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Reliability of the point-of care analyzer "StatStrip® Xpress™" for measurement of fetal blood lactate

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ABSTRACT

Objectives: Measurement of lactate in fetal blood is used to assess the degree of anaerobic metabolism. The technical difficulties in obtaining enough scalp blood for analysis by a bloodgas-analyzer advocates for the use of a point-of-care device. StatStrip®Xpress™ (SSX) has shown promising properties but needs further evaluation before implementation into fetal surveillance.

Methods: Arterial/venous umbilical cord blood from 112 newborns were analyzed simultaneously with SSX and the reference method ABL800™. From 321 fetuses with abnormal heart rate scalp blood was sampled and analyzed repeatedly with SSX.

Results: ABL800™ -lactate ranged from 1.9–13.3 mmol/L in arterial to 1.5–10.2 mmol/L in venous cord blood with excellent correlation to SSX (R^2 = 0.95). SSX-values were lower compared to the reference method ranging from −0.79 mmol/L for low values to −1.68 mmol/L for high values. The mean CV for SSX-values in cord respectively scalp blood was: lactate ≤3 mmol/L 7.1% respectively 8.4%; lactate > 3 mmol/L 3.8% respectively 6.8%. Repeated measurements of the same sample with SSX where without significant difference in cord/scalp blood (p = 0.11).

Conclusion: SSX-lactate values were constantly lower but correlated excellent to the reference method. The reproducibility was good for cord and scalp blood. We suggest SSX as an attractive device for measurement of fetal lactate.

1. Introduction

Lactate in whole blood can easily be measured by hand-held point-of-care (POC) devices, primarily developed for athletics. Presumably because of the consumer friendly and minimal invasive technology, the method gradually has been adopted into prehospital emergency care, adult and neonatal intensive care units [1,2].

In the 1960s, fetal scalp blood sampling (FBS) during labor with measurement of pH was introduced as a supplement to intermittent auscultation of the fetal heart rate for monitoring fetal wellbeing [3] and when continuous registration cardiotocography (CTG) became routine practice, FBS remained as a second line tool to CTG. Since CTG alone has a high sensitivity but low specificity for fetal distress during labor, a secondary test such as FBS is essential to intervene appropriately [4,5]. In the 90's point-of-care analysis of lactate became an alternative to pH [6,7]. PH does not discriminate between respiratory (low pH and high pCO_2) and metabolic acidosis (low pH and high base-deficit and high lactate), whereas lactate only reflects the degree of the metabolic component. There is a correlation between severe metabolic acidosis in umbilical cord blood and impaired neonatal condition at birth, as well as to permanent organ damage [8–10].

The internationally accepted reference interval for normality and acidosis during labor is based on "LactatePro™" which is now out of industrial manufacturing [7]. Therefore, it is urgent to introduce a substitute with optimal reliability and reproducibility. An updated version "LactatePro2™" from the same manufacturer showed unacceptable high CV in cord blood [11].

The FBS Lactate Study was initiated to investigate a new lactate POC-device for clinical use in fetal blood sampling. Part one of the study was to evaluate the reliability of the POC before defining clinical

Abbreviations: POC, point-of-care; FBS, fetal scalp blood sampling; CTG, cardiotocography; SSX, StatStrip Xpress; CV, coefficient of variation; pCO_2, partial pressure of carbon dioxide; pO_2, partial pressure of oxygen; BD_{ecf}, base deficit measured in extracellular fluid; HCO_3^-, bicarbonate; Hct, hematocrit; Hb, hemoglobin; MA, metabolic academia; HIE, hypoxic neonatal encephalopathy

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cut-off for normality.

StatStrip®Xpress™ (SSX) measures lactate in whole blood from only 0.6 μL blood and with the result displayed within 13 s. SSX is FDA approved and CE/ISO certified and is the only lactate meter developed specifically for hospital use, employing technology reducing interference of hematocrit, paracetamol and bilirubin among others [12]. Until today, it is only recommended for use in adults, but recent studies have demonstrated promising properties for measurement of lactate also in fetal blood [13–15]. Since SSX lactate meter has shown advantageous properties in adult blood [1,16] and fetal blood in comparison to other POC lactate meters on the market as well is the only lactate meter designed for hospital use it was selected for the study [13,17].

In this study the primary aim was to evaluate the analytical performance of SSX for measurement of lactate in fetal blood, with specific focus on the CV with different lactate values. Secondary, to correlate lactate values measured by SSX and ABL800™ in relation to each other, respectively to correlate SSX lactate to pH, partial pressure of carbon dioxide (pCO_2) and oxygen (pO_2), base deficit in extracellular fluid (BD_{ecf}), bicarbonate (HCO_3^-), hematocrit (Hct), hemoglobin (Hb) and glucose.

