Induction of parturition in cattle: Effect of triamcinolone pretreatment on the incidence of retained placenta

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Abstract

Two experiments were designed to determine whether pretreatment with triamcinolone acetonide (TRI) prior to induction of parturition with dexamethasone (DEX) and cloprostenol (CLO) would reduce the incidence of retained placenta. Experiment 1 was conducted to determine the optimum dosage of TRI and to approximate the optimum interval from TRI to induction with DEX+CLO. All cows received TRI on day 270 of gestation. Cows in group I received 1 mg/30 kg of body weight (BW) of TRI and were induced to calve with DEX+CLO on day 276. Cows in groups II and III received 1 mg/45 kg BW and were induced on days 276 or 277, respectively. Cows in groups IV and V received 1 mg/60 kg BW and were induced on days 277 or 278, respectively. Group VI cows served as untreated controls. There was no difference in the incidence of retained placenta among the treated and control groups.

Experiment 2 was conducted to more precisely determine the optimum interval from pretreatment to induction treatment with the chosen dose of TRI. All cows in groups I, II, and III were pretreated with 1 mg/60 kg BW of TRI on day 270 of gestation and received DEX+CLO on days 275, 276 or 277, respectively. Group IV cows served as untreated controls. The incidence of retained placenta was higher ($p < 0.05$) in groups I and II than in the control group, with group III intermediate and not different from the others. Cows that retained their placentas had higher ($p < 0.05$) body temperatures from day 2 to day 7 after calving and tended to have a lower pregnancy rate in the subsequent breeding season than cows that did not retain their placentas. Results indicate that pretreatment with TRI seven days prior to induction of parturition with DEX+CLO resulted in a reduced incidence of retained placenta, apparently by advancing placental maturation.

Resumé

Induction de la parturition chez les bovins : Étude de l'incidence de la rétention placentaire à la suite de l'administration de triamcinolone en prétraitement

Deux protocoles expérimentaux ont été élaborés afin de déterminer si le triamcinolone (TRI) pourrait diminuer l'incidence de la rétention placentaire lorsqu'il est administré avant d'induire la parturition avec de la dexaméthazone (DEX) et du cloprosténol (CLO). La première partie de l'expérience consistait à déterminer la posologie et l'intervalle de temps optimal entre l'administration de TRI et de DEX+CLO. Toutes les vaches ont reçu le TRI au 270^{e} jour de gestation. Les vaches du groupe 1 ont reçu 1 mg/30 kg de poids corporel (PC) de TRI et ont été induites à vêler avec de la DEX−CLO au 276^{e} jour. Les vaches des groupes II et III ont reçu 1 mg/45 kg PC et ont été induites respectivement aux 276^{e} et 277^{e} jours. Les vaches des groupes IV et V ont reçu 1 mg/60 kg PC et ont été induites respectivement aux 277^{e} et 278^{e} jours. Le groupe VI était le groupe témoin sans traitement. Les résultats ont démontré qu'il n'y avait pas de différence dans l'incidence de la rétention placentaire entre les groupes traités et le groupe témoin.

La deuxième partie de l'expérience consistait à déterminer, pour un dosage choisi de TRI, l'intervalle de temps optimal entre le prétraitement et l'induction. Toutes les vaches des groupes I, II et III ont reçu 1 mg/60 kg PC de TRI au 270^{e} jour de gestation et ont reçu de la DEX−CLO respectivement aux 275^{e} et 276^{e} jours. Le groupe IV était le groupe témoin. L'incidence de la rétention placentaire était plus élevée ($p < 0,05$) pour les groupes I et II comparativement au groupe témoin. Le groupe III présentait une incidence intermédiaire et ne différait pas des autres groupes. Les vaches qui présentaient une rétention placentaire avaient une température corporelle plus élevée ($p < 0,05$) entre les 2^{e} et 7^{e} jours après la parturition et avaient tendance à avoir un taux de conception plus bas lors des saillies sub-

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séquentes. Les résultats montrent que l'administration de TRI 7 jours avant l'induction de la parturition avec de la DEX−CLO réduit l'incidence de la rétention placentaire, apparamment en devançant la maturation placentaire.

