

A study of piglets born by spontaneous parturition under uncontrolled conditions: could this be a naturalistic model for the study of intrapartum asphyxia?

María E. Trujillo-Ortega¹, Daniel Mota-Rojas², Adriana Olmos-Hernández^{2, 3}, María Alonso-Spilsbury², Miguel González^{2, 3}, Héctor Orozco^{2, 3}, Ramiro Ramírez-Necoechea², Alejandro A. Nava-Ocampo^{4, 5}

¹ Department of Animal Medicine and Production: Swine, Faculty of Veterinary and Animal Production, Universidad Nacional Autónoma de México, Ciudad Universitaria, ² Department of Animal Production & Agriculture, Área de Investigación; Ecodesarrollo de la Producción Animal, Universidad Autónoma Metropolitana-Xochimilco, and ³ Postgraduate Division of Animal Science and Health, Faculty of Veterinary and Animal Production, Universidad Nacional Autónoma de México, México DF, México; ⁴ Division of Clinical Pharmacology & Toxicology, The Hospital for Sick Children, and ⁵ PharmaReasons, Toronto ON, Canada

Abstract. In order to evaluate how spontaneously born piglets could be a suitable model for the study of intrapartum hypoxia, 230 newborn piglets were studied. Out them, 8.3% (n = 19) died intrapartum, 21.7% (n = 50) were born with moderate-to-severe intrapartum hypoxia, and 70% (n = 161) were born with mild or no evidence of intrapartum distress. Piglets born without any evidence of intrapartum asphyxia weighed approximately 240 g lower than those born with intrapartum hypoxia and intrapartum-dead piglets ($P < 0.0001$). The viability score was approximately 3 units lower and the latency to contact the udder was two times longer in the piglets surviving intrapartum hypoxia than in controls ($P < 0.0001$). In comparison with the control group, metabolic acidosis was most severe among intrapartum-dead piglets followed by piglets surviving intrapartum asphyxia ($P = 0.002$). According to a multiple linear regression analysis, pCO₂ and lactate blood levels, and birth weight were identified as explanatory variables of viability score (r: 0.78; $P < 0.001$). Viability score, K⁺ and lactate blood levels, and birth weight were identified as explanatory variables of latency to contact the udder (r: 0.80; $P < 0.001$). In conclusion, the spontaneously-born asphyxiated piglet could be considered as a naturalistic model for the study of intrapartum asphyxia. Histopathologic and more rigorous functional and behavioral evaluations are still required to further characterize the model. (www.actabiomedica.it)

Key words: Acidosis, animal disease models, asphyxia neonatorum, oxygen deficiency

Introduction

Intrapartum related neonatal deaths may account for approximately 10% of deaths in children aged below 5 years (1). Intrapartum asphyxia may occur in 26 out of 1,000 live births of term pregnancies and in 73 out of 1,000 live births of preterm deliveries (2); 15% and 48% of them had moderate to severe asphyxia, respectively. The link between fetal asphyxia and brain damage has been extensively established (2). For future

development of neuroprotective strategies, animal models may help in better understanding the complex interaction between biochemical and metabolic alterations produced at birth and their negative impact in brain function. In pigs, intrapartum stillbirths are predominantly a result of fetal asphyxia (3-5). In a previous study, Herpin et al. (6) did a thorough evaluation of changes in umbilical cord blood gases as surrogated markers of intrapartum asphyxia at birth in piglets and correlated the changes with early postnatal viability.

As expected, the authors found that piglets suffering from asphyxia during delivery were less viable at birth and less prone to adapt to extrauterine life. However, the authors excluded the data obtained from stillbirth piglets from the analysis. The present study was designed to extend the evaluation on the relationship between gross neurological dysfunction and the clinical characteristics and metabolic disturbances in piglets born by spontaneous parturition to multiparous sows. Our results would help to gain attention to piglets born by spontaneous parturition under uncontrolled conditions as a naturalistic model for the study of intrapartum asphyxia.