2. Materials and methods

2.1. Study design

This study was a prospective quality study. The first part was carried out from March until July 2016, and the second part from September 2016 until October 2018 at the delivery department, Skåne University Hospital, Sweden.

2.2. Clinical samples

Paired cord blood samples were routinely collected directly after delivery and before the baby's first cry in marked A (arterial) or V (venous) preheparinized plastic syringes (Radiometer) containing maximum 2 mL. After removal of the needle, syringes were emptied for air bubbles, closed and analyzed within five minutes by the stationary blood gas analyzer (ABL800™, Radiometer, Copenhagen, Denmark). The ABL is a mini-laboratory with optional wet chemistry determinations such as pH, pCO_2, pO_2, BD_{ecf}, HCO_3^-, Hct, Hb, glucose and lactate and the analyzing time is approximately three minutes for a full blood gas status [18]. According to the power calculation published by Reif et al. in 2014 (the sample size should be at least 100 to identify a standard error of a 95% confidence interval for the level of agreement between two methods), we decided to stop the inclusion after 112 umbilical cord collections [14]. All samples were analyzed by one of the authors (NW) by following standard procedure: first the arterial blood was analyzed, thereafter the venous. Simultaneously with analysis by ABL800 ™, the residual blood in the syringe was tested in duplicate or triplicate by the point-of-care device StatStrip®Xpress™, (Nova Biomedical, Waltham, MA, USA).

For the second part of the study scalp blood was collected from 324 fetuses showing a suspicious or pathological CTG-tracing. In 75 of the cases, FBS was performed repeatedly during labor. The blood was collected in pre-heparinized plastic capillary tubes (Radiometer®) with a maximum of 85 μL. Due to the small amount of collected scalp blood, we were not able to analyze the level of agreement between lactate measured by SSX and ABL800™.

2.3. Measurements and laboratory analysis

Lactate was measured in plasma by ABL800™ and in whole blood by SSX, which in fact entails that the absolute values are not comparable [19]. However, the technology behind the measurement is the same: lactate is converted into pyruvate and hydrogen peroxide which is then oxidized. The resulting electric current is proportional to the lactate level and measured by an amperometric electrode and interferences of hematocrit, bilirubin, acetaminophen, ascorbic and uric acid are eliminated by algorithms. Operation ranges are: temperature 15–40 °C (59–104 °F), altitude up to 4500 m (15,000 ft), humidity 10–90% and a hematocrit value within 20–65% [20].

2.4. Statistical analysis

Correlation coefficients (R^2) were calculated by simple linear correlation with 95% prediction interval. Accuracy, discrepancies and bias of the different methods were assessed by Bland-Altman plot, Kruskal-Wallis test and Student's *t*-test. All p-values were two-sided and p-values below 0.05 were considered significant. Statistical analysis was undertaken using Graph Pad Prism, La Jolla, California.

2.5. Ethical approval

The study was approved by the Regional Medical Ethics Committee in Lund, Sweden (diary number 2016/1038).

3. Results

Cord blood samples were collected from 112 patients directly after vaginal delivery. 101 arterial and 111 venous cord blood samples were of sufficient volume to be analyzed successfully by ABL800™ for pH, pCO_2 and pO_2 and for repeated measurements with SSX. In 95 arterial and 109 venous samples, also other parameters (including lactate) could be analyzed by ABL800™. Each sample was tested two or three times by SSX. The mean, median with interquartile ranges (IQR) and ranges for pH and lactate measurements are presented in Table 1.

There were no differences between the correlations of ABL800™ artery lactate and SSX-artery lactate ($y = 0.8353\times + 0.1711$: $R^2 = 0.96$) or ABL800™ venous lactate and SSX-venous lactate ($y = 0.7772\times + 0.0298$: $R^2 = 0.94$) why the ABL800™ artery and venous lactate values were merged for further calculations. The correlation between the composite ABL800™ lactate and SSX-lactate was $R^2 = 0.95$ (Fig. 1).

Absolute SSX-lactate values were lower compared to values measured by ABL800™ and the difference increased with higher values. The bias (the mean difference between the two methods) was significant and increased from −0.79 mmol/L (−21.1%) to −1.68 mmol/L (−15.1%) for low to high lactate values ($p < 0.05$) (Fig. 2).

The CV in umbilical cord blood was calculated from 140 cases with enough blood allowing repeated (triple) analysis with SSX. With low lactate values ≤3 mmol/L the mean CV was 7.1% whereas, for lactate values > 3 mmol/L the mean CV was 3.8%. (Fig. 3). There was no statistical difference between repeated measurements of the same blood drop with SSX ($p = 0.75$).

