Physiological response to hypoxia in piglets of different birth weight

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Abstract

In the present study, we aimed to extend the characterization of the proposed naturalistic experimental model of piglets born with hypoxia by assessing the relationship between birth weight, intra partum asphyxia and gross indicators of neurophysiological alterations in newborn piglets. Three groups of 50 piglets each were classified according to their birth weight into normal (1000-1350 g), low (below 1000 g), and high (over 1350 g). In comparison to piglets within normal weight, those born with high birth weights showed acid-base imbalance as reflected by lower pH levels (7.03±0.01), hypercapnia (88.50±13.20 mmHg), and lactic acidosis (lactate levels: 89.40±26.30). These piglets had lower viability scores (5.40±0.60) and longer periods of time to contact the udder (52.30±28.30) than piglets with normal birth weight. In conclusion, data show that piglets with birth weight over 1350 g are at a higher risk of gross neurophysiological deficits, probably secondary to neonatal hypoxia.

Introduction

In humans, intra partum asphyxia may occur in 26 out of 1000 live births of preterm deliveries (Low, 2004) and intra partum-related neonatal deaths may account for approximately 10% of deaths in children aged below five years (Lawn et al., 2005). In pigs, intra partum stillbirths are predominantly a result of fetal asphyxia (Jezkova and Smrckova, 1990; Alonso-Spilsbury et al., 2005; Olmos-Hernández et al., 2008; Orozco-Gregorio et al., 2010; Orozco-Gregorio et al., 2011). The uterotonic drugs frequently used to diminish mortality at birth effectively reduce the length of the piglet birth process (Mota-Rojas et al., 2002; 2005a,b; González-Lozano et al., 2009; 2010). In a previous study, our group had shown that fetal growth of guinea pigs was critical for surviving induced intra partum asphyxia; larger foetuses had better chances of survival (Sánchez-Aparicio et al., 2008). In contrast, we observed a higher rate of neonatal complications among larger piglets while studying a naturalistic model of newborn hypoxia and neurological damage (Trujillo-Ortega et al., 2007). Our observations in piglets were in agreement with another study in which we noticed that larger piglets born to sows treated with growth hormone during pregnancy had higher mortality rates (Trujillo-Ortega et al., 2006).

In the present study, we aimed to extend the characterization of the proposed naturalistic experimental model of piglets born with hypoxia by assessing the relationship between birth weight, intra partum asphyxia and gross indicators of neurophysiological alterations of newborn piglets.

Materials and methods

Ethical approval for the study was obtained from the Universidad Autónoma Metropolitana-Xochimilco, Mexico DF, Mexico, and the study was conducted in accordance with the guidelines of the ethical use of animals in applied ethological studies described elsewhere (Sherwin et al., 2003). The study was performed at a commercial swine farm located in the State of Mexico, Mexico.

Cardiotoographic monitoring of pregnant sows started 72 h before intramuscular administration of F2-alfa prostaglandins (10 mg) 24 h prior to the expected delivery date. Sows were assisted by two of the investigators.

Piglets

Live-born piglets, selected from those born to 40 hybrid Yorkshire-Landrace crated multiparous sows, were classified into three different groups according to their birth weight (Group 1: 1000-1350 g; Group 2: <1000 g; Group 3: >1350 g). Piglets were selected in a consecutive order until a sample size of 50 piglets per group was obtained. The sample size was considered to be adequate to identify statistical differences in the main outcomes among groups.

Blood tests

Blood samples were obtained from the anterior vena cava of piglets immediately after birth, according to the Mexican regulation NOM-062-ZOO-1999. The blood samples were placed in glass tubes containing lithium heparin. Glucose (mg/dL), electrolytes [Na+, K+ and Ca2+] (mEq/L) and lactate (mg/dL) levels, and partial pressure of carbon dioxide (pCO2 [mm Hg]) and oxygen (pO2 [mm Hg]), were obtained by means of an automatic blood gas and electrolyte analyzer (GEM Premier 3000, Instrumentation Laboratory Diagnostics, Milan, Italy).

