

Manuscript Number: THERIO-D-20-00661

Title: PERIPARTUM FINDINGS AND BLOOD GAS ANALYSIS IN NEWBORN FOALS BORN AFTER SPONTANEOUS OR INDUCED PARTURITION

Article Type: Original Research Article

Keywords: mares, foals, induced parturition, oxytocin, blood-gas analysis, lactate

Corresponding Author: Professor Micaela Sgorbini, Ph.D

Corresponding Author's Institution: University of Pisa

First Author: Micaela Sgorbini, Ph.D

Order of Authors: Micaela Sgorbini, Ph.D; Francesca Freccero; Carolina Castagnetti; Jole Mariella; Aliai Lanci; Paola Marmorini; Francesco camillo

Abstract: Induction of parturition in horses is still not well accepted due to the potential peripartum complications for mares and newborn foals.

We assessed differences after spontaneous and induced parturition with low doses of oxytocin (OX) in 1) incidence of peripartum complications in mares; 2) viability, behavioral, physical, and venous blood gas analyses in foals.

In this study 61 mares were included; 45/61 were enrolled in the spontaneous foaling group (SF) and 16/61 in the induced foaling group (IF). In the IF group, when the calcium in mammary secretion reached concentrations of  $\geq 250$  ppm, mares received a single injection of 2.5 IU of oxytocin IV once a day until foaling.

Mares' breed, age, parity, gestational and stage II length, and peripartum complications were recorded.

Foal maturity, vital (Apgar score), behavioral and physical parameters were assessed at birth, and the foal clinical condition was monitored for one week. A jugular venous blood sample was collected at birth for blood gas analysis, acid-base status, and lactate assessment.

The median gestational length was within the reference interval in all the mares included and did not differ between the two groups. No statistical differences in the II stage length nor in incidence of peripartum complications were observed between the two groups.

All the foals were born alive and showed no signs of prematurity/dysmaturity. No statistical differences were found in foal viability between the two groups. Time to stand and nurse from the mare, and body temperature were significantly higher in the IF compared to the SF group. Venous blood pH,  $SO_2\%$  and BE were lower, while  $pCO_2$  and lactate were higher in the IF than in the SF group. All the foals in both groups remained clinically healthy during the observation period.

In conclusion, at term induction of parturition with a low dose of oxytocin does not have adverse effects on peripartum in mares. Our findings suggest that at term induced foals suffer slightly greater, but

not clinically significant, hypoxia, hypercapnia and acidosis than spontaneously delivered foals.

## Highlights

1. Induction of delivery by a low dose of OX does not adversely affect peripartum in mares at term.
2. At term induction by a low dose of OX did not impair clinical status of the newborns.
3. Induced foals showed slightly longer behavioural signs vs. spontaneously delivered.
4. Induced foals suffered greater hypercapnia and acidosis than spontaneously delivered foals.
5. In foals no clinical signs were present at birth and during the first week of life.

## Research article

### PERIPARTUM FINDINGS AND BLOOD GAS ANALYSIS IN NEWBORN FOALS BORN AFTER SPONTANEOUS OR INDUCED PARTURITION

Micaela Sgorbini<sup>1</sup>, Francesca Freccero<sup>2</sup>, Carolina Castagnetti<sup>2,3</sup>, Jole Mariella<sup>2</sup>, Aliai Lanci<sup>2</sup>, Paola Marmorini<sup>4</sup>, Francesco Camillo<sup>1</sup>.

<sup>1</sup>Department of Veterinary Sciences. Veterinary Teaching Hospital “Mario Modenato”, Pisa (Italy).

<sup>2</sup>Department of Veterinary Medical Sciences, Via Tolara di Sopra 50, 40064 Ozzano dell’Emilia, Bologna (Italy).

<sup>3</sup>Health Science and Technologies Interdepartmental Center for Industrial Research (HST-ICIR), University of Bologna, Bologna (Italy).

<sup>4</sup>Veterinarian, Pisa, Italy

#### Corresponding Author

Micaela Sgorbini

Department of Veterinary Sciences, Via Livornese snc, 56122 San Piero a Grado, Pisa (Italy)

Phone number: +390502210117 – Fax number: +390502210182

Email: [micaela.sgorbini@unipi.it](mailto:micaela.sgorbini@unipi.it)

#### Abstract

Induction of parturition in horses is still not well accepted due to the potential peripartum complications for mares and newborn foals.

We assessed differences after spontaneous and induced parturition with low doses of oxytocin (OX) in 1) incidence of peripartum complications in mares; 2) viability, behavioral, physical, and venous blood gas analyses in foals.

In this study 61 mares were included; 45/61 were enrolled in the spontaneous foaling group (SF) and 16/61 in the induced foaling group (IF). In the IF group, when the calcium in mammary secretion reached concentrations of  $\geq 250$  ppm, mares received a single injection of 2.5 IU of oxytocin IV once a day until foaling.

Mares' breed, age, parity, gestational and stage II length, and peripartum complications were recorded.

Foal maturity, vital (Apgar score), behavioral and physical parameters were assessed at birth, and the foal clinical condition was monitored for one week. A jugular venous blood sample was collected at birth for blood gas analysis, acid-base status, and lactate assessment.

