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Research Article

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Umbilical Cord Blood Lactate Levels in Newborns with Perinatal Asphyxia

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Abstract

Objectives: *This present study aims to evaluate whether increasing levels of cord blood lactate is associated with perinatal asphyxia by using the commonly practised APGAR score as the gold standard.*

Methods: *We performed a descriptive cross sectional study between April 2014 and April 2015 at Hue Medical University Hospital, Vietnam. 106 newborn babies (41 asphyxiaand 65 normal babies) were included in the study. Umbilical cord blood is sampled for lactate analysis.*

Results: *Umbilical cord blood lactate levels were significantly higher among infants born with asphyxia (mean 7.71± 0.27, range 4.74 – 11.96) compared to that with normal infants (mean 5.56± 1.71, range 1.32 – 10.82). Overall accuracy was very good, with area under ROC curve of 0.803 (95% CI: 0.750–0.936). The optimal cutoff point for umbilical cord blood lactate level of 6.97 mmol/l to diagnose asphyxia had a sensitivity 58.5% (95% CI: 42.1 - 73.7), specificity 89.2% (95% CI: 79.1 - 95.6), +ve LR (likelihood ratio) 5.44, -ve LR 0.46.*

Conclusion: *Umbilical cord blood lactate is very good in confirming the diagnosis of asphyxia and following up in newborn babies.*

Keywords: Umbilical Cord Blood Lactate, Perinatal Asphyxia, Apgar

Introduction

Perinatal asphyxia is defined as an oxygen deprivation that occurs around the time of birth and may be caused by several perinatal events. It is also stated as evolution from the utilization of a single indicator such as low Apgar score or delayed respiration to a multiple indicators approaches focusing especially on the neurological damage [1]. About one-quarter of all neonatal deaths are caused by perinatal asphyxia in worldwide [2]. Perinatal asphyxia is responsible for 23% neonatal deaths in low-income countries. This finding underlines that perinatal asphyxia is still a burden of the world [3-6]. The outcome of perinatal asphyxia includes immediate complications like hypoxic ischemic encephalopathy, shock or even death and long term problems like mild cognitive defects, seizure disorders and mild to severe neurological disability [6].

It is difficult to accurately assess the incidence of perinatal asphyxia because of non uniform clinical criteria on which different institutions base their definition. The incidence of asphyxia varies between 1% and 5% depending on the criteria used in making the diagnosis [7]. There is no ideal measure to assess perinatal asphyxia in clinical practice. The commonly used Apgar score has been shown to be not specific for hypoxia and has a weak relationship with biochemical evidence of asphyxia [8-11].

The challenge is to identify markers that can help to nullify the subjective errors that may arise while using APGAR score to diagnose asphyxia in new born clinically and to predict the risk of future problems objectively. Lactate in the cord blood, the specific end product of anaerobic metabolism may have the potential for this purpose. It is wiser to rely on two efficient parameters than a single one to make a critical diagnosis of a disease [12-13].

This present study aims to evaluate whether increasing levels of cord blood lactate isassociated with perinatal asphyxia by using the commonly practised APGAR score as the gold standard.

Materials and Methods

Patients

We performed a descriptive cross sectional study between April 2014 and April 2015 at Hue Medical University Hospital, Vietnam. 106 newborn babies (41 asphyxia and 65 normal babies) were included in the study. A proforma was prepared to collect relevant information of each baby. Approval was obtained from institutional ethics committee. Informed written consent was obtained from the parents of the babies considered for the study. Apgar score was used to differentiate normal babies and those babies subjected to asphyxial insult

Measurements

Umbilical cord blood is sampled by nursing personnel immediately after delivery for all infants deemed to be viable. Umbilical blood samples were drawn from a double-clamped segment of the umbilical

cord into 2-ml plastic syringes flushed with a heparin solution. Blood lactate were measured using whole blood in automated benchtop analyzers. The DXC-800 Automated Chemistry Analyser (Beckman Coulter) was used for lactate assays. Obtained data was recorded in a newborn's notes. Apgar score at 1 minute after birthwas determined by a trained midwife, an obstetrician or a pediatrician.

