



Brief Report

Base excess is an accurate predictor of elevated lactate in ED septic patients

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Received 10 September 2010; revised 25 September 2010; accepted 26 September 2010

Abstract

Background: Prior studies showed that lactate is a useful marker in sepsis. However, lactate is often not routinely drawn or rapidly available in the emergency department (ED).

Objective: The study aimed to determine if base excess (BE), widely and rapidly available in the ED, could be used as a surrogate marker for elevated lactate in ED septic patients.

Methods: This was a prospective and observational cohort study. From March 2009 to March 2010, consecutive patients 18 years or older who presented to the ED with a suspected severe sepsis were enrolled in the study. Lactate and BE measurements were performed. We defined, a priori, a clinically significant lactate to be greater than 3 mmol/L and BE less than -4 mmol/L.

Results: A total of 224 patients were enrolled in the study. The average BE was -4.5 mmol/L (SD, 4.9) and the average lactate was 3.5 mmol/L (SD, 2.9). The sensitivity of a BE less than -4 mmol/L in predicting elevated lactate greater than 3 mmol/L was 91.1% (95% confidence interval, 85.5%-96.6%) and the specificity was 88.6% (95% confidence interval, 83.0%-94.2%). The area under the curve was 0.95.

Conclusion: Base excess is an accurate marker for the prediction of elevated lactate in the ED. The measurement of BE, obtained in a few minutes in the ED, provides a secure and quick method, similar to the electrocardiogram at triage for patients with chest pain, to determine the patients with sepsis who need an early aggressive resuscitation.

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1. Introduction

1.1. Background

The management of septic patients remains a challenge. Early and accurate identification of at-risk patients is difficult

at emergency department (ED) admission, as the presentation of sepsis is often subtle. However, a prior study of early goal-directed therapy (EGDT) for patients with sepsis and an elevated lactate or with fluid nonresponsive hypotension showed a 16% absolute reduction in 28-day mortality, indicating the time sensitivity of the sepsis syndrome [1]. Thus, the Surviving Sepsis Campaign recommended that lactate may be available within minutes in the management of severe sepsis and septic shock [2].

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1.2. Importance

Elevated ED lactate is an indicator of increased likelihood of death in septic patients [3]. However, lactate may not be routinely drawn or immediately available in the ED. Moreover, lactate measurement through point-of-care testing is not currently developed in all the EDs, whereas base excess (BE) is obtained within few minutes, simply and faster than lactate in all the EDs. We hypothesized that using BE, as a surrogate marker for elevated lactate, we could rapidly identify at-risk patients with sepsis in the ED and obtain benefit from a precocious and aggressive resuscitation, as well as allow intensive care unit (ICU) admission.

1.3. Goal of this investigation

We promote a prospective observational study to evaluate the accuracy of BE as a predictor of elevated lactate in ED septic patients.

2. Methods

2.1. Study design

Our prospective observational cohort study took place at the teaching hospital ED of the city of Nantes. The annual ED census is approximately 70 000 patients. The study subjects were enrolled from March 2009 to March 2010.

2.2. Setting and selection of participations

Inclusion criteria consisted of a suspected infection with temperature greater than 38.5°C or less than 36°C and 2 or more of the following criteria: systolic blood pressure less than 100 mm Hg, tachycardia greater than 120 per minute, respiratory rate greater than 30 per minute, signs of tissue hypoperfusion (eg, altered mental state, mottled skin). Patients were excluded if they were younger than 18 years, had already received fluid resuscitation, had already received a vasopressor agent, or had a serious arrhythmia such as rapid atrial fibrillation or ventricular tachycardia. Eligible patients were screened at ED triage using an emergency nurse classification.

2.3. Measurements and data collection

Lactate and BE samples were drawn and lactate was obtained using a gray-top tube (Vacutainer BD, Franklin Lakes, NJ) and BE was obtained using a self-filling arterial sampler (PIC070, Radiometer Medical ApS, Bronshoj, Denmark). Both were analyzed on a GEM Premier 4000 Analyzer (Instrumentation Laboratory, Bedford, Mass), operated according to the manufacturer's recommendations. Based on prior studies, which have used this as their cutoff for more aggressive therapy, we defined a clinically significant lactate to

be greater than 3 mmol/L and BE less than -4 mmol/L [1,4,5]. Triage vital signs, infectious source, patient demographics, and laboratory test results were recorded and collected. All the patients included in the study underwent a confirmatory review by an independent researcher, blinded to the initial BE and lactate results, to affirm the presence of an infection. If the independent researcher subsequently determined that the patient did not have sepsis, the case was then excluded, although initial BE and lactate were already done.

2.4. Data analysis

The data were entered into a custom database (Excel, Microsoft Corp, Redmond, Wash) and analyzed using the Stata 11.0 statistical package (StataCorp LP, College Station, Tex). Categorical data were reported as percentages and 95% confidence interval (95% CI). The analysis was performed with the Pearson χ^2 test. Quantitative data were reported as means \pm SD. The area under the receiver operating characteristic (ROC) curve for BE as a predictor of lactate greater than 3 mmol/L was also calculated. All statistical tests were 2-tailed, and a *P* value of less than .05 was considered statistically significant.

