Screening of foetal distress by assessment of umbilical cord lactate

F. Borruto[1], C. Comparetto[2], E. Wegher[3], A. Treisser[3]

[1]Department of Obstetrics and Gynaecology and Genetic Biology, University of Verona (Italy)
[2]Division of Obstetrics and Gynaecology, City Hospital, Azienda U.S.L. 4 Prato (Italy)
[3]Department of Obstetrics and Gynaecology, Princess Grace Hospital, Monaco (Principality of Monaco)

Summary

Purpose of investigation: Studies on umbilical cord blood for determination of lactate indicate that high levels seem to be correlated to foetal metabolism for anaerobic glycolysis taking place in oxygen-deprived tissues of the foetus. These findings may be of particular-deprived clinical importance when foetal distress or foetal hypoxemia is caused by perinatal events.

Methods: The maternal and foetal heart rates, acid-base values measured and the outcome of 94 pregnancies complicated by intrapartum foetal asphyxia have been reviewed, and the maternal and foetal acid-base and lactate levels during the course of labour and at delivery were studied in patients with evidence of metabolic acidosis. Lactate concentrations were measured during labour and at delivery in blood samples obtained from the foetal presenting part and from the umbilical cord with the use of a rapid electrochemical technique. The foetuses were evaluated by means of the Apgar score, intrapartum cardiotocography, observation of the presence of meconium stained amniotic fluid, and clinical features of distress at birth.

Results: Evidence of clinical foetal distress was not related to the severity of the asphyxia. An increased lactate level was found in asphyctic infants and a clear correlation between lactic acidosis and foetal distress was documented. Low Apgar scores were observed in infants with moderate or severe asphyxia at delivery. Scalp lactate correlated significantly with umbilical artery lactate, but not with 1-min or 5-min Apgar scores. The lactate concentration was higher in cases of instrumental delivery compared to spontaneous delivery. No perfect correlation was found between lactate level and neonatal outcome but there were not a significant number of neonates with immediate complications. The rate of forceps delivery in the distress group was significantly higher than that of the healthy foetuses, so spontaneous labour was less frequently associated with foetal distress than instrumental delivery. In the distress group, severe variable decelerations were generally recorded in the second stage of labour. The incidence of neonatal Apgar score ≤ 7 in neonates with abnormal baseline foetal heart rate (FHR) was higher than in those with severe variable decelerations, mild variable decelerations, and transient tachycardia. Duration of the active second stage of labour was significantly with the presence of foetal lactate at the time of crowning of the foetal head and the presence of lactate in umbilical arterial and vein blood at delivery. Expulsion time ≥ 45 minutes, compared with shorter active second stage, and acidaemia at birth implied larger arterial-venous lactate differences. The presence of foetal lactate at crowning was also significantly associated with the level of umbilical arterial-venous lactate difference.

Conclusion: Lactate and pH values provide the best parameters to distinguish between asphyctic and normal newborns, with lactate having the most discriminating power. The prospective value of the discrimination functions derived from lactate and pH data is good when the foetuses are allocated into normal parameters but poor when an attempt is made to allocate the foetuses into pathologic ones, with a high false-negative rate. However, the discriminating ability is improved when pathologic foetuses are included into one single abnormal group. These results confirm the potential use of rapid foetal blood lactate measurements for the early diagnosis of intrapartum foetal distress.

Key words: Lactate; Foetal distress; Umbilical cord; Foetal asphyxia; Metabolic acidosis.

Introduction

Acid-base assessment of foetal blood with identification of metabolic acidosis provides an accurate objective diagnosis of intrapartum foetal asphyxia.

Metabolic acidosis at delivery is principally caused by hyperlactatemia resulting from the tissue oxygen debt accompanying foetal asphyxia. Hypoxemia is one mechanism contributing to this foetal asphyxia and tissue oxygen debt. This evidence of foetal asphyxia develops during the last half and principally during the last two hours of the intrapartum period [1].