Data analysis

Apgar score was used to identify perinatal asphyxia in the new born. Those babies with apgar score of ≤ 7 were considered to have had perinatal asphyxial insult and those with ≥ 8 were taken as normal. The latter were the reference babies for validating the biochemical parameters against the gold standard apgar score in diagnosing perinatal asphyxia. Receiver-operating characteristic curve (Med CALC) was employed to know the clinical decision limit and diagnostic ability of these biochemical variables to diagnose perinatal asphyxia. The cut off values thus obtained for lactate were used in the further validation of these biochemical variables (sensitivity, specificity, likelihood ratios and predictive values) by comparison with Apgar score taken as the gold standard.

Results

106 babies (41 asphyxia and 65 normal babies) with singleton, liveborn infants with no major anomalies delivering between April 2015 to April 2016 were analysed. Gestational age ranged from 35 to 41 weeks (mean 37,41 ± 0,31 weeks). Umbilical cord blood lactate levels were significantly higher among infants born with asphyxia (mean 7.71± 0.27, range 4.74 – 11.96) compared to that with normal infants (mean 5.56± 1.71, range 1.32 – 10.82), p<0.05 (figure 1). Each step-wise increase in the umbilical cord blood lactate level cutoff point lowered the sensitivity, but increased the specificity for perinatal asphyxia (Table 1). Next we present a ROC curve for umbilical cord blood lactate level for asphyxia (Figure 2). Using ROC analysis, we selected an optimal cutoff point for umbilical cord blood lactate level of 6.97 mmol/l to diagnose asphyxia (area under the curve 0.803). Umbilical cord blood lactate level ≥ 6.97 mmol/l had a sensitivity 58.5% (95% CI: 42.1 - 73.7), specificity 89.2% (95% CI: 79.1 - 95.6), +ve LR (likelihood ratio) 5.44, -ve LR 0.46 for asphyxia (Table 1).

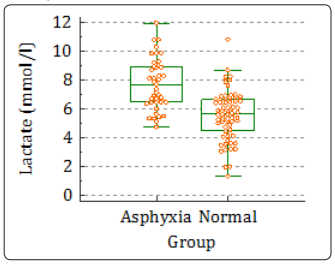

Figure 1: Comparision umbilical cord blood lactate level between asphyxia and normal group

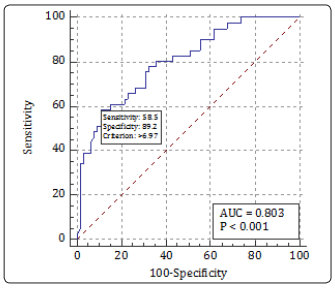

Figure 2: ROC (Receiver –operating characteristic) curves of cord blood Lactate in the diagnosis Perinatal asphyxia. Overall accuracy was very good, with area under ROC curve of 0.803 (95% CI: 0.750–0.936), p<0.001.