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Introduction

Since a cow can calve at any time of the day or night, labor input by the producer increases greatly during the calving season. Induction of parturition can be used to synchronize calving times in cows with known breeding dates and over the past two decades there have been many reports on methods for induction of parturition in cattle (1–13). Most have been used as a treatment for overdue pregnancies (2); however, the complication of retained placenta (1,6,14,15) and the unpredictability of calving times (10,13) have resulted in the induction of parturition not being used as a routine management tool. An induction protocol utilizing a combination of dexamethasone and prostaglandin has been shown to be highly efficacious and to result in predictable calving times; however, this approach also resulted in a very high incidence of retained placenta (6).

Placental retention with induction of parturition has been postulated to be due to placental immaturity or the hormonal imbalance that may occur with synthetic hormone treatments (16,17). In the last week of gestation, rising levels of fetal cortisol have been shown to initiate endocrine events that culminate in the onset of parturition (3,18,19). Uteroplacental progesterone synthesis is gradually reduced (19,20), and estrogen production is increased (19). Estrogens apparently stimulate the production and release of prostaglandins (21), which, in turn, induce luteolysis, and parturition is initiated. Results of a recent study in our laboratory demonstrated that pretreatment with a long-acting corticosteroid (dexamethasone trimethylacetate) six days prior to induction of parturition resulted in a low incidence of retained placenta (1). The long-acting corticosteroid treatment was intended to mimic the slowly rising levels of cortisol secreted by the unborn calf (3,18,19), allowing the placenta to mature prior to induction of parturition. In addition, the long-acting corticosteroid pretreatment followed by induction of parturition with a combination of cloprostenol (CLO) and dexamethasone (DEX) resulted in 95% of calvings occurring between 0700 and 1900 (1). Unfortunately, dexamethasone trimethylacetate is not available for commercial use in North America.

The objective of the present study was to evaluate the effectiveness of another long-acting corticosteroid, triamcinolone acetonide (TRI) as a pretreatment agent for reducing the incidence of retained placenta after induction of parturition with the combination of DEX and CLO. We hypothesized that elevated blood corticosteroid levels prior to induction of parturition would induce placental maturation and reduce the incidence of retained placenta.

Experiment 1 was conducted to determine the optimum dosage and to approximate the optimal interval from pretreatment with TRI to induction with a combination of DEX and CLO. Experiment 2 was designed to more precisely determine the optimal interval between pretreatment with the chosen dose of TRI and induction of parturition for predictable onset of calving and reduced incidence of retained placenta.

Materials and methods

Experiments were done at the University of Saskatchewan Goodale Farm during March and April of 1991 (Experiment 1) and 1992 (Experiment 2). Breeding dates were determined by twice daily observations of bulls fitted with chin-ball markers during a 60-day breeding season, and duration of pregnancy was confirmed by transrectal palpation and ultrasonographic examination six weeks after the end of the breeding season (1).

Experiment 1

One hundred and sixteen, cross-bred, beef cows were used in this experiment. Seventy-five cows with known breeding dates were randomly placed in one of five treatment groups as the calving season progressed, so that approximately equal numbers in each treatment group would calve daily. The remaining 41 cows served as non-treated controls (group VI). Cows in group I were pretreated with 1 mg/30 kg body weight (BW) of TRI (Vetalog, Ciba-Geigy Canada Ltd., Mississauga, Ontario) on day 270 of gestation and were induced to calve on day 276 with a combination of 25 mg of DEX (Dexamone "2", rogar/STB, Pointe Claire/Dorval, Quebec) and 500 μg of CLO (Estrumate, Coopers Agropharm Inc., Ajax, Ontario). Cows in groups II and III were pretreated with 1 mg/45 kg BW of TRI on day 270 of gestation and were induced to calve with DEX+CLO on days 276 or 277, respectively. Cows in groups IV and V were pretreated with 1 mg/60 kg BW of TRI on day 270 and induced with DEX+CLO on days 277 or 278 of gestation, respectively.

