



Efficacy and outcome of foaling augmented with oxytocin using mammary calcium and pH criteria to guide the timing of augmentation



Soon Hon Cheong^{a,*}, Juan M. Castillo Herrera^{a,b}, Jenna C. Dockweiler^{a,c},
Callum G. Donnelly^{a,d}, Jennifer L. Sones^{a,e}, Robyn E. Ellerbrock^{a,f}, Sonya M. Lawlis^a,
Robert O. Gilbert^{a,g}, Mariana Diel de Amorim^a

^a Department of Clinical Sciences, College of Veterinary Medicine, Cornell University, Ithaca, NY, USA

^b Department of Veterinary Clinical and Diagnostic Sciences, Faculty of Veterinary Medicine, University of Calgary, Calgary, AB, Canada

^c Wheat Ridge Animal Hospital by Ethos Veterinary Health, Wheat Ridge, CO, USA

^d Department of Medicine and Epidemiology, School of Veterinary Medicine, University of California-Davis, Davis, CA, USA

^e Department of Veterinary Clinical Sciences, Louisiana State University School of Veterinary Medicine, Baton Rouge, LA, USA

^f Department of Large Animal Medicine, College of Veterinary Medicine, University of Georgia, Athens, GA, USA

^g Department of Clinical Sciences, Ross University School of Veterinary Medicine, Basseterre, St Kitts, West Indies

ARTICLE INFO

Keywords:

Oxytocin
Foaling
Augmentation

ABSTRACT

Augmentation of parturition can be used to advance labor in mares to occur at a time when personnel is available to assist if necessary. We performed a retrospective study to determine the efficacy and safety of augmentation to manage foalings. Augmentation was performed with 3 IU oxytocin i.v. when mammary calcium concentrations were ≥ 250 ppm, mammary secretion pH ≤ 6.5 , and the mare showed impending signs of parturition. Augmented parturitions ($n = 19$) were compared with three different control groups. The three control groups were: 1) Time Match control ($n = 37$) which were non-augmented foalings in the barn during the same time period; 2) Mare Match control ($n = 32$) which were the non-augmented parturitions of the augmented mares in previous years; and 3) Historic Match control ($n = 165$) consisted of foalings that occurred from 2006 to 2016 in the facility. All augmented mares foaled within two h with an average of 44 min (range 20–75) after oxytocin injection. The interval between foaling and the foal standing was shorter in augmented parturitions compared with historic match controls. The interval between foaling and the foal nursing was longer with augmented parturitions compared with time match and historic match controls. Duration of fetal membrane retention was not different between all groups. Augmentation of imminent parturition is potentially a safe and effective treatment for mares and foals. Implementation of augmentation as a routine procedure may increase the likelihood of enteral administration of colostrum to foals.

1. Introduction

Foaling management is an integral part of successful horse breeding. Foals quickly become compromised in cases of dystocia, and timely interventions are required to minimize the adverse effects on foal survival and health (Emberton, 1999). Most mares foal at

* Corresponding author.

E-mail address: cheong@cornell.edu (S.H. Cheong).

<https://doi.org/10.1016/j.anireprosci.2019.02.002>

Received 30 November 2018; Received in revised form 26 January 2019; Accepted 6 February 2019

Available online 08 February 2019

0378-4320/ © 2019 Elsevier B.V. All rights reserved.

night when personnel availability are limited (McCue and Ferris, 2012). It, therefore, is desirable to have the capacity to advance the progress of parturition to a time when personnel is available to assist. Augmentation of parturition generally involves advancement of this process, usually with oxytocin treatments. Augmentation of parturition is used without reports of complications in mares that are imminently in labor or in the early stage of labor (Britton, 1963; Purvis, 1972), as distinct from induction, which occurs before signs of impending foaling are observed. A variety of protocols have been described to advance the timing of parturition in imminently foaling mares to times when personnel are available of assistance (Camillo et al., 2000; Chavatte-Palmer et al., 2002; Duggan et al., 2007; Hillman, 1975; Hillman and Ganjam, 1979; Jeffcott and Rossdale, 1977; Klem et al., 1982; Ley et al., 1989a,b; Ousey, 2003; Pashen, 1980; Purvis, 1972; Rossdale and Jeffcott, 1975; Villani and Romano, 2008). There has only been one study on foaling augmentation since 2014 (Witkowski et al., 2014) and the management of foaling mares, particularly in identifying mares that will foal imminently, has changed during this period with the inclusion of mammary secretion pH testing. Clinically, assessment of imminence of parturition is determined using a combination of physical changes in the mare and changes in the composition of mammary secretions. Physical changes associated with impending parturition include relaxation of pelvic ligaments, elongation of the vulva, mammary gland development, filling of teats, and waxing of teats. Electrolyte changes of mammary secretions are considered more accurate than physical changes for predicting parturition, and this includes inversion of the sodium and potassium ratio and an increase in calcium concentration (Ley et al., 1989a,b; Ousey et al., 1984). An increase of calcium in mammary secretions is typically used to identify the appropriate timing to advance the labor process (Camillo et al., 2000; Chavatte-Palmer et al., 2002; Duggan et al., 2007; Ley et al., 1989a,b; Macpherson et al., 1997; Rigby et al., 1998; Villani and Romano, 2008). More recently, the use of mammary secretion pH has been shown to be a specific and sensitive test to determine if parturition is imminent (Canisso et al., 2013; Korosue et al., 2013). The use of mammary secretion pH in conjunction with calcium concentration and other signs of impending foaling to improve the selection of mares for augmentation has not been evaluated.