For the 321 FBS cases, the blood was successfully analyzed twice

Table 1
pH and lactate (mmol/L) values in fresh umbilical cord blood measured by the stationary blood gas analyzer ABL800™ (Radiometer, Copenhagen, Denmark) and the point-of-care device StatStrip® Express™ (SSX) (Nova Biomedical, Waltham, MA, USA). Mean, median with interquartile range (IQR), minimum and maximum values are presented.

	n	Mean	Median (IQR)	Minimum	Maximum
Art ABL-pH	101	7.24	7.24 (7.19–7.29)	7.00	7.29
Art ABL-lactate	95	5.2	4.8 (3.7–6.2)	1.9	13.3
Art SSX-lactate	286	4.1	3.7 (2.8–5.2)	1.2	11.5
Ven ABL-pH	111	7.33	7.34 (7.31–7.37)	7.15	7.49
Ven ABL-lactate	109	4.3	4.2 (3.2–5.2)	1.5	10.2
Ven SSX-lactate	300	3.4	3.1 (2.4–4.2)	1.2	9.4

Art = Arterial blood, Ven = Venous blood.

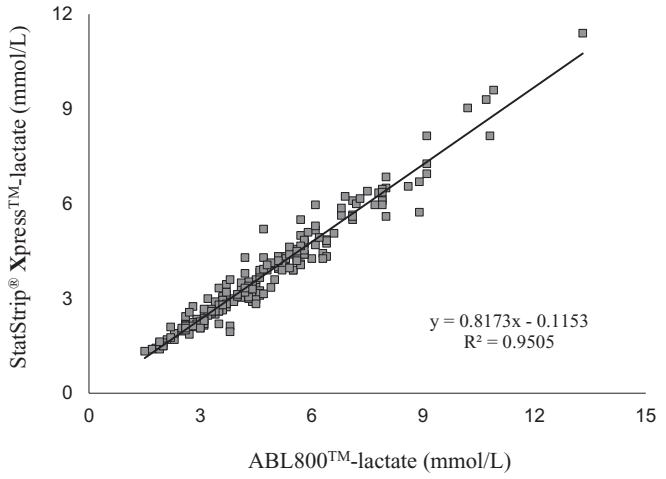

Fig. 1. The correlation between lactate values in umbilical cord blood measured by the point-of-care device StatStrip® Xpress™ (SSX) and the stationary blood gas analyzer ABL800™ (Radiometer). Due to a similar correlation between SSX with arterial and venous blood, the values were merged.

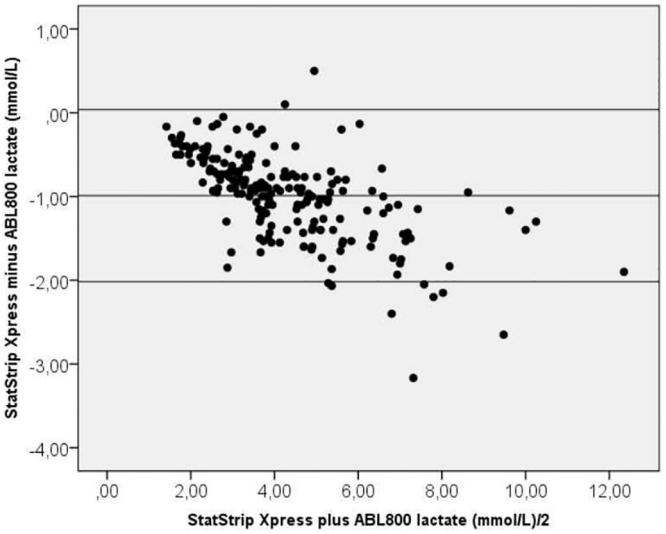

Fig. 2. Bland Altman plot illustrating the mean difference in lactate values in arterial and venous umbilical cord blood samples between the two instruments for lactate measurement (SSX and ABL800™) with prediction limits ± 1,96 SD.

and in 25 of the cases there was enough blood for triple analysis with SSX. With lactate values ≤ 3 mmol/L the mean CV was 8.4% whereas and with values > 3 mmol/L the mean CV was 6.8% (Fig. 4). There was no statistical difference between repeated measurements of the same blood drop with SSX (p = 0.11).

The correlations between umbilical cord SSX- and ABL800™-lactate to the other measured acid-base values (pH, pCO_2, pO_2, BD_{ecf}, HCO_3^-, Hct, Hb, glucose) were similar and are presented for both arterial and venous blood in Table 2. pH, HCO_3^- and BD showed the best correlations to lactate with a stronger correlation in arterial blood. There was a poor correlation between SSX lactate and hematocrit and glucose in cord blood.

