Practical Laboratory Medicine 4 (2016) 41–49

Contents lists available at ScienceDirect

Practical Laboratory Medicine

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

Lactate point-of-care testing for acidosis: Cross-comparison of two devices with routine laboratory results

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ARTICLE INFO

Article history:
Received 20 July 2015
Received in revised form
18 December 2015
Accepted 22 December 2015
Available online 24 December 2015

Keywords:
Lactate
Point-of-care testing
Blood gas
Fetal acidosis

ABSTRACT

Objectives: Lactate is a major parameter in medical decision making. During labor, it is an indicator for fetal acidosis and immediate intervention. In the Emergency Department (ED), rapid analysis of lactate/blood gas is crucial for optimal patient care. Our objectives were to cross-compare-for the first time-two point-of-care testing (POCT) lactate devices with routine laboratory results using novel tight precision targets and evaluate different lactate cut-off concentrations to predict metabolic acidosis.
Design and methods: Blood samples from the delivery room ($n=66$) and from the ED ($n=85$) were analyzed on two POCT devices, the StatStrip-Lactate (Nova Biomedical) and the iSTAT-1 (CG4+ cassettes, Abbott), and compared to the routine laboratory analyzer (ABL-735, Radiometer). Lactate concentrations were cross-compared between these analyzers.
Results: The StatStrip correlated well with the ABL-735 ($R=0.9737$) and with the iSTAT-1 ($R=0.9774$) for lactate in umbilical cord blood. Lactate concentrations in ED samples measured on the iSTAT-1 and ABL-735 showed a correlation coefficient of $R=0.9953$. Analytical imprecision was excellent for lactate and pH, while for pO_2 and pCO_2 the coefficient of variation was relatively high using the iSTAT-1.
Conclusion: Both POCT devices showed adequate analytical performance to measure lactate. The StatStrip can indicate metabolic acidosis in 1 µl blood and will be implemented at the delivery room.

1. Introduction

Lactate is a crucial metabolite produced under stress conditions, like hypoxia. In the absence of oxygen, glucose is converted into lactate, while normally glucose is fully oxidized in the cell mitochondria to efficiently produce energy (adenosine triphosphate, ATP). Intracellular produced lactate is secreted as lactic acid, resulting in metabolic acidosis. In case of severe sepsis, lactate is produced by micro-organisms, as these do not have mitochondria.

Blood lactate is an indicator for metabolic acidosis and can serve as a single marker for immediate medical intervention. In the Emergency Department (ED) it can indicate sepsis and ischemia. In critically ill patients lactate concentrations are

Abbreviations: ; POCT, point-of-care testing; ED, Emergency Department; CCU, Critical Care Unit; CV, coefficient of variation; SD, standard deviation; SEE, Standard Error of Estimate; TEa, Total Allowable Error

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http://dx.doi.org/10.1016/j.plabm.2015.12.005