The median gestational length was within the reference interval in all the mares included and did not differ between the two groups. No statistical differences in the II stage length nor in incidence of peripartum complications were observed between the two groups.

All the foals were born alive and showed no signs of prematurity/dysmaturity. No statistical differences were found in foal viability between the two groups. Time to stand and nurse from the mare, and body temperature were significantly higher in the IF compared to the SF group. Venous blood pH,  $SO_2\%$  and BE were lower, while  $pCO_2$  and lactate were higher in the IF than in the SF group. All the foals in both groups remained clinically healthy during the observation period.

In conclusion, at term induction of parturition with a low dose of oxytocin does not have adverse effects on peripartum in mares. Our findings suggest that at term induced foals suffer slightly greater, but not clinically significant, hypoxia, hypercapnia and acidosis than spontaneously delivered foals.

**Keywords:** mares, foals, induced parturition, oxytocin, blood-gas analysis, lactate.

## **1. Introduction**

In equine species, foaling is considered a critical event because signs of impending parturition are not clear and constant, and the rapidity of stage II of parturition is life threatening for the foal in case of dystocia. In fact, the period from the onset of stage II of parturition to delivery has important effects on the outcome of both the mare and foal [1].

In mares, the induction of parturition is mainly performed to ensure the presence of the stud farm personnel and, in the case of high-risk pregnancy, the availability of optimal veterinary assistance. In fact, most foalings happen during the night [2], when the possibility of assistance is decreased due to economic issues (non-business hours). Thus, the induction of foaling could be scheduled during a more comfortable day time.

Several agents and methods have been used to induce parturition in mares, such as glucocorticoids, prostaglandins, and oxytocin [3]. In many previous reports [4-10] the induction of delivery in healthy mares was associated with greater risks than spontaneous parturition for both mares and foals, such as a higher prevalence of dystocia, premature placental separation, retained placental membranes and delivery of premature or weak foals.

The most frequently used inducing agent in mares is oxytocin (OX). However, Chavatte-Palmer and colleagues [10] reported the delivery of a premature foal following induction with OX in a mare at >320 days of pregnancy with a milk calcium concentration of >13 mmol/L. Ousey [3] reported that OX can induce mares to deliver prematurely, especially when given repeatedly.

In more recent studies, parturition in mares at term was induced by low doses of OX once a day, and the authors [11-13] reported that this procedure was safe for both mares and foals. However, there are currently no data on the clinical outcome or subclinical effects in newborns after this method of induction compared to spontaneous delivery.

The aims of the present study were to assess differences after spontaneous and induced parturition with low doses of OX in the incidence of peripartum complications in mares and in the viability, behavioural, physical, and venous blood gas analyses in foals.

## **2. Materials and methods**

The research protocol was approved by the Institutional Animal Care and Use Committee of the University of Pisa (33476/2016) and the written consent was obtained from the owners of the mares.

The two-year study was conducted on mares and their newborn foals admitted to a stud farm associated with a Veterinary Teaching Hospital (VTH) Pisa and at a second VTH (Bologna). All the mares enrolled in this study were housed because the owners requested an attended parturition.

Inclusion criteria for the mares were as follows: 1) healthy on the basis of clinical examination performed weekly during the last month of gestation; 2) fetal anterior presentation confirmed by ultrasound examination at admission. All the mares were managed under similar circumstances. They were bedded on straw and fed with hay ad libitum and flaked grain, and turned out during the day. Mares were checked daily and moved to a foaling-box for continuous monitoring with video cameras as soon as udder enlargement was detected and/or when they reached 320 days of gestation. Calcium concentration in mammary secretion was evaluated at 05:00 pm using a commercial test kit (Foal Watch® Test Kit, Chemetrics, USA) and the induction of the delivery was performed as previously described [11]. In brief, mares received a single injection of 2.5 IU of oxytocin (Neurofisin®, Fatro, Italy) IV at 06:00 pm when calcium concentrations reached  $\geq 250$  ppm [14]. The mares not showing signs of labor within 60 min of treatment were judged not to be ready to foal and were not injected again. Treatment was repeated on the following days at the same time using the same protocol until delivery.

During foaling, mares were continuously monitored by personnel and the II stage length was recorded. No intervention was employed unless necessary. Information on mares' breed, age, parity, gestational and stage II length was recorded. Placenta retention, defined as no expulsion of foetal membranes within three hours from foaling [15] was assessed.

Foal viability was evaluated using a 5-parameter Apgar score [16] five minutes after birth. In addition, heart rate (HR) ( $>60$  beats/min) [17], respiratory rate (RR) (60-80 breaths/min) [17], and rectal body temperature (BT) (37.2-38.9°C) [18] values were also recorded. Foal maturity was assessed as previously reported [7]. Behavioural parameters, such as time to acquire sternal recumbency ( $<2$  minutes) [17], standing position ( $<120$  minutes) [17] and to nurse from the dams ( $<240$  minutes) [17] were also recorded. The foals were clinically evaluated at least twice a day up to seven days of life.

