American Journal of Emergency Medicine xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Determination of plasma lactate in the emergency department for the early detection of tissue hypoperfusion in septic patients

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ARTICLE INFO

Article history:
Received 17 August 2017
Received in revised form 27 December 2017
Accepted 28 December 2017
Available online xxxx

Keywords:
Sepsis
Lactate
Infection
Hypoxia
Septic shock

ABSTRACT

Objective: To determine the validity of plasma lactate in the emergency department for the early detection of tissue hypoperfusion in septic patients.
Materials and methods: Longitudinal descriptive study. Non probabilistic sampling for convenience. Plasma lactate levels were determined in patients admitted to the emergency department with systemic inflammatory response data and clinical suspicion or documented infection. Follow-up was seven days. Complications were considered if the patients presented septic shock, severe sepsis, entry to intensive care or death.
Results: Ninety patients were included. The mean age was 57.4 ± 20.31. Fifty five percent (n = 49) were women. 25% (n = 22) of the patients showed complications. Plasma lactate levels were 1.55 mmol/L in uncomplicated patients and 3.72 mmol/L for complicated patients ($p < 0.001$). The area under the ROC curve was 0.72 (95% CI, 0.575–0.829). The cutoff point that best described the relationship with the probability of complications was that set at 4.2 mmol/L. The variables studied that showed a significant association with the probability of complications were edema ($p = 0.004$), and infections of the respiratory tract ($p = 0.037$). A model that included lactate levels, using as adjustment variables edema and the presence of low respiratory tract infection explained between 0.234 and 0.349 of the dependent variant, correctly classifying 80% of the cases.
Conclusion: Plasma lactate is useful in emergency departments as a predictive test for the early detection of patients with tissue hypoperfusion that evolve to severe sepsis, septic shock or death.

1. Introduction

Sepsis is one of the major health problems. Up to 19 million cases per year around the world are estimated [1]. The rapidity with which the initial management is established is determinant in the morbi-mortality in the short, medium and long term [2].

In 2001, approximately 750,000 cases of severe sepsis were estimated annually in the United States; with a mortality rate of 28.6% [3,4]. In Mexico, an annual incidence of 11,183 cases (27.3%) was estimated in 2009, with an estimated mortality of 30.4% [5].

The Consensus of the Surviving Sepsis Campaign of 2012, defined it as: the presence (probable or documented) of infection along with systemic manifestations of infection [2]. When the systemic response is perpetuated, hypotension, hypoperfusion and white organ damage may develop [6]. However, some patients report global tissue hypoxia, evidenced by a lactate greater than or equal to 4 mmol/L in the presence of normotension, a condition referred to as cryptic shock [7]. The evidence supports that early intervention and diagnosis result in a significant reduction in morbidity and mortality [6].

Recently, attention has focused on lactate as a biomarker and even as a therapeutic target [8].

Under normal circumstances, tissues can be considered as lactate producers or metabolizers [9]. The arterial plasma concentration of lactate reflects the balance between production, and its consumption/clearance. This concentration is generally <2 mmol/L [10]. Most of the situations that lead to excess production and reduction in clearance are predominantly pathological, reflecting tissue hypoxia or non-hypoxic tissue injury [8].

However, although we found lactate levels >4 mmol/L in septic patients, as a clear indication of tissue hypoperfusion; there is no clarity in the intervention that should be done in the patient with hyperlactatemia but without hemodynamic alteration [6].

According to the management guidelines, an elevated lactate is sufficient to diagnose shock, regardless of whether or not there is

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https://doi.org/10.1016/j.ajem.2017.12.068
0735-6757/

hypotension. Sepsis with elevated levels of lactate (> 4 mmol/L) is associated with high mortality, and is an indication for initiating management protocols and packages. It has also been reported an inverse relationship between lactate clearance and mortality in severe sepsis and septic shock [11].

Although a formal characterization of the possible progression from an infection without systemic manifestations to septic shock or death has not been achieved; traditionally, the natural process of sepsis has been understood as a linear sequence, covering different clinical stages [12].

The present study seeks to know if the measurement of plasma lactate can be used as a prognostic marker of complications in septic patients admitted to an emergency department.

2. Materials and method

This observational study was designed to determine whether the measurement of plasma lactate as a result of tissue hypoperfusion in septic patients can be used as a prognostic marker for complications in an emergency department. It was carried out in the period from May to September 2013 in the Emergency Service of the Regional General Hospital No. 46 of the Mexican Institute of Social Security in Guadalajara, Jalisco. The study was previously authorized by the Hospital Research Committee (1306).