Table 1: Criterion values and coordinates of the ROC curve

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	-LR
≥1.32	100.00	91.4 - 100.0	0.00	0.0 - 5.5	1.00	
>4.52	100.00	91.4 - 100.0	26.15	16.0 - 38.5	1.35	0.00
>4.74	97.56	87.1 - 99.9	26.15	16.0 - 38.5	1.32	0.093
>5.12	97.56	87.1 - 99.9	32.31	21.2 - 45.1	1.44	0.075
>5.12	95.12	83.5 - 99.4	32.31	21.2 - 45.1	1.41	0.15
>5.26	95.12	83.5 - 99.4	38.46	26.7 - 51.4	1.55	0.13
>5.32	90.24	76.9 - 97.3	38.46	26.7 - 51.4	1.47	0.25
>5.36	90.24	76.9 - 97.3	44.62	32.3 - 57.5	1.63	0.22
>5.48	85.37	70.8 - 94.4	44.62	32.3 - 57.5	1.54	0.33
>5.61	85.37	70.8 - 94.4	49.23	36.6 - 61.9	1.68	0.30
>5.64	82.93	67.9 - 92.8	49.23	36.6 - 61.9	1.63	0.35
>5.89	82.93	67.9 - 92.8	56.92	44.0 - 69.2	1.93	0.30
>5.99	80.49	65.1 - 91.2	56.92	44.0 - 69.2	1.87	0.34
>6.1	80.49	65.1 - 91.2	64.62	51.8 - 76.1	2.27	0.30
>6.37	78.05	62.4 - 89.4	64.62	51.8 - 76.1	2.21	0.34
>6.42	78.05	62.4 - 89.4	67.69	54.9 - 78.8	2.42	0.32
>6.43	75.61	59.7 - 87.6	67.69	54.9 - 78.8	2.34	0.36
>6.43	75.61	59.7 - 87.6	69.23	56.6 - 80.1	2.46	0.35
>6.48	68.29	51.9 - 81.9	69.23	56.6 - 80.1	2.22	0.46
>6.54	68.29	51.9 - 81.9	73.85	61.5 - 84.0	2.61	0.43
>6.67	65.85	49.4 - 79.9	73.85	61.5 - 84.0	2.52	0.46
>6.69	65.85	49.4 - 79.9	76.92	64.8 - 86.5	2.85	0.44
>6.71	63.41	46.9 - 77.9	76.92	64.8 - 86.5	2.75	0.48
>6.73	63.41	46.9 - 77.9	78.46	66.5 - 87.7	2.94	0.47
>6.74	60.98	44.5 - 75.8	78.46	66.5 - 87.7	2.83	0.50
>6.88	60.98	44.5 - 75.8	84.62	73.5 - 92.4	3.96	0.46
>6.9	58.54	42.1 - 73.7	84.62	73.5 - 92.4	3.80	0.49
>6.97	**58.54**	**42.1 - 73.7**	**89.23**	**79.1 - 95.6**	**5.44**	**0.46**
>7.36	51.22	35.1 - 67.1	89.23	79.1 - 95.6	4.76	0.55
>7.62	51.22	35.1 - 67.1	90.77	81.0 - 96.5	5.55	0.54
>7.7	48.78	32.9 - 64.9	90.77	81.0 - 96.5	5.28	0.56
>7.86	48.78	32.9 - 64.9	92.31	83.0 - 97.5	6.34	0.55
>7.89	46.34	30.7 - 62.6	92.31	83.0 - 97.5	6.02	0.58
>8.02	43.90	28.5 - 60.3	93.85	85.0 - 98.3	7.13	0.60
>8.13	39.02	24.2 - 55.5	93.85	85.0 - 98.3	6.34	0.65
>8.25	39.02	24.2 - 55.5	96.92	89.3 - 99.6	12.68	0.63
>8.29	34.15	20.1 - 50.6	96.92	89.3 - 99.6	11.10	0.68
>8.67	34.15	20.1 - 50.6	98.46	91.7 - 100.0	22.20	0.67
>10.77	4.88	0.6 - 16.5	98.46	91.7 - 100.0	3.17	0.97
>10.82	2.44	0.06 - 12.9	100.00	94.5 - 100.0		0.98
>11.96	0.00	0.0 - 8.6	100.00	94.5 - 100.0		1.00

Discussion

Birth Asphyxia is defined by the World Health Organization as "the failure to initiate and sustainbreathing at birth" [14]. Early and

prompt diagnosis of asphyxia has remained a matter of controversy and a challenge due to lack of clear objective signs and symptoms, sensitive and specific biomarkers and inherent differences in the definitions used in hospital and home births. With birth asphyxia being a frequent event in the developing world it is essential to find an appropriate tool for its early detection. In developed countries one current routinely used parameter is the assessment of fetal and neonatal acid base balance with umbilical cordlactate, forming key markers towards predicting and diagnosing birth asphyxia [15].

