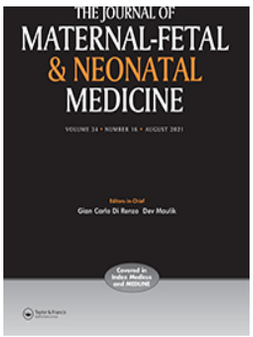

The Journal of Maternal-Fetal & Neonatal Medicine

ISSN: 1476-7058 (Print) 1476-4954 (Online) Journal homepage: https://www.tandfonline.com/loi/ijmf20

# Fetal scalp blood sampling during second stage of labor – analyzing lactate or pH? A secondary analysis of a randomized controlled trial

Ingrid Stål, Ulla-Britt Wennerholm, Lennart Nordstrom, Lars Ladfors & Eva Wiberg-Itzel

**To cite this article:** Ingrid Stål, Ulla-Britt Wennerholm, Lennart Nordstrom, Lars Ladfors & Eva Wiberg-Itzel (2020): Fetal scalp blood sampling during second stage of labor – analyzing lactate or pH? A secondary analysis of a randomized controlled trial, The Journal of Maternal-Fetal & Neonatal Medicine, DOI: 10.1080/14767058.2020.1743656

**To link to this article:** https://doi.org/10.1080/14767058.2020.1743656



Published online: 31 Mar 2020.

THE JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE
https://doi.org/10.1080/14767058.2020.1743656

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

OPEN ACCESS Check for updates

# Fetal scalp blood sampling during second stage of labor – analyzing lactate or pH? A secondary analysis of a randomized controlled trial

Ingrid Stål[a], Ulla-Britt Wennerholm[a], Lennart Nordstrom[b,c], Lars Ladfors[a] and Eva Wiberg-Itzel[d]

[a]Department of Obstetrics and Gynecology, Institute of Clinical Sciences at Sahlgrenska Academy, University of Gothenburg, Sahlgrenska University Hospital East, Gothenburg, Sweden; [b]Department of Women and Children's Health, Karolinska Institute, Stockholm, Sweden; [c]Department of Pregnancy and Delivery, Karolinska University Hospital, Stockholm, Sweden; [d]Department of Clinical Science and Education, Section of Obstetrics and Gynecology, Karolinska Institute, Womens clinic Sodersjukhuset, Stockholm, Sweden

**ABSTRACT**

**Background:** Cardiotocography (CTG) is a widely used method for assessing fetal wellbeing during labor. It is well-known that CTG has high sensitivity but low specificity. To avoid unnecessary operative interventions, adjunctive methods such as fetal blood sampling (FBS) are used. Few studies have looked into whether FBS can be used during second stage of labor, and in that case, which of the methods (lactate or pH) are preferred.

**Objective:** To evaluate clinical effectiveness of measuring lactate versus pH in preventing birth acidemia when FBS was performed during second stage of labor.

**Methods:** Secondary analysis of a randomized controlled trial . Thousand three hundred and thirty-eight women with a singleton pregnancy, cephalic presentation, gestational age ≥34 weeks, and indication for FBS during second stage of labor were included.

**Main outcome measures:** Metabolic acidemia (pH <7.05 and base deficit >12 mmol/l) or pH < 7.00 in cord arterial blood at birth.

**Secondary outcomes:** A composite outcome (metabolic acidemia, pH <7 or Apgar score <4), and rates of operative deliveries.

**Results:** Metabolic acidemia occurred in 4.1% in the lactate versus 5.1% in the pH group (relative risk (RR): 0.80; 95% confidence interval (CI): 0.48–1.35) and pH <7 in 1.4% versus 2.8% (RR: 0.51, 95% CI: 0.23–1.13). Composite outcome was found in 3.8 versus 4.9%, respectively (RR: 0.76; 95% CI: 0.46–1.26). No difference in total operative interventions was found. More cesarean deliveries were performed in the lactate group (16.5 vs. 12.4%; RR: 1.33; 95% CI: 1.02–1.74).

**Conclusion:** When analyzing lactate or pH in fetal scalp blood during second stage of labor neonatal outcomes were comparable. The frequency of total operative interventions was similar but more cesarean deliveries were performed in the lactate group.

**ARTICLE HISTORY**
Received 31 July 2019
Revised 25 February 2020
Accepted 13 March 2020

**KEYWORDS**
Fetal scalp blood sampling; lactate; pH; second stage of labor; metabolic acidosis; neonatal outcome; cesarean section

## Introduction

Cardiotocography (CTG) is a widely used method for assessing fetal wellbeing in labor. CTG has high sensitivity but low specificity [1]. To avoid unnecessary operative deliveries when CTG gives a non-reassuring result, adjunctive methods to monitor fetal wellbeing are needed. Fetal blood sampling (FBS) was introduced in the 1960s by Saling using pH measurements of fetal blood to detect suspected fetal acidosis [2]. However, pH analysis is not suitable for discriminating between metabolic and respiratory acidosis. Respiratory acidosis due to accumulation of carbon dioxide during labor has no long-term consequences but metabolic acidemia due to prolonged hypoxia may result in irreversible organ damage.

