

Three methods of oxytocin-induced parturition and their effects on foals

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Objective—To compare effects of 3 oxytocin-based induction techniques on fetal and neonatal foals.

Design—Prospective randomized controlled trial.

Animals—16 pregnant mares.

Procedure—Parturition was induced in mares by use of 3 treatments: group 1, 75 U of oxytocin, IM; group 2, 15 U of oxytocin, IM, q 15 minutes, for a maximum of 75 U; group 3, 75 U of oxytocin in 1 L of 0.9% NaCl solution, IV (1 U/min), for a maximum of 75 U. Blood gas values and indices of vitality were measured in foals, and variables describing parturition were measured in mares.

Results—Group-3 mares had a shorter interval from administration of oxytocin to rupture of the chorioallantois (OTCA) than group-2 mares. More foals were abnormal when the interval from oxytocin administration to delivery of the foal (OTDE) was \geq 60 minutes. Arterial blood gas values, measurements of vitality, and plasma cortisol concentrations did not differ among foals in various treatment groups. Increased interval for OTCA and OTDE resulted in higher neonatal P_{aCO_2} , and a longer interval for OTCA resulted in lower arterial pH. Time required for birth was shorter in mares with a dilated cervix. More abnormal foals than normal foals were delivered after premature placental separation or dystocia. Abnormal foals took longer to stand and suckle than normal foals. Interval from delivery to suckling was positively correlated with OTCA, OTDE, and P_{aCO_2} .

Clinical Implications—Method of oxytocin-induced parturition did not impact neonatal outcome. Interval from induction until parturition, degree of cervical dilatation, and intrapartum complications influenced induction success. (*J Am Vet Med Assoc* 1997; 210:799–803)

Induction of parturition has been used in mares for management of high-risk pregnancies and for research, teaching, and convenience.¹⁻³ Several agents and methods have been used to induce parturition in mares, including glucocorticoids,^{4,5} prostaglandins,¹ and oxytocin.⁶

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Oxytocin is generally considered to be the drug of choice for induction of parturition in mares.^{1,7} It has a rapid effect and usually results in delivery within 15 to 90 minutes after administration.^{1,8,9} In addition, the patterns of induction are consistent, and it seems to have little untoward effect on full-term foals.^{1,8-10} Various methods of oxytocin induction have been described, including bolus IM or IV injection of 60 to 120 U of oxytocin, IM or SC injection of 2.5 to 20 U of oxytocin at 15-minute intervals, and IV administration of 60 to 120 U of oxytocin in 1 L of 0.9% NaCl solution at a rate of 1 U/min.^{1,8,9}

Subjective impressions about various induction methods in which oxytocin was used have been reported; however, physiologic effects on mares and neonates have not been assessed. Critical comparison of the effects of each method of oxytocin induction would be helpful to determine the efficacy of regimens for inducing parturition in mares, the magnitude of fetal stress resulting from induction methods, and a prediction of survivability of foals after induced parturition. The purpose of the study reported here was to compare the effects of 3 oxytocin-based induction techniques on fetal and neonatal foals.

Materials and Methods

Horses—Sixteen pregnant, light-breed mares were maintained on pasture or free-choice grass hay; diets were supplemented with a 14%-crude-protein concentrate. All mares were artificially inseminated. The day of ovulation was considered to be the first day of gestation.

Study design—The following criteria were used to determine the appropriate time for induction of parturition in the mares: minimum gestational length of 330 days, adequate udder development with evidence of colostral filling in the teats, and testing of mammary secretions by use of a commercially available calcium test kit^a resulting in a color change of \geq 3 test zones (\geq 269 ppm of $CaCO_3$), indicative of \geq 40% chance of foaling within 12 hours. Mares were monitored for evidence of udder development beginning approximately on day 326 of gestation. Mammary secretion testing began on the first day after day 329 of gestation on which secretions were obtainable.