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Viability score and neurofunctional assessment

The viability score of the piglets was obtained according to the scale described by Zaleski and Hacker (1993) and modified by Mota-Rojas et al. (2005b). Briefly, heart rate (<110, 121-160, or >161 beats/min), time interval between birth and first breath (>1 min, 16 sec-1 min, or <15 sec), skin color (pale, cyanotic, or pink), time interval between birth and first stand (>5 min, 1.5 min, or <1 min), and skin stained with meconium (severe, mild or absent) were rated from zero (the worst) to two (the best) and a global score ranging from 1 to 10 was obtained for each piglet. Heart rate was measured by one of the investigators with a stethoscope before taking the blood sample. The time to first breath was recorded from birth to the moment when thoracic movements were noticed accompanied by air exhalation from the piglet’s muzzle. Time to stand was considered from birth to the time when the piglet gained the standing position supported by all four legs. Meconium staining was considered severe when more than 40% of the piglet’s legs. Meconium staining was considered from birth to the time when the piglet gained the standing position supported by all four legs. Meconium staining was considered severe when more than 40% of the piglet’s body surface was stained (Mota-Rojas et al., 2006). In addition to the scale, time to first udder contact was also registered.

Since piglets were manipulated by investigators in order to take a blood sample and tachypnic membrane temperature, both the time to stand and the time to first udder contact were registered starting from the time at which the piglets returned to the mother close to the vulva to allow the piglets to try to find the maternal teat by themselves.

**Weight and temperature**

After taking blood samples, piglets were weighed in a digital bascule (Salter Weight-Tronix Ltd., West Bromwich, UK), and their temperature was taken using a tympanic membrane thermometer (ThermoScan Braun GMBH, Kronberg, Germany). For the purpose of this study, piglets in Groups 2 (<1000 g) and 3 (>1350 g) were considered to be underweight and overweight animals, respectively.

**Data analysis**

Continuous data were summarized as mean ± SD and were compared among the three groups by means of an ANOVA test followed by Bonferroni-type multiple t-test. A Kruskal-Wallis test followed by Bonferroni-type multiple comparisons were used to compare pH blood values at birth among the three groups. Linear regression analysis was performed as an exploratory analysis in order to investigate whether there was a linear relationship between outcome and piglet birth weight. A two-tailed P<0.05 was considered significant. Statistical analyses were performed with SAS (1997).

**Results and discussion**

Blood gases, electrolytes and glucose levels at birth in under- or overweight piglets were compared to the levels observed in piglets weighing 1000-1350 g (Table 1). The main differences between overweight and normal piglets were observed in pH, pCO2, pO2 and lactate blood levels. Other parameters showed only minor differences or were similar between groups. Although there was no significant difference in glucose levels, the mean value in the high birth weight group was substantially higher.

In relation to the viability score, significant differences (P<0.001) were observed among the three groups (Table 2). The worst score was observed in the bigger piglets (5.40±0.60). There was also a significant difference in time to connect the udder (min) among the weight groups (P<0.001). The linear regression analysis did not show any significant relationship between birth weight and either the viability score or the time to connect to the udder (P>0.05).

Our study further characterizes a proposed naturalistic model of brain damage in neonate piglets by identifying that bigger piglets (>1350 g) are at greater risk of showing gross neurophysiological dysfunctions than smaller piglets. In a study of 230 newborn piglets born with different degrees of hypoxia, our group had previously reported some evidence that birth weight was inversely related to time to first udder contact and to viability score, and piglets born without any evidence of intra partum asphyxia weighed approximately 240 g less than those born with intra partum hypoxia and intra partum-dead piglets (Trujillo-Ortega et al., 2007). In addition, in a study administering growth hormone in late pregnancy to primiparous sows, weight of piglets increased an average 100 g in comparison to control animals but the mortality rate was twice higher in the treated group (Trujillo-Ortega et al., 2006). Although in the present study we did not identify any linear relationship between birth weight and viability scores, the weight categories used in the study clearly identified an increased risk of intra partum hypoxia for bigger piglets, and our results are consistent with our previously published observations. On the other hand, Canario et al. (2006) report that the probability of stillbirths is 7.8 times higher in piglets that weighed below the average of their litter.