4. Discussion

For the first time the reliability and reproducibility of the POC-device StatStrip®Xpress™ in fetal blood is assessed in a large sample size over a wide range of lactate levels and the correlation to other parameters in a standard blood gas sample is described. For lactate values > 3 mmol/L, the CV was constant and favorable whereas for lactate values ≤ 3 mmol/L, the CV was unacceptable high. The CV in scalp blood was higher than in cord blood but showed similar patterns.

FBS is a recognized second-line tool for the assessment of fetal wellbeing in laboring women with pathological CTG tracing and is recommended by most of the obstetrical societies [21–24]. FBS with measurement of pH was introduced during the 1960´s and from 77 cases suggested reference values were published [3]. Secondary analysis with approximately 300 new cases showed good agreement with the first results, where after the method successively got credibility into obstetrical practice [25]. Unfortunately sampling of pH has a high failure rate (11–20%) and pH cannot discriminate between respiratory and metabolic acidosis [26]. Respiratory acidosis during labor is a normal phenomenon and is due to impaired gas-exchange over the placenta caused by uterine contractions. The condition is harmless and is quickly solved after birth, as the baby breathes, and the accumulated carbon dioxide is eliminated. In contrast, metabolic acidosis is the result of persisting hypoxia and is potentially harmful to the neonate. Umbilical cord blood lactate has competitive advantages in reflecting serious metabolic acidosis associated to neonatal morbidity and to the need of transfer to the neonatal intensive care unit (NICU) better than other parameters alone or in combination [10,27]. Brain lactate measured by magnetic resonance imaging (MRI) in the neonatal period is also an established biomarker of long-term neurologic morbidity in infants with hypoxic neonatal encephalopathy (HIE) and recently a correlation between the lactate level in umbilical cord blood and in the brain was

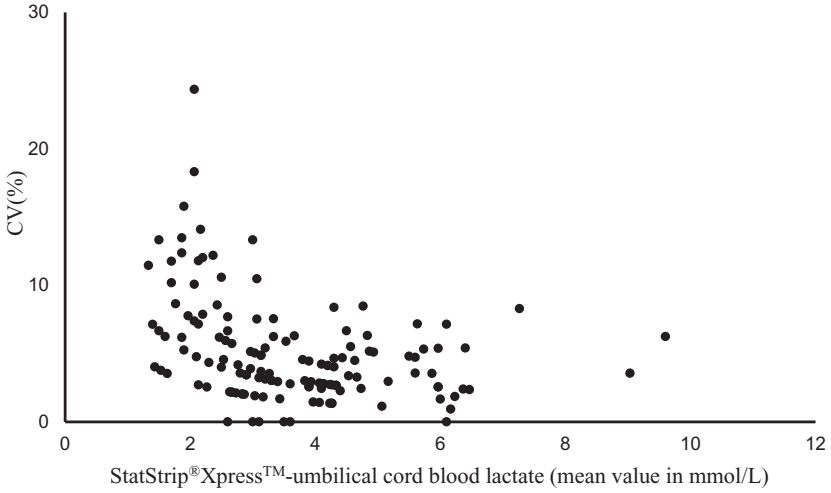

Fig. 3. Coefficient of variation (CV) for SSX calculated in arterial and venous cord blood at different levels of lactate.

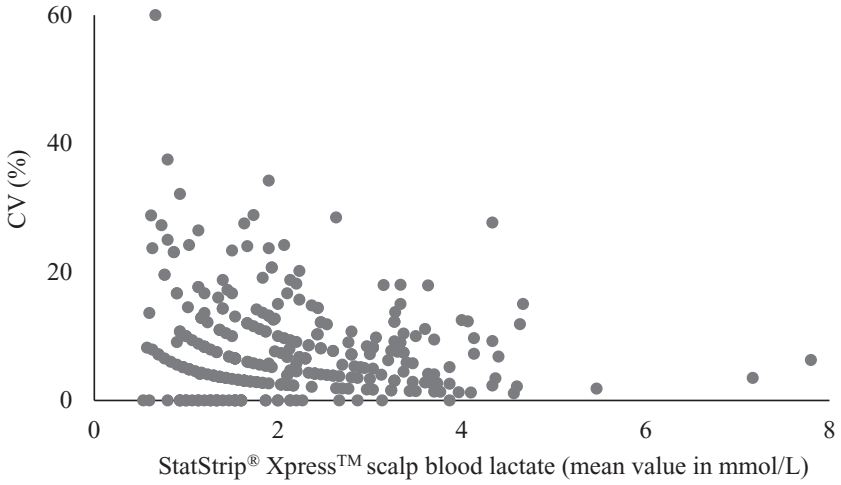

Fig. 4. Coefficient of variation (CV) for SSX calculated in scalp blood at different levels of lactate.