Within five minutes after birth, a jugular blood sample was collected from all foals using anaerobic conditions with a blood gas syringe containing lyophilized heparin (Safe PICO Self-fill arterial sampler, Radiometer Medical ApS-Denmark, [www.Radiometer.com](http://www.Radiometer.com)). An adjunctive

0.5 mL sample of jugular whole blood was collected for direct lactate measurement. Foals were only manually restrained, no clipping was performed, and only alcohol was rubbed on the skin for a better visualization of the vessels.

Whole blood lactate was evaluated within 1 min using a hand-held point-of-care (POC) blood lactate analyzer (Lactate Scout, SensLab GmbH, Leipzig, Germany) [19]. Blood gas and electrolytes analysis of heparinized samples was performed using a hand-held POC blood gas analyzer (VetStat Electrolyte and Blood Gas Analyzer, Idexx, USA) with the respiratory cartridge. This cartridge measured the following parameters: pH, pCO<sub>2</sub> (mmHg), pO<sub>2</sub> (mmHg), Na<sup>++</sup> (mmol/L), K<sup>+</sup> (mmol/L) and Cl<sup>-</sup> (mmol/L), while Hb (gr/dL), BE (mmol/L), Anion Gap (mmol/L), HCO<sub>3</sub><sup>-</sup> (mmol/L), total CO<sub>2</sub> (tCO<sub>2</sub> expressed in mmol/L), SO<sub>2</sub> (%) were calculated automatically. Temperature correction for pH and blood gases was applied. POC blood gas analyzer calibration and automatic sample integrity and quality check were performed according to the manufacturer's instructions.

## **2.2. Statistical analysis**

Analyses were performed using a Graph Pad Prism v. 6.0e. The Shapiro-Wilk normality test was carried out to verify data distribution. Since data showed different distributions (Gaussian vs non-Gaussian), the results were shown as median, minimum, and maximum values.

Fisher's exact test and the Yates's correction were applied to verify differences between the two groups regarding the foals' sex. These tests were also performed to verify differences in the incidence of dystocia, Apgar score, behavioral and clinical parameters between SF and IF groups.

A Mann-Whitney test was performed to verify differences between the two groups regarding mares' age, parity, gestational length and stage II length. A Mann-Whitney was also applied to verify differences between the two groups as regards: behavioral and clinical parameters (time to acquire sternal recumbency and standing position, to nurse from the mare, HR, RR and BT), blood-gas parameters, electrolytes and blood lactate concentrations. The value of P was set at <0.05.

## **3. Results**

Sixty-one mares were included in the study. In particular, 42/61 mares were admitted to the stud farm associated with the VTH in Pisa and 19/61 to the one in Bologna. Forty-five/61



mares were included in the spontaneous foaling group (SF) (26/45 housed in Pisa, 19/45 in Bologna) and 16/61 in the induced foaling group (IF) (16/16 housed in Pisa). Mares in the IF group were Standardbred (15/16) along with one Quarter Horse (1/16), while mares in the SF group were Standardbred (42/45) and Warmbloods (3/45). The mares' median age was 11 (6-24) and 11 (7-19) years and median parity was 4 (1-14) and 3.5 (2-6) in the SF and IF groups, respectively. Six mares in the SF group were primiparous. No differences were observed between the two groups in terms of age and parity.

The median gestational length was within the reference interval (320-360 days) [20], and not significantly different between the SF group (339 days; 320-359) and IF group (335 days; 330-347).

In the IF group, a single dose of OX was sufficient to induce parturition in 15/16 (93.8%) mares, while 1/16 (6.2%) was treated for two consecutive days.

The median length of stage II of parturition was 15.5 minutes (6-29) and 10 minutes (4-21) in the SF and IF groups, respectively, and no statistical differences were found between the two groups.

One premature separation of the placenta occurred in each group (2.2% SF and 6.2% IF). There were two dystocia (4.4%) due to malposition (1/2 carpal flexion and 1/2 lateral deviation of the head) corrected by vaginal-assisted delivery in the SF group, while no dystocia was observed in IF group. No statistical differences in the incidence of dystocia (6.7% vs 6.2% in SF and IF, respectively) were observed between the two groups. No placental retention was observed in either group.

All the foals were born alive and showed no signs of prematurity/dysmaturity. Thirty-one/45 (68.9%) fillies and 14/45 (31.1%) colts were born after spontaneous delivery, and 8/16 (50%) fillies and 8/16 (50%) colts after induced delivery. No difference in sex distribution was observed between the two groups.

In the SF group, the Apgar score was 9-10 in 41/45 (91.1%) and 7-8 in 4/45 (8.9%) foals. In the IF group, the Apgar score was 9-10 in 15/16 (93.5%), and 8 in one foal (6.5%). No statistical differences were found in the Apgar score between the two groups.

The respiratory rate was lower than the reference values in 14/45 (31.1%) and 5/16 (31.2%) in SF and IF foals, respectively, while HR was within reference range in all the foals of both groups. BT was lower than the reference interval values in 2/45 (4.4%) and 1/16 (6.2%) foals in SF and IF, respectively. The incidence of abnormal RR and BT was similar between the

two groups and no statistical differences were found.

In SF foals, the time for sternal recumbency, time to stand and to nurse were longer than normal in 20/45 (44.4%), 7/45 (15.5%), and 2/45 (4.4%) foals, respectively. In IF foals, the time for sternal recumbency, time to stand and to nurse were longer than normal in 4/16 (25%), 6/16 (37.5%) and 3/16 (18.7%) foals, respectively. The incidence of abnormal behavioral parameters was similar between the two groups and no statistical differences were found.