2.1. Inclusion criteria

Patients older than 18 years with at least two signs of systemic inflammatory response (SIRS) according to the general and inflammatory variables proposed by the Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012, which are detailed in Table 1.

2.2. Criteria for non-inclusion

Patients presenting with chronic renal failure on renal replacement therapy, patients with hepatic failure at any stage, and patients on biguanide therapy.

2.3. Exclusion criteria

Patients who presented to the emergency department with a diagnosis of severe sepsis or septic shock, patients who presented with some SIRS criteria, suspected infection or documented infection; Or a diagnosis of sepsis, and which rapidly evolved to severe sepsis or septic shock before sampling for serum lactate and patients who met inclusion criteria and who were definitively transferred to another hospital to continue their study driving.

Table 1
Diagnostic criteria for sepsis.

Documented or suspected infection, and some of the following:
General variables
Fever (>38.3 °C)
Hypothermia <36 °C)
Heart rate > 90 beats per min, or more than two SDs above normal for age.
Tachypnea
Altered mental state
Significant edema or a positive fluid balance (>20 mL/kg in 24 h)
Hyperglycemia (plasma glucose > 140 mg/dL) in the absence of diabetes
Inflammatory variables
Leukocytosis (leukocyte count > 12,000)
Leukopenia (leukocyte count <4000)
Normal leukocytes with >10% immature forms

Abbreviations: SD, standard deviation; °C, degrees centigrade; ml, milliliters; kg, kilograms; mg, milligrams; dl, deciliter.

2.4. Intervention

Patients were identified and classified in the first contact area of the emergency department, the clinical data were collected and the venous blood sample was collected for plasma lactate determination. The blood sample was analyzed using the VITROS® Chemistry Products LAC DT slides, to quantitatively determine the lactate concentration in plasma using the VITROS® 5600 Integrated System Biochemistry Analyzer, based on colorimetric spectrophotometry. Measuring range 0.5–12 mmol/L (reference range 0.6–2.1 mmol/L).

2.5. Data collection and analysis

We identified patients who presented complications and those who did not. The independent variables studied were chosen from the set of signs, symptoms and laboratory data included as part of the systemic inflammatory response and exposed in the last update of the Surviving Sepsis Campaign; as part of the selection criteria for these variables, the ease of collection in an emergency department was considered, as well as the feasibility and opportunity with which a laboratory study could be processed.

To determine the utility of lactate values, patients were followed up for 7 days. Possible complications were ICU admission, death, and progression to severe sepsis or septic shock according to the medical diagnosis at the time of the evaluation.

In order to establish the validity and usefulness of determination of lactate plasma levels, inferential statistics were used in the cases that merited (Student's *t*, square chi, area under the ROC curve and bivariate logistic regression calculation). A significant $p < 0.05$ was considered.

3. Results

We included 98 patients who requested medical attention in the adult emergency department. All patients had at least two diagnostic criteria for systemic inflammatory response, more suspicion of infection, or documented infection. Table 2 shows the distribution by sex, comorbid, some clinical characteristics and basal lactate levels.

The usefulness of plasma lactate for the early detection of tissue hypoperfusion in septic patients was assessed through the ability of this test to discriminate those patients likely to present complications (evolution to severe sepsis or septic shock, ICU admission or death for any reason) within seven days of your hospitalization.

Table 2
Clinical and demographic characteristics of patients

Variable	Values
Age[a]	59 (±20.31)
Sex[b]	
Men	54 (49)
Women	46 (41)
Comorbidities[b]	
Systemic arterial hypertension	41 (37)
Diabetes mellitus type 2	30 (27)
Clinical features[a]	
Systolic blood pressure (mm Hg)	114 (±20.73)
Diastolic blood pressure (mm Hg)	70 (±11.93)
Mean blood pressure (mm Hg)	86 (±13.73)
Heart rate (bpm)	103 (±16.39)
Respiratory rate (bpm)	23 (±5.66)
Significant edema[b]	27 (30)
Temperature (°C)	36 (±0.94)
Oxygen saturation by pulse oximetry (%)	95 (±5.98)
Glasgow Coma Scale (score)	15 (±2.83)
Laboratory studies[a]	
Plasma lactate (mmol/L)	1.4 (±2.32)

Abbreviations: mmol/L, millimoles per liter; mmHg, millimeters of mercury; bpm, breaths per minute; bpm, beats per minute; °C, degrees Celsius.
[a] Median and standard deviation.
[b] Percentage.

Please cite this article as: Gómez-Ramos JJ, et al, Determination of plasma lactate in the emergency department for the early detection of tissue hypoperfusion in septic patients, American Journal of Emergency Medicine (2017), https://doi.org/10.1016/j.ajem.2017.12.068