End points recorded were induction success rate, interval from treatment to calving, length of stage II of labor, interval from calving to placental release, body temperature changes after calving, incidence of placental retention, calving difficulty, calf viability, and subsequent fertility. Induction success was defined as cows calving 24–72 h after induction treatment with DEX+CLO. Cows calving less than 24 h after induction treatment were considered to have calved as a result of the TRI pretreatment (early calving) and were reassigned to groups Ib, IIb, IIIb, and IVb, respectively, for the purpose of comparison of the incidence of retained placentas. Placentas were considered retained when they were not expelled by 24 h after calving. Calving difficulty was scored on a scale from 1 to 4 as follows: 1-normal calving, 2-moderate assistance (up to two people), 3-major assistance (calf-puller), and 4-cesarean section. Calf viability was recorded as normal if the calf was able to stand and nurse within two hours of birth.

Experiment 2

Based on the results of experiment 1, a dose of 1 mg/60 kg BW of TRI was considered optimum for pretreatment prior to induction with DEX+CLO. One

Table 1. The effect of different doses of triamcinolone (TRI) pretreatment on day 270 of gestation and the day of dexamethasone plus cloprostenol (DEX+CLO) treatment on the intervals (h) to calving and calving to placental release and the incidence of retained placenta (experiment 1)

Group	n	Dose TRI on day 270	Day of DEX+CLO	DEX+CLO to calving (h)	Placental release (h)	RP (%)
Ia[a]	8	1 mg/30 kg	276	26.3 ± 0.9	24.5 ± 15.5	1/8 (12.5)
Ib[b]	10	1 mg/30 kg	—	—	4.7 ± 0.9	0/10 (0)
IIa[a]	9	1 mg/45 kg	276	31.8 ± 1.6	15.5 ± 7.2	1/9 (11)
IIb[b]	4	1 mg/45 kg	—	—	13.8 ± 7.2	1/4 (25)
IIIa[a]	13	1 mg/45 kg	277	29.8 ± 1.5	26.4 ± 12.3	3/13 (23)
IIIb[b]	4	1 mg/45 kg	—	—	37.4 ± 31.5	1/4 (25)
IVa[a]	10	1 mg/60 kg	277	29.9 ± 1.4	23.8 ± 8.5	2/10 (20)
IVb[b]	4	1 mg/60 kg	—	—	5.6 ± 1.7	0/4 (0)
Va[a]	5	1 mg/60 kg	278	31.0 ± 2.0	6.9 ± 1.7	0/5 (0)
Vb[b]	8	1 mg/60 kg	—	—	6.8 ± 1.1	0/8 (0)
Control	41	—	—	—	18.8 ± 9.2	2/41 (5)

[a] Cows that calved 24 to 48 h after DEX+CLO
[b] Cows that calved early (prior to or less than 24 h after DEX+CLO)

hundred and two cows with known breeding dates and selected from the same herd as in experiment 1 were utilized in this experiment. Seventy-eight cows were pretreated with 1 mg/60 kg BW of TRI on day 270 of gestation and induced to calve with the DEX+CLO on days 275, 276, or 277 in groups I, II, and III, respectively. The remaining 24 cows served as nontreated controls (group IV). End points were recorded as in experiment 1.

Postpartum temperatures

Cows in both experiments were divided into two groups, namely, retained placenta (RP) and nonretained placenta (NRP), for statistical analysis of postpartum temperatures. Rectal temperatures were measured daily at 0800 for 10 consecutive days, starting one day after calving (day 1). Rectal temperatures were taken from 6 RP and 28 NRP cows in experiment 1, and from 14 RP and 26 NRP cows in experiment 2.

Estradiol analysis

In experiment 2, blood was collected daily into heparinized tubes at 0900 from six cows in each group from day 270 of gestation (day of pretreatment with TRI) to one day after calving. Within one hour of collection, plasma was collected and frozen at −20°C. Plasma concentrations of estradiol were measured in duplicate 500 μg samples, using a validated radioimmunoassay (22). Standards were prepared in charcoal-stripped bovine serum; the standard curve ranged from 7 pmol/L to 735 pmol/L. The sensitivity of the assay was 3.7 pmol/L. The intraassay coefficient of variation was 14% and the interassay coefficient of variation was 15% (mean 52.1 pmol/L).

Statistical analysis

Differences in time from DEX+CLO treatment to calving and from calving to placental release were analyzed using one-way analysis of variance (ANOVA), and means were compared by protected least significant difference. Differences in postpartum temperatures between groups (RP and NRP) were analyzed using ANOVA for repeated measures (23). Qualitative data were analyzed by the chi-square test.