Inducing parturition in mares that are not going to imminently foal can be potentially disastrous for both mare and foal, therefore, induction of foaling is generally not recommended (Jeffcott and Rossdale, 1977; Townsend et al., 1983). When foaling, however, is advanced in mares that have mature fetuses, as indicated by mammary secretions and signs of impending parturition, there are generally few adverse effects of augmentation on mares and foals (Britton, 1963; Camillo et al., 2000; Purvis, 1972; Villani and Romano, 2008). Appropriate control groups are necessary to evaluate the effects of augmentation on foaling outcomes, but obtaining controls can be challenging in retrospective studies. The purpose of this retrospective study was to compare the outcomes of foaling in augmented mares where there is the anticipation of imminent foaling to the outcomes of three control mare groups with there being shortfalls with use of each control group. We hypothesize that augmented parturitions do not have prolonged intervals between foaling and foal standing, foal suckling, or the mare expulsion of the fetal membranes compared with controls.

2. Materials and methods

2.1. Animals

Data were collected from foaling records at the Cornell Equine Park. Foaling mares were brought into the foaling barn approximately 1 month before the anticipated due date, which was defined as 340 days subsequent to the time of ovulation that resulted in the respective pregnancy. Parturition augmentation was initiated as a routine management technique of university-owned foaling mares in 2013 to ensure the presence of attending veterinarians during the critical period of foaling, and to allow students to observe all stages of parturition.

As foalings were not randomly allocated to groups, there were no controls for which there were not shortfalls for utilization for comparison with the parturitions that were augmented, and three different datasets were produced each containing the augmented group and one of three control groups. The first group of controls was 'Time Match' controls ($n = 37$); these were both the client and university-owned mares that were not augmented and foaled in the same facility during the 2013–2016 foaling seasons. The Time Match control mares had the same management conditions imposed as those for the augmented mares including feed, water, bedding, and the same housing environment. The second control group was the 'Mare Match' controls ($n = 32$), for which data were collected from the foaling records from the same mares that were augmented. The control data were from the foaling of these augmented mares in previous years when mares foaled naturally. Mare Match is essentially a case-control matched-pairs design and with this approach there was controlling for the breed and individual variation but not for control of the year-to-year variations in foaling processes. The third control group was the 'Historic Match' ($n = 165$) which consists of all the foaling records from the 2007–2016 foaling season. The Historic Match consists of the largest number of foalings and includes the Time and Mare match records in addition to data from other mares. Historic Match controls provide the most reliable information on the occurrences of dystocia and other conditions in the foaling program in which the present study was conducted.

2.2. Foaling management

Mares were confirmed pregnant and evaluated for the presence of placentitis by measuring the combined thickness of the uterus and placenta, evaluating the characteristics of the fetal fluids by trans-rectal ultrasonic examination, and fetal heart rate via trans-abdominal ultrasonography after being placed in the foaling barn. Mares were evaluated twice daily for signs of impending parturition. Physical changes evaluated included: relaxation of the pelvic ligaments, elongation of the vulva, mammary gland development, filling of the teats with secretions, and waxing of the teats. Mammary secretions were evaluated daily in the evening. When sufficient volume of mammary secretion could not be collected, the tests were prioritized in the following order of importance: 1) the

pH of mammary secretion was the most important variable and was determined using pH colorimetric strips with an increment of 0.2–0.3 (GmbH & Co.KG, Düren, Germany); 2) when possible calcium concentrations were determined using a commercial water hardness test strip (EMD Chemicals Inc., Gibbstown, NJ, USA) when the quantity of mammary secretion was less than optimal; or 3) using FoalWatch™ (CHEMetrics Inc., Calverton, VA, USA) when sufficient mammary secretions were collected (1.5 ml) and the commercial water hardness test strip indicated there were increased calcium concentrations.

Foaling monitoring was accomplished by video monitoring and a magnetic transmitter system (Foalert Inc., Acworth, GA, USA). Veterinarians and veterinary students attended foalings and the following information was collected: time of chorioallantois rupture, time of foaling, ease of foaling (no assistance, slight traction, moderate traction, or severe dystocia), time of foal standing, time of foal suckling, time of fetal membranes passing, quality of colostrum (taken prior to foal nursing), foal immunoglobulin concentration at 24 h post-foaling. Slight traction was defined as minimal assistance and traction provided when the mares are not making substantial progress as determined by the attending veterinarian. Moderate traction was defined as foaling that required a vaginal examination to correct minor maldispositions, or the foaling process required more than the minimal traction to deliver the foal. Severe dystocia was defined as major obstetrical manipulations including extensive vaginal manipulations to deliver the foal. Foals were assisted to stand if they had not stood at 60 min after foaling, tube-fed with colostrum if suckling had not occurred by 120 min after foaling and the mares were treated for retained fetal membranes if fetal membranes had not been expelled within 180 min of foaling. Retained fetal membrane treatment varied depending on the clinician practices for managing the case but typically consisted of administration of 5 IU oxytocin (various commercial manufacturers) i.m. every 30 min initially with decreasing intervals between administrations every 2–6 hours depending on the case, uterine lavage at least twice a day until fetal membranes were expelled, and metritis was resolved, antibiotics which may include trimethoprim sulfamethoxazole (various commercial manufacturers) approximately 15–30 mg/kg p.o. b.i.d., ceftiofur sodium (Zoetis, Kalamazoo, MI, USA) approximately 2.2–4.4 mg/kg i.m. and procaine penicillin G (various commercial manufacturers) approximately 44,000 IU/kg i.m. b.i.d.; non-steroidal anti-inflammatory drugs typically flunixin meglumine (Intervet / Merck Animal Health, Madison, NJ, USA) at 1.1 mg/kg i.v. s.i.d, intravenous fluids and close monitoring for signs of laminitis. All fetal membranes were evaluated carefully for completeness, signs of placentitis, and other abnormalities shortly after expulsion. Foal immunoglobulin G (IgG) concentrations were evaluated at approximately 12 h after birth using the SNAP® foal IgG test (IDEXX pharmaceutical Inc., Westbrook, ME, USA) and considered to be adequate if foal IgG concentrations were ≥ 800 mg/dL. Foals with IgG concentrations less than this threshold were treated with intravenous hyper-immune plasma (various commercial manufacturers), typically 1 L by slow i.v. administration until circulating IgG concentrations exceeded 800 mg/dL.