The evidence of foetal asphyxia tends to appear earlier in patients with maternal medical and obstetric complications than in those with labour complications [2].

The blood present in the human umbilical cord increases its lactate concentration by about + 4 mg/l/min, on average. This is due to the high metabolic activity of foetal erythrocytes, but is also a result of the action of the cord tissue itself. This tissue, after elimination of blood, results in a high concentration of lactate, which increases when the cord is kept at room temperature, reaching and rising above 1 or 2 g/kg after many hours. This glycolytic process indicates that cord tissue has a metabolic activity which seems to be in relation to the high lactate concentration of the amniotic fluid [3].

Venous-blood lactate level is highest in women and in the umbilical card blood of newborns at the time of delivery (in particular, during the passage of the foetal head through the genital canal). The return of normal lactate values occurs at the same time in mothers and newborns.

Preliminary data of this work were presented at the national SIGO conference in Bologna, September 20-24, 2005 and received the "Francesco Bottiglioni" award for best scientific presentation.

Revised manuscript accepted for publication October 9, 2006

In several cases of labour with complications which were not induced pharmacologically, the lactate levels are no different from those observed during spontaneous labour [4].

Delay in cord clamping after vaginal delivery increases the blood volume of the newborn. Similar effects have also been observed in caesarean section births. Other effects of delayed cord clamping in caesarean section have not been investigated. Significantly lowered PO_2 and pH values and elevated plasma lactate levels have been observed in infants with three minutes' delay in clamping when compared with the early clamping group. Thus, when healthy mature newborns are considered, early clamping of umbilical cord in caesarean section with general anaesthesia is preferable to late clamping [5].

Materials and Methods

To assess the predictive value of acidosis at birth for perinatal brain damage, alone or in combination with the 5-min Apgar score, a cohort of 94 liveborn infants delivered over a two-year time period (2004-2005) was studied prospectively. This prospective observational study was conducted on foetal scalp blood samplings. We compared the measurement of lactate in foetal scalp and umbilical artery blood and reviewed the clinical characteristics of the pregnancies complicated by intrapartum foetal asphyxia (14 cases, 14.9%). Foetal lactate characteristics were also analysed in patients who delivered an infant with evidence of metabolic acidosis at delivery by reviewing the clinical situation and foetal heart rate (FHR) and their sequelae. We measured umbilical cord blood lactate levels by analysing umbilical arterial and venous blood samples at delivery which allowed for the measurement of infant lactic acid levels. All samples were analysed immediately for lactate levels. The umbilical cord was double clamped, and lactate concentration was successfully determined in all infants. Reference values defining acidosis (mean ± 2 standard deviations, SD) were obtained from the infants who had no complications (80 cases, 85.1%). Foetal scalp blood samples were obtained during labour and umbilical artery blood samples were obtained at birth. Foetal scalp blood samples were collected at cervical dilatations between 4 cm and 10 cm. In this way, we evaluated the validity and the feasibility of foetal scalp lactate sampling during labour in the assessment of non reassuring foetal status. Scalp lactate measurements were compared to neonatal cord blood lactate levels and Apgar scores. Values were considered pathological when scalp lactate was > 5 mmol/l, cord arterial lactate > 6.35 mmol/l, and Apgar score < 7 at 1 and 5 min. Our series included neonates with a mean gestational age of 38 (± 3.1) weeks. All neonates in the distress group had abnormal foetal heart monitoring patterns. The abnormal patterns included abnormal baseline FHR, severe variable decelerations, mild variable decelerations, and tachycardia. Twenty-minute foetal heart monitoring was performed during the second stage of labour.

Statistical analysis was carried out with the Student's t-test.