Table 2
The correlation between lactate values in umbilical cord blood measured by the point-of-care device "StatStrip® Xpress™" (SSX) and the stationary blood gas analyzer ABL800™ (Radiometer, Copenhagen, DK) to biochemical parameters measured by the ABL800™. P-values for the correlations are shown in parenthesis.

	Artery SSX-lactate R^2	Artery ABL800™-lactate R^2	Vein SSX-lactate R^2	Vein ABL800™-lactate R^2
	$n = 286$	$n = 95$	$n = 300$	$n = 109$
ABL800™ pH	0.62 ($p < 0.0001$)	0.63 ($p < 0.0001$)	0.34 ($p < 0.0001$)	0.34 ($p < 0.0001$)
ABL800™ pCO_2	0.22 ($p < 0.0001$)	0.19 ($p < 0.0001$)	0.002 ($p = 0.66$)	0.0004 ($p = 0.83$)
ABL800™ pO_2	0.005 ($p = 0.50$)	0.017 ($p = 0.20$)	0.004 ($p = 0.50$)	0.0001 ($p = 0.91$)
ABL800™ BD_{ecf}	0.66 ($p < 0.0001$)	0.68 ($p < 0.0001$)	0.50 ($p < 0.0001$)	0.56 ($p < 0.0001$)
ABL800™ HCO_3^-	0.76 ($p < 0.0001$)	0.78 ($p < 0.0001$)	0.66 ($p < 0.0001$)	0.68 ($p < 0.0001$)
ABL800™ Hct	0.016 ($p = 0.23$)	0.034 ($p = 0.08$)	0.02 ($p = 0.13$)	0.053 ($p = 0.02$)
ABL800™ Hb	0.013 ($p = 0.27$)	0.034 ($p = 0.07$)	0.03 ($p = 0.10$)	0.059 ($p = 0.01$)
ABL800™ glucose	0.25 ($p < 0.0001$)	0.26 ($p < 0.0001$)	0.30 ($p < 0.0001$)	0.34 ($p < 0.0001$)

R^2: correlation coefficient.
pCO_2: partial pressure of carbon dioxide in kPa.
pO_2: partial pressure of oxygen in kPa.
BD_{ecf}: base deficit in extracellular fluid.
HCO_3^-: bicarbonate.
Hct: hematocrit.
Hb: hemoglobin.

shown also in newborns without signs of HIE [28,29].

In a setting lacking a BGA, as in low income countries, the use of SSX could be an appropriate alternative to easily assess the degree of lactate-acidosis in the newborn and thereby predict those neonates who will benefit from observation and care [30].

Based on this and in the context of the easy, quick, cheap measurement of lactate, the method is preferable to the measurement of pH and in the 1990´s the suggested cut-offs for normality and acidosis for lactate in scalp blood were proposed [6]. The cut-offs were calculated by conversion and comparison of the accepted cut-offs for pH and without testing the performance and reliability of the device LactatePro™. The device has been discontinued and new cut-off values for new devices need to be established. An updated version (LactatePro2™) from the same manufacturer, has shown completely different reference values for normality and acidosis as well as an unacceptable high CV between measurements originated from the same umbilical cord blood sample. For a lactate value of 6.9 mmol/L with is closest to the recommended cut-off for normality the CV was 7.2% [11]. From our clinical daily life, we know that the CV in scalp blood with this meter is even higher.

SSX is the only commercial FDA/ISO approved lactate meter launched for medical use. It adjusts for several interferences in the blood; an important factor for improved accuracy, since for example the levels of hematocrit in fetal blood varies to a higher extent [31]. High hematocrit levels lead to false low lactate values and hence metabolic acidosis could falsely be dismissed by the use of a POC device lacking this correction.

SSX is found to have the lowest bias among bench top blood gas analyzers (BGA) and the lowest inter-device variation [13,16]. In accordance with previous studies, we found that SSX had acceptable reproducibility at clinically relevant lactate levels in cord blood [16,32,33]. The goal of 8% bias based on biological variability was not met and we found a significant negative bias in arterial blood of up to 2.6 mmol/L (low levels −0.79 (−21.1%), high levels −1.68 (−15.1%) [34]. However, the bias to the reference method is not the key point in this scenario. The cut-offs for SSX used in clinical practice must be derived from the lactate meter and related to the clinical outcome and not to values originated from a BGA or approximation of previously accepted cut-offs. Besides, reference values for lactate in scalp blood measured by a BGA has not even been proposed or published.

