Determination of pH or lactate in fetal scalp blood in management of intrapartum fetal distress: randomised controlled multicentre trial


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Determination of pH or lactate in fetal scalp blood in management of intrapartum fetal distress: randomised controlled multicentre trial


ABSTRACT
Objective To examine the effectiveness of pH analysis of fetal scalp blood compared with lactate analysis in identifying hypoxia in labour to prevent acidaemia at birth.

Design Randomised controlled multicentre trial.

Setting Labour wards.

Participants Women with a singleton pregnancy, cephalic presentation, gestational age ≥34 weeks, and clinical indication for fetal scalp blood sampling.

Interventions Standard pH analysis (n=1496) or lactate analysis (n=1496) with an electrochemical microvolume method (5 μl test strip device). The cut-off levels for intervention were pH <7.21 and lactate >4.8 mmol/l, respectively.

Main outcome measure Metabolic acidemia (pH <7.05 and base deficit ≥12 mmol/l) or pH <7.00 in cord artery blood.

Results Metabolic acidemia occurred in 3.2% in the lactate group and in 3.6% in the pH group (relative risk 0.91, 95% confidence interval 0.61 to 1.36). pH <7.00 occurred in 1.5% in the lactate group and in 1.8% in the pH group (0.84, 0.47 to 1.50). There was no significant difference in Apgar scores 7 at 5 minutes (1.15, 0.76 to 1.75) or operative deliveries for fetal distress (1.02, 0.93 to 1.11).

Conclusion There were no significant differences in rate of acidemia at birth after use of lactate analysis or pH analysis of fetal scalp blood samples to determine hypoxia during labour.

Trial registration ISRCT No 1606064.

INTRODUCTION

Sampling of blood from the fetus’s scalp during labour to analyse pH is regarded as the ideal method of identifying intrapartum fetal hypoxia.1 Arbitrarily, a pH <7.20 is chosen as cut-off value to recommend intervention. The analysis of pH needs a relatively large amount of blood (30-50 μl), and sampling failure rates of 11-20% have been reported.2-4 It also does not discriminate between respiratory and metabolic acidemia, the latter being associated with neonatal morbidity.

Observational studies have shown that determination of lactate in blood from the fetus’s scalp during labour has similar or better predictive properties compared with pH analysis in the identification of short term neonatal morbidity. It has been an option in clinical practice since a reliable electrochemical microvolume method became available, which needs only 5 μl of blood.1 A randomised controlled trial comparing analyses of pH and lactate in fetal scalp blood showed significantly fewer failures in sampling with lactate analysis (odds ratio 16.1, 95% confidence interval 5.8 to 44.7) and no differences in short term neonatal outcome.2 The limited size of the study (341 cases), however, meant it could not compare metabolic acidemia at birth or hypoxic ischaemic encephalopathy.3

We compared pH and lactate analyses of fetal scalp blood in the clinical management of intrapartum fetal distress to prevent severe acidaemia at birth.

METHODS

Participants—Ten labour wards in Sweden participated and enrolled women between December 2002 and the autumn of 2003. The study closed for all departments on 31 December 2005 (see bmj.com for further details).

Recruitment
Inclusion criteria were: singleton pregnancy, cephalic presentation, gestational age ≥34 weeks, and a non-reassuring fetal heart rate trace that the clinician in charge considered an indication for sampling fetal scalp blood. In total 3007 women were randomised. Fifteen were excluded because of multiple pregnancies or gestational age <34 weeks, leaving 2992 for analysis.

Randomisation and stratification—When the clinician decided to sample fetal scalp blood, the woman was randomised to either pH or lactate analysis. If sampling or analysis failed, management was carried out on the basis of other clinical information. No change to randomised analysis was allowed, and if crossover occurred it was regarded as protocol violation. To adjust for differences in management routines or selection of patients, randomisation was stratified for the number of patients within each department and whether or not the departments used fetal
electrocardiography (the STAN monitor) as an adjunct to cardiotocography.

**End points**—Primary end points were metabolic acidaemia in cord artery blood at birth (pH <7.05 and base deficit >12 mmol/l) and pH <7.00, both of which are associated with neonatal morbidity.6-8 Secondary end points were operative interventions (cesarean, ventouse, and forceps deliveries), Apgar scores <7 at five minutes, and admissions to neonatal intensive care units.