In the present study, we did not observe any case of severe neurological dysfunction including seizures, loss of muscular tone or spastic muscular contractions, or spontaneous death.

**Table 1. Blood gases, electrolytes, and glucose levels in piglets of different birth weights.**

| Weight and temperature | Normal birth weight, no. 50 | Low birth weight, no. 50 | High birth weight, no. 50 |
|------------------------|-----------------------------|--------------------------|---------------------------|
| Weight, g<sup>°</sup>  | 1250.6±74.7                 | 917.8±45.0<sup>^</sup>     | 1518.6±163.8<sup>^</sup>   |
| Temperature<sup>°</sup>| 37.8±0.5                    | 37.5±0.6                 | 37.1±0.8                  |
| pH<sup>°</sup>         | 7.26±0.14                   | 7.24±0.41                | 7.03±0.11<sup>^</sup>      |
| PCO<sub>2</sub>, mm Hg<sup>°</sup>| 52.1±7.3                   | 49.9±8.2                 | 88.5±13.2<sup>^</sup>      |
| Pco<sub>2</sub>, mm Hg<sup>°</sup>| 25.8±3.5                   | 26.5±3.8                 | 18.8±4.7<sup>^</sup>       |
| Lactate, mg/dL<sup>°</sup>| 40.8±5.4                   | 35.7±2.8                 | 89.4±26.3<sup>^</sup>      |
| Glucose, mg/dL<sup>°</sup>| 77.0±10.8                   | 65.8±6.0                 | 84.8±43.9                 |
| Na<sup>+</sup>, mmol/L  | 135.8±3.7                   | 136.6±3.4                | 134.5±3.0                 |
| K<sup>+</sup>, mmol/L  | 6.5±0.5                    | 6.6±0.5                  | 6.3±0.7                   |
| Ca<sup>2+</sup>, mmol/L<sup>°</sup>| 1.6±0.9                     | 1.6±0.8                  | 1.7±0.1<sup>^</sup>        |
| Hematocrite, %         | 37.1±3.8                    | 36.8±3.8                 | 37.5±6.8                  |
| HCO<sub>3</sub> mmol/L<sup>°</sup>| 21.9±1.6                   | 21.9±2.5                 | 21.1±2.5                  |

Values are means ± SD; *ANOVA P<0.05; #Kruskal-Wallis P=0.05; ^normal vs low birth weight, P<0.05; â normal vs high birth weight, P<0.05.

**Table 2. Influence of birth weight and gross neurophysiological parameters.**

| Weight and temperature | Normal birth weight, no. 50 | Low birth weight, no. 50 | High birth weight, no. 50 |
|------------------------|-----------------------------|--------------------------|---------------------------|
| Viability score<sup>°</sup>| 8.7±0.4                     | 7.7±0.8<sup>^</sup>      | 5.4±0.8<sup>^</sup>       |
| Latency to first udder contact, min<sup>°</sup>| 22.4±4.5                    | 28.2±5.1<sup>^</sup>     | 52.3±8.3<sup>^</sup>      |

Values are means ± SD; *ANOVA P<0.001; #normal vs low birth weight, P<0.05; ânormal vs high birth weight, P<0.05.
in the live-born piglets studied. However, there was a clear difference in neurological achievement among the three groups, as judged by the approximately 40% lower scores in the neonatal viability scale and the more than 2-fold longer times to first udder contact in the piglets with birth weights over 1350 g. In contrast, in a recent study in guinea piglets undergoing intra partum asphyxia by clamping their umbilical cord, we observed that bigger piglets had better outcomes (Sánchez-Aparicio et al., 2008). However, guinea piglets were delivered by cesarean section which likely altered the results. Another possible explanation is that there may be differences in the neurological sensitivity to intra partum asphyxia across different species. In that context, the present study supports previous observations in human babies showing that birth weight was positively related to intra partum hypoxia and neurological dysfunction at birth, despite the fact that more than 50% of cases were born by cesarean section (Salhab and Perlman, 2005).