2.3. Parturition augmentation and exclusions

Mares that had augmented parturition received 3 IU oxytocin i.v. when all of the following criteria were met: 1) the mare was at least 330 days in gestation; 2) calcium concentrations in mammary secretions ≥ 250 ppm; mammary secretion pH ≤ 6.5 ; and 3) the mare had impending signs of parturition (elongated vulva, relaxed pelvic ligaments, waxed teats).

To ensure that the comparisons reported were between appropriately augmented mares and control mares that had normal foalings, the following groups were excluded. Mares that received oxytocin without meeting the augmentation criteria were considered to have been induced to foal ($n = 3$) and mares that were administered a second dose of oxytocin 3 IU i.v. ($n = 2$) were excluded from the analyses. In addition, mares were excluded from the control group if the mare had a fetal abortion, delivered a stillborn foal ($n = 2$), was diagnosed with placentitis ($n = 6$), or had body-wall tears ($n = 2$) as our goal was to compare foaling outcomes of augmentation with normal healthy foalings. None of the augmented mares had any of these conditions that are described.

After excluding the three mares that did not satisfy the augmentation criteria and the two mares that received a second dose of oxytocin, the augmented group consisted of 19 parturitions from 15 individual mares (five mares had two parturitions that were augmented).

2.4. Statistical analysis

Three datasets were produced as previously described in this manuscript, each with the augmented group and one of the three control groups. There was no analysis used for which there was a direct comparison of one control group to another. Descriptive statistics are presented as means \pm standard error. Comparisons of continuous variables such as mammary calcium, pH, were performed using a Wilcoxon Rank Sum test. Comparison of values for categorical variables such as dystocia risk and risk of premature separation of the chorioallantois between augmented and the Historic Match control group occurred using a mixed-model logistic regression (PROC GLIMMIX) of SAS version 9.4 (SAS Institute, Cary, NC, USA) with 'mare' identity as the random variable. Results were reported as the Odds Ratio 'OR' for the event occurring in augmented mares with the 95% confidence intervals (95% C.I.). Analysis of time-to-event such as time from foaling to foal standing, foal suckling, and the expulsion of fetal membranes was performed using a frailty model in the PHREG procedure of SAS. Time from foaling to standing was not right-censored. Time to foal suckling was right-censored after 120 min as most foals that failed to suckle by 120 min were tube-fed colostrum. Time to the expulsion of fetal membranes was right-censored at 180 min. Mares were considered to have retained fetal membranes if they were not expelled within 180 min. For analysis using Time Match controls, the variable 'year' was included as a random variable. For analysis using Mare Match controls, the variable 'mare' was included as a random variable. For the Historic Match controls, the variable 'year' and 'mare' were evaluated for the best model fit and the variable 'year' was better than 'mare' for all the models and was, therefore, used as the random variable. The effects of foal sex (colt versus filly) was included in all models and the effects of

Table 1
Outcomes by foaling group.

| | Augmented (<i>n</i> = 19) | Time Match (<i>n</i> = 37) | Mare Match (<i>n</i> = 32) | Historic Match (<i>n</i> = 165) |
|---|---|---|---|---|
| Mammary secretion on day of foaling | | | | |
| Calcium (ppm) | 341.8 ± 17.8 | 278.6 ± 15.3 ^a | 320.0 ± 15.6 ^a | 280.1 ± 7.6 ^a |
| ≥250ppm calcium (%) | 100% | 77.1% ^a | 83.9% ^a | 75.2% ^a |
| pH | 6.2 ± 0.05 | 6.5 ± 0.10 ^a | NA | NA |
| ≤6.5 pH (%) | 100% | 77.8% ^a | NA | NA |
| Foaling | | | | |
| No assistance (%) | 36.8% | 45.9% | 59.4% | 57.6% |
| Slight traction (%) | 42.1% | 40.5% | 34.4% | 30.3% |
| Moderate traction (%) | 21.1% | 13.5% | 6.3% | 10.3% |
| Severe dystocia (%) | 0% | 0% | 0% | 1.8% |
| Premature separation of the chorioallantois | 5.3% | 2.7% | 6.3% | 2.5% |
| Stage II duration (min) | 15.4 ± 2.5 | 13.6 ± 1.6 | 18.9 ± 2.8 | 18.1 ± 1.0 |
| Stage III duration (min) | 75.1 ± 14.1 | 51.1 ± 8.0 | 67.9 ± 9.7 | 59.1 ± 5.0 |
| Retained Fetal membranes (%) | 9.5% | 8.1% | 12.5% | 9.1% |
| Foal vitality | | | | |
| Foaling to stand (min) | 41 ± 3.7 | 46 ± 3.4 ^b | 51 ± 4.2 ^b | 52 ± 1.9 ^a |
| Foal to suckle (min) | 105 ± 4 | 99 ± 4 ^a | 99 ± 4 ^b | 93 ± 2 ^a |
| Failed to suckle in 120 minutes (%) | 47.4 % | 18.9% | 21.9% | 25.5% |
| IgG < 800 at 12 h (%) | 10.5% | 16.2% | 12.5% | 17.6% |
| Mare signalment | | | | |
| Breed | Quarterhorse = 2 Saddlebred = 1 Thoroughbred = 2 Warmblood = 11 Warmblood X = 3 | Arabian = 2 Morgan = 3 Appendix = 1 Quarterhorse = 6 Standardbred = 4 Thoroughbred = 3 Warmblood = 15 Warmblood X = 2 Belgian = 1 | Quarterhorse = 1 Thoroughbred = 2 Warmblood = 23 Warmblood X = 6 | Appaloosa = 2 Arabian = 4 Morgan = 9 Paint = 1 Appendix = 3 Quarterhorse = 12 Saddlebred = 1 Standardbred = 8 Thoroughbred = 29 Warmblood = 85 Warmblood X = 9 Belgian = 1 Clydesdale = 1 |
| Maiden mares (%) | 10.5% | 40.5% | 3.1% | 19.4% |
| Foal sex (Colt/Filly) | 9/10 | 16/21 | 20/12 | 90/75 |