Failures in sampling or analysis of pH measurements occur in 10–20% [3]. An alternative method in FBS is measuring lactate which has been used since the 1990s. It requires a smaller amount of blood, the analysis is done within minutes, failure rate is low (1.3–1.7%) and theoretically only metabolic acidemia is detected [3–8].

In an randomized controlled trial (RCT) we compared lactate and pH analyses of fetal scalp blood in the clinical management of intrapartum fetal distress, to prevent acidemia at birth [7]. There were no

CONTACT Eva Wiberg-Itzel eva@itzel.eu Department of Clinical Science and Education, Karolinska Institute, Women's Clinic, Sodersjukhuset, Stockholm, 118 83, Sweden

significant differences in rates of acidemia at birth after use of lactate or pH analysis, or operative deliveries for fetal distress although the sampling failure rate was higher for pH (11%).

In the active second stage of labor, there are periods of diminished blood perfusion through the placenta. It is well established that fetal pH is lower at the end of the second stage than the first stage of labor. The question is whether this decrease in pH during the second stage depends on maternal transferred lactate or on lactic acidosis in the fetus itself [9,10]. Both maternal and fetal lactate increase during second stage of labor, but it is most likely that fetal anaerobic metabolism contributes to lactate increase in the fetus [11].

We performed a secondary analysis of data from the original study [7]. The aim of this project was to evaluate which method of FBS, lactate or pH analysis that is most reliable in the second stage of labor in preventing birth acidemia. We also studied rates of operative vaginal deliveries, cesarean section (CS), sampling, and failure rates.

## Material and methods

This study is a secondary analysis of an RCT conducted by Wiberg-Itzel et al. [7] in 10 Swedish labor wards. In that study, 3007 women with a pathological CTG were randomly assigned to FBS with either lactate or pH analysis. The women participating in the study had given their informed consent before randomization. Inclusion criteria for the trial were: singleton pregnancy, cephalic presentation, gestational age $\geq$34 weeks, and a pathological fetal heart rate trace, considered by the clinician in charge as an indication for FBS. Fifteen of the randomized women were excluded because they did not meet the inclusion criteria. A total of 2992 woman were randomized to either pH ($n = 1496$) or lactate analysis ($n = 1496$).

In 1387 of these women, the FBS was performed in the second stage of labor (which begins when the cervix is fully dilated and ends when the baby is born). Time intervals of more than four hours from the last FBS to delivery were regarded as outliers due to incorrect registration, and 49 women were subsequently excluded. We analyzed 1338 women with a time interval of four hours or less between the last FBS and delivery (Figure 1). Subgroup analyses were performed where an FBS was done from 0 to 30 min ($n = 478$) before delivery. A subgroup analysis was also performed where an FBS was carried out during the active second stage of labor (defined as active pushing; $n = 175$).

### Biochemical analyses and clinical guidelines

This has been described in the previous paper [7]. Lactate was measured using a commercially available micro volume test strip device (Lactate Pro™, Arkray, Kyoto, Japan) [5,6,8,12]. Regular quality checks of the acid–base measurements were performed by a commercial company (Equalis AB, Uppsala, Sweden).

Base deficit (BD) was calculated for the blood compartment with the algorithm used by radiometer blood gas analyzers [13]. As hemoglobin concentration in cord blood was not known, the approximation of a hemoglobin concentration of 150 g/l was used in calculations.

Guidelines for interpretation of the fetal scalp blood analyses were as follows: lactate samples were defined as acidemia when the value was above 4.8 mmol/l, preacidemia between 4.2 mmol/l and 4.8 mmol/l, and normal below 4.2 mmol/l as recommended by Kruger et al. [8]. The corresponding values for the pH samples were: acidemia when the value was $<$7.21, preacidemia between 7.21 and 7.25, and normal above 7.25 [2,7]. During the study period a repeat FBS was recommended within 20–30 min in cases of preacidemia if no other indication for intervention was present. The clinician in charge decided on interventions in fetuses with preacidemia and acidemia.

### Outcome measures

#### Primary endpoints

1. Metabolic acidemia in umbilical cord arterial blood at birth (pH $<$7.05 and BD $>$12 mmol/l).
2. pH $<$7.00 in umbilical cord arterial blood at birth.

#### Secondary endpoints

1. Operative deliveries (cesarean delivery, vacuum extraction, or forceps deliveries),
2. Operative deliveries for fetal distress.
3. pH $<$ 7.10 in umbilical cord arterial blood at birth.
4. Apgar score $<$4 and $<$7 at five minutes.
5. Admission to neonatal intensive care unit (NICU).
6. Sampling/analysis failure rates.

A new composite outcome, defined as any of metabolic acidemia, pH $<$7 or Apgar score $<$4 at five minutes, was included in the present study.

The diagnostic accuracy of FBS using lactate or pH measurements was calculated by analyzing metabolic acidemia in umbilical cord arterial blood at birth in relation to the results of FBS.