One of the interesting findings in our study was that of all the biochemical assessments, only pCO2 was clearly elevated and pO2 was substantially decreased in piglets with high birth weight. These differences had already been observed in a study comparing piglets born without asphyxia to animals surviving intra partum asphyxia (Castro-Najera et al., Orozco-Gregorio et al., 2008; Mota-Rojas et al., 2011). However, in that study we found no significant differences in pH and pCO2 between control and asphyxiated piglets probably because of the small sample size (n=10 piglets in each group) and large variability of these parameters. In contrast, in the present study, these two parameters, as well as other parameters of asphyxia such as lower pH and higher lactate blood levels, reflected the severity of asphyxia at birth in large piglets (van Dijk et al., 2008). Soon after birth and once the piglet starts adapting to extraterine life, these parameters are expected to return to physiological levels in a short period of time (Orozco-Gregorio et al., 2008). However, the consequences of neurophysiological alterations in the piglets may be permanent.

Glucose is a good marker of neonatal distress and may reflect the capability of the piglets to compensate the process. At birth, the increments in glucose plasma levels may be explained by a release of catecholamines and stimulation of liver glycogenolysis secondary to the intra partum asphyxia (Randall, 1979; Herpin et al., 1996). High glucose blood levels have been reported in stillbirth and weak-born piglets (Lauterbach et al., 1987; Tuchscherer et al., 2000), in piglets born during the later stages of parturition, in highly asphyxiated piglets (Herpin et al., 1996), and in piglets who died within the first ten days of life (Tuchscherer et al., 2000). In our study, glucose blood levels were higher in piglets over 1.35 kg in comparison with the normal- and low-weight piglets. However, these differences did not reach significance in the post-hoc analysis, mainly due to the large variability in the bigger piglets.

The proposed naturalistic model still needs further characterization. For example, glycine is an inhibitory neurotransmitter amino acid that acts as neuromodulator of N-methyl-D-aspartate (NMDA) receptors, critically involved in the process of ischemic brain injury. Several drugs that inhibit the presynaptic glutamate release have been tested as potential neuroprotective agents (Nava-Ocampo et al., 2000), and a recent study showed that glycine administered i.p. to rats with permanent left carotid occlusion limited the ischemic brain damage, probably by increasing the neurological availability of glycine concentration enough to prevent the desensitization of NMDA receptors and consequently altering the cascade of events that lead to cellular death (Uribe-Escamilla et al., 2010). Whether the naturalistic model of neurological dysfunction in piglets also responds to pharmacological manipulations of glycine remains to be clarified in further studies.

In relation to the more favorable outcome of piglets born with low birth weight in comparison with piglets over 1350 g, our study has the following potential flaws. We only included live-born piglets in the study. Although this could be overcome by incorporating neurohistological examinations of stillbirths, gross neurophysiological alterations can only be assessed in live-born piglets. In addition, the criterion normal used in our study for piglets of a mean birth weight of 1250.60±74.70 g was somewhat arbitrary. A recent report on average litter weight in Landrace (5178 litter size records and a pedigree file of 8800 individuals) and Yorkshire pigs (3958 litter size records and a pedigree file of 7143 individuals) reported 1.36 kg±0.35 kg and 1.30 kg±0.22 kg, respectively (Varona et al., 2007). Thus, our overweight animals would be within expected normal weights. However, differences across populations of sows from different countries cannot be ruled out. For example, the rate of stillbirths is 0.36 per litter in Mexico, 0.70 in Canada and 0.98 in the USA (Dewey and Straw, 2006). In this context, our classification system, although somewhat arbitrary, successfully classified the animals with high-risk of neurophysiological dysfunction. However, the normal weight has yet to be confirmed as it may cover a different range in other piglet populations.

Conclusions

Our results further characterize the naturalistic model of neonatal hypoxia in piglets by showing that piglets with birth weight over 1350 g are at a higher risk of neurological deficit secondary to neonatal hypoxia. We propose that, when using this experimental model, piglets weighing more than 1350 g should be preferred to piglets born with lower birth weights.

