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Induction of Parturition (29 Sept 2000)

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Introduction

Induction of parturition has been used in the mare for management of high risk pregnancies, research, teaching and convenience [1-3]. Elective, attended foalings are advantageous for monitoring mares that have experienced dystocia or premature placental separation in previous deliveries. Mares with gestational abnormalities such as rupture of the prepubic tendon (Fig. 1) or hydrallantois may require assistance delivering foals. However, induced parturition in the mare is associated with side effects such as dystocia, premature placental separation (Fig. 2), fetal hypoxia and dysmaturity [1,4]. Careful case selection prior to induction of parturition is critical for facilitating a successful delivery.

Figure 1. Mare with a ruptured prepubic tendon (Courtesy of Dr. Peter Daels). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 2. Premature separation and expulsion of the chorioallantoic membranes (Courtesy of Dr. Peter Daels). - To view this image in full size go to the IVIS website at www.ivis.org . -

Criteria for Induction of Parturition

A prerequisite to inducing labor in a mare is determining whether the fetus is capable of surviving extrauterine life. Several physiologic processes occur within the fetus prior to delivery ensuring that it will survive after birth. The normal fetus must have appropriate energy reserves, functional lungs and gut, and the ability to suck, swallow and maintain body temperature after delivery [5]. In most domestic species, fetal maturation is associated with a prenatal increase in adrenocortical activity a few weeks prior to birth [6]. The equine fetus is unique in that there is little adrenocortical activity until 24 - 48 hours before birth. Final maturation of the equine fetus occurs during this period. Consequently, the equine fetus is at substantially greater risk of dysmaturity/prematurity if delivered at an inappropriate time.
Several indicators have been identified that suggest fetal and maternal "readiness for birth". Purvis [7] described three criteria considered essential prior to inducing parturition in the mare:

1. Adequate gestational length,
2. Mammary development and milk/colostrum production,
3. Cervical softening.

Gestational length - the first criterion, adequate gestational length, was defined by Purvis as at least 330 days from the last day of breeding. Purvis reported consistently positive outcomes when inducing mares that were no less than 330 days from last breeding. However, gestational length is highly variable between mares,

ranging from 320 to 360 (mean - 340) days [8]. Season can also impact on gestational length [9,10]. Mares foaling during short days typically have a longer gestation, while mares foaling during long days have a shorter gestation. Therefore, all fetuses are not necessarily mature 330 days from the last breeding. Purvis acknowledged that gestational length, alone, would not be an adequate means of determining fetal readiness for birth.

Mammary Development and Secretions (Fig. 3) - mammary development and colostrum production in the mare are presently the most reliable indicators of fetal maturity and "readiness for birth". Colostrum is paramount to the survival of the neonate both as a source of nourishment and immunoglobulins. Furthermore, Ousey and co-workers [11] described a correlation between concentration of mammary secretion electrolytes and fetal maturity. The group showed that 24 to 48 hours prior to foaling, calcium concentration rose sharply in mammary secretions of 16 normal mares. Additionally, sodium concentration was much higher than potassium until 3 to 5 days before birth at which time the sodium to potassium ratio inverted. Changes in mammary secretion electrolytes (calcium, sodium and potassium) were compared to neonatal parameters that were indicative of adequate maturity at birth. The group concluded that a rise in mammary secretion calcium greater than 10 mmol/L and inversion of the sodium-potassium ratio were well correlated with fetal maturity.

Figure 3. Well developed mammary gland on a mare (Courtesy of Dr. Peter Daels). - To view this image in full size go to the IVIS website at www.ivis.org . -

Precise measurement of mammary secretion electrolyte concentrations requires a flame spectrophotometer or a laboratory chemistry analyzer. Using these systems, elevation of mammary secretion calcium above 40 mg/dL and potassium concentration greater than sodium (potassium $\geq$ 30 mEQ/ml and sodium $\leq$ 30 mEQ/ml) generally indicates fetal maturity in the normal equine pregnancy. Changes in mammary secretion electrolytes most commonly occurs at night, coincident with the period when the majority of mares foal. Stall-side tests are available to measure calcium (Ca^{++}) or calcium carbonate ($CaCO_3$) concentration. Test kits measuring mammary secretion Ca^{++} typically employ a colorimetric change of pads on a test strip from green to red (Predict-A-Foal ^{tm}) or titration of a diluted sample until an indicator dye changes from pink to blue (Titret ^{tm}). The dilution kits are somewhat more labor intensive than the test strip kits. Of the commercially available mammary secretion test kits, Ley [12] found the Titret^{tm} test kit to be the most reliable and repeatable test for predicting foaling within 24 hours. Using this kit, mares with mammary secretion $CaCO_3 \geq$ 200 ppm had a 54% probability of foaling within 24 hours, 84% probability of foaling within 48 hours and 97% probability of foaling within 72 hours. Most mares foaled within a short period of time if the mammary secretion $CaCO_3$ was between 300 and 500 ppm. Mares with mammary secretion $CaCO_3 <$ 200 ppm had a less than 1% chance of foaling within 24 hours of testing [13].