The CV target of 5% required for serial lactate measurement in the range 4-10 mmol/L based on a 0.5 ratio of biological variability as desirable performance was met at lactate values > 3 mmol/L in umbilical cord blood. However, in scalp blood the CV was higher compared to umbilical cord blood. The phenomena can be explained by; 1) the scalp blood was mainly double analyzed whereas the umbilical cord blood was triple analyzed 2) the umbilical cord blood is sampled by injection of a needle directly into a vessel without the risk of contamination whereas the scalp blood is sampled by puncturing the skin to access capillary blood with risk for contamination of amnion fluid and fetal tissue, for example fat. By the small amount of blood (0.6 μL) used for the measurement, variations in the blood composition will automatically have an impact on the result. Based on our results, we therefore highlight the importance of carefully cleaning the scalp before performing a FBS and when high lactate values (> 3 mmol/L) also to double analyze the same blood sample. In case of a variation > 7% we recommend to repeat the scalp sample for a new analysis.

For both SSX-lactate and ABL800™-lactate the correlations to the

other parameters in the blood gas sample were strongest for arterial umbilical cord blood except for glucose where the correlation was stronger in venous blood. Theoretically this can be due to different blood compositions, the venous blood flows directly from the placenta whereas the arterial blood originates from the fetus but also due to a certain degree of anaerobic metabolism in low-priority organs as for example the muscles, the phenomena know as hidden acidosis [35]. Overall the correlations between SSX-lactate and ABL 800 lactate to the different parameters shown in Table 2 were similar. Arterial and venous SSX-lactate concentrations are not significantly associated with hematocrit most likely due to the algorithms in SSX that corrects for hematocrit interference. Furthermore, there was no correlation between SSX lactate and glucose, an important finding supporting that maternal hyperglycemia has no association to fetal lactate production. A previous study has shown that maternal diabetes does not hamper the ability of LGA fetuses to mobilize glycogen stores for the production of glucose and lactate in strenuous situations during labor [36].

4.1. Conclusions

Assessment of fetal blood lactate concentration is easy and quickly performed with SSX. The POC has an acceptable variation in umbilical cord blood, but due to the risk of contaminated scalp blood we recommend to repeat measurements for lactate levels > 3 mmol/L. Proposal of clinical useable cut offs for normality and need of intervention remains to be shown.

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Declaration of interest

None.

Author contributions statement

LI, KP, KK and NW designed the study. NW was responsible for the sampling, analyzing and configuration of the database. NW and LI wrote the first draft of the manuscript. KP performed statistical analyses. KP and KK revised the subsequent drafts. All authors approved the final version of the manuscript.

References

[1] T. Léguillier, R. Jouffroy, M. Boisson, A. Boussaroque, C. Chenevier-Gobeaux, T. Chaabouni, B. Vivien, V. Nivet-Antoine, J.-L. Beaudeux, Lactate POCT in mobile intensive care units for septic patients? A comparison of capillary blood method versus venous blood and plasma-based reference methods, Clin Biochem. (2018), https://doi.org/10.1016/j.clinbiochem.2018.03.006.

[2] A. Rhodes, L.E. Evans, W. Alhazzani, M.M. Levy, M. Antonelli, R. Ferrer, A. Kumar, J.E. Sevransky, C.L. Sprung, M.E. Nunnally, B. Rochwerg, G.D. Rubenfeld, D.C. Angus, D. Annane, R.J. Beale, G.J. Bellinghan, G.R. Bernard, J.D. Chiche, C. Coopersmith, D.P. De Backer, C.J. French, S. Fujishima, H. Gerlach, J.L. Hidalgo, S.M. Hollenberg, A.E. Jones, D.R. Karnad, R.M. Kleinpell, Y. Koh, T.C. Lisboa, F.R. Machado, J.J. Marini, J.C. Marshall, J.E. Mazuski, L.A. McIntyre, A.S. McLean, S. Mehta, R.P. Moreno, J. Myburgh, P. Navalesi, O. Nishida, T.M. Osborn, A. Perner, C.M. Plunkett, M. Ranieri, C.A. Schorr, M.A. Seckel, C.W. Seymour, L. Shieh, K.A. Shukri, S.Q. Simpson, M. Singer, B.T. Thompson, S.R. Townsend, T. Van der Poll, J.L. Vincent, W.J. Wiersinga, J.L. Zimmerman, R.P. Dellinger, Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016, Springer, Berlin Heidelberg, 2017, https://doi.org/10.1007/s00134-017-4683-6.

[3] E. Saling, A new method for examination of the fetus during labor:introduction,technic and basics, Arch Gynak. 197 (1962) 108–122.

