Asphyxia in Newborn Canines

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Morphological variability in canines is associated with the mother's size and weight, which likely affects the birth weight of the puppies and their metabolic status. Identifying physio-metabolic alterations in the blood from the umbilical vein to evaluate the concentration of gases, glucose, lactate, calcium, hematocrit levels, and blood pH of newborn puppies will make it possible to determine the risk of complications due to intrauterine asphyxia.

Keywords: animal perinatology ; asphyxia ; physiological blood profile

1. Introduction

Mortality in dogs during the neonatal period has been estimated to reach 40% [1]. Deaths may occur in the uterus, during expulsion, immediately postpartum, or during the first weeks of life [2][3][4], but the highest number of stillbirths occurs during birth [5] and the first 7 days of life [6]. Approximately 60% of these deaths are associated with intrapartum asphyxiation [7] caused by dystocic deliveries [5][6][8]. Asphyxia during the birthing process also negatively impacts the newborns' adaptation to extrauterine life [9] by limiting their viability and vitality [6][10][11][12][13]. A high neurologic morbidity increases the risk of neonatal mortality [14]. The birthing process is the most critical phase for newborns [15] because the transition from fetus to neonate involves physiological, biochemical, and anatomical changes accompanied by flows of hormones that trigger the respiratory function, vascular changes, and the activation of energy metabolism [16][17]; additionally, the maternal behavior is critical for the parturition to take place in favorable conditions for the newborn puppy [18][19][20][21]. Studies of dogs have reported that a certain level of transitory asphyxiation occurs during delivery. Though this is normal, it produces hypercapnia and transitory acidosis in puppies [22][23]. If these conditions persist, they will alter gas exchange [24], delay the onset of respiration, and generate metabolic acidosis in newborns [25]. The challenges of the birthing process, together with these risk factors can determine the proportion of the liveborn (LP) vs. stillbirth (SB) puppies and the viability of the former [26][27][28]. Morphological variability in canines is associated with the mother's size and weight [23], for these likely affect the birth weight of the puppies [26][28][29][30] and their metabolic status. In both veterinary and human perinatology, analyzing blood gases and metabolites has emerged as an important tool for evaluating newborns [13][31], but reports on dogs are scarce. Studying physiological indicators provides crucial information and allows researchers to estimate variations in oxygenation levels, metabolic profiles, and the acid–base balance [32] that help determine the level of fetal hypoxia suffered during birth. Gasometry allows the monitoring of the respiratory function by measuring the concentration of certain gases (pO_2, O_2 saturation (SaO_2), pCO_2) and blood pH [11][12][33][34][35][36] and the evaluation of the acid-base balance—to estimate the newborns' metabolic status [13][33][37][38]. Variations in metabolite levels, including lactate, play an important role in metabolic acidosis [39][40] associated with hypoxic events [1][41], high blood glucose levels [36], and a general compensatory metabolism marked by excess base and bicarbonate in the blood [25]. Identifying physio-metabolic alterations in the blood of newborn puppies will make it possible to determine the risk of complications due to intrauterine asphyxia. However, evidence on hypoxia in canines, its effects, and its relations to the mother's weight as a risk factor is scant or has not been fully evaluated.

2. Weight

It was proposed that the weight of puppies at birth can be influenced by diverse factors, as occurs in other mammals. These include the duration of pregnancy [27][42][43], restrictions on intrauterine growth [42][44][45], the mother's nutritional status [27], breed [46], and the weight and size of the placenta [47]. However, the results of our study suggest that the mother's weight before giving birth exerts an effect on the weight of the newborn puppies since this varied significantly among the four categories tested. A broad weight range was observed that might be attributable to this species' extensive morphological variability characteristic [48]. The recorded weights of the 272 puppies born and classified according to the weight of the dam (based on FCI guidelines, [49]) showed a mean from 204.48 to 407.39 g (157–453 g), with a mean variation of 77.46 to 202.91 g. We believe that the weight of the neonates reflected the mother's weight because our study did not consider breed as a variable. A study by Vassalo et al. [6] observed a similar effect, the mothers' body weight

influenced the weight of puppies born by eutocic births and cesarean section. While it is true that the dam's nutritional status can affect the weight of the puppies—as occurs in humans [50]—this variable was not controlled in this study.

