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Umbilical cord clamping in term piglets: A useful model to study perinatal asphyxia?

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Abstract

Perinatal asphyxia results in tissue and cellular changes during the reperfusion period and clinical signs like perinatal mortality and decreased vitality at birth in newborn piglets. This study aimed to develop and validate a model of birth asphyxia, mimicking the evolvement of birth asphyxia in natural farrowings by conducting umbilical cord clamping (UCC) in term piglets during caesarean sections under general anaesthesia. In total 23 piglets were subjected to 5–8 min of UCC and 24 piglets served as controls. Acid–base balance values and heart rates measured before UCC remained fairly constant throughout the surgical procedure, indicating nearly identical starting conditions of piglets within and between litters. UCC resulted in a significant, mild, mixed respiratory-metabolic acidosis (pH 7.22, pCO_2 9.8 kPa, BE_{ecf} 2 mmol/L, lactate 6.5 mmol/L; controls: pH 7.31, pCO_2 8.5 kPa, BE_{ecf} 5 mmol/L, lactate 4 mmol/L) at 10 min after birth (defined as simultaneous cutting of the umbilical cord and removal of a plastic bag that had been placed over the head to avoid air intake). Heart rates were significantly decreased during UCC (range: 83–107 beats/min versus 128–134 beats/min in controls). Rectal temperatures and changes in body weight until 72 h of life were not affected by UCC. Interestingly, four control and seven clamped piglets did not survive as no independent respiration could be attained. Birth weights and duration of UCC of these piglets did not differ significantly from those in surviving control and clamped piglets. In conclusion the mixed respiratory-metabolic acidosis arising in the surviving clamped piglets is not as severe as can be expected in highly asphyxiated, vaginally delivered newborn piglets. Repeatability of the model is compromised by considerable variation in the individual response to UCC.

Keywords: Perinatal asphyxia; Newborn piglets; Umbilical cord clamping; Acid–base balance values; Heart rates

1. Introduction

Besides the directly visible adverse effects of perinatal asphyxia, like high perinatal mortality rates [1] and reduced postnatal vitality [2,3] observed in piglets born under farm conditions, numerous detrimental changes at tissue and cellular level arise in the post-ischemic reperfusion period [4]. For example, in newborn piglets that have been subjected to hypoxia-ischemia in laboratory experiments, modified expression patterns of stress related proteins have been demonstrated in brain, heart and intestines [5–7]. Apparently this attributes to clinical signs, varying from

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delivery of less viable piglets [1,2] and reduced early postnatal vitality [2,3] to decreased growth and survival rates until the age of 10 days [3].

The evolvement of neurological deficits due to brain damage in surviving human neonates [8] has urged research to focus on strategies to prevent the severe, adverse outcome arising from birth asphyxia. Newborn (1–3-day-old) piglets are commonly used as experimental animal in these studies [9]. The various methods applied to induce hypoxia and/or ischemia include, among others, reduction of the fraction of inspired oxygen, either by placing newborn piglets in a hypoxia chamber with a reduced ambient oxygen tension [7] or by decreasing the inspiratory oxygen percentage in mechanically ventilated piglets [10]. The latter method has also been conducted with simultaneous occlusion of both carotid arteries [11,12].

Apart from the fact that in some models only the brain is exposed to a significant degree of hypoxia, all these models have in common that any relation with the natural expulsion of piglets and the concomitant risk factors for the evolvement of birth asphyxia, like occlusion, damage or even rupture of the umbilical cord [3], is lacking. This seriously limits the use of such models to study (pharmacological) intervention methods aimed at reducing or preventing adverse effects arising from birth asphyxia in piglets kept under normal farm conditions.

As both the incidence and the degree of birth asphyxia experienced in newborn piglets during birth are highly variable and rather unpredictable [13,14], Herpin et al. [13] developed a model of acute asphyxia by providing anteriorly presented piglets with a facemask to prevent breathing during the first 4 min of life. Although a quick recovery from the resulting respiratory acidosis was observed, plasma lactate values of the asphyxiated piglets remained significantly elevated during the first 75 min of life [13]. However, a major disadvantage of this model is that the hypoxia that the newborn piglets are exposed to might well be superimposed on a more or less severe degree of acidosis, already experienced during the expulsive stage of farrowing [15].

To design a model of asphyxia, which is in more close agreement with the development of birth asphyxia that occurs during vaginal deliveries, the main causes of birth asphyxia have to be considered.

According to Randall [1] and Christianson [16], the loss of umbilical cord functionality is an inevitable risk factor in the evolvement of birth asphyxia and thus perinatal mortality. This is emphasized by the finding that over 90% of the intra-partum stillborn piglets are born with a ruptured umbilical cord [17]. Mota-Rojas et al. [18] provided indirect evidence for the vital importance of the umbilical cord by demonstrating that administration of oxytocin resulted in a significantly higher percentage of stillbirths with haemorrhage and rupture of the umbilical cord. In piglets born alive but with broken umbilical cords, significantly lower pH values at birth have been found [15]. Furthermore, a more pronounced mixed respiratory-metabolic acidosis is observed in umbilical artery blood of liveborn piglets towards the end of the expulsive stage of farrowing [15]. These acid–base balance values are, however, still not comparable to those found in asphyxiated piglets [3] which implies that additional, deteriorating factors play a role in affecting the condition of the piglet at birth.

The aim of the study presented here was to develop and validate a model of birth asphyxia that mimics the evolvement of birth asphyxia in natural farrowings, by exposing term piglets to several minutes of umbilical cord clamping during caesarean sections in late pregnant sows. Such a standardised model would allow controlled studies of (non-)pharmacological intervention methods for reduction or prevention of the adverse effects resulting from birth asphyxia in newborn piglets. Outcome parameters of this model included analysis of acid–base balance values in blood samples from the umbilical vein and artery, measurement of heart rate and rectal temperatures, and evaluation of daily changes in body weight during the first 72 h of life.

2. Materials and methods

The experiment was approved by the Ethical Committee of the Veterinary Faculty of Utrecht University (the Netherlands).

2.1. Animals and experimental procedures

For this study, four late pregnant sows (gestational age 112–113 days) of second (three animals) and third (one animal) parity of the Topigs 20 breed were used. The sows were accommodated at the experimental pig farm The Tolakker, Faculty of Veterinary Medicine, Utrecht. Prior to surgery animals were weighed and fasted overnight but had ad libitum access to water. On the day of surgery, animals were transported to the surgical unit. Upon their arrival in this unit, sows were allowed to accommodate for 1 h before intramuscular premedication with azaperone (5.5 mg/kg) (Stresnil®, Janssen-Cilag, Tilburg, the Netherlands), ketamine (2 mg/kg) (Narketan®, Vétoquinol B.V., 's Hertogenbosch, the Netherlands) and midazolam (0.03 mg/kg)