[4] J.S. Jørgensen, T. Weber, Fetal scalp blood sampling in labor – a review, Acta Obstet. Gynecol. Scand. 93 (2014) 548–555, https://doi.org/10.1111/aogs.12421.

[5] B. Carbonne, K. Pons, E. Maisonneuve, Foetal scalp blood sampling during labour for pH and lactate measurements, Best Pract. Res. Clin. Obstet. Gynaecol. 30 (2016) 62–67, https://doi.org/10.1016/j.bpobgyn.2015.05.006.

[6] K. Kruger, B. Hallberg, M. Blennow, M. Kublickas, M. Westgren, Predictive value of fetal scalp blood lactate concentration and pH as markers of neurologic disability, Am. J. Obstet. Gynecol. 181 (1999) 1072–1078.

[7] L. Nordström, I. Ingemarsson, M. Kublickas, B. Persson, N. Shimojo, M. Westgren, Scalp blood lactate: a new test strip method for monitoring fetal wellbeing in labour, Br. J. Obstet. Gynaecol. 102 (1995) 894–899.

[8] T.M. Goodwin, I. Belai, P. Hernandez, M. Durand, R.H. Paul, Asphyxial complications in the term newborn with severe umbilical acidemia, Am. J. Obstet. Gynecol. 167 (1992) 1506–1512.

[9] J.A. Low, C. Panagiotopoulos, E.J. Derrick, Newborn complications after intrapartum asphyxia with metabolic acidosis in the term fetus, Am. J. Obstet. Gynecol. 170 (1994) 1081–1087.

[10] N. Wiberg, K. Källén, A. Herbst, P. Olofsson, Relation between umbilical cord blood pH, base deficit, lactate, 5-minute Apgar score and development of hypoxic ischemic encephalopathy, Acta Obstet. Gynecol. Scand. 89 (2010) 1263–1269, https://doi.org/10.3109/00016349.2010.513426.

[11] L. Iorizzo, T.W. Klausen, E. Wiberg-Itzel, F. Ovin, N. Wiberg, Use of Lactate Pro™2 for measurement of fetal scalp blood lactate during labor – proposing new cutoffs for normality, preacidemia and acidemia: a cross-sectional study, J. Matern. Neonatal Med. (2018), https://doi.org/10.1080/14767058.2017.1416603.

[12] Statstrip xpress user manual, Https://Www.Kruuse.Com/Ecommerce/Userfiles/Kno/296200_NovaVet_usermanual_EN.Pdf. (n.d.).

[13] M. Wang, S.C. Chua, L. Bouhadir, E.L. Treadwell, E. Gibbs, T.M. McGee, Point-of-care measurement of fetal blood lactate - Time to trust a new device, Aust. New Zeal. J. Obstet. Gynaecol. 58 (2018) 72–78, https://doi.org/10.1111/ajo.12671.

[14] P. Reif, I. Lakovschek, C. Tappauf, J. Haas, U. Lang, W. Schöll, Validation of a point-of-care (POC) lactate testing device for fetal scalp blood sampling during labor: clinical considerations, practicalities and realities, Clin. Chem. Lab. Med. 52 (2014) 825–833, https://doi.org/10.1515/cclm-2013-0732.

[15] A. Heinis, J. van Dillen, J. Oosting, S. Rhöse, F. Vandenbussche, J. van Drongelen, Clinical evaluation of statstrip®lactate for use in fetal scalp blood sampling, Acta Obstet. Gynecol. Scand. 96 (2017) 334–341, https://doi.org/10.1111/aogs.13078.

[16] J.M. Bonaventura, K. Sharpe, E. Knight, K.L. Fuller, R.K. Tanner, C.J. Gore, Reliability and accuracy of six hand-held blood lactate analysers, J. Sport. Sci. Med. 14 (2014) 203–214.

[17] A.M.F. Heinis, J. Dinnissen, M.E.A. Spaanderman, F.K. Lotgering, J.M.T.K. Gunnewiek, Comparison of two point-of-care testing (POCT) devices for fetal lactate during labor, Clin. Chem. Lab. Med. 50 (2012) 89–93, https://doi.org/10.1515/CCLM.2011.734.

[18] Radiometer Medical Aps, ABL800 FLEX, Reference manual, n.d.

[19] J. Toffaletti, M.E. Hammes, R. Gray, B. Lineberry, B. Abrams, Lactate measured in diluted and undiluted whole blood and plasma: Comparison of methods and effect of hematocrit, Clin. Chem. 38 (1992) 2430–2434.

[20] C. Systems, S. Critical, C. Xpress, S.L. Strips, S.C. Meter, S.X. Meter, StatStrip Lactate Specifications Other Nova Biomedical Stat and Point-of-Care Products Nova StatStrip Lactate Point-of-Care Measuring System A True Point-of-Care Lactate Test System Accuracy Comparable to Hospital, (2010), pp. 5–6.

