two groups, depending on serum lactate levels; Group1 with > 2mmol / l-high and Group2 with ≤ 2mmol / l-normal.

Statistical analysis

For all the variables, summary measures were used, the qualitative ones were expressed by absolute numbers and percentage. The quantitative ones as the mean(SD) or the median with 25-75% interquartile range (IQR) according to the distribution of normality of the population. Comparison between the study groups was performed using the Chi-square test ($\chi 2$) or Fisher's exact test. For the quantitative variables, the Mann-Whitney U test was used. The Kaplan-Meier method was used to estimate the survival probability of patients admitted to the ICU and the Log-Rank statistic to determine the difference between patients with and without elevated serum lactate levels and the occurrence of the event. The Cox proportional hazard model with adjusting hazard ratio (AHR) and 95% confidence interval (CI) was used. Statistical tests were considered significant at a two-sided p-value less than 0.05. Statistical analysis was carried out using the IBM® SPSS® program, version 23 (Chicago, IL, USA).

Results

During the study period, 170 patients were admitted to the ICU, of which 15 patients were excluded because they did not present serum lactate level determinations in the first six hours after admission and a further twenty due to incomplete clinical records in the database. A total of 145 subjects were enrolled in the study (85%)of which twenty-eight died in the ICU (19%).

The general characteristics of the population studied, stratified according to serum lactate levels in the first six hours after admission to the ICU are shown in (Table 1). Traumatic (p = 0.05) and infectious (p = 0.041) causes and the distribution of the APACHE II prognostic score (p = 0.002) were significantly related to high serum lactate levels and the highest probability of death in the ICU. A good association was also observed in patients who required hemodynamic support (p = 0.008) and mechanical ventilation (p<0,0001).

The median serum lactate was 2.1 mmol / l (RIQ 1.4-4.2 mmol / l). Table 2 shows the analytical values and physiological variables in the first 6 hours after admission to the ICU. It was found that the distribution of serum lactate was higher in the group of patients who presented high creatinine levels while the mean blood pressure was lower in that group, with a statistically significant relationship in relation to mortality in the ICU.

When the analysis of the Kaplan-Meier curve was performed (figure 1), patients who presented serum lactate ≤ 2mmol / l had a higher probability of survival with a median stay of 14 days in the ICU, which

Table 1. General characteristics of the population, stratified according to serum lactate values in the first six hours after admission to the ICU.

Variable	Serum lactate >2mmol/l (N=80)	Serum lactate ≤ 2mmol/l (N=65)	P
Age, average (SD)	53,9 (16,8)	45,1 (17,6)	0,203
Sex, n (%)			
Male	46 (57,5)	26 (40,0)	0,860
Female	34 (42,5)	39 (60,0)	
Apache II, median (IQR **)	14 (11,0-20,0)	8 (5,0-13,0)	0,002
SOFA, median (IQR **)	10,5 (6,0-15,0)	5 (1,5-8,0)	0,098
Cause of admission to the ICU, n (%)			
Cardiovascular	8 (10,0)	1 (1,5)	0,520
Pulmonary	6 (7,5)	7 (10,8)	0,463
Neurological	6 (7,5)	5 (7,7)	0,691
Traumatic	26 (32,5)	19 (29,2)	0,05
Infectious	16 (20,0)	11 (16,9)	0,041
Gastrointestinal	8 (10,0)	8 (12,3)	0,738
Poisoning	1 (1,3)	4 (6,2)	0,583
Other	9 (11,3)	10 (15,4)	0,124
Hemodynamic support, n (%)	14 (17,5)	4 (6,2)	0,008
Use Mechanical Ventilation, n (%)	25 (31,3)	21(32,3)	<0,0001
Stay in ICU, median (IQR **)	5,0 (4,0-7,0)	6,0 (4,0-7,5)	0,756

SD *, standard deviation; IQR **, interquartile range; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment; ICU, intensive care unit.

Table 2. Analytical values and physiological variables in the first six hours after admission to the ICU.