reported to correlate well with disease state, have prognostic value and can be used for monitoring [1,2]. A short turn-around-time for lactate measurements, preferably as a component of full blood gas analysis, will support prompt medical decision making. Measurement by POCT devices can be an adequate method to achieve this, but one should always consider analytical performance, user competences and costs-benefits ratios. In the department of Obstetrics, fetal lactate is a direct indicator of metabolic acidosis and can therefore be used to assess the need for intervention during labor. Currently, along with intra-partum cardiotocography to measure fetal heart rate and uterine activity, fetal scalp blood can be collected to monitor fetal status. Blood tests include fetal pH, combined with other blood gas parameters (base excess, pCO_2) to identify fetal acidosis [3–5]. It is necessary to distinguish between respiratory and metabolic acidosis, as poor neonatal outcome is associated with the latter. However, a major drawback is the amount of sample needed to perform full blood gas analysis (40–90 μL), which results in very high failure rates, up to 23% [6,7]. Since lactate is responsible for metabolic acidosis and, moreover, can be measured in very small volumes of blood (1 μL), direct measurement of lactate is a very attractive alternative. A number of studies have evaluated whether lactate can replace pH, measured in umbilical cord or fetal scalp blood [7–10]. The common conclusion of these studies is that lactate concentrations represent fetal status equivalently to pH measurement. To evaluate the analytical performance of lactate POCT devices in this setting, several studies have compared lactate concentrations in umbilical cord and fetal scalp blood. Frequently evaluated lactate POCT devices are strip-analyzers, like the Lactate-Pro (Arkray) and StatStrip Lactate (Nova Biomedical), which have been shown to have satisfactory analytical performance. The StatStrip Lactate was found to perform the best, based on interference studies and imprecision (coefficient of variation, CV) measurements [11,12]. Recently, these conclusions were confirmed in a large study population resulting in a strong reduction in failure rates, compared with fetal scalp blood sampling, mainly caused by a shortage of sample resulting in no measurement on blood gas analyzers [6]. Noticeably, the cut-off value of lactate used to predict fetal metabolic acidosis differs strongly between the studies (5.1 mmol/L versus 6.6 mmol/L), which is primarily explained by the use of different analyzers.. The possibilities of lactate measurement with POCT devices at the bedside of patients in the ED and Critical Care are also explored in the literature [13–15]. Interestingly, for patients with metabolic acidosis, biological variability of lactate was shown to be about half that of healthy individuals, which is clearly important for validation of lactate POCT devices [16].

In view of the above mentioned clinical settings and recent literature, we set up a study, comparing two POCT devices (which have not previously been compared) with routine blood gas analysis. The StatStrip Lactate and the iSTAT-1 (for full blood gas analysis, including lactate) were compared with a routine blood gas analyzer (ABL-735) and with each other. We also evaluated the published cut-off values for fetal lactate and incorporated the new insights of biological variation of lactate concentrations in critically ill patients.

2. Materials and methods

2.1. Patient samples

151 blood samples from patients were used, including 66 umbilical cord samples from the Department of Obstetrics and 85 arterial samples from the ED and Critical Care Unit (CCU). This study was done on surplus material and patients who refused re-use of their blood were excluded. According to Dutch legislation covering this kind of validation research, no informed consent and approval of the Medical Ethics Review Board is necessary, and this was confirmed by the local Medical Ethics Review Board of the Elisabeth-TweeSteden Hospital under reference number: METC-Brabant/15.147. This implies that there is no extra handling for subjects, there is no difference in treatment, no difference in analysis, no effect on diagnosis and also no in- or exclusion criteria as in comparative diagnostic studies with control and study groups. For this reason the STARDChecklist was not used as most issues are not applicable to this study [17]. Umbilical cord blood was drawn in the delivery room after the baby was born. Samples from the ED and CCU were collected within the timeframe of the study, after routine analysis was complete. Measurements were performed by laboratory specialists and technicians. All samples were anonymised by removal of the patient identification number.

2.2. Comparison of lactate and blood gas measurements

Multiple instrument comparison was performed for the routine blood gas analyzer, ABL-735 (Radiometer, Copenhagen, Denmark) and two POCT devices: the StatStrip-Lactate (Nova Biomedical, Waltham, MA, USA) and the iSTAT-1 (CG4+ cassettes, Abbott Point of Care, Princeton, NJ, USA). All blood samples were measured routinely on the ABL-735. Simultaneously to this routine measurement, lactate concentrations were analyzed in 1 μL blood on the StatStrip. For all blood samples that contained sufficient material, a full blood gas was measured in 90 μL blood on the iSTAT-1 using in the CG4+ cassette. To ensure inclusion of the whole measurement range for lactate, a small subset of blood samples was measured again after 2–6 h. Using this protocol, all parameters in the CG4+ cassette (pH, pCO_2, pO_2, base excess, HCO_3^-, sO_2 and lactate) were measured for 54 umbilical cord blood samples and 77 ED/CCU blood samples on the ABL-735. Lactate concentrations were cross-compared between the two POCT devices and the routine laboratory analyzer for all blood samples.