References

Alonso-Spilsbury, M., Mota-Rojas, D., Villanueva-García, D., Martínez-Burnes, J., Orozco, G.H., Ramírez-Necoechea, R., López, A., Trujillo-Ortega, M.E., 2005. Perinatal asphyxia pathophysiology in pig and human: a review. Anim. Reprod. Sci. 90:1-30.
Canario, L.E., Cantoni, E., Le Bihan, D., Cartíte, J.C., Billon, Y., Bidanet, J.P., Fouillé, J.L., 2006. Between-breed variability of stillbirth and its relationship with sow and characteristics. J. Anim. Sci. 84:3185-3196.
Castro-Najera, J.A., Martínez-Burnes, J., Mota-Rojas, D., Cuevas-Reyes, H., López, A., Ramírez-Necoechea, R., Gallegos-Sagredo, R., Alonso-Spilsbury, M., 2006. Morphological changes in the lungs of meconium-stained piglets. J. Vet. Diagn. Invest. 18: 622-627.
Dewey, C.E., Straw, B.E., 2006. Herd examination. In: B.E. Straw, J.J. Zimmermann, S. D’Allaire and D.J. Taylor (eds.) Disease of Swine. Blackwell Publ., Malden, MA, USA, pp 3-14.
González-Lozano, M., Trujillo-Ortega, M.E., Becerril-Herrera, M., Alonso-Spilsbury, M., Ramírez-Necoechea, R., Hernández-González, R., Mota-Rojas, D., 2009. Effects of oxytocin on critical blood variables from dystocic sows. Vet. Mex. 40:231-245.
González-Lozano, M., Trujillo-Ortega, M.E., Becerril-Herrera, M., Alonso-Spilsbury, M., Ramírez-Necoechea, R., 2010. Uterine activity and fetal electronic monitoring in parturient sows treated with vetrabutin chlorhydrate. J. Vet. Pharmacol. Ther. 33:28-34.
Herpin, P., Le Dividich, J., Claude, H.J., Fillault, M., De Marco, F., Bertin, R., 1996. Effects of the level of asphyxia during delivery on viability at birth and early postnatal vitality of newborn pigs. J. Anim. Sci. 74:2067-2075.

Jezkova, D., Smrckova, M., 1990. Variations of glucoasemia and lactacidemia in pregnant sows, fetuses and in sows and piglets till the 10th day after delivery. Vet. Med. 35:613-620.

Lauterbach, K.E., Kolb, V., Gerisch, G., Grundel, C., Schmidt, U., 1987. Levels of hemoglobin in the blood and of glucose, lactate and free fatty acids in blood plasma from still-born piglets of various birth weight. Arch. Exp. Vet. Med. 41:522-530.

Lawn, J., Shibuya, K., Stein, C., 2005. No cry at birth: global estimates of intrapartum stillbirths and intrapartum-related neonatal deaths. B. World Health Organ. 83:409-417.

Low, J.A., 2004. Determining the contribution of asphyxia to brain damage in the neonate. J. Obstet. Gynaecol. Re. 30:276-286.

Mota-Rojas, D., Martinez-Burnes, J., Ramírez-Necochea, R., Trujillo-Ortega, M.E., Albores-Torres, V., Gallegos-Sagredo, R., 2006. Meconium staining of the skin and meconium aspiration in porcine intrapartum stillbirths. Livest. Sci. 102:155-162.

Mota-Rojas, D., Martinez-Burnes, J., Trujillo-Ortega, M.E., López-Mayagoitia, A., Rosales-Torres, A.M., Ramírez-Necochea, R., Alonso-Spilsbury, M., 2005a. Uterine and fetal asphyxiation in parturient sows treated with oxytocin. Anim. Reprod. Sci. 86:131-141.

Mota-Rojas, D., Martinez-Burnes, J., Trujillo-Ortega, M.E., Ramírez-Necochea, R., López-Mayagoitia, A., 2002. Oxytocin administration during parturition and effects on umbilical cord and neonatal mortality in pigs. Am. J. Vet. Res. 63:1571-1574.

Mota-Rojas, D., Nava-Ocampo, A.A., Trujillo-Ortega, M.E., Velázquez-Armenta, Y., Ramírez-Necochea, R., Martinez-Burnes, J., Alonso-Spilsbury, M., 2005b. Dose minimization study of oxytocin in early labor in sows: uterine activity and fetal outcome. Reprod. Toxicol. 20:255-259.