Methods

Ethical approval for the study was obtained from the Universidad Autónoma Metropolitana-Xochimilco, México DF, Mexico. The study was performed in a commercial swine farm, located in the State of Mexico, in accordance with the guidelines of the ethical use of animals in applied ethologic studies described elsewhere (7).

Animals and neonatal evaluations

All piglets born to 20 hybrid Yorkshire-Landrace created sows were included in the study. The sows were in their 2nd to 5th pregnancy and weighted from 172 to 284 kg at term. Parturition was not induced, and piglets were not assisted at birth although sows and offspring were closely monitored for the purpose of the study. There was no manipulation to the sows. The number of live-born, meconium-stained and intrapartum-dead piglets was obtained. Fetal deaths were classified as antepartum (type I) or intrapartum (type II) deaths, according with the criteria previously described in detail elsewhere (8, 9). Briefly, type I, or antepartum stillbirths, had a rather characteristic edematous and hemorrhagic appearance, some had a grayish-brown discoloration due to the initial stages of mummification, and if the process was more advanced the fetuses were dehydrated and started to lose hair. Type II or intrapartum stillbirths had the exact appearance of their normal littermates with the excep-

tion that they did not breathe. Immediately after birth, temperature was obtained by means of a tympanic membrane thermometer (ThermoScan Braun GMBH, Kronberg, Germany) and piglets were weighted in a digital bascule (Salter WeightTronix Ltd., West Bromwich, United Kingdom). Within the first minute after birth and with the piglets still in apnea, a single 1-ml blood sample was obtained from the caval vein by anterior neck puncture using a syringe containing lithium heparin. In our experience, the blood sampling took approximately 20-30 seconds. Hematocrite (%), glucose (mg/dL), serum electrolytes [Na^+ , K^+ and Ca^{2+} (mmol/L)] and blood lactate (mg/dL) levels, oxygen saturation [SaO_2 (%)], and partial pressure of carbon dioxide [PaCO_2 (mm Hg)] and oxygen [PaO_2 (mm Hg)], were obtained by means of an automatic blood gas and electrolyte analyzer (GEM Premier 3000, Instrumentation Laboratory Diagnostics S.A. de C.V. México).

The piglets' viability was scored according to the modified version of a scale previously described by Mota-Rojas et al. (5). Briefly, heart rates were classified in categories as less than 110, between 111 and 160, or more than 161 beats per min; time interval between birth and first breath as more than 1 min, between 16 sec and 59 sec, or less than 15 sec; muzzle skin color as pale, cyanotic, or pink; time interval between birth and first stand as more than 5 min, between 1 and 5 min, or less than 1 min; and the skin stain with meconium as severe, mild, or absent. Each category was rated from 0 (the worst) to 2 (the best), and an overall score of 0 to 10 points was obtained in each piglet.

The heart rate was obtained using a stethoscope by one of the investigators. The first breath was considered when thoracic movements were noticed for the first time after birth followed by air exhalation from the piglet's muzzle. Meconium stains were classified as severe when more than 40% of the piglet's body surface was stained and as mild when the stained surface was 40% or less. In addition to the viability scale, the latency to contact the udder was also recorded. Since piglets were manipulated by investigators in order to obtain a blood sample and tympanic membrane temperature, both the time to stand and the latency to contact the udder were registered starting

when the piglets were returned to their mothers, close to the vulva, and finishing when the animals reached the stand position supported by their four legs or reached the udder for the first time, respectively.

Data analysis

Weight, temperature, glucose, electrolytes, and blood gases were summarized as mean \pm SD. Since pH blood levels correspond to log units, these data were summarized as medians (ranges). Piglets were allocated into 3 different groups. Intrapartum-dead piglets were included in group 1. Piglets born with evidence of moderate-to-severe intrapartum hypoxia including an edematous or ruptured umbilical cord and meconium stain in more than 40% of the body surface were included in group 2. Finally, piglets born with minor or no evidence of intrapartum hypoxia including meconium stain in 40% or less of the body surface and normal or adhered umbilical cord were included in group 3. Study data were compared among the 3 groups by means of an Analysis of Variance followed, if applicable, by a Tukey test for comparison of pairs of groups. For comparisons of pH blood values at birth among the 3 groups, a Kruskal-Wallis test was performed and followed, if applicable, by a Mann-Whitney U test for comparison of pairs of groups. As naturally expected, some of the parameters (e.g. viability scores) were not measured in Group 1. In such cases, comparisons between Groups 2 and 3 were performed by an unpaired Student t test.