Evaluation of mammary secretion pH was only initiated in the 2013 foaling season.

^a Indicate a significant difference from the augmented group $P < 0.05$.

^b Indicate a tendency to be different from the augmented group $P \geq 0.05$ but < 0.10 .

parity (primiparous versus multiparous), and breed (category 1: Morgan, Quarterhorse, Saddlebred, Appaloosa, Paint, and Arabian; category 2: Warmblood breeds and crosses; category 3: Thoroughbred and Standardbred; and category 4: Clydesdale, Belgian) were included in the Time Match and Historic Match models and retained in the model if $P < 0.10$. Results of the frailty models are presented as Hazard Ratio (HR) and the 95% Confidence Limits (C.L.). The significance level was set at $P < 0.05$ and a tendency was reported when $P < 0.10$ but ≥ 0.05 .

3. Results

3.1. Foaling outcomes

The Time Match control consisted of 37 foalings, the Mare Match control consisted of 32 foalings, and the Historic Match controls consisted of 165 foalings. There were 21 mares augmented, of which two mares required a second treatment with oxytocin. The average time from oxytocin injection until foal delivery was 44 min (range 20 to 75 min).

There were no significant effects of augmentation on dystocia risk at either threshold of ‘No assistance’ (OR = 2.01, 95% C.I. 0.63–6.41; $P = 0.204$) or ‘Moderate traction’ (OR = 1.43, 95% C.I. 0.35–5.76; $P = 0.574$). Seven of the 19 augmented mares foaled without assistance (37% in Augmented compared with 58% in Historic Match), eight mares (42% in Augmented compared with 30% in Historic Match) had slight traction applied to deliver the foal and the remaining four mares (21% in Augmented compared with 10% in Historic Match) had moderate traction applied to deliver the foal. One of the augmented mares had a foal with lateral deviation of the neck which required obstetrical intervention and one of the Time Matched mares had a shoulder flexion which also required obstetrical interventions. There were no augmented mares that had severe dystocia and the proportion of mares with severe dystocia in the Historic Match group was 1.8%. Results are summarized in Table 1.

One of the augmented mares (5.3%) had premature separation of the chorioallantois (red-bag), and the incidence of red-bag deliveries in the Historic Match controls was 2.4% (4/165); however, this difference was not significant (OR = 2.24, 95% C.I. 0.16 to

31.83; $P = 0.50$). Two foals from augmented mares (2/19; 10.5%) had IgG concentrations of < 800 mg/dL at approximately 12 h after birth. In the Time Match controls, six foals (6/37; 16.2%) had IgG concentrations < 800 mg/dL at 12 h.

There were three mares that were induced without reaching the mammary secretion thresholds and excluded in all data analyses. One mare had retained fetal membranes, two foals did not suckle by 2 h subsequent to foaling and were tube fed, and the one foal that was not tube fed had a failure of passive transfer. In addition, there were two augmented parturitions for which there was a second oxytocin injection and data from these parturitions were also excluded from the augmented group. Both mares foaled within 75 min of the first injection. One foal did not nurse by 2 h subsequent to foaling and was tube fed with colostrum. Both foals had adequate IgG (> 800 mg/dL) at 12 h after foaling and both mares had placental expulsions within 90 min of foaling. One mare had premature separation of the chorioallantois.

All of the foals that were born from mares that were augmented survived without any significant health complications to weaning.

3.2. Foaling to time of standing

The mean time from foaling to the foal standing was 41 ± 3.7 min in the augmented group, and 46 ± 3.4 , 51 ± 4.2 , and 52 ± 1.9 min for the Time Match, Mare Match, and Historic Match controls, respectively. Parity and breed were not significant in any model and were not retained in the final model for analyses. There was a tendency for foal sex to affect the interval from foaling to standing of the foal in the Time Match control group but the values for this variable were not significant in the Mare Match or Historic Match models. There was a tendency for foals born from mares that were augmented to have a shorter interval from time of foaling to standing compared with the Time Match (HR = 0.53, 95%C.L. 0.27 to 1.02; $P = 0.056$) but when Mare Match controls were used, the difference was not significant (HR = 0.62, 95%C.L. 0.33 to 1.16; $P = 0.12$). For the Historic Match control foals, there was a longer interval from foaling to the time of standing compared with the foals from augmented mares (HR = 0.58, 95%C.L. 0.33 to 0.99; $P = 0.044$). For colts, there tended to be a longer interval from time of foaling to the time of standing compared with fillies in the Time Match (HR = 0.54, 95%C.L. 0.28 to 1.03; $P = 0.061$). The intervals between time of foaling to time of foal standing are depicted in Fig. 1.