**Biochemical analyses and clinical guidelines**—Lactate was measured with a commercially available micro-volume test strip device. A commercial company performed regular quality checks of the acid-base measurements. Each month we sent all departments water soluble standard solutions for analysis and compared results between the different analysers. The microvolume test device was also tested for lactate content in the solutions. Guidelines for interpretation of the blood analyses were as follows: pH >7.25 normal, 7.21-7.25 pre-acidaemia, <7.21 acidaemia. Corresponding values for lactate were <4.2 mmol/l normal, 4.2-4.8 mmol/l pre-acidaemia, >4.8 mmol/l acidaemia.9 In cases of pre-acidaemia, we recommended repeat sampling of fetal scalp blood within 20-30 minutes if no other indication for intervention was present.

**Statistical analyses**—From our sample size calculation we needed 2872 participants (1436 in each arm). See bmj.com. An independent steering committee recommended we close the study after 3000 cases. We used χ² tests and relative risks with 95% confidence intervals to compare the pH and lactate groups.

**RESULTS**

Of the 2992 included women, 1496 were equally randomised to management by scalp blood pH and lactate determinations. There were no significant differences between the two groups in metabolic acidaemia or pH <7.00 in cord artery blood at birth. Operative interventions and the indication of fetal distress were also similar in the study groups (table 1).

The number of missing samples for measuring cord artery blood pH or full acid-base balance was higher in the pH group than in the lactate group. Among these cases, the rates of Apgar scores <7 at five minutes, operative interventions, and admissions to neonatal intensive care units were similar to the rates in the whole trial.

Scalp blood was sampled from one to nine times in each fetus. In the pH group, successful sampling or analysis was performed in 1908 fetuses with a total of 1628 analyses of pH. Corresponding figures in the lactate group were 1355 and 2301. For all pH analyses the mean value was 7.29 (SD 0.08, range 6.88-7.54). Mean lactate concentration in scalp blood was 3.5 (SD 1.8) mmol/l (range 0.8-15.9 mmol/l). Table 2 shows primary and secondary outcomes in relation to scalp blood pH or lactate values.

Protocol violation, when the patient was randomised to management by one of the methods but the clinician changed to the alternative method, occurred six times more often in the pH group than in the lactate group.

We carried out a subanalysis of outcome according to use of ST analysis of the fetal electrocardiogram as an adjunct to cardiotocography and found no significant difference in the rate of metabolic acidaemia. See bmj.com.

**DISCUSSION**

This large randomised trial of the effectiveness of pH and lactate analyses in fetal scalp blood in the clinical management of intrapartum fetal distress and prevention of acidaemia at birth found no significant difference in the rate of metabolic acidaemia with either method. The risk difference of −0.3 percentage point was present.

20-30 minutes if no other indication for intervention was present. We changed to the alternative method, occurred six times more often in the pH group than in the lactate group.

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**Table 1** Obstetric and neonatal outcome in groups according to method of monitoring for hypoxia analysed according to intention to treat. Figures are numbers (percentages)

<table>
<thead>
<tr>
<th></th>
<th>pH (n=1496)</th>
<th>Lactate (n=1496)</th>
<th>Relative risk for lactate vs pH (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic acidaemia*</td>
<td>47 (3.6)</td>
<td>44 (3.2)</td>
<td>0.91 (0.61 to 1.36)</td>
<td>0.63</td>
</tr>
<tr>
<td>pH&lt;7.00</td>
<td>24 (1.8)</td>
<td>21 (1.5)</td>
<td>0.84 (0.47 to 1.50)</td>
<td>0.56</td>
</tr>
<tr>
<td>pH&lt;7.10</td>
<td>131 (9.9)</td>
<td>121 (8.8)</td>
<td>0.89 (0.70 to 1.12)</td>
<td>0.32</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>415 (27.7)</td>
<td>452 (30.2)</td>
<td>1.09 (0.97 to 1.22)</td>
<td>0.14</td>
</tr>
<tr>
<td>Forceps/ventouse‡</td>
<td>416 (38.5)</td>
<td>370 (35.4)</td>
<td>0.92 (0.82 to 1.03)</td>
<td>0.15</td>
</tr>
<tr>
<td>ODFD</td>
<td>571 (38.2)</td>
<td>580 (38.8)</td>
<td>1.02 (0.93 to 1.11)</td>
<td>0.77</td>
</tr>
<tr>
<td>Apgar &lt;7 at 5 min</td>
<td>40 (2.7)</td>
<td>46 (3.1)</td>
<td>1.15 (0.76 to 1.75)</td>
<td>0.51</td>
</tr>
<tr>
<td>NICU admission</td>
<td>164 (11.0)</td>
<td>167 (11.2)</td>
<td>1.02 (0.83 to 1.25)</td>
<td>0.86</td>
</tr>
</tbody>
</table>