In addition, a set of linear regression analyses was performed between viability scores as a dependent variable and either tympanic membrane temperature, birth weight or each of the electrolyte or blood gas parameters as the independent variable. Viability scores were entered as a numeric variable in the analysis assuming that in live-born piglets the intervals between 0 and 10 are equal due to the continuous nature of the concept being measured. A similar process was performed with latency to contact the udder as the dependent variable.

Once the independent variables significantly correlated to either viability scores or latency to first udder contact were identified, a multiple linear regression analysis was performed. The colinearity among

independent variables was tested by the Variance Inflation Factor (VIF) that measured the "inflation" of the standard error of each regression parameter (coefficient) for an independent variable due to redundant information in other independent variables. If the variance inflation factor was less than 4, it was considered to have no redundant information in the other independent variables.

Statistical analyses were performed by SigmaStat for Windows v. 3.5 (Systat Software Inc., San Jose, California, United States of America) by one of the investigators ignoring the data allocation group. The limit of significance was fixed to a two-sided $P < 0.05$.

Results

Two hundred and thirty piglets were born to the 20 sows included in the study. Out of them, 8.3% ($n = 19$) died intrapartum, 21.7% ($n = 50$) born with moderate-to-severe intrapartum hypoxia, and 70% ($n = 161$) were born minor or no evidence of intrapartum distress. All the piglets were successfully sampled and had the study evaluations completed. Piglets born minor or no any evidence of intrapartum asphyxia weighed approximately 240 g less than those born with hypoxia or dead ($P < 0.0001$) (Table 1). Body temperature in the intrapartum-dead piglets was on average 0.4°C to 0.7°C lower than in the other two groups. Viability scores were moderate-to-severe approximately 3 units lower in the piglets surviving intrapartum hypoxia than in control piglets. Latency to first udder contact was two times longer in the piglets with intrapartum asphyxia than in controls ($P < 0.0001$). Glucose blood levels were approximately 2.5 times higher in intrapartum-dead piglets than in the other two groups (Table 1). Sodium serum levels were modestly but significantly higher in the former group. Potassium serum levels were 9.9 ± 1.3 in dead piglets, 6.4 ± 0.8 in piglets surviving moderate-to-severe intrapartum asphyxia, and 6.6 ± 0.7 in the controls ($P < 0.0001$), respectively; calcium plasma levels followed a similar pattern. As expected, in comparison to controls, intrapartum-dead piglets had evidence of severe metabolic acidosis followed by the group of piglets surviving moderate-to-severe intrapartum asphyxia ($P = 0.002$;

Table 1. Clinical and laboratory parameters in newborn piglets born with different degrees of intrapartum asphyxia