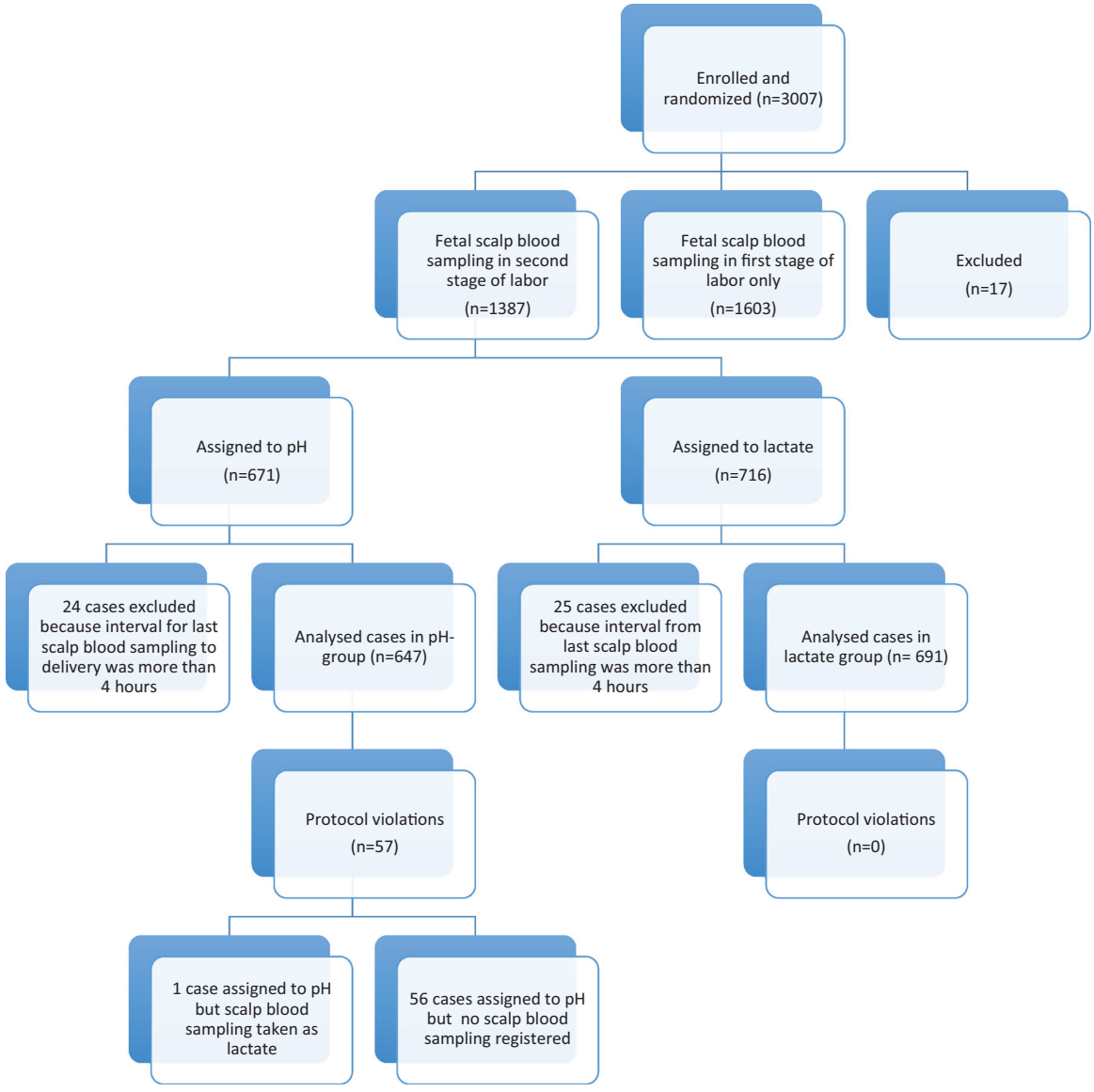


Figure 1. Study flowchart.

### Statistical analyses

Data was analyzed according to "intention to treat". We present results as numbers and percentages. *p* Values were calculated by a Mann–Whitney *U*-test for continuous variables, and Fisher's exact test for categorical variables. Relative risks (RR) with 95% confidence interval (CI) were calculated. Adjustments were made for differences between groups (gestational age, use of STAN monitoring). Statistical Package for the Social Science (SPSS, version 21.0 and 24.0, Chicago, IL) was used for the statistical analyses.

### Sample size

Since this study had 1338 participants (691 and 647 in each arm, respectively) it had the power to detect differences in the incidence of metabolic acidemia in umbilical cord arterial blood at birth between 1.2% in one arm and 3.6% in the other arm (80% power at 5% significance level, two tailed.)

### Ethical approval

Ethical approval was obtained from Karolinska Institute, Stockholm, Sweden (file record 109/02).

The original study was registered with ISRCTN.com number 1606064.