**Hypoxic ischaemic encephalopathy:**

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Moderate</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

NICU=neonatal intensive care unit; ODFD=operative delivery because of fetal distress.
*pH <7.05 +base deficit >12 mmol/l. Samples for measuring cord artery acid-base balance missing in 181 in pH group and 136 in lactate group.
‡Samples for measuring pH missing in 174 in pH group and 120 in lactate group.
*Percentage calculated in vaginal deliveries.
points and the confidence interval for the difference (−1.6 to 1.0 percentage points) indicate that there is no clinically significant difference either. Blood sampling and assessments were more successful for lactate than for pH, mainly because of the smaller amount of blood needed for lactate analysis.

Failure of sampling and analysis
The higher failure rate with pH determination was significant and led to protocol violations on 155 (10.4%) occasions in this group compared with 18 cases (1.2%) in the lactate group. Previous publications have reported failure rates with pH blood sampling or analysis in 11–21%.[2,23] Our failure rate with lactate analyses (1.2%) was similar to that previously reported (1.7%).[4] Both sampling and analysis are much quicker with lactate analysis,[2] thus minimising the risk of delay in clinical management.

Neonatal outcome
We found no significant differences in the rates of acidaemia at birth between the study arms or any differences in the rates of low Apgar scores at five minutes or admissions to neonatal intensive care units. A previous randomised controlled trial found similar results.[2] See bmj.com.

The prevalence of hypoxic ischaemic encephalopathy was only 4/1000 making it impossible for us to use it as an end point to be able to show significant differences. Our primary end points—metabolic acidaemia and pH <7.00—were also rare. The low prevalence of acidaemia at birth in Western populations made calculations of sample size realistic only for showing large differences in outcome (50–100%). This is also why the confidence intervals are wide. As the actual rate of metabolic acidaemia in the pH arm was higher than initially estimated, however, the study had the power to evaluate smaller differences between the study arms than initially expected.

Operative interventions
As expected (because of how we derived cut-off values for recommended interventions) operative interventions in terms of instrumental vaginal or caesarean deliveries were evenly distributed. Fetal scalp blood sampling has not been used in the United States for many years.[10] Availability of a simple bedside method might reintroduce it into clinical practice and could help to reduce their high rate of caesarean section.

Fetal scalp blood acidaemia
We had around 40% more lactate analyses than pH analyses to evaluate. Scalp blood analysis also identified a higher proportion of acidaemia in the lactate arm than in the pH arm. The proportion of neonates with acidaemia at birth was slightly lower when we used lactate analyses, a difference that was not significant. The only significant difference between the study arms was an increased proportion of operative delivery indicated by acidaemia or pre-acidaemia in the lactate group. Clinicians claimed that previous experience with pH analysis made them more confident in managing timing for intervention with this method compared with the new lactate device.

Sampling fetal scalp blood is a diagnostic test in cases with worrying results on cardiotocography. When one test has yielded alarming results, it is extremely important that an additional test has a low frequency of “false negatives.” In this study six babies had pH <7.00 and 10 had metabolic acidaemia at birth when fetal scalp blood pH was >7.20 determined within 60 minutes of delivery. Corresponding figures for cases with scalp blood lactate <4.8 mmol/l were none with pH<7.00 and six with metabolic acidaemia.

Single or combined analyses
The combined measurement of pH and lactate is no better at predicting abnormal outcome than each method individually.[9,11] If combined analyses are carried out, however, a high lactate value indicates action, even if the pH is normal. Severely depressed newborns have been reported with this combination of findings.[9]

Weakness of the trial
A potential cause of bias was that larger numbers of values for cord artery acid-base balance were missing in the pH group, which theoretically could have concealed cases with acidaemia at birth.