	Group 1 (n = 19)	Group 2 (n = 50)	Group 3 (n = 161)	P value
Sex [M:F (%)]	9:10 (47.4%:52.6%)	27:23 (54%:46%)	87:74 (54%:46%)	$\chi^2 = 0.31, P = 0.86$
Birth weight (g)	1,565.5 ± 77.7	1,578.4 ± 177.8	1,322 ± 208 ^{ab}	< 0.0001
Temperature (°C)	36.9 ± 0.5	37.3 ± 0.8	37.6 ± 0.7 ^{a,b}	< 0.0001
Viability score	--	5.4 ± 0.7	8.7 ± 0.8	< 0.0001
Latency to first udder contact (min)	--	53.7 ± 7.2	25.7 ± 7.6	< 0.0001
Glucose (mg/dL)	148.6 ± 34.3	66.3 ± 36.5 ^c	62.3 ± 8.9 ^a	< 0.0001
Na ⁺ (mmol/L)	137.9 ± 1.6	134.1 ± 3.0 ^c	135.4 ± 3.7 ^a	0.0003
K ⁺ (mmol/L)	9.9 ± 1.3	6.4 ± 0.8 ^c	6.6 ± 0.7 ^a	< 0.0001
Ca ²⁺ (mmol/L)	2.2 ± 0.2	1.8 ± 0.1 ^c	1.6 ± 0.1 ^{a,b}	< 0.0001
pH	6.70 (6.50-6.90)	7.08 (6.87-7.43) ^c	7.20 (7.00-7.50) ^{ab}	< 0.0001*
PaCO ₂ (mm/Hg)	150 ± 9.0	85.0 ± 13.9 ^c	52.5 ± 9.3 ^{a,b}	< 0.0001
PaO ₂ (mm/Hg)	11.3 ± 2.4	21.2 ± 7.1 ^c	25.9 ± 6.3 ^{a,b}	< 0.0001
Lactate (mg/dL)	129.7 ± 4.8	86.3 ± 28.4 ^c	35.2 ± 3.8 ^{a,b}	< 0.0001
Bicarbonate (mmol/L)	--	20.7 ± 2.4	22.0 ± 2.6	0.002

Group 1: intrapartum death piglets; group 2: piglets surviving severe-to-moderate intrapartum asphyxia; group 3: piglets born with mild or no evidence of intrapartum asphyxia. Comparisons among 3 groups were performed by either chi-squared, ANOVA or *Kruskal-Wallis test. Comparison of viability score, latency to first udder contact and bicarbonate levels were performed between groups 2 and 3 by an unpaired Student t test. Temperature was obtained in the tympanic membrane. Superscript letters a, b and c indicate *post-hoc* comparisons statistically significant between groups 1 and 3, 2 and 3, and 1 and 2, respectively.

Table 2. Clinical and laboratory variables that significantly correlated with viability score in 230 piglets

Dependent variable (y)	Independent variable (x)	Linear equation ($y = b + mx$)		R	F and P values
		$b \pm SE$	$m \pm SE$		
Viability score	Lactate (mg/dL)	10.0 ± 0.1	-0.04 ± 0.002	-0.74	264.5; < 0.001
	PaCO ₂ (mm/Hg)	11.7 ± 0.2	-0.06 ± 0.004	-0.70	196.7; < 0.001
	pH	-30.2 ± 5.2	5.3 ± 0.7	0.45	53.2; < 0.001
	Birth weight (g)	11.8 ± 0.6	-0.002 ± 0.0004	-0.41	42.0; < 0.0001
	Ca ²⁺ (mmol/L)	14.1 ± 1.2	-3.7 ± 0.7	-0.32	24.0; < 0.001
	PaO ₂ (mm/Hg)	6.3 ± 0.4	0.06 ± 0.01	0.26	15.7; < 0.001
	Temperature (°C)	-4.0 ± 5.6	0.3 ± 0.1	0.15	4.5; 0.03
	Bicarbonate (mmol/L)	5.9 ± 0.9	0.09 ± 0.04	0.14	4.7; 0.03
Latency to first udder contact	Viability score	84.7 ± 3.2	-6.6 ± 0.3	-0.75	276.3; < 0.001
	Lactate (mg/dL)	14.0 ± 1.4	0.3 ± 0.02	0.71	212.4; < 0.001
	PaCO ₂ (mm/Hg)	1.0 ± 2.6	0.51 ± 0.04	0.64	146.5; < 0.001
	Birth weight (g)	-2.7 ± 5.4	0.02 ± 0.003	0.41	42.5; < 0.001
	pH	339.2 ± 46.9	-42.6 ± 6.5	-0.41	42.8; < 0.001
	Ca ²⁺ (mmol/L)	-28.9 ± 10.9	36.5 ± 6.5	0.36	31.3; < 0.001
	K ⁺ (mmol/L)	61.3 ± 8.9	-4.4 ± 1.3	-0.21	10.5; 0.001
	PaO ₂ (mm/Hg)	42.7 ± 3.6	-0.4 ± 0.1	-0.20	8.8; 0.003
Bicarbonate (mmol/L)	49.3 ± 8.0	-0.7 ± 0.3	-0.14	4.5; 0.03	