## Results

The study population consisted of 1338 women. Of these, 691 women were assigned to lactate analysis

Table 1. Descriptive data of groups according to method of monitoring for hypoxia.[a]

| | Lactate ($n = 691$) | pH ($n = 647$) | $p$ Value[b] |
|---|---|---|---|
| Maternal age, years | 32.9 (19.9–46.9) | 32.9 (18.9–48.9) | .67 |
| Parity[c], *n* (%) | | | |
| *Primiparous* | 554 (80.2) | 537 (83.0) | .2 |
| *Multiparous* | 137 (19.8) | 110 (17.0) | |
| Gestational age, days | 284 (243–302) | 283 (240–304) | .02 |
| Birthweight[d], g | 3565 (1860–4980) | 3560 (1985–5680) | .96 |
| Birthweight <2500 g, *n* (%) | 15 (2.1) | 18 (2.7) | .49 |
| Sex, *n* (%) | | | |
| *Female* | 337 (48.8) | 289 (44.7) | .14 |
| *Male* | 354 (51.2) | 358 (55.3) | |
| Use of STAN-monitor, *n* (%) | 128 (18.5) | 153 (23.6) | .02 |
| Time interval from last scalp blood sampling to delivery (min) | 39 (0–240) | 43 (1–237) | .08 |

[a]Figures are medians unless stated otherwise.
[b]Mann–Whitney *U*-test or Fisher's exact test.
[c]Data missing in two cases in pH group.
[d]Data missing in two cases in pH group.

and 647 were assigned to pH analysis. In the lactate group there were no sampling failures or protocol violations. In the pH group no results were registered for 57 women (8.8%) ($p < .0001$), and in one case FBS was analyzed as lactate (Figure 1).

Table 1 shows descriptive data for the lactate and pH groups. Significant differences between the two groups were found for gestational age (lactate 284 vs. pH 283 days; $p = .02$) and in the use of ST analysis (STAN; lactate 18.5% vs. pH 23.6%; $p = .02$).

Table 2 shows the neonatal and obstetric outcomes in the two groups according to intention to treat. There was no significant difference between the lactate and pH groups in the incidence of neonatal metabolic acidemia (4.1 vs. 5.1%; $p = .11$), in the rate of pH <7 (1.4 vs. 2.8%; $p = .11$), in composite outcome (3.8 vs. 4.9%; $p = .07$) or in total operative interventions (54.1 vs. 52.9%; $p = .66$). However, significant differences in the rate of total CS (lactate 16.5% vs. pH 12.4%; $p = .04$) and the rate of CS for fetal distress (12.7 vs.7.6%; $p = .002$) were found.

Adjustment for gestational age and use of ST analysis only marginally changed the results (metabolic acidemia): $p = .48$; pH <7: $p = .13$; composite outcome: $p = .33$; cesarean delivery: $p = .04$.

Data was analyzed for women where FBS was performed during the active second stage of labor (Table 3). The number of women who fulfilled these criteria was 175 (94 in lactate group and 81 in pH group). There was no significant difference in primary neonatal outcome or in the numbers of newborns with a composite outcome. No woman was delivered by CS, and there was no significant difference in the rate of forceps or vacuum extraction delivery (lactate 47.9% vs. pH 46.9%) during active pushing.

Table 4 shows the groups divided according to the value of the last FBS, categorized as acidemia, preacidemia, or normal, performed within 30 min prior to delivery. Diagnostic accuracy for the last FBS, categorized as acidemia (pH <7.21) and lactate (>4.8 mmol/l) analysis performed within 30 min prior to delivery in relation to metabolic acidemia at birth, is presented in Table 5. The positive likelihood ratio was 1.89 for lactate and 2.30 for pH. The corresponding negative likelihood ratios were 0.33 and 0.34, respectively. There were no cases with normal FBS results at the time of sampling and pH <7 at delivery, but two cases of metabolic acidemia in the lactate group and one in the pH group.

## Discussion

This study compared the effectiveness of lactate and pH analysis in fetal scalp blood in the management of pathological CTG during the second stage of labor. No significant differences were found in the rates of metabolic acidemia, pH <7 or low Apgar scores at birth when comparing management guided by concentrations of lactate or pH in fetal scalp blood. This study provides no evidence that either lactate or pH is more reliable than the other in predicting the actual condition of the neonate. When lactate sampling was performed in the second stage of labor, significantly more women were delivered by CS. No failed sampling/analysis occurred in the lactate group but one in 11 attempts in the pH group.