After mares met the criteria for induction, they were randomly assigned to 1 of 3 treatment groups, and induction of parturition was initiated. Group-1 mares ($n = 5$) received 75 U of oxytocin in a single IM injection. Group-2 mares ($n = 5$) received 15 U of oxytocin, IM, at 15-minute intervals (0, 15, 30, 45, and 60 minutes) until rupture of the chorioallantois (ie, release of allantoic fluid) was detected or until 75 U had been administered. Group-3 mares ($n = 6$) received 75 U of oxytocin mixed in 1 L of sterile 0.9% NaCl solution. The solution was administered IV via an infusion pump^b at a rate of 1 U/min (13.33 ml/min) until rupture of the chorioallantois was detected or administration of the liter was completed.

Vaginal examination was performed on each mare prior to induction and at 30-minute intervals thereafter to determine the degree of cervical dilatation. Examinations continued until the chorioallantois ruptured. Fetal heart rate was recorded prior to induction and thereafter at 30-minute intervals until the chorioallantois ruptured, using transcutaneous ultrasonography.^{11,c}

Peripartum intervals were recorded as follows: from initial oxytocin administration to rupture of the chorioallantois (OTCA), from rupture of the chorioallantois to delivery of the foal (CADE), and from initial oxytocin administration to delivery of the foal (OTDE). Intrapartum complications were recorded. Specifically, premature placental separation was defined as observation of the chorion at the vulvar lips. Dystocia was defined as complications requiring obstetric manipulation of the fetus to facilitate delivery. Interval from delivery of the foal to passage of the placenta was recorded. The placenta was grossly examined, and placental abnormalities were recorded.

Immediately after birth, a 19-gauge, 12-in catheter^d was placed in the umbilical artery of each foal. The catheter was secured in place with glue and suture material and was wrapped in elasticized tape. Blood samples for gas analysis^e were obtained from the catheter immediately after placement and at 30 and 60 minutes after delivery. Samples for determination of plasma cortisol concentrations^f were obtained immediately after catheter placement and at 60 minutes after delivery. Respiratory rate, heart rate, and rectal temperature of foals were recorded at delivery and at 30 and 60 minutes and 12 and 24 hours after delivery.

The association between intervals (OTCA, CADE, OTDE) and neonatal outcome (ie, normal vs abnormal) was evaluated. Normal foals stood and suckled ≤ 2 hours after delivery,¹² had a strong suckle reflex and suckled 4 to 6 times/h, consistently stood without assistance, and ambulated freely. Abnormal foals remained recumbent for > 2 hours after birth or did not suckle during that time frame. Some abnormal foals also required assistance to stand, locate the dam's udder, were unable to suckle, or required stimulation to stand and suckle. Intervals from delivery to standing (DEST) and delivery to suckling (DESU) also were recorded.

Statistical analyses—Treatment differences for fetal heart rate and for neonatal heart rate, respiratory rate, arterial pH, Pa_{CO₂}, and Pa_{O₂} were analyzed by ANOVA,¹³ as were treatment differences for the mean intervals of OTCA, CADE, and OTDE. To examine associations between OTCA, OTDE, and CADE and the initial and 1-hour neonatal arterial pH, Pa_{CO₂}, and Pa_{O₂}, simple correlation coefficients were determined.¹⁴

To examine associations between preinduction dilatation of the cervix and OTCA, CADE, and OTDE, mares retrospectively were assigned to 1 of 2 groups: mares with a nondilated cervix (n = 12) and with a dilated cervix (n = 4). Group differences in mean OTCA, CADE, and OTDE were analyzed by ANOVA.¹³

Maximum expected intervals^{7,12} were assigned to the following intervals: OTCA of \leq or > 40 minutes, CADE of \leq or > 20 minutes, OTDE of \leq or > 60 minutes, and DEST and DESU of \leq or > 120 minutes. The association between treatment and duration of interval was evaluated, using Fisher's exact test.¹⁵ To examine associations between neonatal outcome and OTCA, CADE, OTDE, DEST, DESU, dystocia, and premature placental separation, foals were retrospectively assigned to 1 of 2 groups: normal neonates (n = 11) and abnormal neonates (n = 5). Group differences in plasma concentrations of cortisol in foals were evaluated by repeated-measures ANOVA.¹³ For all tests, differences were considered significant at $P < 0.05$.