3.3. Time interval from foaling to suckling

Parity and breed were not significant in any model and were not retained in further analyses using the models. Foal sex was only significant in the Historic Match model. The interval between time of foaling and foal suckling was longer in the augmented foals (105 ± 4 min) compared with the Time Match (99 ± 4 min; HR = 2.58, 95%C.L. 1.16 to 5.75; $P = 0.020$). The augmented group also had a longer interval from the time of foaling to the time of suckling compared with the Historic Match control group (93 ± 2 min; HR = 2.16, 95%C.L. 1.09 to 4.28; $P = 0.027$) and this interval tended to be longer when compared with the Mare Match controls (99 ± 4 min; HR = 2.00, 95%C.L. 0.92 to 4.35; $P = 0.079$). Almost half (9/19) of the foals from the augmented

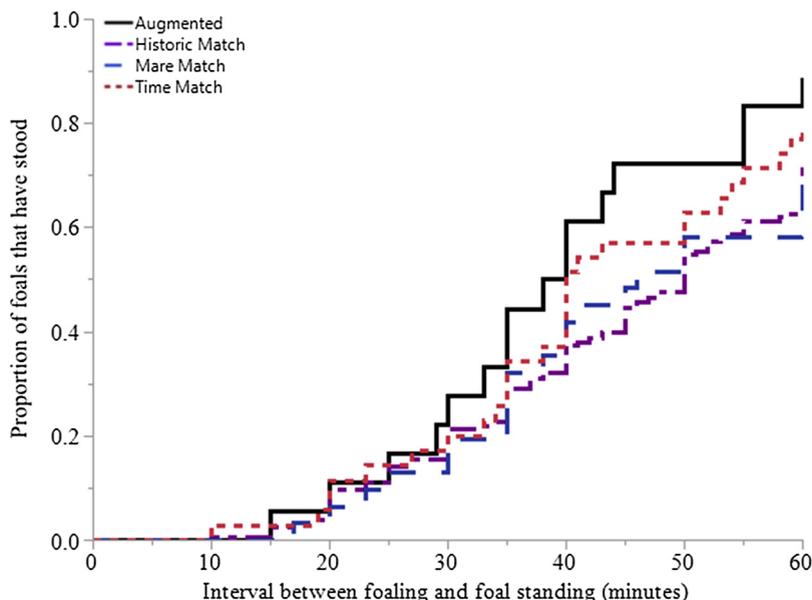


Fig. 1. Failure plot for the time interval between foaling and foal standing. There was a tendency for foals born from mares that were augmented (solid black line) to induce foaling to stand in after a shorter time interval subsequent to foaling, indicated by a steeper slope, compared with the Time Match (dotted red line; $P = 0.075$), not different from Mare Match controls (dashed blue line; $P = 0.11$) but at a shorter interval than the Historic Match control (dash and dot purple line; $P = 0.049$) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

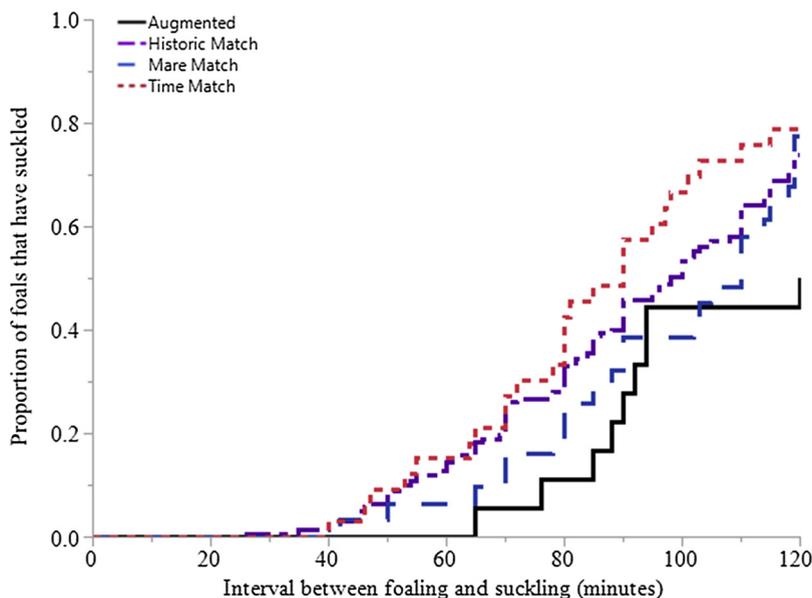


Fig. 2. Failure plot for the time interval between foaling and foal nursing. The interval between foaling and the foal suckling was less, indicated by a right shift in the line, in the augmented foals (solid black line) compared with the Time Match (dotted red line; $P = 0.026$) and Historic Match (dash and dot purple line; $P = 0.033$) and tended to be less than the Mare Match controls (dashed blue line; $P = 0.074$) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

mares were administered colostrum via nasogastric intubation after 120 min and all of the foals were able to nurse without assistance by 180 min post-foaling. The proportion of foals that failed to suckle within 120 min was 18.9%, 21.9% and 25.5% for the Time Match, Mare Match, and Historic Match respectively. For the Historic Match group, colts had a longer interval from foaling to suckling compared with fillies (HR = 0.56, 95%C.L. 0.39 to 0.81; $P = 0.0017$). The data for intervals between foaling and foal suckling are depicted in Fig. 2.