Mota-Rojas, D., Orozco-Gregorio, H., Villanueva-Garcia, D., Bonilla-Jaime, H., Suarez-Bonilla, X., Hernandez-Gonzalez, R., Roldan-Santiago, P., Trujillo-Ortega, M.E., 2011. Foetal and neonatal energy metabolism in pigs and humans: a review. Vet. Med. 56:215-225.

Nava-Ocampo, A.A., Reyes-Pérez, H., Belo-Ramírez, A.M., Mansilla-Olivares, A., Ponce-Monter, H., 2000. For ischemic brain damage, is preclinical evidence of neuroprotection by presynaptic blockade of glutamate release enough? Med. Hypotheses 54:77-79.

Olmos-Hernández, A., Trujillo-Ortega, M.E., Alonso-Spilsbury, M., Ramírez-Necochea, R., Mota-Rojas, D., 2008. Foetal monitoring, uterine dynamics and reproductive performance in spontaneous farrowing sows. J. Appl. Anim. Res. 33:181-185.

Orozco-Gregorio, H., Mota-Rojas, D., Bonilla-Jaime, H., Trujillo-Ortega, M.E., Becerril-Herrera, M., Hernández-González, R., Villanueva-García, D., 2010. Effects of administration of caffeine on metabolic variables in neonatal pigs with peripartum asphyxia. Am. J. Vet. Res. 71:1214-1219.

Orozco-Gregorio, H., Mota-Rojas, D., Ramírez-Necochea, R., Velázquez-Armenta, Y., Nava-Ocampo A., Hernández-González, R., Trujillo-Ortega, M.E., Villanueva-Garcia, D., 2008. Short-term neurophysiologic consequences of intrapartum asphyxia in piglets born by spontaneous parturition. Int. J. Neurosci. 118:1299-1315.

Orozco-Gregorio, H., Mota-Rojas, D., Villanueva-Garcia, D., Bonilla-Jaime, H., Suárez-Bonilla, X., Torres-Gonzalez, R., Bolaños, D., Hernández-González, R., Martínez-Rodríguez, R., Trujillo-Ortega, M.E., 2011. Caffeine therapy for apnoea of prematurity: a pharmacological treatment. Afr. J. Pharm. Pharmacol. 5:564-571.

Randall, G.C., 1979. Studies on the effect of caffeine on metabolic variables in neonatal pigs with peripartum asphyxia. Am. J. Obstet. Gynecol. 198:582.

Trujillo-Ortega, M.E., Hernández-Gonzalez, R., Becerril-Herrera, M., Alonso-Spilsbury, M., 2006. Obstetric and neonatal outcomes to recombinant porcine somatotropin administered in the last third of pregnancy to primiparous sows. J. Endocrinol. 189:575-582.

Trujillo-Ortega, M.E., Mota-Rojas, D., González, M., Orozco, H., Ramírez-Necochea, R., Nava-Ocampo, A.A., 2007. A study of piglets born by spontaneous parturition under uncontrolled conditions: could this be a naturalistic model for the study of intrapartum asphyxia? Acta Biomedica 78:29-35.

Tuchscherer, M., Puppe, B., Tuchscherer, A., Tiemann, U., 2000. Early identification of neonates at risk: traits of newborn piglets with respect to survival. Theriogenology 54:371-388.

Uribé-Escamilla, R., Padilla-Martín, K., González-Maciej, A., Arch-Tirado, E., Nava-Ocampo, A.A., Alfaro-Rodríguez, A., 2010. Neuroprotective effects of glycine in rats with permanent cerebral ischemia. J. Theor. Exp. Pharmacol. 1:72-75.

van Dijk, A.J., van Loon, J.P., Taverne, M.A., Jonker, F.H., 2008. Umbilical cord clamping in term piglets: A useful model to study perinatal asphyxia? Theriogenology 70:662-674.

Varona, L., Soenssen, D., Thompson, R., 2007. Analysis of litter size and average litter weight in pigs using a recursive model. Genetics 177:1791-1799.

Zaleski, H.M., Hacker, R.R., 1993. Variables related to the progress of parturition and probability of stillbirth in swine. Can. Vet. J. 34:109-113.