Results

Evidence of clinical foetal distress was present in 11 newborns (11.7%) and was not related to the severity of the asphyxia. An increased lactate level was found in asphyctic infants. Nine cases (9.5%) presented lactic acidosis which continued to be persistent in five of them one hour after delivery. A clear correlation between lactic acidosis and foetal distress was documented. The incidence of high lactate concentration was 8.5% (8 out of 94), and low Apgar score at 5 min (≤ 7) 6.3% (6 out of 94). Low Apgar scores occurred in infants with moderate or severe asphyxia at delivery. Two of the eight infants with acidosis (25%) had low Apgar scores, and one out of two infants (50%) with low Apgar scores had acidosis. The mean lactate value was 1.8 ± 0.7 mmol/l. The mean lactate concentration in the umbilical artery immediately after delivery was 3.8 ± 1.1 mmol/l. Scalp lactate correlated significantly with umbilical artery lactate ($p = 0.49$, $p = 0.01$), but with neither Apgar score at 1 min ($R = -0.21$, ns) nor at 5 min ($R = -0.11$, ns). Data were presented as mean and SD. In the series the mean umbilical artery lactate concentration was 3.82 (± 1.70) mmol/l. The 97th percentile of lactate was 7.64 mmol/l. Lactate concentration was higher in cases of instrumental delivery compared to spontaneous delivery: 4.76 versus 3.87 mmol/l ($p = 0.0001$). No perfect correlation was found between lactate level and neonatal outcome but the number of neonates with immediate complications was not significant. The rate of forceps delivery in the distress group was significantly higher than that of the healthy foetuses ($p < 0.01$), thus the rate of spontaneous labour was significantly lower than the instrumental delivery rate ($p < 0.01$) in the distress group. Severe variable decelerations generally were recorded in the distress group in the second stage of labour. The incidence of neonatal Apgar score ≤ 7 in neonates with abnormal baseline FHR was higher than for those with severe variable decelerations, mild variable decelerations, and transient tachycardia ($p < 0.05$). As for the neonatal umbilical artery lactate levels, the average for neonates with abnormal baseline FHR was 4.66 (± 0.12) mmol/l and for neonates with severe variable decelerations it was 3.95 (± 0.29) mmol/l, all significantly higher than the other groups ($p < 0.01$). In the neonates with mild variable decelerations it was 2.74 (± 0.21) mmol/l, in neonates with tachycardia it was 2.66 (± 0.35) mmol/l, and there were no significant differences between the neonates with mild variable decelerations and tachycardia and the others ($p > 0.05$). Duration of the active second stage was significantly associated with foetal lactate ($p < 0.001$) at the time of crowning of the foetal head, and lactate levels in umbilical arterial and venous blood at delivery ($p < 0.001$). Expulsion time ≥ 45 minutes, compared with a shorter active second stage of labour, and acidaemia at birth implied larger arterial-venous lactate differences ($p < 0.001$). Foetal lactate levels at crowning were also significantly associated with the umbilical arterial-venous lactate difference ($p = 0.03$). In newborn infants clinical evidence of cerebral abnormality was observed in 0.3%, and evidence of respiratory distress syndrome (RDS) was seen in 0.3% of the study group. At one year of age two infants (2.1%) were lost to follow-up and two (2.1%) had an adverse outcome unrelated to asphyxia; 90 infants (95.7%) showed normal development but the possible sequelae of asphyxia included one death (1%), slight

abnormalities in five infants (5.3%), and clear abnormalities in two (2.1%). The sensitivity and the positive predictive value of high lactate concentrations for adverse outcome were, respectively, 14% and 7%, and of low 5-min Apgar score 14% and 21%.

Discussion

Arterial blood lactate is a reliable indicator of tissue oxygen debt and is of value in expressing the degree and prognosis of circulatory failure as a result of various diseases [6].

Relevant clinical factors in cases of asphyxia include the preterm foetus, the intrauterine growth retarded (IUGR) foetus, maternal toxemia, and midforceps delivery. Duration of developing metabolic acidosis in asphyxia ranges from terminal to the last two hours of labour. Marked patterns of total decelerations and moderate and marked patterns of late decelerations are of predictive value in the diagnosis of intrapartum foetal asphyxia with a trend to an increased incidence in the longer duration categories, between four and two hours prior to delivery, and a significant increase in all categories during the last two hours of labour. The significance of intrapartum foetal asphyxia in the newborn infant is evident from the low Apgar scores, increased incidence of moderate and severe RDS, and central nervous system (CNS) complications in the asphyxia group in relation to a normal group [7].