The independent variables were listed according to the coefficient of correlation (R value). The F and P values shown in the table are from the Analysis of Variance of the linear regression analysis. The parameters *b* and *m* in the linear equation are shown with their corresponding ± standard errors (SE).

ANOVA). The linear regression analyses identified that lactate and PaCO₂ blood levels were highly correlated with the viability scores at birth. The pH, birth weight, Ca²⁺, PaO₂, and, although less evident but still

significant, the tympanic membrane temperature and blood bicarbonate levels also correlated with the viability scores at birth (Table 2). In the multiple linear regression analysis, the PaCO₂, lactate blood levels and

Table 3. Multiple linear regression analysis between clinical and laboratory parameters and functional outcomes at birth in piglets born by spontaneous parturition

Dependent variable	Multiple linear equation	R	Adjusted r ²	F and P values
Viability score	12.2 - 0.02 PaCO ₂ (mmol/L) - 0.03 lactate (mg/dL) - 0.001 birth weight (g)	0.78	0.60	108.5; <0.001
Latency to contact the udder	62.7 - 4.0 viability score - 2.4 K ⁺ + 0.1 lactate + 0.006 birth weight	0.80	0.63	92.0; <0.001

R is the correlation coefficient, and r² the coefficient of determination obtained in the multiple regression analysis. There was no evidence of colinearity among the parameters included in the multiple equations shown in the table

birth weight were identified as explanatory variables of viability scores (adjusted r² = 0.60; *P* < 0.001) (Table 3).

Latency to first udder contact was inversely related to viability scores (*r* = 0.75; *P* < 0.0001), i.e. longer latency times were observed among piglets with lower viability scores. It was also importantly correlated with lactate and PaCO₂ blood levels and less evident, although still significant, with birth weight, pH, PaO₂ and bicarbonate blood levels, and to Ca²⁺ and K⁺ serum levels (Table 2). In the multiple linear regression analysis, viability score, K⁺ and lactate blood levels, and birth weight were selected as explanatory variables of latency to first udder contact (corrected r² = 0.63; *P* < 0.001) (Table 3).

Discussion

In this study, an association was found between certain clinical characteristics as well as electrolyte and metabolic imbalance at birth and gross neurological dysfunction in newborn piglets. Hypoxia followed by respiratory and metabolic acidosis secondary to anaerobic metabolism essentially describes asphyxia. A recent retrospective study with full-term human neonates suspected of having suffered a significant degree of intrapartum asphyxia reported that lactate levels obtained from an indwelling arterial catheter within 1 hour after birth were important predictors of moderate-to-severe hypoxic ischemic encephalopathy (10). In another retrospective cohort study of 87 human newborns with pathologic acidosis, an umbilical artery pH ≤ 6.92 was found to be the threshold linked with neonatal organ dysfunction (11). A third retrospective study showed that babies born with an umbi-

lical artery pH level < 7.00 had an increased risk of intraventricular hemorrhages and seizures (12). In our study, intrapartum death piglets had pH blood levels < 6.90. In addition, PaCO₂ and lactate blood levels were included as significant predictors of viability in the piglets, further supporting the current knowledge that severity of metabolic acidosis secondary to hypoxia is a good indicator of intrapartum death. Furthermore, lactate levels and birth weight were positively associated with latency to first udder contact whereas the viability status at birth and K⁺ serum levels were negatively associated. A problem with lactate levels is how to discriminate between the increase of lactate due to pyruvate and accelerated glucose metabolism and the lactate due to hypoxia. Glucose levels were more than 2 times higher in intrapartum-dead piglets than in piglets with mild-to-no intrapartum asphyxia or piglets with severe asphyxia, whereas the difference between the means of the two latter groups was of 4 mg/dL. In contrast, the differences in the lactate levels among the 3 study groups were 40–45 mg/dL on average. It is therefore more likely that the differences in lactate levels among the three study groups were secondary to hypoxia rather than to changes in glucose metabolism.