Regression analysis was used to calculate the rate of increase in plasma estradiol concentrations (slope) for individual animals in experiment 2. Slopes were calculated from days 270 to 275 for group I, from days 270 to 276 for group II, and from days 270 to 277 for group III. Slopes representing cows in the control group were calculated from day 270 to the day of induction in each treatment group (days 275, 276, and 277, respectively). Differences in the rate of increase in estradiol by group were analyzed using analysis of covariance, controlling for the effect of initial estradiol level on day 270 (23).

Results

Experiment 1

Overall, 30 of 75 (40%) cows pretreated with TRI calved before or within 24 h of the scheduled induction treatment (groups Ib, IIb, IIIb, IVb, and Vb, Table 1). All cows that were induced calved within 48 h of the DEX+CLO treatment, and 93% began to calve between 0700 and 1900; whereas, only 45% of control cows began to calve during the same period of the day ($p < 0.001$). The mean interval from DEX+CLO treatment to calving did not differ ($p > 0.12$) among treatment groups (Table 1). The mean interval from calving to placental release and the incidence of RP was not different ($p > 0.1$) among groups (Table 1). The length of stage II of labor, birth weights, calving difficulty, and calf viability were not different among groups ($p > 0.3$).

In the following breeding season, the first-service pregnancy rate and final pregnancy rate for the breeding season in RP cows were lower (43% and 63.6%, respec-

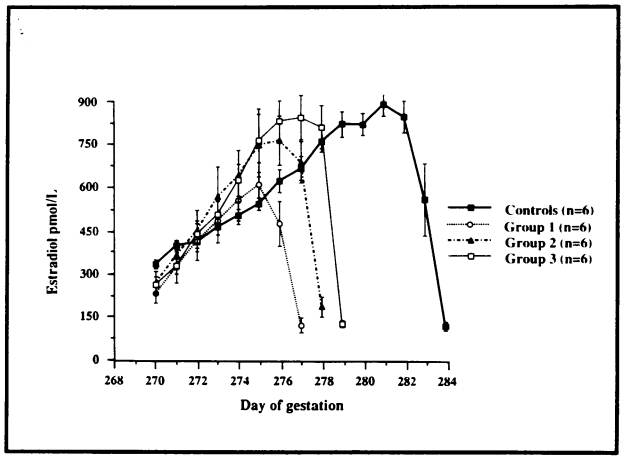

Figure 1. Mean (± SEM) plasma estradiol concentrations from day 270 of gestation to day 1 after calving in cows induced to calve with DEX+CLO, five (group 1), six (group 2), or seven (group 3) days after TRI pretreatment at day 270 and in untreated control cows. The rate of increase in estradiol levels, measured by slopes, was greater ($p < 0.05$) for cows pretreated with TRI than for the control cows. Significant and precipitous declines in plasma estradiol concentrations occurred 24 h before calving in all groups and were not different, whether calving was natural (control) or induced with DEX+CLO (groups 1, 2, and 3).

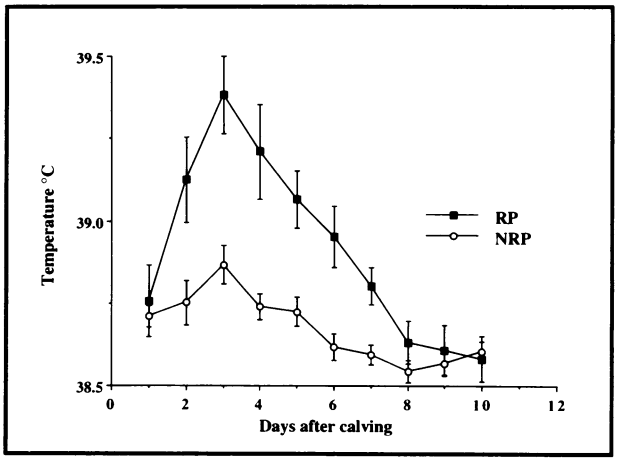

Figure 2. Mean (± SEM) rectal temperatures from days 1 to 10 after calving in cows with retained placenta (RP) and cows without retained placenta (NRP; both experiments combined). Temperatures of RP cows were higher and differed from NRP cows from days 2 to 7 after calving.

tively; $p < 0.05$) than in NRP cows (76% and 87.7%, respectively). However, the final pregnancy rate for induced cows (83%) did not differ from that of noninduced control cows (88%).