The second stage of labor is defined as the period from the time cervix is fully dilated until the fetus is born. During this period, the fetal head descends through the birth canal. The active second stage is the

**Table 2.** Obstetric and neonatal outcomes in groups according to method of monitoring for hypoxia: second stage of labor.[a]

| | Lactate ($n = 691$) | pH ($n = 647$) | RR (95 % CI) lactate versus pH | $p$ Value[b] |
|---|---|---|---|---|
| Metabolic acidemia[c] | 26 (4.1) | 29 (5.1) | 0.80 (0.48–1.35) | .49 |
| pH < 7.00[d] | 9 (1.4) | 16 (2.8) | 0.51 (0.23–1.13) | .11 |
| pH < 7.10[e] | 68 (10.5) | 77 (13.3) | 0.79 (0.58–1.08) | .16 |
| Cesarean delivery | 114 (16.5) | 80 (12.4) | 1.33 (1.02–1.74) | .04 |
| Immediate cesarean delivery | 30 (4.3) | 17 (2.6) | 1.65 (0.92–2.97) | .10 |
| Cesarean delivery for fetal distress | 88 (12.7) | 49 (7.6) | 1.78 (1.23–2.57) | .002 |
| Forceps/vacuum extraction | 260 (37.6) | 262 (40.5) | 0.93 (0.81– 1.06) | .29 |
| Spontaneous vaginal delivery | 317 (45.9) | 305 (47.1) | 0.97 (0.87–1.09) | .66 |
| ODFD | 278 (40.2) | 250 (38.6) | 1.04 (0.91–1.19) | .58 |
| Apgar score <7 at 5 min | 18 (2.6) | 28 (4.3) | 0.60 (0.34–1.08) | .10 |
| Apgar score <4 at 5 min | 1 (0.1) | 4 (0.6) | 0.23 (0.30–2.09) | .20 |
| NICU admission | 58 (8.4) | 73 (11.3) | 0.74 (0.54– 1.03) | .08 |
| Composite outcome (any of metabolic acidemia, pH <7, or Apgar <4 at 5 min if cord artery sampling is missing) | 26 (3.8) | 32 (4.9) | 0.76 (0.46–1.26) | .34 |

[a]Figures are for fetal scalp blood sampling performed during second stage of labor.
[b]Fisher's exact test.
[c]Metabolic acidemia defined as pH < 7.05 and base deficit >12 mmol/l. Samples for measuring umbilical cord arterial blood gases missing in 77 cases (11.9%) in pH group and 58 cases (8.4%) in lactate group.
dSamples for measuring umbilical cord arterial blood pH missing in 67 cases (10.4%) in pH group and in 45 cases (6.5 %) in lactate group.

**Table 3.** Obstetric and neonatal outcomes in groups according to method of monitoring for hypoxia: active second stage.[a]

| | Lactate ($n = 94$) | pH ($n = 81$) | RR (95 % CI) lactate versus pH | $p$ Value[b] |
|---|---|---|---|---|
| Metabolic acidemia[c] | 5 (5.5) | 4 (5.5) | 1.00 (0.28–3.60) | 1.0 |
| pH < 7.00[d] | 2 (2.2) | 2 (2.7) | 0.79 (0.12–5.5) | 1.0 |
| pH < 7.10[e] | 13 (14.1) | 10 (13.7) | 1.03 (0.48–2.22) | 1.0 |
| CS | 0 | 0 | | |
| Forceps/vacuum extraction | 45 (47.9) | 38 (46.9) | 1.02 (0.75–1.40) | 1.0 |
| Spontaneous vaginal delivery | 49 (52.1) | 43 (53.1) | 0.98 (0.74–1.30) | 1.0 |
| ODFD | 35 (37.2) | 33 (40.7) | 0.91 (0.63–1.33) | .64 |
| Apgar score <7 at 5 min | 2 (2.1) | 1 (1.2) | 1.72 (0.16–18.66) | 1.0 |
| Apgar score <4 at 5 min | 0 | 0 | | |
| NICU admission | 6 (6.4) | 7 (8.6) | 0.74 (0.26– 2.11) | .58 |
| Composite outcome (any of metabolic acidemia, pH <7, and Apgar <4 at 5 min if umbilical cord artery sampling is missing) | 5 (5.3) | 4 (4.9) | 1.08 (0.30–3.88) | 1.0 |

[a]Fetal scalp blood sampling taken during active second stage.
[b]Fisher's exact test.
[c]Metabolic acidemia defined as pH < 7.05 and base deficit >12 mmol/l.
[d]Sample for measuring umbilical cord arterial blood gases missing in eight cases (9.9%) in pH group and four cases (4.3%) in lactate group.
[e]Samples for measuring umbilical cord arterial pH missing in eight cases (9.9%) in pH group and in two cases (2.1%) in lactate group.

period when the woman is actively pushing, implicating intermittent hypoxia for the fetus. During active second stage, fetal scalp blood lactate increases with 1 mmol/l per 30 min of bearing down [11]. Some obstetricians will argue that FBS should not be performed during active pushing when an ominous CTG is present, as it may delay the delivery if an instrumental delivery is an alternative. In this study, 13% of the FBS's during the second stage of labor were actually performed during active pushing.