Variable	Serum lactate >2 mmol/l (N= 80)	Serum lactate ≤ 2 mmol/l (N= 65)	P
Leukocytes / mm3, median (IQR **)	12,5 (8,7-18,9)	11,6 (8,5-14,3)	0,055
Hematocrit (%), median (IQR **)	31,2 (5,8)	32 (8,3)	0,482
Platelet count / mm3, median (IQR **)	200 (164,3-279,0)	200 (170,0-239,0)	0,510
Blood Glucose (mmol/l), median (IQR **)	7,2 (5,9-8,9)	6,8 (58,7-9,6)	0,066
Aminotransferase Aspartate (u/l), median (IQR **)	42,5 (29,3-75,6)	41,0 (31,5-69,5)	0,469
Aminotransferase Alanine (u/l), median (IQR **)	40,0 (28,3-60,0)	40,0 (29,0-58,0)	0,124
Albumin (g/l), median (IQR **)	33,0 (27,3-37,0)	35,0 (28,0-38,0)	0,164
Creatinine (Mmol / l), median (IQR **)	90,5 (66,3-129,5)	86 (68,5-114,0)	0,044
PH, median (IQR **)	7,41 (7,35-7,45)	7,42 (7,37-7,45)	0,225
PCO2 (mmHg), median (IQR **)	35,3 (21,1-42,8)	35,0 (30,1-42,6)	0,08
PO2 (mmHg), median (IQR **)	86,5 (70,0-115,3)	90,0(72,9-115,0)	0,175
Base Excess, median (IQR **)	-0,7 (-4,1-2,6)	-0,1 (-3,6-2,2)	0,341
Bicarbonate, median (IQR **)	23,4 (20,9-26,0)	24,0 (19,9-26,3)	0,407
PO2 / FiO2, average (SD *)	306,9 (137,8)	341,5 (117,9)	0,232
D(A-a)O2, median (IQR **)	81,0 (29,2-140,6)	56,6 (17,5-97,7)	0,241
Sodium (mmol / l), median (IQR **)	136,0 (132,0-141,0)	133,0 (130,0-138,5)	0,056
Potassium (mmol / l), median (IQR **)	3,8 (3,4-4,2)	3,7 (3,4-4,2)	0,845
Heart Rate (bpm), average (SD *)	93,9 (21,0)	97,3 (18,5)	0,374
Respiratory rate (rpm), median (IQR **)	22,0 (19,0-25,8)	21,0 (20,0-25,0)	0,252
Medium Arterial Tension (mmHg), median (IQR **)	92,3 (82,1-99,8)	93 (80,5-102,2)	0,021

SD *, standard deviation; IQR **, interquartile range.

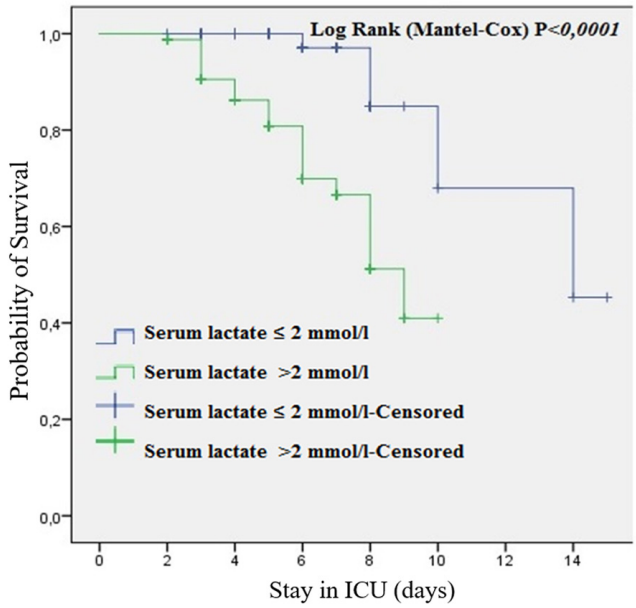

Fig. 1. Kaplan-Meier curve for the probability of survival in patients admitted to the ICU concerning serum lactate levels.

revealed a statistically significant difference in relationship to the group of patients who presented elevated serum lactate with a Log Rank (Mantel-Cox) (p <0.0001).

In the Cox regression analysis (Table 3), of all the variables studied, only serum lactate was an independent predictor of mortality with a statistically significant relationship (AHR 1.28 [1.07-1.53], p = 0.008).

Discussion

In every patient, but especially in the critically ill patient, a doctor has to establish a diagnosis, determine the severity of the disease, decide on a treatment, predict and monitor the degree of response in order to make all necessary adjustments before the critical condition take the patient to the point of no return. To achieve this, it is essential to have a biomarker as an aid to treatment planning in those critical moments. Serum lactate levels have been proposed as a useful tool in such situations [4].