In some cases, mammary secretion electrolyte concentrations may not reliably indicate impending parturition. Ley [13] reported that 2% of mares in one study population foaled within 24 hours of mammary secretion testing and $CaCO_3$ was < 200 ppm. Samples taken early in the day may not reflect electrolyte changes that occur in the evening or at night, shortly before parturition. Rapid or no change in mammary secretion electrolytes can be especially true for mares foaling for the first time. "Maiden" mares often do not have significant mammary development and colostrum production until immediately prior to parturition. Conversely, precocious mammary gland development and secretion electrolyte changes may occur in mares with placental pathology. Rossdale and co-workers [14] monitored mammary secretion electrolytes in 25 mares with abnormal pregnancies. Seventeen mares (17/25, 68%) had elevation of mammary secretion calcium greater than 10 mmol/L before 310 days of gestation. Placental pathology was identified in sixteen of the seventeen (16/17, 94%) mares with prematurely elevated mammary secretion calcium. Ten of the sixteen foals (10/16, 63%) were either delivered dead or died shortly after birth. Results from these studies indicate that electrolyte changes in mammary secretions from maiden mares or mares with abnormal pregnancies should be interpreted cautiously.

Cervical Softening - cervical softening is the final criterion cited by Purvis [7] as critical to the success of induced parturition. Importance of cervical relaxation is a controversial point with regard to induction of

parturition in the mare. Numerous studies [15] cited in the human medical literature associate poor cervical relaxation with failed induction, prolonged labor and a high cesarean birth rate. Reports in the veterinary medical 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 a recent study [16], mares with a spontaneously dilated cervix (determined by digital examination per vagina) prior to induction delivered their foals more quickly than those mares with a closed cervix. Foals with a shorter interval from initial administration of oxytocin to delivery were better adapted after birth. Foals from mares with a dilated cervix stood and nursed more quickly and had fewer signs of intrapartum asphyxia (hypercapnia, maladjustment) than foals from mares with a closed cervix. Mares suffering intrapartum complications (premature placental separation, dystocia) all had a non-dilated cervix prior to induction.

Rigby and co-workers [17] further investigated the role of pre-induction cervical dilation on foal outcome by using prostaglandin E-2 (PGE-2) for cervical relaxation prior to induction. Prostaglandin E-2 is routinely administered to women to promote cervical softening and dilation before inducing labor [18,19]. In several human studies, PGE-2 treatment significantly enhanced cervical dilation and effacement, shortened the induction-delivery interval, reduced induction failures, and lowered cesarean section rate [19,20]. Rigby, et al. treated 7 mares with 2.5 mg intracervical PGE-2 and 4 mares with intracervical saline. Pretreatment cervical dilation was assessed in all mares by determining how many fingers would easily penetrate the cervix. Differences were not seen between PGE-2-treated and saline-treated mares for number of oxytocin treatments required to induce chorioallantois rupture. Mean intervals from initial injection of oxytocin to rupture of the chorioallantois or delivery of the foal also did not differ between treatment groups. Mares treated with PGE-2 tended to have more cervical dilation prior to induction than saline-treated mares. Foals delivered from PGE-2-treated mares suckled more quickly than foals from saline-treated mares. The authors concluded from the study that cervical softening prior to induction of parturition favored a shorter delivery period and positively impacted neonatal adaptability. Additionally, the authors acknowledged that PGE-2 treatment enhanced cervical softening, but they speculated whether cervical manipulation alone may have contributed to cervical changes seen prior to induction.

In summary, no one criterion effectively predicts the success of an induced parturition in the mare. Adequate udder development, changes in mammary secretion electrolytes and cervical softening are all important considerations prior to induction.

Methods of Induction

Induction Agents - a variety of agents and methods have been used to induce parturition in the mare, including glucocorticoids, prostaglandins and oxytocin. Glucocorticoids have limited efficacy for inducing parturition in the mare [4,21,22], although this agent is useful for induction in many other species. High doses and prolonged treatment intervals preclude routine use of glucocorticoids for induction in the mare.

Exogenous prostaglandins have been successful in initiating parturition in the mare. Both natural (PGF-2α) and synthetic products (fluprostenol, fenprostalene, prostalene) produce potent myometrial activity,[23-25] however, natural prostaglandin is not a reliable induction agent [4]. Parturition has been effectively induced using fluprostenol [1,23] fenprostalene and prostalene [25]. The induction-parturition interval with fluprostenol [11] and fenprostalene or prostalene [25] is more variable (1 - 6 hours) and may take longer than spontaneously foaling mares or those induced with oxytocin [23]. Neonatal adaptation abnormalities, neonatal weakness and fractured ribs have resulted from prostaglandin-induced parturition [1]. Currently, fluprostenol, fenprostalene and prostalene are not available on the veterinary market.