One important finding involves the weight of the SB, as this was always higher than that of the LP in all four cases (C1–C4). These differences mean 29.16–52.77 g, but categories C3 and C4 had both the highest mean weights (419.86 and 433.79 g, respectively) and the highest mortality rates (C3 = 20.58%, C4 = 24.58%). On one side, and such as other species, including humans, swine, and bovines, low birth weight is considered an important risk factor for neonatal mortality [34][51][52]. Reports on dogs affirm that low birth weight is strongly related to mortality. In this regard, Groppetti et al. [53] and Mila et al. [54] pointed out that there is a twelve-fold higher mortality risk for the lightest puppies than those with normal weight. Though low birth weight has been deemed a disadvantageous condition for neonatal survival [3][53][55][56] and has been associated with a higher risk of fetal death, our study did not reveal signs of this because the heaviest puppies presented a higher risk of fetal death than those with the lowest weight (12.5 vs. 24.58% mortality). On the other side, previous results indicate that higher birth weights reduce postnatal mortality but increase the rate of intrapartum mortality due to the difficulties of birth caused by cephalopelvic disproportion and prolonged labor that can cause hypoxia or death [28][57][58]. The mortality rate in this study was 17.27%, counting only the pups that died intrapartum. While it is true that the cause of perinatal mortality in dogs is multifactorial, the mother's weight must be considered a risk factor due to its impact on the weight of type II SB puppies, physiological alterations, and the acid–base imbalance present in puppies born in natural births.

3. Physiometabolic Profiles

Fetuses commonly suffer intermittent periods of light hypoxia due to uterine contractions and the mechanical pressure inherent to the birth process [59]. Vassalo et al. [6] affirmed that a state of fetal hypoxia during the perinatal period is common in newborn puppies. We measured the physiological and metabolic changes that LP experienced during eutocic births, including increases in blood levels of pCO_2 and lactate of 17.38% and 51.45%, respectively, and decreases in blood pH of 1.22%, and levels of pO_2 (15.27%) and bicarbonate HCO_3^- (9.48%), with high EB (45.91%), all due to hypercapnia (an indicator of respiratory acidosis) as the main factor. The most evident alterations occurred in the LP groups with the heaviest dams (C2, C3, C4). These alterations in gases and blood metabolites indicated respiratory and metabolic acidosis (mixed acidosis) resulting from intermittent asphyxia in utero during natural birth. Compensatory alkalosis began as a response to the respiratory and metabolic acidosis in the LP in all groups (C1–C4) due to hypoxia. This explains why pH did not decrease drastically [60][61]. Hypoxia-induced stress increases circulating epinephrine that breaks down muscular glycogen; thus, increasing lactate concentrations [62][63][64]. The above slows metabolism and triggers delayed anaerobiosis, a mechanism known as a tolerance to fetal hypoxia [65].

Regarding the metabolite glucose, no significant differences were observed in the LP during the first minute of life in any of the four categories, since measurements were in a range of 94.92–103.91 mg/dL. Mila et al. [17] reported a mean plasma glucose concentration of 97 mg/dL between 10 min and 8 h postpartum. The blood glucose level of puppies in the first 24 h postpartum was established in a range of 88–133 mg/dL [66][67]. Adequate energy reserves are extremely important for neonatal survival and resistance to adverse climatic conditions [68]. However, during the first hours of life, a decrease in glucose concentrations may be seen in diverse species because the glucose supply is interrupted abruptly during birth. This decrease is associated with the rapid exhaustion of hepatic glycogen. Hypoglycemia increases blood glucagon, cortisol, and catecholamine levels, leading to gluconeogenesis, lipolysis, glycogenolysis, and the consumption of ketone bodies. Ingesting colostrum post-birth increases and maintains glucose levels. In humans, for example, values below 50 mg/dL have been observed, though these may increase to 81 mg/dL during daytime [69][70]. A similar situation has been seen in foals [71]. On another point, an increase in blood glucose in newborn piglets can be considered an accurate indicator of neonatal distress because it shows their incapacity to regulate, or compensate for, the physiological processes during birth [13][37][72]. Mota-Rojas et al. [73] mention that high glucose concentrations in piglets are a sign of a short episode of asphyxia compared to those that manage to maintain their energy reserves. Therefore, lower glucose levels are associated with a more extended period of asphyxia and higher a consumption of energy reserves. It is important to mention that a prolonged or intermittent asphyxia in utero during birth does not necessarily lead to intrapartum stillbirth. However, these conditions can weaken newborns and reduce their capacity to adapt to extrauterine life, as documented in piglet studies [36]. The events that occur during an acute process of asphyxiation—such as metabolic acidosis and hypoxia—impact the welfare of newborns and their postnatal development.