Median, minimum and maximum values for the time to acquire sternal recumbency and standing position, and to nurse from the mare are reported in Table 1, both for IF and SF foals, along with HR, RR and BT values. Significant differences were found between the two groups for the time to stand ( $p=0.039$ ) and to nurse from the mare ( $p=0.010$ ) and for body temperature ( $p=0.0004$ ).

Results on blood gas analysis, electrolytes and blood lactate are reported in Table 2. In particular, pH ( $P=0.0008$ ),  $SO_2\%$  ( $P=0.0019$ ) and BE ( $P=0.0146$ ) were lower in IF foals, while  $pCO_2$  ( $P=0.0304$ ) and lactate ( $P=0.0007$ ) were higher.

#### **4. Discussion**

In mares, induction of delivery is still not well-accepted due to the potential complications, such as dystocia, premature placental separation, retained placental membranes, fetal hypoxia or failure of passive transfer [4-10, 21].

Our aim was to assess the differences in the incidence of peripartum complications in mares, together with the viability, behavioral, physical, and venous blood gas analysis parameters in foals after spontaneous and induced parturition with low doses of OX.

Overall, the time to stand and to nurse, the body temperature, and venous blood gas and acid-base status at birth of the newborns differed significantly between the SF and IF groups, while neither the clinical status of the mares or foals was negatively affected by the induction of parturition.

We found that gestational length was within the reference range and was similar in SF and IF groups, which suggests that low-doses of OX successfully induce parturition if mares are ready for parturition, as previously demonstrated [11-13].

The length of the II stage of parturition was within the reference interval (<30 minutes) [1, 22] in both groups and no differences were found between SF and IF mares. Although these re-

sults do not agree with Panzani et al. [13] who reported a shorter expulsion time in treated mares, they are in line with others who reported similar lengths both in treated and control mares using either low-dose OX [12] or other OX-based induction protocols [8].

The prevalence of premature placental separation or dystocia in both groups was slightly higher than in previous studies [11,12], but in line with findings previously reported by others (4-10%) [23, 24].

The main problem related to the induction of delivery is the increased risk of prematurity [3]. In our study, all induced mares were over 330 days of pregnancy, and the foals' maturity was determined by dosing the calcium content in the mammary secretion, and all foals were assessed for maturity using the criteria suggested by Rossdale et al. [7].

Our results on the viability and behavioural parameters of foals are in agreement with studies [11-13] that evaluated the efficacy of daily low-dose OX injections for the induction of parturition and assessed the outcome of mares and foals. In fact, most of the foals in both groups showed a normal viability and behavioral parameters within the reference intervals.

The SF foals achieved first standing and nursing from the mares slightly faster than the IF foals. These results are in contrast with Villani and Romano [12] who reported that foals from induced mares achieved first standing and first sucking faster. However, our results are in agreement with others [11,13,25] who found that foals born after induced delivery were slightly slower to stand and nurse.

Our results showed similar HR and RR values between SF and IF foals; whereas, BT values were higher in IF foals, though still in the normal range [18]. Moreover, the difference in this parameter was marginal with no long-term clinical effects. In fact, all the foals subsequently showed normal BT and remained clinically healthy during the first week of life.

Some studies have investigated the blood gas concentrations and acid-base parameters from umbilical vessels immediately after birth in spontaneously delivered and at term induced foals [26-29]. To the best of our knowledge, only a few papers have reported jugular venous blood gas analyses performed immediately after spontaneous normal and dystocic delivery [30, 31].

Overall, our results are in line with previous findings that, even at term, spontaneously delivered foals suffer a degree of hypercapnia and acidosis at birth [26, 27, 29-31]. A very slight acidemia was present in our SF foals, and consistent with the pH values, the pCO<sub>2</sub> was slightly high, suggesting some respiratory acidosis.

According to Stewart et al. [28], foals do not suffer the same level of asphyxia at birth as hu-

man neonates. It has also been suggested that newborn foals might have greater levels of blood bicarbonate compared to human neonates [26]. This mildly alteration in acid-base status normalizes in the early hours in healthy foals which rapidly achieve effective ventilation [26-28], as supported by both arterial [26-28] and venous [32] blood gas analyses over the subsequent hours up to one day after birth.

In the study by Kimura et al. [30], in heavy draft foals, pH, and AG were slightly lower, and pCO<sub>2</sub> and lactate were higher, while HCO<sub>3</sub>, tCO<sub>2</sub>, BE were comparable to median values that we obtained. The II stage length (21.2±5.7 min) of normal deliveries reported by Kimura et al. [30] was slightly longer than the duration we found. This might explain some of the differences in the absolute values of pH, pCO<sub>2</sub> and lactate. Breed-related differences in foaling and in post-natal adaptation are more likely compared to the light breeds enrolled in the present study.