Experiment 2

One cow in group I, six cows in group II, and seven cows in group III calved before or within 24 h of the scheduled induction treatment and were regrouped as in experiment 1. All induced cows calved between 24 h and 48 h after DEX+CLO treatment, and 94% began to calve between 0700 and 1900; whereas, only 58% of the control cows calved during the same period of time ($p < 0.001$). The length of stage II of labor, birth weights, calving difficulty, and calf viability were not different among groups ($p > 0.3$).

Overall, none of the early calving cows had a retained placenta and the mean interval from calving to placental release was not different ($p > 0.5$) from the control group (Table 2). The mean interval from DEX+CLO treatment to calving was not different ($p > 0.4$) among treatment groups (Table 2). Cows in groups I and II had a longer ($p < 0.05$) mean interval from calving to placental release and a higher ($p < 0.05$) incidence of RP than controls. Cows in group III had a shorter ($p < 0.05$) mean interval to placental release than cows in group II, but the interval to placental release and incidence of RP did not differ from the other groups. The first-service pregnancy rate and final pregnancy rate in the following breeding season were not different ($p > 0.5$) in RP cows (77%, and 87.5%, respectively) compared to NRP cows (80%, and 92.5%, respectively).

Estradiol analysis

Plasma estradiol concentrations of cows in experiment 2 are illustrated in Figure 1. The rate of increase in estradiol levels, measured by comparing the slopes of the lines defining the estradiol profiles for individual cows, was greater ($p < 0.05$) for cows in the pretreated groups compared to the control group. Significant and precipitous declines in plasma estradiol concentration occurred 24 h before calving in all groups and were not different, whether calving was natural (control) or induced with DEX+CLO.

Postpartum temperatures

Because no year effect ($p > 0.32$) was detected between experiment 1 (1991) and experiment 2 (1992), postpartum temperature data were combined. Univariate analysis revealed a group effect ($p < 0.0001$), a day effect ($p < 0.001$), a day-by-group interaction ($p < 0.0006$). Differences were attributed to a higher ($p < 0.05$) mean rectal temperature in RP cows than in NRP cows from days 2 to 7. Although body temperatures were elevated in RP cows, no signs of systemic illness were noticed and no antibiotics were administered in either experiment.

Discussion

The interval from induction treatment to calving and calving to placental release and the incidence of RP did not differ among treatment groups; however, the numbers of cows used, particularly in experiment 1, may have been too small to detect statistical differences. Nevertheless, the results of these studies support the hypothesis that exposure to elevated blood corticosteroid levels prior to the induction of parturition with DEX+CLO in combination will result in a lower incidence of RP than previously reported for this method of induction (6). In three previous studies done in this laboratory, the induction of parturition in 101 cows with the combination of DEX+CLO resulted in a combined incidence of RP of 61.4% (1,6,15). The combined incidence of RP in 29 cows pretreated with 1 mg/60 kg BW of TRI on day 270 of gestation and induced to calve with DEX+CLO on day 277 of gestation in these two studies was 13.8%. In addition, results indicate that a period of seven days between pretreatment with TRI and induction with DEX+CLO is required

Table 2. The effect of the day of dexamethasone plus cloprostenol (DEX+CLO) treatment following triamcinolone (TRI) pretreatment (1 mg/60 kg BW) on day 270 on the intervals (h) from DEX+CLO to calving and calving to placental release and the incidence of retained placenta (experiment 2).

Group	n	Day of DEX+CLO	DEX+CLO to calving (h)	Placental release (h)	RP (%)
Ia*	24	275	30.4 ± 0.9	43.4 ± 13.4^{bc}	7 (29%)^{b}
Ib*	1	—	—	6.0	0 (0%)
IIa*	21	276	30.8 ± 1.0	68.4 ± 19.4^{c}	7 (33%)^{b}
IIb**	6	—	—	7.7 ± 1.2	0 (0%)
IIIa*	19	277	29.3 ± 1.0	22.2 ± 9.8^{ab}	2 (11%)^{ab}
IIIb**	7	—	—	9.8 ± 1.8	0 (0%)
Control	24	—	—	6.1 ± 0.8^{a}	0 (0%)^{a}

^{abc} Means and percentages within a column with superscripts not in common are different ($p<0.05$)
* Cows that calved 24 to 48 h after DEX+CLO
** Cows that calved early (prior to or less than 24 h after DEX+CLO)

for placental maturation, so that RP does not occur. Unfortunately, this period of time causes some loss of precision in our ability to predict the time of calving after DEX+CLO induction.