In critically ill patients, elevated serum lactate levels at the time of admission to the hospital as a static value over time are related to higher mortality. In 2010, Soliman et al studied the lactate levels of 433 patients of a medical-surgical ICU defining hyperlactatemia as a serum concentration greater than or equal to 2 mEq / L 45% of the patients had hyperlactatemia and found a direct relationship between lactate levels and risk of death, reaching a mortality of 17% with lactate concentrations between 2-4 mEq / l and 64% in those with concentrations greater than 8 mEq / l. Also, it was correlated with a longer hospital stay in the ICU and higher APACHE II and SOFA scores [4,8]. The same results were found in the present study, in which the median Apache II score was 14 points in patients with serum lactate greater than 2 mmol / l, obtaining a powerful association between this group of patients and the probability of death in ICU.

At present, it is proposed that in the patient with polytrauma, serum lactate levels rise not only due to the hemodynamic instability that arises as a result of circulatory shock, but also due to the trauma caused by an increase in stimulation of β2 receptors, big producers of adrenaline. All this leads to an increase in pyruvate that saturates the capacity of the enzyme pyruvate dehydrogenase, which causes the metabolism to deviate and produce an increase in lactate levels.[5].

A previous study on traumatized patients showed that an initial lactate level of more than 4 mmol / L is associated with an increase in the probability of death in the acute phase [9]. Zachary et al. retrospectively evaluated lactate levels in patients with closed or open trauma, at least twice in the first twenty-four hours of admission [10]. The recorded mortality was 7.3%. The average initial lactate levels of the survivors were lower than the deceased, with a statistically significant difference [10]. In a recent study at the San Vicente Foundation University Hospital (Medellin, Colombia), 251 polytrauma patients were evaluated, who were given lactate measures at admission, at 6 and 24 hours, 15.5% died, serum lactate upon admission was 4.6 mmol / L (IQR = 2.9-6.9) and an important association with

Table 3. Results of the Cox regression analysis.

Variable	AHR	95% IC	P
Serum lactate	1,28	1,07-1,53	0,008
APACHE II	1,07	1,00-1,14	0,06
SOFA	0,96	0,89-1,03	0,258
Excess Base	1,02	0,97-1,07	0,417

AHR, adjust hazards ratio; IC, confidence interval; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment.

mortality was found in the adjusted logistic regression model [11]. In our study, traumatic causes and serum lactate greater than 2 mmol / l were significantly related to death in the ICU.

According to world literature, there are multiple reports that show the relationship between the elevation of serum lactate and the occurrence of septic states [6,12-15], this is due to the presence of an imbalance between the genesis and clearance of serum lactate. It is proposed that there is a state of critical tissue hypoperfusion that affects the synthesis of ATP by blocking the pyruvate dehydrogenase enzyme due to hypoxia this, in turn, alters with the conversion of pyruvate to lactate [16]. In one study, 830 patients admitted to an emergency ward, with a diagnosis of severe sepsis, were classified into three groups according to the level of lactate in low risk. The three groups were defined as; a level of lactate less than 2; intermediate from 2 to 3.9 and high greater than 4. At twenty-eight post-admission days, mortality was of 15.4%, 37% and 46.9%, respectively for the three defined lactate levels. In contrast, in patients who did not present with shock, mortality was 8.7%, 16.4% and 31.8%, respectively [4].

Our results concur with the literature, since the cause of admission of infectious origin, and the presence of elevated serum lactate levels showed a significant relationship with mortality in the ICU.

Concerning the need for mechanical ventilation, hemodynamic support and presence of arterial hypotension, in the present study, an association with hyperlactatemia and death in ICU was also found. Despite the effect that mechanical ventilation has on cardiac output and tissue perfusion, this alone did not influence the elevated levels of serum lactate. It is concluded that the cause may be related to the fact that many of these patients presented in a state of shock, with hemodynamic instability and need for support with vasoactive amines, which in turn results in a decreased blood flow to the tissues, favouring anaerobic metabolism, with lactic acidosis and hyperlactatemia.

Concerning the ICU survival time, patients who presented high serum lactate levels died more quickly than those who presented normal parameters, with significant statistical differences between both groups of studies (figure 1). On the other hand, in the Cox regression analysis, serum lactate levels were only associated with an increased risk of dying in the ICU (AHR 1.28 [1.07-1.53], p = 0.008).

It is accepted that observational studies such as the present one, do not allow stratified randomization. The study was restricted to one ICU, but never the less addressed an ICU population with diverse medical, surgical, traumatic and infectious conditions, which we feel moderates its limitations.

Conclusions

The assessment of a critically ill patient by determining serum lactate levels provides useful and valuable information. Its measurement is not expensive, it is fast, and it is available.

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