In this study, hyperlactatemia was present in the SF group, and the values were within the physiological range reported by Castagnetti et al. [19], but higher compared to ranges reported by Pirrone et al. [33] in healthy light breed foals at birth. Besides other potential causes, a rise in blood lactate is most commonly associated with tissue hypoxia [34], which could be due to a degree of asphyxia during parturition [28]. The high concentrations measured at birth could also be due to cortisol and catecholamine release [19]. To the best of our knowledge, no previous studies reported venous whole blood electrolytes in foals immediately after delivery. Electrolyte concentrations in equine neonates show a wide variation in the reference intervals, especially concerning the Na<sup>+</sup> concentration (123-159 mEq Na<sup>+</sup>/L) during the first days of life [35]. Overall, concentrations of Na<sup>+</sup>, K<sup>+</sup>, and Cl<sup>-</sup> recorded in both groups in this study were in the upper ranges reported in serum samples in healthy foals < 12 h of age [36].

Comparing the at term induced foals with those spontaneously delivered, significantly higher pCO<sub>2</sub> and lactate values were found in the former group, but with lower pH, BE and SO<sub>2</sub>% values. In line with the lower pH values, pCO<sub>2</sub> was higher in the IF group, highlighting greater respiratory acidosis. This suggests a decreased alveolar ventilation in the IF than the SF group in this early post-natal period, however this needs further evaluation.

The median concentration of lactate was significantly higher in the induced foals. In previous studies [19,33] no difference was found in blood lactate between healthy and sick foals at birth and during the first six hours of life. In our study, since lactatemia was within the refer-

ence intervals at birth and all the foals were clinically healthy, the difference found between the SF and IF groups does not seem to be clinically significant.

BE was significantly lower in the IF group, likely due to lactatemia, but still within the normal limits in both groups [37]. BE is used as an indicator of metabolic acid-base disturbance. In addition,  $\text{HCO}_3$  concentrations have also been suggested as a surrogate for BE and may represent a means to evaluate acid-base status [28]. In our study, no difference in  $\text{HCO}_3$  was found between the two groups. In addition, the AG was within the normal range for newborn foals [36], and also not different between the two groups. On balance, this might support a leading contribution of the respiratory component to the lower pH in IF group. However, factors such as a degree of compensatory response, hypoproteinemia, or coexisting metabolic alkalosis could partly mask a metabolic disturbance and thus further evaluation is warranted. Venous  $\text{SO}_2\%$  is one indirect measure of tissue hypoxia [39]. Consistent with the pH and lactate levels, in our study the  $\text{SO}_2\%$  was lower in the IF than the SF group. Moreover, this parameter was slightly lower in both groups at birth than in older foals [38]. The reduction in pH could interfere with the hemoglobin ability to bind oxygen, with a subsequent shift to the right of the oxygen dissociation curve [40]. However, many factors influence  $\text{SO}_2\%$ , such as the concentration of hemoglobin,  $\text{SaO}_2$ , cardiac output, and oxygen consumption [38]. Further investigations are needed regarding the pathophysiological mechanisms employed in the differences between groups. An arterial blood gas analysis could help to assess the respiratory function in these foals, despite the fact that no sign of respiratory distress was detected in our study.

As venous blood was used in our study, we found no agreement with previous studies [27,28] reported no significant differences in umbilical artery blood gas and acid-base parameters between spontaneously delivered and at term induced foals. In fact, these previous studies [27,28] only foals prematurely induced showed lower pH,  $\text{HCO}_3$ , BE and  $\text{pO}_2$  and higher  $\text{pCO}_2$ .

Factors that may affect the outcome in foals born after being induced may be parity, environment, cervical dilatation, and intrapartum complications [8]. We found no differences concerning the above-mentioned factors between SF and IF mares. However, it is our clinical impression that the II stage length needs to be reassessed with a larger number of cases.

Cervical ripening at the time of induction was not specifically assessed in our mares. However, induction of parturition with a low-dose of OX is successful only in subjects in which

readiness for parturition had been already achieved [11-13]. Thus, in our opinion this factor is negligible relative to the foals' outcome in this study.

In light of our findings, the relationship between at term parturition induction and a possible mild degree of subclinical dysmaturity or less prompt adaptation of the foals in the immediate post-natal period still needs to be clarified. However, it is essential to stress the fact that no clinical signs were manifest at birth and during the first week of life.

One limitation of the study is that foals born from induced mares were included in only one of the two facilities, thus it is not possible to completely rule out some management or environmental effect on the findings. The lack of statistical difference in some factors, such as the stage II length, might be due to the limited number of subjects included in the IF group. Moreover, no blood-gas follow up analysis was included to monitor any persistent subclinical difference between groups over the subsequent days after birth, in face of a clinically healthy status.

We found that a jugular venous sample and a POC analyzer were useful and practical for stall-side blood gas, acid-base and electrolyte measurements and for comparisons between groups. Another study reported that the POC analyser that we used in this study provided reliable results with regards to pH, pCO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup> and K<sup>+</sup> in horses and older foals, while Na<sup>+</sup>, Cl<sup>-</sup> and pO<sub>2</sub> values should be interpreted with caution [41]. This should therefore be considered in clinical assessments and decision-making based on single measurements, especially in sick foals. It would be advisable to determine device-specific reference intervals in newborn foals in order to minimize interpretation errors.