Birth weight was reported as a risk factor for intrapartum hypoxia because newborns with a low birth weight are more likely to suffer oxygen restriction and the secondary effects of hypoxemia [74][75]. Present findings, however, indicate otherwise. The blood samples collected from the umbilical cords for the gas and metabolic analyses of the intrapartum SB indicated that the fetuses showed signs of severe metabolic acidosis moments before birth due to the low pH (range:

6.79–6.88), increased pCO_2 levels up to double those registered in the LP (94.66 vs. 47.69 mmHg), lactate values as many as four times higher than in the LP (13.08 vs. 4.80 mg/dL), EB in a range of −14.26 to −15.33, and a decrease in pO_2 (6.22%) and bicarbonate HCO_3^- levels (6.97%). We also observed that the Type II SB showed a significant decrease in plasma glucose concentrations in every group (C1–C4), with a range of 38.78–51.11 mg/dL. This result coincides with the values < 40 mg/dL reported by Lawler [76], related to hypoglycemia, which indicate a depletion of the newborns' energy reserves, as a by-product of a previous hypoxic process [7][76] accompanied by a delay in eliminating excess liquid from the lungs, a decrease in uterine blood circulation, deficient gas exchange, and an alteration of energy metabolism [16]. We, therefore, infer that prolonged uterine contractions without fetal expulsion, caused by the prolonged birth process characteristic of this species, trigger hypoxia by increasing anaerobic glycogenolysis and the development of metabolic acidosis, as has been seen in piglets [73][77][78], humans [79], foals [80], and domesticated animals, including buffaloes [81] [82]. These are conditions that reduce vitality and increase mortality [83].

Fetal asphyxia, defined as a condition of hypoxemia with hypercapnia and acidosis, caused the death of the pups at birth in this study. Fetal asphyxia caused the death of 17.27% of the puppies in this study, but the highest percentages of intrapartum deaths were seen in C3 and C4, which together represented 55.31% of the mortality of the pups from natural births.

Acid–Base Balance

In LP, a pH below the reference values was observed (7.35–7.45) in C2, C3, and C4, but this parameter on its own does not permit measuring the accumulated exposure to hypoxia because it is expressed logarithmically [39]. It does, however, establish the existence of acidosis in newborns and reflects fetal hypoxic stress that occurred during birth. Hence, the relation among pH, bicarbonate, and pCO_2 indicates a process of metabolic acidosis [84]. In addition, the concentration of excess base (EB) must be determined, as this is an indicator of a linear tendency that determines the accumulation of acidosis after being adjusted for variations in pCO_2 [85].

The intense, constant uterine contractions necessary for fetal expulsion can compress the umbilical cord, drastically decreasing both placental and umbilical blood circulation [86]. The decrease in pO_2 and the increase in pCO_2 combined to lower the pH, but bicarbonate in the plasma mitigated this imbalance. As a result, the high concentration of bicarbonate generated a mixed acidosis that exacerbated the increase in ionized calcium and the decrease in protein-bonded calcium [87], producing hypocalcemia at birth. Andres et al. [25] indicate that delayed breathing and metabolic acidosis are related to mortality at birth.

During pregnancy, fetuses depend on their mother for gas exchange and correct oxygenation through the placenta. This exchange is determined by the size of the fetuses, blood gas concentrations in the mother, and the latter's capacity for transfer and transport. Thus, modifications to any of these parameters can generate a state of hypoxia and subsequent disruptions of the acid–base balance, such as metabolic acidosis [59]. It is believed that the fetus' capacity to withstand birth stress and welfare depends on both its condition at birth and the birthing process itself (duration, number of contractions, fetus thermoregulation, physiological, and metabolic changes. In addition, the newborn has to make several adjustments to adapt to extrauterine life, such as maintaining normoglycemia, thermoregulation, etc.) [18][88][89][90][91][92][93].

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