3.4. Time from foaling to fetal membrane expulsion

Breed and foal sex was not significant with use of any of the models and these variables were excluded with further analyses. Parity was significant in the Historic Match model and was retained for subsequent analyses. There were no differences in the mean interval from foaling until the fetal membranes were expelled between the augmented group (75.1 ± 14.1 min) and the Time Match 48 ± 7.4 min (HR = 1.53, 95%C.L. 0.77 to 3.03; $P = 0.21$), Mare Match 72 ± 10.7 (HR = 1.12, 95%C.L. 0.56 to 2.24; $P = 0.69$) or Historic Match 58 ± 3.8 (HR = 1.13, 95%C.L. 0.67 to 1.90; $P = 0.64$) groups. Primiparous mares had a shorter interval between foaling and passing fetal membranes compared with multiparous mares (HR = 0.652, 95%C.L. 0.44 to 0.97; $P = 0.037$). The data for interval between foaling and expulsion of fetal membranes are depicted in Fig. 3.

4. Discussion

Augmentation of parturition is a potentially safe and effective method to schedule time of foaling with personnel availability to assist with foaling if needed if the treated mares are properly selected, and are showing signs of imminent parturition. All 19 augmented mares foaled within 75 min of the time of the oxytocin injection, with a mean time from injection to foaling of 44 min. This interval is similar to the 30 to 60 min reported previously for augmentation of foaling with the use of oxytocin (Britton, 1963; Pashen, 1980; Purvis, 1972). There were two augmented mares that were administered a second oxytocin injection but the foaling outcomes of these two mares were similar to other augmented mares and including these two mares in the analyses did not change any of the findings.

In several previous studies, there was evaluation of the use of daily small-dose (2.5–3.5 IU) oxytocin injections as a management technique to advance time of parturition in mares that were determined to be near-term and foaling occurred within 2 h of treatment (Camillo et al., 2000; Chavatte-Palmer et al., 2002; Villani and Romano, 2008). Of these studies, Camillo et al. (2000) reported the most desirable outcomes, with 63% of 51 multiparous Haflinger mares foaling on the first day of treatment and 95% of mares foaling within 2-hours after the time of the oxytocin injection. Chavatte-Palmer et al. (2002) reported that 61% of 18 mares of light or draft mixed breeding foaled within 2 h when administered 2 IU of oxytocin i.v., but only 7% to 14% of mares treated with smaller doses (1, 0.5, or 0.1 IU oxytocin) foaled within 2 h. Results from the largest study (Villani and Romano, 2008) indicated that 51.3% of 148 Standardbred mares treated with 3 IU oxytocin i.m. foaled within 2 h on the first day of treatment and only 68.9% of foalings occurred within 2 h of treatment on subsequent days. The primary concern of daily oxytocin administration is the induction of

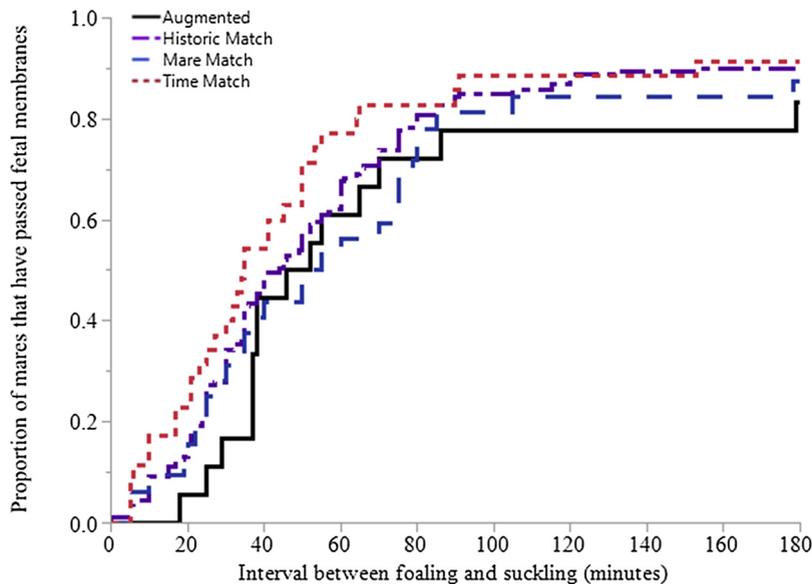


Fig. 3. Failure plot for the time interval between foaling and mare expelling fetal membranes. There were no differences in the interval from foaling until the fetal membranes were expelled in the augmented group (solid black line) and the Time Match (dotted red line; $P = 0.25$), Mare Match (dashed blue line; $P = 0.72$) and Historic Match (dash and dot purple line; $P = 0.29$); Most mares will have expulsion of the fetal membranes within 90 min after foaling and those that still retained fetal membranes at 90 min subsequent to foaling and certainly by 120 min are likely to have retained fetal membranes at 180 min after foaling (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

parturition before it is naturally imminent and the resulting birth of premature foals (Ousey, 2003). The use of mammary secretion pH in the present study increased the likelihood that the augmented mares were imminently close to foaling. In some disease conditions such as placentitis, mares may have a premature increase in calcium concentrations and pH decrease in mammary secretions and the mammary parameters for augmentation would occur but these mares would likely be in earlier stages of gestation (< 320 days) and would not be suitable candidates for augmentation. The additional criteria, therefore, such as being at least 330 days in gestation, and have other impending signs of parturition such as an elongated vulva, relaxed pelvic ligaments, waxed teats are very important factors in determining the suitability of the mare to undergo the parturition augmentation treatments.