Table 1—Effect of oxytocin administration on intervals (mean \pm SD) from oxytocin administration to rupture of chorioallantois (OTCA), from rupture of chorioallantois to delivery (CADE), and from oxytocin administration to delivery (OTDE) in 16 pregnant mares

Group	Oxytocin	No. of mares	Intervals (min)		
			OTCA	CADE	OTDE
1	75 IU, single injection	5	48 \pm 15	19 \pm 13	68 \pm 8
2	15 IU, 5 injections	5	69 \pm 34	13 \pm 7	83 \pm 32
3	75 IU, IV drip	6	34 \pm 19	17 \pm 8	51 \pm 25

Table 2—Effect of preinduction cervical dilatation on intervals (mean \pm SD) in 16 pregnant mares

Dilated Cervix	No. of mares	Intervals (min)		
		OTCA	CADE	OTDE
No	12	55 \pm 27	17 \pm 10	72 \pm 26 ^a
Yes	4	32 \pm 17	16 \pm 9	48 \pm 19 ^b

^{a, b}Means with different superscripts are different ($P < 0.05$). See Table 1 for key.

Results

In the 16 mares, significant differences were not detected among mares in the various oxytocin-treatment groups for CADE and OTDE intervals (Table 1). Mean OTCA was shorter, but not significantly so, for mares given an infusion of oxytocin in 1 L of fluid (group 3) than for mares given IM injections of oxytocins at 15-minute intervals (group 2).

Significant differences were not noticed between normal and abnormal foals for duration of OTCA and CADE. The OTDE was significantly ($P < 0.05$) greater in abnormal foals (range, 62 to 124 minutes) than in normal foals (range, 25 to 110 minutes).

Significant differences were not found for OTCA and CADE for mares with a dilated cervix versus those with a nondilated cervix (Table 2). Mean OTDE duration was shorter ($P < 0.05$) for mares with a dilated cervix than for those with a nondilated cervix. Mean neonatal Pa_{CO₂} at the first hour after birth was lower, but not significantly so, for foals born to mares with a dilated cervix than for those born to mares with a nondilated cervix. Differences were not evident in neonatal outcome (normal vs abnormal foals) between mares with a dilated cervix versus mares with a nondilated cervix.

Differences were not evident for neonatal pH, Pa_{CO₂}, Pa_{O₂}, and respiratory rate at delivery and at 30 and 60 minutes later among foals born to mares in various treatment groups. At delivery, heart rate was lower, but not significantly so, in foals born to group-1 mares than in those born to group-2 mares. Heart rate was significantly ($P = 0.03$) lower for foals born to group-3 mares than to those from group-1 and group-2 mares at 30 minutes. At 60 minutes, rectal temperature was lower, but not significantly so, in foals from group-3 mares than those from group-2 mares.

When overall means (combined data for all 16 foals) were examined, arterial pH, Pa_{CO₂}, and heart rate changed with time as follows: arterial pH increased with time after delivery; Pa_{CO₂} decreased with time after delivery; and heart rate was lowest at birth, peaked

Table 3—Overall values (mean ± SD) for arterial pH, PaCO₂, PaO₂, respiratory rate (RR), heart rate (HR), and rectal temperature (TEMP) for all 16 foals, determined at delivery and 30 and 60 minutes after delivery

