Clinical Biochemistry xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Clinical Biochemistry

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

Lactate POCT in mobile intensive care units for septic patients? A comparison of capillary blood method versus venous blood and plasma-based reference methods

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ARTICLE INFO

Keywords:
Lactate
Septic patients
Analytical performances
Sepsis
Point-of-care testing (POCT)

ABSTRACT

Aim of the study: We evaluated if the StatStrip Xpress Meter, a Lactate point of care testing (POCT) handled device, could be a valuable tool in the mobile intensive care units (MICU) to assess the severity of septic patients.
Methods: We first investigated POCT analytical performance, then, using samples collected from 50 identified septic patients admitted to the intensive care unit (ICU), we compared lactate values obtained with the device to those obtained with four central laboratory analysers: one whole blood and three plasma-based methods.
Results: Results were compared by least squares regression, Bland-Altman plot and by comparing concordance within clinically relevant lactate ranges. We observed a reliable analytical performance of the POCT (CVs < 3.8% for repeatability and < 5.0% for reproducibility) an excellent correlation between POCT and central laboratory analysers (R^2: 0.96–0.98, slopes:0.83–0.90, intercepts: 0.02–0.03) and an excellent concordance of the POCT results to the central laboratory analyser results (98–100%).
Conclusion: Whatever the methodology used, lactate values obtained are comparable and transferable between POCT and central laboratory analysers meaning that POCT could be a valuable tool in the MICU to evaluate the severity of septic patients and to better manage their hospital triage.

1. Introduction

Measurement of blood lactate level for septic patients is actually used to differentiate sepsis from septic shock [1–4]. This differentiation is a fundamental step in influencing the prehospital patient pathway between the emergency department (ED) and the intensive care unit (ICU) [5]. Many of septic patients are transported by mobile intensive care units (MICU) to hospital [6,7]. Thus, measurement of blood lactate level during the pre-hospital phase could help MICU to determine the prognostic severity of these patients and, thus, better manage their hospital management pathway [5]. In this context, the use of a point of care (POC) blood lactate monitoring system (BLMS) seems to be clinically justified. However, no study has compared lactate values measured with central laboratory analysers (plasma and venous whole blood methods) and POC BLMS (capillary whole blood method) in real conditions of use. In this study, we compared lactate values obtained with POC BLMS and central laboratory analysers using capillary whole blood, venous whole blood and plasma samples collected from septic patients admitted to the ICU. In accordance with French Good Laboratory practice, we both evaluated the analytical performance of a POC BLMS, the StatStrip Lactate Xpress Meter, and compared it to plasma based lactate central laboratory methods used at the three hospital sites in Paris [8].

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https://doi.org/10.1016/j.clinbiochem.2018.03.006
Received 5 January 2018; Received in revised form 20 February 2018; Accepted 6 March 2018

2. Materials and methods

2.1. Sample collection and blood lactate measurement

The study was conducted using whole blood and plasma samples collected from identified septic patients admitted to the intensive care unit during their hospitalisation (n = 50). The study was approved by the Ethics Committee (CPP n°2015-08-03 SC, Paris, France). For each patient, three samples were collected at the same time for lactate concentration measurements. Sample 1 was a capillary whole blood sample obtained from a finger-stick using a lancet, directly analysed at the patient's bedside with the StatStrip Lactate Xpress Meter. Sample 2 was a venous whole blood sample collected with a preheparinized syringe that was sent to the central laboratory at room temperature and analysed with a blood gas analyser within 30 min. Sample 3 was a venous whole blood sample collected into a potassium oxalate/sodium fluoride tube that was sent to the central laboratory on ice. Sample 3 tubes were then centrifuged, and the separated plasma analysed using the C16000 Abbott analyser within 60 min. At the same time the remaining plasma was aliquoted in 2 fractions and immediately frozen at −80 °C for further analysis. Frozen aliquots were transferred on dry ice for testing on central laboratory analysers (Siemens and Roche analysers) at two other hospital sites (Bichat-Claude Bernard and Cochin hospitals, Paris) and defrosted at ambient temperature and centrifuged before immediate analysis.

2.2. Analytical performances

The analytical performance of the StatStrip Lactate Xpress Meter were determined according to the ISO 15189 guideline [9]. To investigate the device coefficients of variation (CVs), lactate concentrations were determined at two different levels (1.65 and 3.35 mmol/L) using commercial controls (Liquid Assayed Multiqual, Biorad # 694 and 695). CVs were determined based on within-day (repeatability) and between-day variation (reproducibility) using commercial controls approved with our lab method (Abbott Diagnostics). The precision was assessed by running control samples at two levels 30 times in a row for repeatability and 30 times during 15 days for reproducibility. An inter-sample contamination assay was performed by running 5 times a low lactate sample (0.7 mmol/L) 3 times in a row, then a high lactate sample (7.0 mmol/L) 3 time in a row. We then investigated the device's ability to measure low lactate concentrations after measuring high lactate concentrations and vice versa [10].