In the present study, the two significant differences between mares that had augmented parturitions imposed as compared with controls is the shorter interval between foaling and standing in foals when there was augmented parturition of mares, and the longer interval between foaling and nursing with augmented parturition as compared to natural foalings. The clinical significance of a decrease from 52 min to 41 min for a foal to stand or an increase from 93 min to 105 min for a foal to suckle is likely marginal. In the situation of the present study, the experimental animals were horses used for teaching purposes, and the opportunity to train students to tube-feed colostrum was an added advantage. From experiences of those conducting the research for the present study, tube-feeding colostrum increases the likelihood that the foal will have an adequate intake of good-quality colostrum in a timely manner and reduces the likelihood of requiring plasma transfusions of antibodies which is economically more costly. Results from other studies do not indicate there is a delay in the interval between foaling and nursing, and tube feeding was not necessary (Camillo et al., 2000; Chavatte-Palmer et al., 2002; Villani and Romano, 2008). In the horse population for the present study, all of the foals that were tube-fed colostrum were able to nurse shortly after the meal and in general had greater IgG concentrations at 12 h. Only one of the 15 foals that were tube-fed colostrum in the present study had IgG concentrations of 400 to 800 mg/dL with the other foals having IgG concentration of > 800 mg/dL; whereas 6% of foals that were not tube-fed colostrum had low IgG at 12 h (≤ 400 mg/dL) and 12% had intermediate IgG concentrations (between 400 and 800 mg/dL). All foals that had IgG concentrations < 800 mg/dL at 24 h postpartum were given i.v. hyper-immune plasma infusions until IgG concentrations in blood were adequate.

Foal IgG concentrations in the current study are consistent with those in some previous studies (Camillo et al., 2000; Duggan et al., 2007; Ley et al., 1989a,b), however, these findings are not consistent with those of Townsend et al. (1983) where prostaglandins were used to induce parturition and it was reported that there were lesser IgG concentrations in foals from mares in which parturition was induced. Further, four of the 11 foals from mares induced to foal in this previous study were euthanized or died during the first 24 h of life. Leadon et al. (1984) used prostaglandin to induce parturition in 11 mares between 301 and 319 days in gestations and reported that the amount of globulin in mammary secretions doubled from prepartum to postpartum but was still less than mares that foaled naturally. In this previous study, there was also very poor foal survival with only one of the foals (the one that was 319 days in gestation) surviving beyond 7 days subsequent to foaling. In the foals of the present study, there were three foalings that were induced when the mammary secretions were less than those of the established thresholds, with one foal having a failure of passive transfer of immunity (IgG < 400 mg/dL), one foal with a partial failure of immunity (IgG between 400 and 800 mg/dL) and one foal being tube fed colostrum that had adequate passive transfer of immunity (> 800 mg/dL). Therefore, case selection of mares

that are imminently close to foaling are augmentation is likely an important factor to prevent failure of passive immunoglobulin transfer from mares to foals.

The interval between foaling and expulsion of fetal membranes was not different between augmented mares and controls. There are differing reports on the effect of augmentation on the duration of fetal membrane retention. From some studies, there have been reports of an increased duration of placental retention in mares that were treated with oxytocin (Chavatte-Palmer et al., 2002; Hillman, 1975). Results from other studies indicate similar results as those in the current study, with a numerically increased duration of retention that was not statistically significant (Camillo et al., 2000; Duggan et al., 2007). From one other study it was reported that there was a slightly shorter duration of placental retention in treated mares (Villani and Romano, 2008). The reason for this range of observed results is not known but may be due to the population of horses used in the study. Most mares will have expulsion of the fetal membranes by 90 min subsequent to foaling, and based on observations depicted in Fig. 3, mares that still retained fetal membranes by 120 min postpartum are very likely to have retained fetal membranes at 180 min post-foaling.

Premature separation of the chorioallantois has been mentioned as a possible problem in mares that are treated with oxytocin (Rigby et al., 1998; Ousey, 2003; Duggan et al., 2007), however, in results from the largest study (176 treated mares) there was not a single treated mare with premature separation of the chorioallantois (Villani and Romano, 2008). The proportion of mares with premature separation of the chorioallantois in the augmented mare group in the current study was 5.3%, compared with 2.5% in the Historic Match group. While this condition is a problem when there are not personnel present to assist with foalings, it is easily corrected by the attending veterinarian in foalings facilitated by the augmentation treatment. One of the augmented mares had premature separation of the chorioallantois in an augmented parity and in the preceding control parity. Both foalings were attended and the chorioallantois ruptured in a timely manner resulting in both foals surviving. The mare did not have any evidence of placentitis parturientum or by gross evaluation of the placenta in either affected parity. Augmentation of foaling, therefore, may be a useful technique to manage foalings in mares with a history of recurrent premature separation of the chorioallantois.

There are a number of mares that do not have ≥ 250 ppm calcium and a $\text{pH} \leq 6.5$ in mammary secretions the evening preceding foaling in the present study. It, therefore, is important to have redundancies to ensure foalings are attended by personnel in case assistance is needed. Also, mares can have fully developed and healthy foals born at < 330 days of gestation. Thus, the application of augmentation in field settings when the gestational age criteria are not met can be discussed with the foaling manager on a case-by-case basis especially in mares that have a history of foaling with shorter than typical gestation lengths. Augmentation of foaling is not a panacea and the adoption into a foaling program must occur after considering the benefits and deficiencies. In the teaching institution scenario where the present study was conducted, this management technique has dramatically enhanced the teaching value and has not had detrimental effects on the outcomes of foalings.

5. Conclusion

Foaling augmentation is a potentially safe and efficacious treatment in mares where there is careful selection based on physical and mammary changes in secretions that indicate mares are imminently close to foaling. This method may benefit farms that need to facilitate personnel to be present during parturition.

Conflict of interest

The authors have no conflicts of interest to declare.