A Cochrane review from 2015 evaluated the effectiveness of fetal scalp lactate sampling compared with no testing or alternative testing [14]. There was no available evidence to determine the effectiveness of fetal scalp blood lactate sampling, compared with no sampling, on clinical outcomes. The review included

**Table 4.** Primary and secondary neonatal and obstetric outcomes in relation to fetal scalp blood values (normal, pre-acidemia, or acidemia). [a, b]

| | Fetal scalp blood lactate (mmol/l) ($n = 280$) | | | Fetal scalp blood pH[c] ($n = 198$) | | |
|---|---|---|---|---|---|---|
| | <4.2 ($n = 114$) | 4.2–-4.8 ($n = 38$) | >4.8 ($n = 128$) | >7.25 ($n = 89$) | 7.25–7.21 ($n = 39$) | <7.21 ($n = 70$) |
| Metabolic acidemia[d] | 2 (1.8) ($n = 106$) | 1 (2.8) ($n = 36$) | 13 (11.0) ($n = 118$) | 1 (1.1) ($n = 79$) | 1 (2.6) ($n = 36$) | 7 (10.8) ($n = 65$) |
| pH <7.0 | 0 ($n = 108$) | 0 ($n = 36$) | 5 (4.2) ($n = 119$) | 0 ($n = 79$) | 1 (2.6) ($n = 36$) | 5 (7.6) ($n = 66$) |
| Apgar score <7 at 5 min | 0 | 0 | 7 (5.5) | 4 (4.5) | 1 (2.6) | 6 (8.6) |
| Apgar score <4 at 5 min | 0 | 0 | 0 | 0 | 0 | 3 (4.3) |
| ODFD | 18 (15.8) | 25 (65.8) | 115 (89.8) | 23 (25.8) | 19 (48.7) | 53 (75.7) |
| Median time interval from last scalp blood sampling to delivery (min) | 19 (0-30) | 17 (6-30) | 15 (3-30) | 20 (3-30) | 21 (5-30) | 16 (2-30) |
| Composite outcome (any of metabolic acidemia, pH <, or Apgar < 4 at 5 min if cord arterial blood sampling is missing) | 2 (1.8) | 1 (2.6) | 13 (10.2) | 1 (1.1) | 1 (2.6) | 9 (12.9) |

[a]Figures are for fetal scalp blood sampling within 30 min prior to delivery.
[b]There are missing values for umbilical cord blood gases ($n = 20$ (7.1%) in lactate and $n = 18$ (9.1%) in pH group) and for umbilical cord arterial blood pH ($n = 17$ (6.1%) in lactate and $n = 17$ (8.6%) in pH group).
[c]Scalp blood sampling value is missing in 31 cases in pH group.
dMetabolic acidemia defined as pH < 7.05 and base deficit >12 mmol/l.

**Table 5.** Diagnostic accuracy of fetal scalp blood sampling of lactate or pH for assessment of metabolic acidemia in umbilical cord arterial at birth.[a]

| | Lactate >4.8 mmol/l Estimate (95% confidence interval) | pH< 7.21 Estimate (95% confidence interval) |
|---|---|---|
| Sensitivity (%) | 81.3 (57.0–93.4) | 77.8 (45.3–93.7) |
| Specificity (%) | 57.0 (50.7–63.0) | 66.1 (58.7–72.8) |
| Positive predictive value (%) | 11.0 (6.6–17.9) | 10.8 (5.3–20.6) |
| Negative predictive value (%) | 97.9 (94.0–99.3) | 98.3 (93.9–99.5) |
| Positive likelihood ratio (LR+) | 1.89 (1.43–2.49) | 2.30 (1.53–3.45) |
| Negative likelihood ratio (LR–) | 0.33 (0.12–0.92) | 0.34 (0.10–1.15) |

[a]Figures are for sampling within 30 min prior to delivery. A test positive result was defined as a scalp lactate >4.8 mmol/l or pH <7.21. Metabolic acidemia is defined as pH < 7.05 and base deficit >12 mmol/l.

two RCTs, both performed in Sweden and both assessing lactate versus pH [3,7]. The largest study included was the Wiberg-Itzel study and this article is a secondary analysis of data from that study. The Cochrane review concluded that lactate testing was more likely to be successful than pH testing, but with no differences in newborn outcomes or rates of Cesareans or instrumental deliveries between the two groups. Similar findings were found in the present study except for a higher frequency of CS in the lactate group. The Cochrane review further recommended studies on the impact on labor of FBS [14].

There are discussions on how to reduce the increasing rate of CS performed globally today. Obstetricians are questioning if FBS actually reduces operative deliveries or not [14–18]. There is only one randomized controlled trial which has compared CTG monitoring with and without FBS as an adjunctive method [19]. They found no significant reduction in CS when FBS was added, but the study was underpowered to show any difference in CS. The International Federation of Gynecology and Obstetrics (FIGO) consensus guideline on intrapartum fetal monitoring concluded that the use of FBS is likely to reduce the CS rate [20]. An ongoing RCT in Australia aims to determine the impact of FBS lactate measurements on rates of CS [21].