Time	pH _a	PaCO ₂	PaO ₂	RR	HR	TEMP
Delivery	7.239 ± .049 ^a	51.6 ± 1.8 ^a	66.7 ± 11.6	75 ± 18	92 ± 14 ^a	100.8 ± .64
30 min	7.313 ± .05 ^b	49.0 ± 4.8 ^{ab}	59.2 ± 9.7	69 ± 30	130 ± 31 ^b	101.2 ± .86
60 min	7.368 ± .052 ^c	46.1 ± 5.3 ^b	65.1 ± 17.3	67 ± 33	108 ± 29 ^a	101.2 ± 1.16

^{a,b,c}Means with different superscripts are different (P < 0.05).

at 30 minutes, and then decreased at 1 hour after delivery (Table 3). For combined data from all foals, PaCO₂ at 60 minutes after birth was positively correlated with duration of OTCA ($r = 0.74$; $P < 0.001$) and OTDE ($r = 0.68$; $P < 0.004$), whereas arterial pH at 60 minutes after birth was negatively correlated with duration of OTCA ($r = -0.50$; $P = 0.05$).

Method of oxytocin treatment in the dams did not affect cortisol secretion in their foals for the first hour of life. However, when means were combined for all foals, plasma cortisol concentrations were higher ($P < 0.0001$) at 60 minutes after birth than at delivery.

Differences were not detected among treatment groups for DEST or DESU for foals from mares in various oxytocin treatment groups. When data were combined for all foals, DEST and DESU were longer, but not significantly so, in foals with abnormal outcomes. Duration of DESU was positively correlated ($r = 0.57$; $P = 0.02$) with duration of OTCA and OTDE at delivery. At 60 minutes, DESU was positively correlated ($r = 0.57$; $P = 0.02$) with duration of OTCA and OTDE as well as with PaCO₂ ($r = 0.52$; $P = 0.04$).

Differences were not noticed among treatment groups for frequency of premature placental separation or dystocia (6/16; 38% and 4/16; 25%, respectively). Dystocia was related to fetal position in 2 mares (dorsoiliac position of torso or head), fetal posture in 1 mare (forelimb rotated 180° and crossed over contralateral limb), and poor abdominal press in 1 mare. When data were combined for all foals, more abnormal foals (4/6; 67%, $P < 0.04$) were delivered after premature placental separation than were delivered without such separation (1/10; 10%). Foals involved in dystocia were more likely (3/4; 75%), but not significantly so, to be abnormal than foals that did not endure dystocia (2/12; 17%).

Discussion

Numerous variables can be considered when evaluating various methods of inducing parturition in mares. In the study reported here, 3 methods of oxytocin delivery (bolus injection, pulsatile injections, and continuous infusion) were evaluated for the effect of treatment on neonates born to treated mares. In naturally foaling mares, specific time limits have been assigned for each of the 3 stages of parturition (stage I: 1 to 4 hours; stage II: 30 to 60 minutes; stage III: 3 hours).¹² Induced foalings generally follow the same time scheme, with the exception of stage I, which often is accelerated in induced parturitions (approx 15 to 90 minutes from induction to delivery).^{1,7,10,16} In our study, intervals defined by OTCA and CADE closely approximated

stages I and II of natural parturition, respectively. Mares given a continuous infusion of oxytocin had a shorter, but not significantly so, OTCA interval than did those in other treatment groups. The CADE and OTDE intervals did not differ among treatment groups. The amount of time required for an induced parturition was similar between treatment groups, suggesting that efficiency in hastening the process of induction did not differ among treatments. When data were combined for all foals, OTDE was greater for abnormal foals. Although method of induction of parturition with oxytocin may not influence neonatal health, expedient delivery of the foal is evidently critical to neonatal adaptability.