A study [8] attempted to determine the major source of lactate in the normal and in the distressed human foetus, in order to assess the applicability of foetal blood lactate measurement for the evaluation of foetal stress during labour. In vigorous newborns (1-min Apgar score ≥ 7), umbilical arterial and venous lactate levels were lowest with elective caesarean section done before the onset of labour, higher with caesarean section performed during labour, and highest at the time of vaginal delivery ($p < 0.001$). Foetal lactate levels were also significantly higher than maternal lactate levels in vigorous newborns ($p < 0.01$), the lactate difference between umbilical artery and maternal artery being lowest with elective caesarean section, higher with caesarean section performed during labour, and highest with vaginal delivery ($p < 0.02$). Distressed newborns (1-min Apgar score < 7) had higher umbilical lactate levels and higher fetomaternal lactate differences than vigorous newborns ($p < 0.01$).

In another study, to assess the predictive value for perinatal brain damage of acidosis at birth, alone or in combination with the 5-min Apgar score, a cohort of liveborn infants delivered over two months was studied prospectively. The sensitivity and the positive predictive values of low pH for adverse outcome were, respectively, 21% and 8%, of high lactate concentration 12% and 5%, and of low 5-min Apgar score 12% and 19%. According to this study, metabolic acidosis determined in the blood from the umbilical artery at birth is a poor predictor of perinatal brain damage [9].

Lactate, pH, PO_2, and PCO_2 were determined in arterial, venous, and free-flowing mixed umbilical cord blood obtained from deliveries of apparently healthy neonates. The goals of this study were to establish reference ranges for lactate and pH against which results in cases of high-risk labour and delivery could be compared, to see how the gases correlated with these values, and to determine whether easily accessible mixed umbilical cord blood can serve as the sample in lieu of cord arterial or cord venous blood. It was concluded that less than 2.5% of deliveries of apparently healthy neonates have arterial, venous, or mixed cord lactate levels ≥ 7.0 mmol/l and pH ≤ 7.15, neither cord venous PO_2 nor PCO_2 correlate well with cord venous lactate, and readily available mixed cord blood is a satisfactory specimen for the measurement of venous cord lactate [10].

Regular cord blood analysis postpartum is regarded by many as one of the most accurate and objective methods of auditing intrapartum care. Emergency caesarean section and ventouse deliveries, due to the threat of asphyxia, are examples where postpartum acid-base data from the umbilical artery ought to be a must. Cord blood acid-base data are a superior method of retrospective analyses of cardiotocographic tracings and partograms within a quality control programme relating to intrapartum care. However, routines for cord blood sampling must be well established in both the delivery room and in the operating theatre to obtain samples from the umbilical artery in cases of threatening intrapartum asphyxia [11].

A prospective observational study was conducted on the effect of delayed sampling from arteries and veins that were double clamped to isolate the blood from the placenta (clamped), and from vessels that were not isolated from the placenta (unclamped). Paired samples taken from clamped and unclamped vessels at 0, 20, 40, and 60 minutes were analysed for lactate, base excess, pH, and PCO_2. Data were analysed as the change from time 0 at 20, 40, and 60 minutes. Arterial and venous lactate levels were significantly higher than at time 0 by 20 minutes in both clamped and unclamped vessels. Changes in unclamped vessels were greater than in clamped vessels. The pH remained unchanged over 60 minutes in clamped vessels but changed markedly in unclamped vessels. Base excess changed significantly in both clamped and unclamped vessels. Cord blood samples taken after a 20-minute delay are unreliable for lactate measurement, even if the vessel has been double-clamped to isolate the blood from the placenta. Current guidelines which state that blood can be sampled from a clamped cord for up to one hour after delivery should not apply to the interpretation of lactate or base excess. Delayed blood gases from unclamped cords are very unreliable [12].