The predictability of calving time in the present study was not as accurate as that observed in a previous report (1). Although the TRI pretreatment dose used in experiment 2 (1 mg/60 kg BW) appeared to be near the optimum dose according to experiment 1, 18% of cows still calved prior to or less than 24 h after induction in experiment 2. Of the cows that calved early, two cows in group II and one cow in group III started to calve around 20 h after DEX+CLO treatment. Although their calving may have been as a result of DEX+CLO induction, by design they were classified as calving early. Interestingly, none of the cows that calved early in experiment 2 had an RP. In a previous study (24), in which TRI was used as a pretreatment and DEX alone was used as an induction agent, TRI apparently facilitated the action of DEX, which resulted in early calving without placental retention. This relationship was also observed in the present study, suggesting that the early calving cows were more endocrinologically prepared for parturition at the time of the induction treatment. Furthermore, the tendency towards a reduced incidence of RP in group III, experiment 2 (TRI on day 270 and DEX+CLO on day 277) indicated that the placenta required exposure to exogenous corticosteroids for a period of seven days to obtain the physiological maturation that would allow induction of parturition without retention of the fetal membranes.

The increased rate of elevation in estradiol levels observed in the pretreatment groups compared to the control group indicated that TRI pretreatment resulted in an increased estradiol production. The level of estrogens at the time of induction treatment with DEX has been shown to be negatively correlated with incidence of retained placentas and induction failures (25). Therefore, circulating estrogen concentrations near term may serve as a useful indicator of placental maturity and the temporal proximity to parturition for subsequent induction treatments.

The interval from DEX+CLO to calving after TRI pretreatment was not different among groups in both experiments. All calvings occurred within 48 h after DEX+CLO. The mean interval from induction to calving (30 h) was similar to the interval (28.3 h) after cows were induced following pretreatment with another long-acting corticosteroid, dexamethasone trimethylacetate (1). In addition, TRI, like dexamethasone trimethyl acetate (1), did not alter calf viability.

Conflicting results on postpartum fertility in cows that retained their placentas have been reported (5,6,8,13, 26–32). We have previously shown that first-service pregnancy rates and final pregnancy rates were either significantly lower (1) or tended to be lower (15) in cows that retained their placenta than in cows that did not retain their placentas. Furthermore, cows with retained placentas tended to have longer intervals from calving to first ovulation and calving to conception than average for the herd (1). The experiments reported herein tended to confirm the detrimental effects of retained placenta on fertility.

We have also reported that postpartum rectal temperatures increased earlier and to a greater extent in cows that retained their placentas than in those that did not (1,15). It has also been reported that higher numbers of bacteria were isolated from the uterus of cows with retained placentas than of cows without (33). Bacterial endotoxins have been shown to increase body temperature during the first few days after delivery (34). When antibiotic therapy was administered, rectal temperatures dropped one day earlier but there was no increase in subsequent fertility (15). In the present study, the increase in the body temperature of cows that retained the placenta was greater between days 2 and 7 after calving than that of cows not retaining the placenta. However, body temperature increases were not associated with illness.

In summary, data from these experiments suggest that pretreatment with 1 mg/60 kg BW of TRI seven days prior to the induction of parturition with a combination

of DEX+CLO results in a low incidence of RP without compromising calf viability. The predictability of calving time was reduced by pretreatment with TRI, with approximately 18% of cows calving prior to induction treatment or within 24 h after induction treatment; however, 94% of induced cows calved between 0700 and 1900 the day after DEX+CLO treatment. Cows that retained their placentas after induction exhibited elevated rectal temperatures between days 2 and 7 after calving and tended to have lower first-service and overall pregnancy rates than their herd-mates that did not retain their placentas. Further studies must be aimed at maintaining the low incidence of placental retention and improving the predictability of calving time by reducing the number of cows that calve after pretreatment prior to the induction of parturition with DEX+CLO.

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