One would expect cervical dilation to play an important role in rapid delivery of the foal in induced parturitions. Indeed, the period from oxytocin administration to delivery of the foal was shorter, but not significantly so, in those mares that had a dilated cervix than in mares with a closed cervix at the onset of induction. However, an association was not identified between normal versus abnormal outcome and preinduction dilatation of the cervix in the dams. The importance of cervical dilation continues to be a controversial point with regard to induction of parturition in mares. In the initial establishment of the criteria for induction, Purvis⁶ stressed the importance of a dilated or softened cervix. Numerous studies¹⁷ involving human beings have been cited that associate poor cervical relaxation with failed induction, prolonged labor, and a high number of cesarean sections. Reports in the veterinary literature^{1,3} suggest that inductions may proceed successfully in mares with a tightly closed, mucus-covered cervix as late as the end of first-stage labor. In the study reported here, only 4 of 16 mares had cervical relaxation prior to induction. All mares induced that had preinduction cervical softening delivered normal foals. Of the 12 mares induced with a nondilated cervix, 5 had foals that were abnormal.

Furthermore, mean neonatal PaCO₂ at 60 minutes after birth was higher, but not significantly so, in foals from mares with a nondilated cervix. Higher neonatal PaCO₂ suggested that induction of parturition in mares with a nondilated cervix may result in a greater degree of hypercapnia in the neonates, probably attributable to peripartum asphyxia. Asphyxia, in turn, could affect multiple organ systems and culminate in an abnormal neonate. A third of the foals in this study were abnormal, and all were from mares that had a nondilated cervix. In addition, all mares with intrapartum complications (premature placental separation, dystocia) had a nondilated cervix. Although a significant difference was not noticed, the higher prevalence of abnormal foals from mares with a nondilated cervix suggested that evaluation of preinduction cervical dilatation may have some merit in predicting success of induced parturition in mares.

Differences were not noticed among foals from dams in various treatment groups for any of the arterial blood gas values or plasma cortisol concentrations. Significant changes in neonatal heart rate and rectal temperature during the first 24 hours after delivery were not consistently observed in any treatment group, so little

could be concluded regarding an effect of treatment modality on these variables. However, these inconclusive findings were interesting when one considers that the rationale for the use of pulsatile or slow-drip administration of oxytocin, rather than bolus injection, is to provide a safer and more physiologic parturition.^{9,18} We suggest that bolus administration of oxytocin in mares may have become less popular because of reported adverse effects of this technique in human beings. Specifically, uterine hyperstimulation and rupture as well as fetal distress have been associated with this technique in induction of parturition in women.^{19,20} To our knowledge, these sequelae have not been reported in mares. Furthermore, these adverse effects in women are attributed largely to overdosing with oxytocin.^{19,21,22} Response to oxytocin activity also has been reported to depend on preexisting uterine activity and sensitivity, more than it depends on dose.²³ If uterine sensitivity to oxytocin controls induction of parturition, then method of oxytocin administration, and possibly dose, may have little impact on the eventual uterine response. Instead, selection of the optimal time to begin induction may figure more importantly in the overall outcome of the induction. Gestational duration and clinical signs of impending parturition, such as udder enlargement, evidence of colostrum, and relaxation of the perineal region and cervix, vary greatly among mares.^{8,10} Changes in electrolyte concentrations in prepartum mammary secretions can be useful in predicting impending parturition in mares.^{24,25} Furthermore, alterations in calcium, potassium, and sodium concentrations in mammary secretions have been correlated with fetal readiness for birth.^{25,26} To date, measurement of electrolyte concentrations in mammary secretions, combined with clinical signs, provide the most reliable indicators for timely induction of parturition in mares.²⁷

Differences were not observed in the prevalence of intrapartum complications (premature placental separation and dystocia) among treatment groups. More abnormal foals, however, were delivered after premature placental separation. In normal-foaling mares, it is believed that the chorion separates from the endometrium only after fetal expulsion and the initiation of third-stage labor.²⁸ Premature placental separation prior to fetal expulsion results in fetal asphyxia and subsequent hypoxemia or ischemia.²⁹ Fetal asphyxia commonly is implicated as a cause of maladjustment syndrome in neonates.³⁰ Similarly, more foals in our study, but not a significantly different number, were abnormal after dystocia than were foals not involved in dystocia. Premature placental separation and dystocia have been associated with induced parturitions as well as with neonatal abnormalities.^{1,5} Personnel and financial constraints precluded the use of a control group of noninduced, natural foaling mares in our study; consequently, ascertaining an association between induction and peripartum complications is difficult. However, the frequency of premature placental separation, dystocia, and neonatal abnormality in this study seemed to support other reports of peripartum complications associated with induced parturition.