## **5. Conclusions**

At term induction of parturition with a low dose of oxytocin did not produce adverse effects in mares and foals. Our findings suggest that at term induced foals suffer a slightly greater, but not clinically significant, hypoxia, hypercapnia and acidosis than spontaneously delivered foals.

A jugular venous blood sample was used to assess and compare the two groups of foals with regard to various acid-base parameters and electrolytes, which may be useful and easy to test in clinical practice.

## Acknowledgments

We are grateful to the studfarm “La Piaggia” (Tuscany, Italy) for the technical support.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## References

1. Norton JL, Dallap BL, Johnston JK, Palmer JE, Sertich PL, Boston R, et al. Retrospective study of the dystocia in mares at a referral hospital. *Equine vet J* 2007; 39(1):37-41. [http://doi: 10.2746/042516407X165414](http://doi:10.2746/042516407X165414).
2. Rossdale PD, Short, RV. The time of foaling in Thoroughbred mares. *J Reprod Fert* 1967; 13:341-3. [http// 10.1530/jrf.0.0130341](http://10.1530/jrf.0.0130341)
3. Ousey J. Induction of parturition in the healthy mare. *Equine vet Educ*, 2002; 5:83-87. [http// http://doi.org/10.1111/j.2042-3292.2003.tb00236.x](http://doi.org/10.1111/j.2042-3292.2003.tb00236.x).
4. Hillmann RB. Induction of parturition in mares. *J Reprod Fert* 1975; Suppl 23:641-4.
5. Jeffcott LB, Rossdale PD. A critical review of current methods for induction of parturition in the mare. *Equine vet J* 1977; 9:208-15.
6. Leadon DP, Rossdale PD, Jeffcott LB, Allen WR. A comparison of agents for inducing parturition in mares in the pre-viable and premature periods of gestation. *Reprod Fert* 1982; 32(S):597-602.
7. Rossdale PD, Ousey JC, Silver M, Fowden A. Studies on equine prematurity 6: guidelines for assessment of foal maturity. *Equine Vet J* 1984; 16:300-2. <http://doi.org/10.1111/j.2042-3306.1984.tb01931.x>.
8. Macpherson ML, Chaffin MK, Carroll GL, Jorgensen J, Arrott C, Varner DD. et al. Three methods of oxytocin-induced parturition and their effects on foals. *J Am Vet Med Assoc* 1997; 210:799-803.
9. Ousey JC, Rossdale PD, Dudan FE, Fowden AL. The effect of intrafetal ACTH administration on the outcome of pregnancy in the mare. *Reprod Fertil Dev* 1998; 10:359-67. <http://doi.org/10.1071/R98045>.

10. Chavatte-Palmer P, Arnaud G, Duvaux-Ponter C, Zanazi C, Gerard M, Ponter A. et al. The use of microdoses of oxytocin in mares to induce parturition. *Theriogenol* 2002; 58:837-40. [http://10.1016/S0093-691X\(02\)00813-0](http://10.1016/S0093-691X(02)00813-0)
11. Camillo F, Marmorini P, Romagnoli S, Cela M, Duchamp G, Palmer E. Clinical studies on daily low dose oxytocin in mares at term. *Equine Vet J* 2000; 32(4):307-10. <http://doi.org/10.2746/042516400777032147>.
12. Villani M, Romano G. Induction of parturition with daily low-dose oxytocin injections in pregnant mares at term: clinical applications and limitations. *Reprod Domest Anim* 2008; 43(4):481-3. <http://doi.org/10.1111/j.1439-0531.2007.00940.x>.
13. Panzani S, Villani M, Govoni N, Kindahl H, Faustini M, Romano G. et al. 15-Ketodihydro-PGF<sub>2α</sub> and cortisol plasma concentrations in newborn foals after spontaneous or oxytocin-induced parturition. *Theriogenol* 2009; 71(5):768-74. <http://doi.org/10.1016/j.theriogenology.2008.09.053>.
14. Ley WB, Bowen, JM, Purswell BJ, Irby M, Greive-Crandell K. The sensitivity, specificity and predictive value of measuring calcium carbonate in mares' prepartum mammary secretions. *Theriogenol* 1993; 40(1):189-98. [http://doi.org/10.1016/0093-691X\(93\)90352-6](http://doi.org/10.1016/0093-691X(93)90352-6).
15. Sager FC. Examination and care of the genital tract of the brood mare. *J Am Vet Med Assoc* 1949; 115:450-5.
16. Vaala WE. Perinatology. *Vet Clin North Am Eq Pract* 1994; 10:237-65.
17. Madigan JE. Normal equine labor, delivery and newborn vital signs. In Madigan HE, editor. *Manual of Equine Neonatal Medicine*. 4<sup>th</sup> Ed. Woodland, California, USA: Live Oak Publishing; 2013, p. 19.
18. Glenton-McDonald P, Green MA, Vaala WE, Cudd TA, Koterba AM. Nursing care of the neonatal foal. In: Koterba AM, Drummond WH, Kosch PC, editors. *Equine Clinical Neonatology*, Baltimore, USA: William and Wilkins; 1990, p. 625-652.
19. Castagnetti C, Pirrone A, Mariella J, Mari G. Venous blood lactate evaluation in equine neonatal intensive care. *Theriogenol* 2010; 73:343-57. <http://doi.org/10.1016/j.theriogenology.2009.09.018>.
20. Davis Morel MCG, Newcombe Jr, Holland SG. Factors affecting gestation length in the Thoroughbred mare. *Anim Reprod Sci* 2002; 74:175-85. [10.1016/s0378-4320\(02\)00171-9](http://10.1016/s0378-4320(02)00171-9).