[21] National institute for health and care excellence, Overview | Intrapartum care for healthy women and babies, Guidance | NICE (2017).

[22] Vägledning till åtgärder, Sfog.Se. (2009).

[23] The Royal Australian and New Zealand College of Obstetricians and Gynaecologists, Intrapartum Fetal Surveillance Clinical Guideline-Third Edition 2014 (2014).

[24] G.H. Visser, D. Ayres-de-Campos, FIGO consensus guidelines on intrapartum fetal monitoring: Adjunctive technologies, Int. J. Gynaecol. Obstet. 131 (2015) 25–29, https://doi.org/10.1016/j.ijgo.2015.06.021.

[25] J. Bretscher, E. Saling, pH values in the human fetus during labor, Am. J. Obstet. Gynecol. 97 (1967) 906–911.

[26] E. Wiberg-Itzel, C. Lipponer, M. Norman, A. Herbst, D. Prebensen, A. Hansson, A.-L. Bryngelsson, M. Christoffersson, M. Sennström, U.-B. Wennerholm, L. Nordström, Determination of pH or lactate in fetal scalp blood in management of intrapartum fetal distress: randomised controlled multicentre trial, BMJ. 336 (2008) 1284–1287, https://doi.org/10.1136/bmj.39553.406991.25.

[27] L. Knutzen, H. Anderson-Knight, E. Svirko, L. Impey, Umbilical cord arterial base deficit and arterial pH as predictors of adverse outcomes among term neonates, Int. J. Gynecol. Obstet. (2018), https://doi.org/10.1002/ijgo.12502.

[28] S. Thayyil, M. Chandrasekaran, A. Taylor, A. Bainbridge, E.B. Cady, W.K.K. Chong, S. Murad, R.Z. Omar, N.J. Robertson, Cerebral Magnetic Resonance Biomarkers in Neonatal Encephalopathy: A Meta-analysis, Pediatrics. 125 (2010) e382 LP-e395 http://pediatrics.aappublications.org/content/125/2/e382.abstract.

[29] A. Cahill, G. Macones, C. Smyser, J. López, T. Inder, A. Mathur, Umbilical Artery Lactate Correlates with Brain Lactate in Term Infants, Am. J. Perinatol. 34 (2016) 535–540, https://doi.org/10.1055/s-0036-1593844.

[30] G.K. Chilinda, L.A. Gadama, W. Stones, Point-of-care umbilical arterial lactate and newborn outcomes in a low resource setting: cohort study, BMC Res. Notes. 11 (2018) 477, https://doi.org/10.1186/s13104-018-3598-9.

[31] J. Jopling, E. Henry, S.E. Wiedmeier, R.D. Christensen, Reference Ranges for Hematocrit and Blood Hemoglobin Concentration During the Neonatal Period: Data From a Multihospital Health Care System, Pediatrics. 123 (2009), https://doi.org/10.1542/peds.2008-2654.

[32] J.M. Colon-Franco, S.F. Lo, S.S. Tarima, D. Gourlay, A.L. Drendel, E. Brook Lerner, Validation of a hand-held point of care device for lactate in adult and pediatric patients using traditional and locally-smoothed median and maximum absolute difference curves, Clin. Chim. Acta. 468 (2017) 145–149, https://doi.org/10.1016/j.cca.2017.02.015.

[33] R. van Horssen, T.N. Schuurman, M.J.M. de Groot, B.S. Jakobs, Lactate point-of-care testing for acidosis: Cross-comparison of two devices with routine laboratory results, Pract. Lab. Med. 4 (2016) 41–49, https://doi.org/10.1016/j.plabm.2015.12.005.

[34] K.A. Versluys, S. Redel, A.N. Kunst, M. Rimkus, D. Chin, D. Tran, D. Holmes, G.S. Cembrowski, Tighter precision target required for lactate testing in patients with lactic acidosis, Clin. Chem. Lab. Med. 52 (2014) 809–813, https://doi.org/10.1515/cclm-2013-0685.

[35] P. Mokarami, N. Wiberg, P. Olofsson, Hidden acidosis: An explanation of acid-base and lactate changes occurring in umbilical cord blood after delayed sampling, BJOG An Int. J. Obstet. Gynaecol. 120 (2013), https://doi.org/10.1111/1471-0528.12234.

[36] M. Zaigham, K. Källén, P. Olofsson, Assessment of lactate production as a response to sustained intrapartum hypoxia in large-for-gestational-age newborns, Acta Obstet. Gynecol. Scand. (2018), https://doi.org/10.1111/aogs.13384.