The question about FBS as a useful diagnostic test is also discussed in two published papers by Chandraharan and Wiberg [15] and Mahendru and Lees [17]. They argue that the studies performed to determine cutoff values before the test was introduced were very small and that the test is assumed to be a "gold standard" in spite of the fact that it has never been validated in humans. Chandraharan and Wiberg [15] also argue that testing peripheral tissue such as the fetal scalp for acidosis reflects a poor understanding of the physiological response to hypoxia. Others argue that peripheral tissue blood tests are early markers in the hypoxic process, making preventive measures possible [20].

The acidemic cutoff levels of lactate and pH have been discussed [22,23]. Traditionally, levels above 4.8 mmol/l for lactate and 7.20 or less for pH have been set as cut off values for intervention in labor. There is no defined distinction in first or second stage of labor. We do not know if the cutoff value for intervention derived during first stage of labor (lactate >4.8 mmol/l) should be used or if a higher cutoff value during active bearing down could be accepted with safety. From an observational study by Wiberg et al. [24] a lactate cutoff value of 5.1 mmol/l for the second stage was suggested.

Bowler et al. [22] studied the diagnostic accuracy of scalp lactate sampling taken the last hour before delivery. They found that a lactate measurement of ≥4.8 mmol/l had a positive predictive value (PPV) of 1% and a negative predictive value (NPV) of 100% in predicting umbilical artery blood levels of pH ≤7 [22]. In our analysis, PPV and NPV for predicting metabolic acidemia was similar for lactate (>4.8 mmol/l) and pH (<7.21; 11 and 98%, respectively).

Recently, a large observational study of FBS from 44 maternity units in the UK was published [25]. The conclusion of the study results was that FBS as an adjunct tool to cardiotocography, offered limited value to predict neonatal acidaemia, low Apgar Scores, and admission to NICU. However, it should be noted that the number of included deliveries in the study was limited, the study was not randomized and that only pH in fetal scalp blood was analyzed.

The aim with intrapartum fetal monitoring is to identify fetuses that do not cope with contractions and intervene before they are severely affected with risk for future morbidity. The most important feature of an adjunctive test is that it has no "false negative tests", i.e. that the FBS is normal but the fetus is severely acidemic. In the present study three cases with normal scalp blood values had metabolic acidemia at birth, but none were severely acidemic, defined as cord blood pH <7. When a fetus had FBS performed within 30 min prior to delivery and lactate or pH did not indicate acidemia, 98–99% of the newborns had normal acid–base status in cord blood. This is a secondary analysis of the largest RCT done on FBS in labor and to our knowledge is the largest study on FBS during the second stage.

## Strength and limitations

However, a major limitation was that the sample size was too small for low prevalence outcomes such as pH <7, metabolic acidemia, and longer-term infant morbidity. Among outcomes not included is maternal satisfaction. Since this is a secondary analysis we were not able to choose the size of the groups according to power calculation or outcomes of interest. FBS with lactate analysis was a newly introduced method, with no experience of dynamics and time frames of lactate changes, which probably have influenced the rate of CS.

The results of FBS analyses of lactate and pH levels during second stage of labor did not differ with regard to the neonates' umbilical cord blood gases, Apgar scores, or admission to the neonatal intensive care unit. The only significant differences between the two modes in the second stage of labor were a higher frequency of CS in the lactate group and more failed samplings in the pH group. However, one should take into account that this was the first instance of the introduction of lactate in clinical practice and most of the clinics had not used the method before.

## Conclusion

When FBS was performed during the second stage of labor, in this randomized study no significant differences were found in the neonatal outcomes when comparing management guided by measurement of lactate or pH in fetal scalp blood. This study provides no evidence that either lactate or pH is more reliable than the other in predicting the actual condition of the neonate during the second stage of labor. When lactate sampling was performed, significantly more women were delivered by CS, but the frequencies of total operative interventions were comparable.

It is important to mention that during second stage of labor, hypoxia, and acidosis may arise rapidly, and therefore, the single point of time tests (scalp pH or lactate) should be used with caution, as the rate of fall depends on the rapidity of fetal hypoxia and the individual fetal reserve.

## Acknowledgements

We thank all the women who took part in the trial and the obstetricians and midwives who recruited patients and managed their labors. The following hospitals took part: Danderyd, Kalmar, Karlstad, Karolinska, Lund, Soder Hospital, Trollhättan, Örebro, Gothenburg, and Linköping.

## Contribution to authorship

IS, UBW, and EWI designed the work. EWI and LN collected the original material. IS, UBW, and LL made the data analysis. All authors interpreted the results and wrote the report.

## Disclosure statement

No potential conflicts of interest was reported by the author(s).

## Funding

This study was financially supported by Signhild-Engqvists-Stiftelse, Allmänna BB, FOU-Västra Götaland, and Medexa foundation.

## ORCID

Lars Ladfors http://orcid.org/0000-0002-7512-2059

## References

[1] Alfirevic Z, Devane D, Gyte GML, et al. Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour. Cochr Database Syst Rev. 2017; 2017.

[2] Bretscher J, Saling E. pH values in the human fetus during labor. Am J Obstet Gynecol. 1967;97(7): 906–911.