Oxytocin is generally considered the drug of choice for induction of parturition in the mare [1,26]. Oxytocin has a rapid effect resulting in delivery within 15 - 90 minutes following administration [1,7,27]. The patterns of induction are consistent with oxytocin and few adverse effects are noted in the term foal [1,7,27,28]. Various methods and doses of oxytocin induction have been described including: bolus injection of 20 - 120 units oxytocin, via intramuscular or intravenous injection; intramuscular or subcutaneous injection of 2.5 - 20 units oxytocin at 15 minute intervals; and intravenous administration of 60 - 120 units oxytocin in 1 liter saline delivered at a rate of 1 unit/minute [1,7,27].

Induction Method Using Oxytocin - workers in Texas [16] recently compared different methods of oxytocin administration for inducing parturition in mares to determine if method of administration had untoward effects on the foal. Three treatments were used to induce parturition: 1) a bolus intramuscular injection of 75 u oxytocin, 2) intramuscular injection of 15 u oxytocin every 15 minutes with a maximum dose of 75 u or 3) intravenous administration of oxytocin in 1L 0.9% NaCl at a rate of 1 u/minute for a maximum dose of 75 u.

Delivery time intervals and foal vitality parameters were measured. The method of oxytocin administration did not affect the overall time interval from initial oxytocin administration to delivery of the foal. Furthermore, neonatal blood gas values, vitality assessments and plasma cortisol concentrations were similar between foals from different treatment groups. Longer delivery times resulted in reduced foal vigor (standing, sucking) and vitality. Mares that had a softened cervix prior to induction had shorter delivery times and more vigorous foals. The authors concluded that method of induction had little impact on foal viability. Case selection and adherence to criteria for induction were cited as critical factors for a successful induction.

Dose of Oxytocin - Purvis [7,29] initially reported little untoward effect of high dose oxytocin (120 u) on the mare or foal when inducing parturition. Hillman [2] used between 20 iu and 100 iu oxytocin, IM, to induce parturition in 37 mares and observed the time of appearance and degree of expression of parturient symptoms. Hillman concluded that lower doses of oxytocin (20 , IM) resulted in quieter, more prolonged foaling. Conversely, he found that higher doses of oxytocin (100 u, IM) hastened parturition and accentuated parturient signs.

Pashen [27] investigated administration of very low doses of oxytocin (2.5 - 10 u, IV) to induce parturition in 4 pony mares and one jenny at 323 - 334 days of gestation. Mares foaled following administration of 2.5 - 10 u, IV, total. Additionally, plasma prostaglandin metabolite (PGFM) profiles were similar to those seen in spontaneously foaling mares [30]. Pashen concluded that low doses of oxytocin were physiologic and efficacious for inducing parturition in mares. Furthermore, he speculated that higher doses of oxytocin were unnecessary and potentially detrimental to the mare and foal based on reported complications in women treated with high dose oxytocin. Camillo and co-workers [31] repeated the work of Pashen with a slight modification in protocol. Mammary secretion calcium concentrations were determined in 24 mares at $\geq$ 320 days gestation. Mares having 8 mmol/L CA^{++} were considered near to foaling and one dose of 2.5 u was administered. Mares that did not foal within one hour of oxytocin were judged not ready to foal. These mares received a second dose of oxytocin (2.5 u, IV) each day until foaling. Fourteen of 17 mares (14/17, 82%) foaled after the first injection of oxytocin, one mare foaled after oxytocin administration on day 2 and 2 mares foaled after oxytocin on day 3. The group concluded that a single, low dose injection of oxytocin (2.5 u, IV) was efficacious for inducing parturition in mares. Furthermore, the workers suggested that this induction scheme would work only in mares that had a mature fetus. They felt that mares foaling on days subsequent to the initial injection did not respond to oxytocin because the fetus was in the final maturational phase.

Using an in vitro model, Ousey et al., [32], recently examined the dose-related effects of oxytocin on myometrial contractility in pregnant mares . Myometrial strips were collected from 33 pregnant mares (gestational age 60 - 340 days) and placed in a muscle bath. Strips were treated with varying doses of oxytocin. Myometrial tension, contractile amplitude and contractile frequency were measured. Treatment with oxytocin resulted in a significant dose dependent increase in myometrial resting tension. Myometrial contraction amplitude increased with oxytocin treatment and contraction frequency decreased with treatment. No correlation was noted between response to oxytocin treatment and gestational age. The results of the study indicated that the response of the myometrium to oxytocin was a dose-related effect.

Conclusions

In summary, several factors impact the success of induced parturition in the mare. Fetal readiness for birth is paramount to survival of the foal after birth. Critical evaluation of mammary secretion electrolytes, cervical relaxation and gestational length facilitates proper mare selection and neonatal survivability with induced parturition. Oxytocin is the current agent of choice for induction of parturition in the mare. Method of oxytocin administration does not impact neonatal adaptability after induced birth. Low dose oxytocin is effective for inducing parturition in the mare. Higher doses of oxytocin are unnecessary, and may be inappropriate, for inducing parturition in the mare.

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