Conclusions
Lactate analysis and pH analysis of fetal scalp blood had comparable results in the management of intra-partum fetal distress. We found no significant differences in birth acidaemia, operative interventions, low

Table 2 | Primary and secondary outcomes in relations to scalp blood values (normal, pre-acidaemia or acidaemia[9]). Figures are fetuses in whom fetal scalp blood was collected within 60 minutes of delivery (percentage of cases in each group)

<table>
<thead>
<tr>
<th>Fetal scalp blood pH (n=508)</th>
<th>Fetal scalp blood lactate (n=684)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic acidaemia &gt;7.25 (n=281)</td>
<td>7.25-7.21 (n=92)</td>
</tr>
<tr>
<td>pH &lt;7.00</td>
<td>4 (1.4)</td>
</tr>
<tr>
<td>Apgar &lt;7 at 5 minutes</td>
<td>9 (3.2)</td>
</tr>
<tr>
<td>ODFD</td>
<td>81 (28.8)</td>
</tr>
</tbody>
</table>

| Metabolic acidaemia | 7 (2.5) | 3 (3.3) | 10 (7.4) | 6 (1.7) | 0 | 19 (7.1) |
| pH <7.00 | 4 (1.4) | 2 (2.2) | 5 (3.7) | 6 (1.7) | 0 | 19 (7.1) |
| Apgar <7 at 5 minutes | 9 (3.2) | 2 (2.2) | 10 (7.4) | 4 (1.2) | 1 (1.4) | 23 (8.6) |
| ODFD | 81 (28.8) | 58 (63.0) | 118 (87.4) | 79 (23.0) | 50 (68.5) | 251 (94.0) |

ODFD=operative delivery because of fetal distress.

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At worst, replacement of pH measurement with lactate measurement could result in a one third increase in acidaemia at delivery.

**WHAT IS ALREADY KNOWN ON THIS TOPIC**

Fetal scalp blood can be tested for hypoxia in fetuses with worrying intrapartum heart rate traces.

pH analysis has a sampling or analysis failure rate of 11-20% and has been excluded from clinical practice in the US.

**WHAT THIS STUDY ADDS**

There was no difference between assessment of fetal acidaemia with lactate analysis or pH analysis.

At worst, replacement of pH measurement with lactate measurement could result in a one third increase in acidaemia at delivery.

Apgar scores at five minutes, or admissions to neonatal intensive care units. Sampling failure was more common in the pH group. Combined analyses are not recommended as they are likely to increase the number of interventions without decreasing metabolic acidaemia at birth.

We thank all the women who took part in the trial and the obstetricians and midwives who recruited patients and managed their labours. The following hospitals took part: Danderyd, Kalmar, Karlstad, Karolinska, Lund, Söder Hospital, Trollhättan, Örebro, Gothenburg, Linköping. We also thank Hans Pettersson, Department of Biostatistics, Karolinska Institute at Söder Hospital, Stockholm, Sweden, for excellent statistical advice. The independent steering committee comprised Sven Cnattingius, Bengt Persson, Magnus Westgren, Karolinska Institutet, Stockholm, Sweden. Contributors: See bmj.com.

**ABSTRACT**

**Objective** To examine whether doctors’ global assessments of treatment effects agree with patients’ global assessments.

**Design** Survey of trials included in systematic reviews of treatments for diverse conditions.

**Data sources** Cochrane database of systematic reviews.

**Data extracted** Data on patients’ global assessments and on doctors’ global assessment for the same treatment against the same comparator.

**Main outcome measures** Relative odds ratio (ratio of odds ratios of global improvement with the experimental intervention versus control according to doctors compared with patients), and improvement rates according to doctors and patients.

**Results** Doctors’ global assessments were compared with patients’ global assessments for 63 different treatment comparisons (240 trials) in 18 conditions. The summary relative odds ratio across the comparisons was not significant (0.98, 95% confidence interval 0.88 to 1.08; I²=0%, 95% confidence interval 0% to 30%). In 62 of the 63 comparisons the effects of treatment rated by patients and by doctors did not differ beyond chance, but for single comparisons the confidence intervals were large. Rates of improvement on average did not differ for single comparisons (summary relative odds ratio 0.98, 0.88 to 1.06; I²=0%, 0% to 24%).

**Conclusion** Doctors’ global assessments of the effects of treatments are on average similar to those of patients.

**INTRODUCTION**

Several studies have evaluated whether global assessment in specific conditions and settings is more appropriate done by patients than by doctors. Some