The DEST and DESU intervals were not different

among foals in various treatment groups. For all foals, these intervals were longer, but not significantly so, in abnormal foals than in normal foals. Furthermore, DEST was positively correlated with longer parturition-related intervals and with neonatal PaCO₂. Given the higher prevalence of neonatal abnormalities seen in foals that were slow to stand or suckle, one might speculate that poor adaptability results from prolonged parturition and fetal asphyxia.

Parturition is a dynamic event with plentiful opportunities for error. Data in our study supported the accepted belief that time is an important variable of the parturition process, whether natural or induced. Positive correlations between neonatal PaCO₂ at 1 hour after delivery and the OTCA and OTDE intervals indicated that an increased amount of time for parturition leads to neonatal hypercapnia. Furthermore, neonatal arterial pH at 1 hour after birth was negatively correlated with the duration of OTCA. Analysis of both correlations suggested that fetal asphyxia was an outcome of delayed parturition. Prolonged parturition was not attributable to method of oxytocin treatment in this study. Factors that may influence induction outcome include cervical dilatation, intrapartum complications, parity, and environment. Although selecting 1 method of induction of parturition as being physiologically most supportive of the neonate would be difficult, the judicious selection of mares for induction and adherence to established criteria for induction would likely facilitate inductions that result in healthy neonates.

*Predict-a-foal, Animal Healthcare Products, Vernon, Calif.

^bIvion IV7200, Ivion Corp, Broomfield, Colo.

^cAusonics Microimager 2000, Universal Medical Systems Inc, Yonkers, NY.

^dIntracath, Becton-Dickinson Vascular Access, Sandy, Utah.

^eCiba-Corning 280, Ciba-Corning, New York, NY.

^fCoat-A-Count Cortisol, Diagnostic Products Corp, Los Angeles, Calif.

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Book Review:

Herd Health and Production Management in Dairy Practice. By A. Brand, J. P. T. M. Noordhuizen, and Y. H. Schukken. 604 pages; illustrated. Wageningen Pers, PO Box 42, NL-6700 AA, Wageningen, The Netherlands. 1996. Price NLG 30.

The author organizes important variables faced by practitioners in dairy production into an outline that bridges the gaps among textbooks on diseases, textbooks on agriculture production, and farm computer programs (eg, DairyChamp 305, DairyComp, and Monitor). In this textbook, examples are provided of ways in which the veterinary profession needs to change its approach to solving herd medicine problems from the passive professional approach, used in the past, to an active interventionist approach.

This textbook supplies a framework that will enable practitioners to build a farm data collection and analysis program. The textbook also supplies an approach that can function for herds consuming a high-concentrate diet or that are on a grass-pasture system (the chapter on lameness is a good example). This is important in light of the fact that many dairy enterprises in the Western hemisphere are once again using pasture systems to supply optimal resources, rather than relying on feeding concentrates.

This is not a textbook for novices, nor is it a reference book on the etiologic agents for a specific problem. It is an organized outline of influential variables in a dairy enterprise. The author assumes readers will have an immense familiarity with the complicated dairy industry and that they have a need to put this knowledge into a program that defines problems, seeks the sources of those problems, and then provides solutions for them. The information in *Herd Health and Production Management* supplies the approach needed to move from a passive veterinarian-client-patient role to an interventionist role.

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