Conclusion

Cord blood lactate at birth is a marker of antenatal hypoxia, and is comparable to pH as a prognostic tool. The blood lactate levels in both mother and foetus increase with labour and reach their highest values at the

time of vaginal delivery. The lactate levels are highest in the umbilical artery, lower in the umbilical vein, and lowest in the maternal artery before the onset of labour. This also suggests that, under conditions that lead to neonatal depression, the foetus is the major source of the increased lactate produced, with a smaller contribution from the placenta. The foetal lactate level may be a good indicator of foetal stress in labour [13].

References

[1] Low J.A., Pancham S.R., Worthington D., Boston R.W.: "The acid-base and biochemical characteristics of intrapartum foetal asphyxia". *Am. J. Obstet. Gynecol.*, 1975, *121*, 446.

[2] Low J.A., Pancham S.R., Worthington D., Boston R.W.: "Clinical characteristics of pregnancies complicated by intrapartum foetal asphyxia". *Am. J. Obstet. Gynecol.*, 1975, *121,* 452.

[3] Vincent D., Notter A.: "Lactic acid in the human umbilical cord. Influence of glycolysis in the blood in cord and in cordonal tissue". *J. Gynecol. Obstet. Biol. Reprod. (Paris)*, 1979, *8*, 289.

[4] Bargiel Z., Kobus E., Wasilewska E.: "Changes in plasma lactate concentration in women in labour and their newborns within the first days of life". *Acta Physiol Pol.*, 1980, *31,* 21.

[5] Erkkola R., Kero P., Kanto J., Korvenranta H., Nanto V., Peltonen T.: "Delayed cord clamping in caesarean section with general anaesthesia". *Am. J. Perinatol.*, 1984, *1,* 165.

[6] Fauchere J.C., Bauschatz A.S., Arlettaz R., Zimmermann-Bar U., Bucher H.U.: "Agreement between capillary and arterial lactate in the newborn". *Acta Paediatr.,* 2002, *91,* 78.

[7] Low J.A., Pancham S.R., Piercy W.N., Worthington D., Karchmar J.: "Intrapartum foetal asphyxia: clinical characteristics, diagnosis, and significance in relation to pattern of development". *Am. J. Obstet. Gynecol.,* 1977, *129*, 857.

[8] Vincent D., Notter A., Cellier-Chapuis C.: "Lactate dehydrogenase and its isoenzymes in human umbilical cord tissue". *C R Seances Soc Biol Fil*, 1978, *172,* 1162.

[9] Ruth V.J., Raivio K.O.: "Perinatal brain damage: predictive value of metabolic acidosis and the Apgar score". *Br. Med. J.,* 1988, *297,* 24.

[10] Shirey T., St Pierre J., Winkelman J.: "Cord lactate, pH, and blood gases from healthy neonates". *Gynecol. Obstet. Invest.,* 1996, *41,* 15.

[11] Bulkmans N., Lyrenas S., Hallberg G., Niklasson F.: "Umbilical cord blood sampling – A tool for delivery quality control?". *Acta Obstet. Gynecol. Scand.*, 1997, *76,* 419.

[12] Armstrong L., Stenson B.: "The effect of delayed sampling on umbilical cord arterial and venous lactate, and blood gases in clamped and unclamped vessels". *Arch. Dis. Child Foetal Neonatal* (ed.), 2006 Apr 25; [Epub ahead of print].

[13] Suidan J.S., Wasserman J.F., Young B.K.: "Placental contribution to lactate production by the human fetoplacental unit". *Am. J. Perinatol.,* 1984, *1*, 306.

Address reprint requests to:
C. COMPARETTO, M.D.
Via Castelfidardo, 33
50137 Firenze (Italy)