Acknowledgments

The authors thank the students, staff and personnel of the Cornell Equine Park and College of Veterinary Medicine that assisted the care and management for the foaling mares. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

- Britton, J.W., 1963. Breeding farm practices. In: Catcott, E.J., Smithcors, J.F. (Eds.), *Equine Medicine and Surgery*. American Veterinary Publications, Wheaton, Illinois.
- Camillo, F., Marmorini, P., Romagnoli, S., Cela, M., Duchamp, G., Palmer, E., 2000. Clinical studies on daily low dose oxytocin in mares at term. *Equine Vet. J.* 32, 307–310.
- Canisso, I.F., Ball, B.A., Troedsson, M.H., Silva, E.S.M., Davolli, G.M., 2013. Decreasing pH of mammary gland secretions is associated with parturition and is correlated with electrolyte concentrations in prefoaling mares. *Vet. Rec.* 173, 218. <https://doi.org/10.1136/vr.101658>.
- Chavatte-Palmer, P., Arnaud, G., Duvaux-Ponter, C., Zanazi, C., Gerard, M., Ponter, A., Kindahl, H., Clement, F., 2002. The use of microdoses of oxytocin in mares to induce parturition. *Theriogenology* 58, 837–840.
- Duggan, V.E., Holyoak, G.R., MacCallister, C.G., Confer, A.W., 2007. Influence of induction of parturition on the neonatal acute phase response in foals. *Theriogenology* 67, 372–381. <https://doi.org/10.1016/j.theriogenology.2006.06.015>.
- Emberson, R.M., 1999. Dystocia and caesarean sections: the importance of duration and good judgement. *Equine Vet. J.* 31, 179–180.
- Hillman, R.B., 1975. Induction of parturition in mares. *J. Reprod. Fertil. Suppl.* 641–644.
- Hillman, R.B., Ganjam, V.K., 1979. Hormonal changes in the mare and foal associated with oxytocin induction of parturition. *J. Reprod. Fertil. Suppl.* 541–546.
- Jeffcott, L.B., Rosedale, P.D., 1977. A critical review of current methods for induction of parturition in the mare. *Equine Vet. J.* 9, 208–215.
- Klem, M.E., Kreider, J.L., Harms, P.G., Potter, G.D., Kraemer, D.C., Godke, R.A., 1982. Induction of parturition in the mare with prostaglandin F2 alpha. *Prostaglandins* 24, 89–96.

- Korosue, K., Murase, H., Sato, F., Ishimaru, M., Kotoyori, Y., Tsujimura, K., Nambo, Y., 2013. Comparison of pH and refractometry index with calcium concentrations in preparturient mammary gland secretions of mares. *J. Am. Vet. Med. Assoc.* 242, 242–248. <https://doi.org/10.2460/javma.242.2.242>.
- Leadon, D.P., Jeffcott, L.B., Rossdale, P.D., 1984. Mammary secretions in normal spontaneous and induced premature parturition in the mare. *Equine Vet. J.* 16, 256–259.
- Ley, W.B., Hoffman, J.L., Crisman, M.V., Meacham, T.N., Kiracofe, R.L., Sullivan, T.L., 1989a. Daytime foaling management of the mare 2: induction of parturition. *J. Equine Vet. Sci.* 9, 95–99. [https://doi.org/10.1016/S0737-0806\(89\)80035-8](https://doi.org/10.1016/S0737-0806(89)80035-8).
- Ley, W.B., Hoffman, J.L., Meacham, T.N., Sullivan, T.L., Kiracofe, R.L., Wilson, M.L., 1989b. Daytime management of the mare: 1: pre-foaling mammary secretions testing. *J. Equine Vet. Sci.* 9, 88–94.
- Macpherson, M.L., Chaffin, M.K., Carroll, G.L., Jorgensen, J., Arrott, C., Varner, D.D., Blanchard, T.L., 1997. Three methods of oxytocin-induced parturition and their effects of foals. *J. Am. Vet. Med. Assoc.* 210, 799–803.
- McCue, P.M., Ferris, R.A., 2012. Parturition, dystocia and foal survival: a retrospective study of 1047 births. *Equine Vet. J. Suppl.* 22–25. <https://doi.org/10.1111/j.2042-3306.2011.00476.x>.
- Ousey, J., 2003. Induction of parturition in the healthy mare. *Equine Vet. Educ.* 15, 164–168.
- Ousey, J.C., Dudan, F., Rossdale, P.D., 1984. Preliminary studies of mammary secretions in the mare to assess foetal readiness for birth. *Equine Vet. J.* 16, 259–263.
- Pashen, R.L., 1980. Low doses of oxytocin can induce foaling at term. *Equine Vet. J.* 12, 85–87.
- Purvis, A.D., 1972. Elective induction of labor and parturition in the mare. *Proceedings of the 18th Ann. Conv. Am. Assoc. Equine Pract.* pp. 113–116.
- Rigby, S., Love, C., Carpenter, K., Varner, D., Blanchard, T., 1998. Use of prostaglandin E2 to ripen the cervix of the mare prior to induction of parturition. *Theriogenology* 50, 897–904.
- Rossdale, P.D., Jeffcott, L.B., 1975. Problems encountered during induced foaling in pony mares. *Vet. Rec.* 97, 371–372.
- Townsend, H.G., Tabel, H., Bristol, F.M., 1983. Induction of parturition in mares: effect on passive transfer of immunity to foals. *J. Am. Vet. Med. Assoc.* 182, 255–257.
- Villani, M., Romano, G., 2008. Induction of parturition with daily low-dose oxytocin injections in pregnant mares at term: clinical applications and limitations. *Reprod. Domest. Anim.* 43, 481–483. <https://doi.org/10.1111/j.1439-0531.2007.00940.x>.
- Witkowski, M., Witkowski, M., Pawłowski, K., 2014. Clinical observations on the course of oxytocin- or prostaglandin E2/oxytocin-induced parturition in mares. *Pol. J. Vet. Sci.* 17, 347–351.