21. Townsend HGG, Tabel H and Bristol FM. Induction of parturition in mares: effect on passive transfer of immunity to foals. *Am Vet Med Ass* 1983; 182:255-7.
22. Christensen BW. Parturition. In: McKinnon AO, Squires EL, Vaala WE, Varner DDD, editors. *Equine reproduction*, 2<sup>nd</sup> Ed. Chichester, UK, Blackwell Publishing Ltd; 2011, p. 2268-2276.
23. Rossdale, PD, Ricketts SW. *The Practice of Equine Stud Medicine*. Baltimore, USA, Williams and Wilkins; 1994; p. 98-146.
24. McCue PM, Ferris A. Parturition, dystocia and foal survival: a retrospective study of 1047 births. *Equine vet J* 2012; 44(41S): 22-5.
25. Cheong SH, Castillo Herrera JM, Dockweiler JC, Donnelly CG, Sones JL, Ellerbrock RE. Efficacy and outcome of foaling augmented with oxytocin using mammary calcium and pH criteria to guide the timing of augmentation. *Anim Reprod Sci* 2019; 202:87-95. <http://doi.org/10.1016/j.anireprosci.2019.02.002>.
26. Rossdale PD. Blood gas tensions and pH values in the normal Thoroughbred foal at birth and in the following 42h. *Biol Neonat* 1968; 13:18-25.
27. Rose RJ, Rossdale PD, Leadon DP. Blood gas and acid-base status in spontaneously delivered, term-induced and induced premature foals. *J Reprod Fert* 1982; 32(S): 521-8.
28. Stewart JH, Rose RJ, Barko AM. Respiratory studies in foals from birth to seven days old. *Equine Vet J* 1984; 16(4):323-8. <http://doi.org/10.1111/j.2042-3306.1984.tb01936.x>.
29. Jeawon SS, Katz LM, Galvin NO, Fogarty UM, Duggan VE. Determination of reference intervals for umbilical cord arterial and venous blood gas analysis of healthy Thoroughbred foals. *Theriogenol* 2018; 118:1-6. <http://doi.org/10.1016/j.theriogenology.2018.05.024>.
30. Kimura Y, Aoki T, Chiba A, Nambo Y. Effects of dystocia on blood gas parameters, acid-base balance and serum lactate concentration in heavy draft newborn foals *J Equine Sci* 2017; 28(1):27-30. <http://doi.org/10.1294/jes.28.27>.
31. Melchert M, Aurich C, Aurich J, Gautier C, Nagel C. Controlled delay of the expulsive phase of foaling affects sympathoadrenal activity and acid base balance of foals in the immediate postnatal phase, *Theriogenol* 2019; 139: 8-15. <https://doi.org/10.1016/j.theriogenology.2019.07.017>.

32. Madigan JE. Blood gases. In Madigan JE, editor. *Manual of Equine Neonatal Medicine*. 4<sup>th</sup> Ed. Woodland, California, USA: Live Oak Publishing; 2013, p. 413-414.
33. Pirrone A, Mariella J, Gentilini F, Castagnetti C. Amniotic fluid and blood lactate concentrations in mares and foals in the early postpartum period. *Theriogenology* 2012; 78(6): 1182-9. <https://doi.org/10.1016/j.theriogenology.2012.02.032>.
34. Magdesian GK. Blood lactate levels in neonatal foals: normal values and temporal effects in the post-partum period. *J Vet Emerg Crit Care* 2003; 3: 174.
35. Viu J, Armengou L, Ríos J, Muñoz A, Jose-Cunilleras E. Simplified strong ion difference approach to acid–base balance in healthy foals. *J Vet Emerg Crit Care* 2016; 26: 549-58. <http://doi:10.1111/vec.12488>.
36. Bauer JE, Harvey JW, Asquith RL, McNulty K, Kivipelto J. Clinical chemistry reference values of foals during the first year of life. *Equine vet J* 1984; 16(4): 361-3.
37. Knottenbelt BE, Holdstock N, Madigan JE. Reference values for hematology and biochemistry, appendix 2. In Knottenbelt BE, Holdstock N, Madigan JE, editors. *Equine neonatology, medicine and surgery*. 1<sup>st</sup> Ed. London, UK: Elsevier Ltd; 2004, 475.
38. Wong DV, Hepworth-Warren KL, Sponseller BT, Howard JM, Wang C. Measured and calculated variables of global oxygenation in healthy neonatal foals. *Am J Vet Res* 2017; 78(2): 230-8. <http://doi: 10.2460/ajvr.78.2.230>.
39. Hartog C, Bloos F. Venous oxygen saturation. *Best Pract Res Clin Anaesthesiol* 2014; 28:419-28. <http://doi.org/10.1016/j.bpa.2014.09.006>.
40. Refsum H, Opdahl H, Leraand S. Effect of extreme metabolic acidosis on the oxygen content of the blood. *Crit Care Med* 1997; 25: 1497-501.
41. Kirsch K, Detilleux J, Serteyn D, Sandersen C. Comparison of two portable clinical analyzers to one stationary analyzer for the determination of blood gas partial pressures and blood electrolyte concentrations in horses. *PLoS ONE* 2019; 14(2): e0211104. <https://doi.org/10.1371/journal.pone.0211104>.