In the present study, we are reporting the association between functional neurological alterations at birth and electrolytes and metabolic disturbances in a large set of piglets born by spontaneous parturition. This naturalistic model of intrapartum asphyxia may provide a unique opportunity for studying neurological sequels and to test neuroprotective strategies. However, several aspects of the evaluation and the model by itself still deserve further studies. Latency to first udder contact was assumed to reflect complex neurological functions in the newborn piglets since it requires the integrity of at least the olfactory, visual

and neuromuscular functions to allow for an oriented search of the maternal teat. Similarly, the viability scale includes the time to stand which may also be altered if a neurological insult is present. Since these parameters may not necessarily represent the best surrogated markers of neurological function in this experimental animal model, more specific neurological evaluations may help to clarify more accurately the extension of neurological alterations. The lack of specific parameters for neurological function in the study probably affected the linear regression analyses, where the best coefficient of correlation was 0.80 ($r^2 = 0.64$). However, despite such limitations, some of the coefficients of correlation observed in our study were higher than those previously reported by Herpin et al. (6). In addition, we did not evaluate whether the neurological insult may remain for a long term, and intrapartum asphyxia may not necessarily be limited to neurological function (13). Our study did not evaluate any adverse impact of hypoxia to other organs.

Interestingly, birth weight was inversely related to the viability score in a significant way. Our findings support two previous studies showing that birth weight was positively related to intrapartum hypoxia and neurological dysfunction at birth in humans despite the fact that more than 50% of cases were born by cesarean section (14). It is probably due to other mechanisms beside anatomical difficulties for crossing the birth channel. Larger newborns may have enhanced requirements of oxygen supply than smaller babies. Another possibility could be that neurological development is more advanced in larger fetuses and cells are therefore less tolerant to hypoxia. The results of the present study, however, contrast with the inverse correlation between birth weight and the time to first udder contact previously reported in neonate piglets surviving intrapartum asphyxia (6), suggesting that bigger piglets may have better adaptation to extrauterine life. These contradictory results deserve further evaluation to clarify the role of birth weight on the postnatal adaptation of mammals.

Impaired oxygen delivery or consumption leads to increased anaerobic glycolysis with terminal conversion of the resulting pyruvate to lactate instead of through the Krebs cycle of aerobic metabolism. Therefo-

re, although no statistical colinearity between $p\text{CO}_2$ and lactate blood levels were found, they are similarly expressing the severity of acidosis occurring in the hypoxic or asphyxiated piglets at birth. It is however very unlikely that there is any potential relationship between these two parameters and birth weight. In addition, the latency to contact the udder is a process that demands a neurological integrity of the piglets in order to establish the initial contact. Therefore, this appears to be a critical parameter when evaluating the neurological insult of asphyxia in newborn piglets and appears to be sensitive to respiratory and metabolic acidosis at birth.

In conclusion, the extent of biochemical and metabolic alterations may explain the severity of neurological dysfunction in the newborn piglet surviving intrapartum asphyxia. The newborn piglet may provide a naturalistic model for the study of intrapartum asphyxia and neuroprotective strategies. Histopathologic and more rigorous functional and behavioral evaluations are still required to further characterize the model.