2.3. Measuring devices

Plasma was measured for lactate using three central laboratory analysers: Architect C16000 (Abbott Diagnostics) at Necker hospital, Cobas 8000 (Roche Diagnostics) at Cochin hospital and Dimension Vista 1500 (Siemens Diagnostics) at Bichat-Claude Bernard hospital. These devices use a spectrophotometric method based on an enzymatic reaction. For all the analysers except for Dimension Vista 1500, lactate is converted to pyruvate and H_2O_2 by lactate oxidase. Peroxidase catalyses the oxidation of chromogen precursor by H_2O_2 to produce a coloured dye. The increase in absorbance at 548 nm is directly proportional to the lactic acid concentration in the sample. In Dimension Vista 1500, lactic dehydrogenase catalyses the oxidation of lactate to pyruvate with simultaneous reduction of NAD^+. One mole of NAD^+ is converted to one mole of NADH, H^+ for each mole of lactate present. NADH, H^+ absorbance is directly proportional to the lactate concentration.

Whole blood was measured for lactate using an ABL 800 Flex (Radiometer) blood gas analyser and the StatStrip Lactate Xpress Meter (Nova Biomedical). The ABL blood gas used an amperometric measurement method based on a lactate selective membrane. As an appropriate potential is applied across the electrodes, lactate is reduced at the cathode producing an electrical current. The magnitude of the current flowing through the circuit is proportional to the concentration of lactate being reduced.

The StatStrip Xpress Meter is a handheld, single use electrochemical strips device with the measurement technology based on an enzymatic reaction with lactate oxidase and potassium ferricyanide as an electron mediator. The electrical signal is produced as a result of the reaction between lactate in the blood and the enzyme lactate oxidase on the inserted sensor strip. The voltage signal corresponds to the lactate concentration of the sample with a correction for interfering substances such as haematocrit, acetaminophen, uric acid and ascorbic acid.

2.4. Statistical analysis and interpretation

Correlation coefficients (R^2) between the different methods were determined using linear least square regression analysis. Student's *t*-test, two tailed, was used to assess inter-sample contamination [10]. Computations were performed using Graph Pad Prism 5.0.

3. Results

3.1. Evaluation of StatStrip Lactate Xpress Meter analytical performances

CVs were 2.95% and 2.50% for repeatability and 4.49% and 4.54% for reproducibility at 1.65 and 3.65 mmol/L lactate concentrations respectively (Table 1). These results are in agreement with guideline of the French Society of Clinical Biology (SFBC) (CV < 3.8% for repeatability and CV < 5.0% for reproducibility). Then, we performed an inter-sample contamination assay using a low (0.7 mmol/L) and a high (7.0 mmol/L) lactate sample concentration. *t*-test statistical analysis revealed no contamination between-samples.

3.2. Assessment of lactate concentration stability between fresh and frozen plasma samples

By comparing lactate values between fresh and frozen plasma samples, we assessed the stability of lactate concentration after the freezing step. We compared paired lactate values before and after the freezing step using the Architect C16000 analyser (Figs. 1A and 2A). Correlation by least square regression yielded $R^2 = 0.99$, a slope of 1.01 and an intercept of 0.01 (Table 2). The Bland-Altman agreement method showed a positive bias value of 0.10 (Table 3). Thus, paired values between fresh and frozen samples could be considered as equivalent.

3.3. Comparison of lactate measurements between the StatStrip Lactate Xpress Meter and the central laboratory analysers

There was an excellent correlation between the values obtained with the POC BLMS and the four central laboratory analysers with: R^2 between 0.96 and 0.98, slopes between 0.83 and 0.90 and intercepts

Table 1
Inter- and intra-assay coefficients of variability for StatStrip BLMS.

	Repeatability		Reproducibility	
	QC Level 1	QC Level 2	QC Level 1	QC Level 2
Mean (mmol/L)	1,66	3,26	1,67	3,39
SD	0,05	0,08	0,07	0,15
%CV calculated	2,95	2,50	4,49	4,54
%CV supplier	NC	NC	NC	NC
%CV approved (SFBC)	3,8	3,8	5,0	5,0
N	30	30	30	30
Matrix	Biorad #694	Biorad #695	Biorad #694	Biorad #695
Conclusion	compliant	compliant	compliant	compliant