Parameters		SF (n=45)	IF (n=16)	P
<b>Time to sternal recumbency</b>	Med m-M	2 1-16	2 1-4	0.335
<b>Time to standing</b>	Med m-M	70* 22-480	90* 35-165	0.039
<b>Time to nurse</b>	Med m-M	123.5* 60-240	143* 65-285	0.010
<b>HR</b>	Med m-M	82 48-142	80 60-100	0.801
<b>RR</b>	Med m-M	60 20-68	60 36-60	0.205
<b>BT</b>	Med m-M	37.6* 36.6-38.2	38* 37-38.8	0.0004

\*statistically different in rows

Table 1 – Median (Med), minimum (m) and maximum (M) values of time to acquire sternal recumbency and quadrupedal standing, time to nurse from the mare, heart (HR) and respiratory (RR) rates, body temperature (BT) evaluated at birth in foals born after spontaneous (SF) and induced (IF) parturition.

Parameter		SF (n=45)	IF (n=16)	P
pH	Med m-M	7.33 7.25-7.42*	7.31 7.24-7.34*	0.001
p <sub>v</sub> O <sub>2</sub> mm Hg	Med m-M	34 22-76	31 21-40	0.222
S <sub>v</sub> O <sub>2</sub> %	Med m-M	65 60-94*	60 60-70*	0.002
p <sub>v</sub> CO <sub>2</sub> mm Hg	Med m-M	59 46-71*	62 54-70*	0.038
HCO <sub>3</sub> <sup>-</sup> mmol/L	Med m-M	28.7 24-33	27.3 25.7-30.6	0.178
Anion Gap mmol/L	Med m-M	19.1 15.8-29.6	19.5 2-33.4	0.603
tCO <sub>2</sub> mmol/L (25±5 mmol/L) [34]	Med m-M	30.55 25.8-34.9	29.05 27.5-32.4	0.228
BE mmol/L	Med m-M	1.1 -4.3-4.9*	-0.1 -2.7-2.1*	0.022
tHb g/dL	Med m-M	17.2 15.0-18.9	16.6 14.7-19	0.394
Na <sup>+</sup> mmol/L [34]	Med m-M	151 146-163	152 144-163	0.576
K <sup>+</sup> mmol/L	Med m-M	4.2 2.9-5.6	4.05 3.1-5.6	0.803
Cl <sup>-</sup> mmol/L	Med m-M	107 103-111	108 104-109	0.864
Blood lactate	Med m-M	4.6 1.5-11.8*	5.8 3.9-7.9*	0.001

\*statistically different in rows

Table 2 – Median (Med), minimum (m) and maximum (M) values of venous blood gas parameters, acid-base and lactate in foals born after spontaneous (SF) and induced (IF) parturition.

Dear Editor,

here is our paper titled “Peripartum findings and blood gas analysis in newborn foals born after spontaneous or induced parturition” authored by Sgorbini et al. We would like to submit our paper for the publication on your journal. The manuscript has not been published or submitted for publication elsewhere. Authors’ contribution to the manuscript is equally distributed and no conflict of interest exists. The paper has the approval of all authors.

Yours sincerely,

Dr Micaela Sgorbini

(corresponding author)



**27 April 2020**

To whom it may concern

This is to declare that I have edited and proofread the English of the following paper:

**PERIPARTUM FINDINGS AND BLOOD GAS ANALYSIS IN NEWBORN FOALS BORN AFTER SPONTANEOUS AND INDUCED PARTURITION**

On behalf of:

**Micaela Sgorbini et al**

My revision did not include the Bibliography. Subsequent to my revision, the authors may have made other changes or chosen not to implement some of the changes that I suggested. The correctness of the technical terms is also the responsibility of the authors.

The final version of the manuscript, as sent to the authors on **27 April 2020**, will be kept in our archives.

I have 30 years of experience of editing the English of scientific papers. I am also the author of *English for Writing Research Papers* published by Springer.

Please do not hesitate to contact me for any further information you may require:

adrian.wallwork@gmail.com

Best regards

A handwritten signature in blue ink that reads 'Adrian Wallwork'.

Adrian Wallwork

## Theriogenology Author Agreement Form

*This Form should be signed by all authors OR by the corresponding (or senior) author who can vouch for all co-authors. A scanned copy of the completed Form may be submitted online.*

The authors confirm the following statements:

1. that there has been no duplicate publication or submission elsewhere of this work
2. that all authors have read and approved the manuscript, are aware of the submission for publication and agree to be listed as co-authors

**Author Name**

**Signature**

Micaela Sgorbini

Micaela Sgorbini

Francesca Freccero

Francesca Freccero

Carolina Castagnetti

Carolina Castagnetti

Jole Mariella

Jole Mariella

Aliai Lanci

Aliai Lanci

Paola Marmorini

Paola Marmorini

Francesco Camillo

Francesco Camillo