Acknowledgements

The study was supported by a grant from the *Programa de Mejoramiento del Profesorado* No. UAMPPTC-028 to the Academic Staff of Etología, Producción Porcina y Fauna Silvestre. Adriana Olmos-Hernández is a member of the program of *Maestría en Ciencias de la Producción y de la Salud Animal*, UNAM, and was supported by the scholarship No. 185983 from CONACYT, Mexico. Daniel Mota-Rojas, M. Alonso-Spilsbury and M.E. Trujillo were supported, as members, by the Sistema Nacional Investigadores. Authors are indebted to Q. Antonio Campos Osorno, Chief of the Branch of Gasometry at I.L. Diagnostics S.A. de C.V., Mexico DF, for temporarily providing the instrument and tools for blood gas and electrolyte analyses, to Pedro Sánchez and Gloria González, postgraduate students, for their technical assistance, and to Ms. Olivia Tischler for her valuable assistance in editing the manuscript.

References

1. Lawn J, Shibuya K, Stein C. No cry at birth: global estimates of intrapartum stillbirths and intrapartum-related neonatal deaths. *Bull World Health Organ* 2005; 83: 409-17.
2. Low JA. Determining the contribution of asphyxia to brain damage in the neonate. *J Obstet Gynaecol Res* 2004; 30: 276-86.

3. Randall GC. The relationship of arterial blood pH and pCO₂ to the viability of the newborn piglet. *Can J Comp Med* 1971; 35: 141-6.
4. Sprecher DJ, Leman AD, Dziuk PD, Cropper M, De-Decker M. Causes and control of swine stillbirths. *J Am Vet Med Assoc* 1974; 165: 698-701.
5. Mota-Rojas D, Martinez-Burnes J, Trujillo ME, et al. Uterine and fetal asphyxia monitoring in parturient sows treated with oxytocin. *Anim Reprod Sci* 2005; 86: 131-41.
6. Herpin P, Le Dividich J, Hulin JC, Fillaut M, De Marco F, Bertin R. Effects of the level of asphyxia during delivery on viability at birth and early postnatal vitality of newborn pigs. *J Anim Sci* 1996; 74: 2067-75.
7. Sherwin CM, Christiansen SB, Duncan IJ, et al. Guidelines for the ethical use of animals in applied ethology studies. *Appl Anim Behav Sci* 2003; 81: 291-305.
8. Randall GC. Observations on parturition in the sow. II. Factors influencing stillbirth and perinatal mortality. *Vet Rec* 1972; 90: 183-6.
9. Mota-Rojas D, Martinez-Burnes J, Trujillo-Ortega ME, Alonso-Spilsbury ML, Ramirez-Necochea R, Lopez A. Effect of oxytocin treatment in sows on umbilical cord morphology, meconium staining, and neonatal mortality of piglets. *Am J Vet Res* 2002; 63: 1571-4.
10. Shah S, Tracy M, Smyth J. Postnatal lactate as an early predictor of short-term outcome after intrapartum asphyxia. *J Perinatol* 2004; 24: 16-20.
11. Chauhan SP, Hendrix NW, Magann EF, et al. Neonatal organ dysfunction among newborns at gestational age 34 weeks and umbilical arterial pH<7.00. *J Matern Fetal Neonatal Med* 2005; 17: 261-8.
12. Lavrijsen SW, Uiterwaal CS, Stigter RH, de Vries LS, Visser GH, Groenendaal F. Severe umbilical cord acidemia and neurological outcome in preterm and full-term neonates. *Biol Neonate* 2005; 88: 27-34.
13. Low JA, Panagiotopoulos C, Derrick EJ. Newborn complications after intrapartum asphyxia with metabolic acidosis in the preterm fetus. *Am J Obstet Gynecol* 1995; 172: 805-10.
14. Salhab WA, Perlman JM. Severe fetal acidemia and subsequent neonatal encephalopathy in the larger premature infant. *Pediatr Neurol* 2005; 32: 25-9.

Accepted: 13th November 2006

Correspondence: Dr. AA Nava-Ocampo,
Division of Clinical Pharmacology & Toxicology,
The Hospital for Sick Children, 555 University Ave.,
Toronto ON, M5G 1X8, Canada
Fax: + (416) 813 7562.

E-mail: navaocampo_aa@yahoo.com, www.actabiomedica.it