[3] Westgren M, Kruger K, Ek S, et al. Lactate compared with pH analysis at fetal scalp blood sampling: a prospective randomised study. BJOG. 1998;105(1):29–33.

[4] Kruger K, Kublickas M, Westgren M. Lactate in scalp and cord blood from fetuses with ominous fetal heart rate patterns. Obs Gynecol. 1998;92(6):918–922.

[5] Nordstrom L, Ingemarsson I, Kublickas M, et al. Scalp blood lactate: a new test strip method for monitoring fetal wellbeing in labour. BJOG. 1995;102(11):894–899.

[6] Shimojo N, Naka K, Uenoyama H, et al. Electrochemical assay system with single-use electrode strip for measuring lactate in whole blood. Clin Chem. 1993;39(11):2312–2314.

[7] Wiberg-Itzel E, Lipponer C, Norman M, et al. Determination of pH or lactate in fetal scalp blood in management of intrapartum fetal distress: randomised controlled multicentre trial. BMJ. 2008; 336(7656):1284–1287.

[8] Kruger K, Hallberg B, Blennow M, et al. Predictive value of fetal scalp blood lactate concentration and pH as markers of neurologic disability. Am J Obstet Gynecol. 1999;181(5):1072–1078.

[9] Nickelsen C, Thomsen SG, Weber T. Continuous acid--base assessment of the human fetus during labour by tissue pH and transcutaneous carbon dioxide monitoring. BJOG. 1985;92(3):220–225.

[10] Piquard F, Schaefer A, Dellenbach P, et al. Is fetal acidosis in the human fetus maternogenic during labor? A reanalysis. Am J Physiol. 1991;261(5): R1294–R1299.

[11] Nordstrom L, Achanna S, Naka K, et al. Fetal and maternal lactate increase during active second stage of labour. BJOG. 2001;108(3):263–268.

[12] Nordstrom L, Chua S, Roy A, et al. Quality assessment of two lactate test strip methods suitable for obstetric use. J Perinat Med. 1998;26(2):83–88.

[13] Wiberg N, Kallen K, Olofsson P. Base deficit estimation in umbilical cord blood is influenced by gestational age, choice of fetal fluid compartment, and algorithm for calculation. Am J Obset Gynecol. 2006;195(6): 1651–1656.

[14] East CE, Leader LR, Sheehan P, et al. Intrapartum fetal scalp lactate sampling for fetal assessment in the presence of a non-reassuring fetal heart rate trace. Cochrane Database Syst Rev. 2015; 5:CD006174.

[15] Chandraharan E, Wiberg N. Fetal scalp blood sampling during labor: an appraisal of the physiological basis and scientific evidence. Acta Obstet Gynecol Scand. 2014;93(6):544–547.

[16] Jørgensen JS, Weber T. Fetal scalp blood sampling in labor – a review. Acta Obstet Gynecol Scand. 2014; 93(6):548–555.

[17] Mahendru AA, Lees CC. Is intrapartum fetal blood sampling a gold standard diagnostic tool for fetal distress?. Eur J Obstet Gynecol Reprod Biol. 2011;156(2): 137–139.

[18] Carbonne B, Pons K, Maisonneuve E. Foetal scalp blood sampling during labour for pH and lactate measurements. Best Pr Res Clin Obs Gynaecol. 2016; 30:62–67.

[19] Haverkamp AD, Orleans M, Langendoerfer S, et al. A controlled trial of the differential effects of intrapartum fetal monitoring. Am J Obstet Gynecol. 1979; 134(4):399–412.

[20] Visser GH, Ayres-de-Campos D. FIGO Intrapartum Fetal Monitoring Expert Consensus PanelAyres. FIGO consensus guidelines on intrapartum fetal monitoring: Adjunctive technologies. Int J Gynecol Obstet. 2015; 131(1):25–29.

[21] East CE, Kane SC, Davey MA, et al. Protocol for a randomised controlled trial of fetal scalp blood lactate measurement to reduce CS during labour: the Flamingo trial [ACTRN12611000172909]. BMC Pregnancy Childbirth. 2015;15(1):285.

[22] Bowler T, Beckmann M. Comparing fetal scalp lactate and umbilical cord arterial blood gas values. Aust NZ J Obstet Gynaecol. 2014;54(1):79–83.

[23] Ramanah R, Martin A, Clement MC, et al. Fetal scalp lactate microsampling for non-reassuring fetal status during labor: a prospective observational study. 2010; 27(1):14–23. Fetal Diagn Ther.

[24] Wiberg N, Källén K. Fetal scalp blood lactate during second stage of labor: determination of reference values and impact of obstetrical interventions. J Matern Neonatal Med. 2017;30(5):612–617.

[25] Al Wattar BH, Lakhiani A, Sacco A, et al. Evaluating the value of intrapartum fetal scalp blood sampling to predict adverse neonatal outcomes: a UK multicentre observational study. Eur J Obstet Gynecol Reprod Biol. 2019;240:62–67.