As results of umbilical cord blood lactate level ≥ 6.97 mmol/l had a sensitivity 58.5% (95% CI: 42.1 - 73.7), specificity 89.2% (95% CI: 79.1 - 95.6), +ve LR (likelihood ratio) 5.44, -ve LR 0.46 for asphyxia (Table 1), our data was consistant to most of previous reports. Determination of lactate levels in blood from the fetus's scalp during labor has been studied since the 1970s [16]. Lactate is a metabolite of anerobic metabolism and reflects tissue hypoxia. Once produced prenatally the placenta excretes it. During neonatal period liver and kidneys control its excretion. Many observational studies have shown that lactate analysis has similar or better predictive properties compared with pH in the identification of short term neonatal morbidity [17] but is free from the sampling error variables mentioned earlier for pH and base excess.

Borruto F et al [18] has screened of foetal distress by assessment of umbilical cord lactate and has reported that 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 asphyxiaat delivery. Scalp lactate correlated significantly with umbilical artery lactate, but not with 1-min or 5-min Apgar scores. Lactate and pH values provide the best parameters to distinguish between asphyctic and normal newborns, with lactate having the most discriminating power.

Geetha Damodaran K et al studied 128 babies born during two months period (April – May 2008). The clinical decision limit of lactate obtained in the study (27 mg %) was found to be significantly associated with perinatal asphyxia diagnosed by Apgar score. Sensitivity and specificity of cord blood lactate at the cut off value of 27 mg% is 68% and 60 % respectively (AUC = 0.679, p =0.0001) [19].

Studies by Nordstrom have shown that the main contributor to the fetal lactate increase during labor is the fetus itself, suggesting cord blood lactate is not significantly influenced by maternalor utero-placental lactate production [20]. There is increasing evidence that elevated lactate levels found in cord blood of anasphyxiated infant has a clear correlation between lactic acidosis and fetal distress. In 2007Franco Borruto et al from Italy demonstrated that fetal scalp lactate correlated significantly with umbilical artery lactate (P = 0.49, 0.01), but not with APGAR score at 1 min (R = -0.21, ns) or at 5min (R = -0.11, ns) [21]. Gjerris et al. from Denmark showed a significant correlation between umbilical cord arterial lactate and pH (r = 0.73) and actual base excess (r=-0.83). Their ROC-curves suggested an arterial lactate value of more than 8mmol/l indicate intra-partum asphyxia [22]. Taking a step further researchers from Australia have demonstrated that plasma lactate concentration of >7.5 mmol/l in neonates within 1 hour of birth has a sensitivity of 94% and a specificity of 67% to predict moderate to severe HIE in babies thus concluding that the predictive value of lactate is more than that of pH or base deficit [15]. Similarly Da Silva et al. found that lactate levels lower than 5mmol/l were not followed by neurological complications while plasma lactate concentration greater than 9 mmol/l was associated with moderate or severe encephalopathy [23].

We would however like to emphasize the point that timing of obtaining a sample from umbilical cord even for lactate measurements is of paramount importance. There is enough evidence to suggest that cord blood samples taken after 20 minutes delay are unreliable for lactate as well as pH and base excess values. Dessolle and colleagues have clearly shown that arterial cord blood lactate levels increased linearly with time, by 0.062 mmol/l per min [24]. Hence it is recommended that blood should be immediately obtained from an artery identified after clamping the cord at both ends and certainly no later than 20 minutes [25].

Conclusion

Umbilical cord blood lactate will give an idea about the impact of anoxia in tissues. Being an objective parameter, it will be more convenient for confirming the diagnosis of asphyxia and for further follow up. It can be used to supplement APGAR score routinely.

Conflicts of interest

The authors declare no conflicts of interest

Authors' contribution

All authors contributed equally to this work.

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