3. Results

A total of 224 patients were enrolled in the study lasting for more than a 12-month period. Of these patients, 120 (53.6%) were men and the mean age was 56.3 years (SD, 18.2 years). The patients had an average lactate of 3.5 mmol/L (SD, 2.9 mmol/L) and an average BE mean of -4.5 mmol/L (SD, 4.9 mmol/L). There were 92 of 101 patients with an elevated lactate (>3 mmol/L) who had a BE less than -4 mmol/L, for a sensitivity of 91.1% (95% CI 85.5%-96.6%) and a specificity of 88.6% (95% CI, 83.0%-94.2%). Positive predictive value and negative predictive value

Table 1 Operating characteristics for a BE less than -4 mmol/L for predicting a lactate greater than 3 mmol/L

	Lactate <3	Lactate >3
BE greater than -4	109	9
	NPV = 92.4%	
	(95% CI, 87.6-97.2)	
	Sp = 88.6%	
	(95% CI, 83.0-94.2)	
BE less than -4	14	92
		PPV = 86.8%
		(95% CI, 80.3-93.2)
		Se = 91.1%
		(95% CI, 85.5-96.6)
Pearson $\chi^2 = 141.3, P < 1.10^{-4}$		

Se indicates sensitivity; Sp, specificity; NPV, negative predictive value; PPV, positive predictive value.

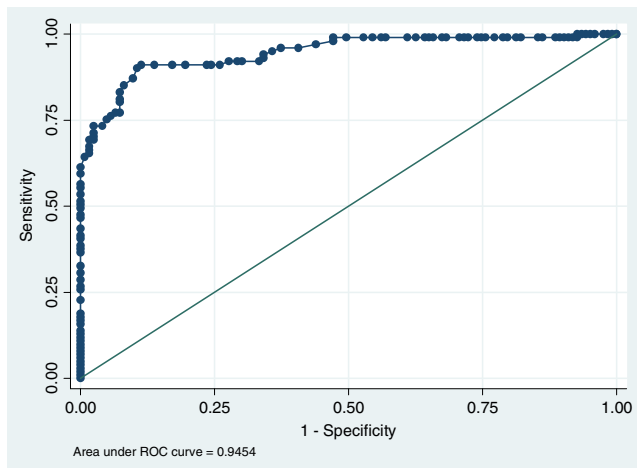


Fig. 1 The ROC curve for BE less than -4 mmol/L as a predictor of lactate greater than 3 mmol/L.

were, respectively, 86.8% (95% CI, 80.3%-93.2%) and 92.4% (95% CI, 87.6%-97.2%). A correlation has been found between lactate greater 3 mmol/L and BE less than -4 mmol/L ($r = -0.67$, $P < 1.10 \cdot 10^{-4}$) (Table 1). The area under the ROC curve for BE less than -4 as a predictor of lactate greater than 3 was 0.95, showing high reliability of the test (Fig. 1). Other thresholds were tested, but BE less than -4 was the most adequate.

4. Discussion

Our data indicate that a BE less than -4 mmol/L is efficient to predict elevated lactate in the ED septic population and may help identify patients who can benefit from quick aggressive resuscitation. A number of prior studies have established lactate as helpful to the clinician assessing patients with suspected sepsis for the identification of ED patients at increased risk of morbidity and mortality [2,3,6]. Considering our findings, the obtaining of BE, in a very short period, can be used to start aggressive resuscitation and to question ICU admission. With earlier recognition of these at-risk patients with suspected sepsis, appropriate resources could be directed and outcome may be improved.

Base excess is defined as the amount of strong acid that must be added to each liter of fully oxygenated blood to return the pH to 7.40 at a temperature of 37°C and a PCO_2 of 40 mm Hg (5.3 kPa). A prior study, based on an ICU with a heterogeneous group of patients, indicated that both BE and lactate, or a combination of the two, may be used to predict outcome in ICU-admitted patients. Smith et al [5] concluded that these variables could be used to identify patients who have a high risk of mortality and thus who should be admitted to ICU. In addition, BE has been also shown to be correlated with intravascular fluid requirement and mortality in patients with pelvic fractures and hepatic injuries and other trauma with hypovolemic shock [7,8]. However, another

ICU study showed that survivors and nonsurvivors of sepsis exhibit different types of metabolic acidosis, more pronounced and less corrected during ICU stay in the nonsurvivors' group, causing differences in the correlation of lactate and BE [9].

Early identification of septic patients is needed because they can benefit from precocious and aggressive resuscitation, and BE makes it possible. These results are supported by the latest guidelines in terms of early identification of ED patients with time-sensitive illnesses such as acute coronary syndrome [10]. Thus, BE could be performed at ED triage for early identification of septic patients such as electrocardiogram performed at ED triage in patients with chest pain. The BE obtained in few minutes could improve sepsis management, commonly showed as inadequate and imperfect in several recent studies [11].

This study has several limitations, the most important being the limited sample size of our single-center observational study. Moreover, we did not measure the turnaround times for BE and lactate nor did we determine if the use of BE actually leads to a significant decrease in the time to EGDT initiation. Furthermore, in our study, the level of acidemia and lactate elevations were overall pretty mild, and a previous study, using an in vitro model, pointed out that the correlations may vary slightly in case of less severe acidemia [12]. Last but not least, other thresholds may have been chosen for lactate and BE.

5. Conclusion

With a sensitivity of 91.1% and a specificity of 88.7%, BE proves to be an efficient tool in the prediction of elevated lactate. The findings of our study support the use of BE as a clinically useful sample for the safe identification of at-risk patients with sepsis, quicker than lactate. Thus, BE provides an accurate method, similar to the electrocardiogram at triage for patients with chest pain, to determine the patients with sepsis who are in need of early aggressive resuscitation and may help to improve sepsis management in the ED.

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