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Induction of Parturition in Beef Cattle using Estrogens in Conjunction with Dexamethasone

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INTRODUCTION

The use of dexamethasone to induce parturition in beef cattle has given highly repeatable results when it is injected after 255 days of gestation. However, a high frequency of retained placentas and concomitant endometritis are a common sequelae (1, 2, 7, 15, 21).

Blood serum estradiol and estrone concentrations in cattle increase approximately tenfold during the month before parturition, with the most dramatic rise occurring during the last five days of gestation (5, 9, 10, 13, 18, 20). It has been suggested that cows induced with corticoids prior to normal term, may calve without sufficient estrogen concentrations to result in normal placental delivery (4, 11, 16). However, the use of estrogens in various induction regimes in an attempt to mimic normal hormonal events at parturition has yielded conflicting results (11, 12, 14, 16, 19). This inconsistency of results may be due to uncontrolled experimental error such as breed and age differences of cattle used in the experiments, the number of days before predicted calving when induced, small numbers of experimental animals and variations in the type, dose and method of administration of estrogens. Estrogens dissolved in oils or absolute alcohol and administered intramuscularly may not have been present long enough or in high enough concentrations to have the desired result.

This study was performed to investigate the effects of estrogens administered in depot forms on placental retention and other factors such as calving difficulty and calf vigor, when parturition is induced by dexamethasone.

MATERIALS AND METHODS

A uniform herd of 127 two year old Hereford heifers, bred to Polled Hereford bulls by artificial insemination, was used in this experiment. Forty days after the end of the calving period, bulls which were known to be fertile were turned in with the herd for a period of two and one-half months. Pregnancy testing was done two months after the end of the breeding season.

In a preliminary study (unpublished) estrone or estradiol 17B in sesame oil was administered to nonpregnant Holstein cows in a single dose of 20 mg intramuscularly. This resulted in peak plasma concentrations of greater than 1000 pg/ml in three to six hours which returned to almost normal levels in 24 hours. A similar dose suspended in 1% methyl cellulose and administered subcutaneously produced maximal levels in three to 12 hours which were maintained at 100–150 pg/ml for 60–72 hours.

The heifers were randomly allocated to five groups as indicated in Table I. All inductions were started on day 273 of gestation. For the purpose of discussion in this project, a successful induction was defined as one in which labour was initiated within 72 hours from the time of dexamethasone injection resulting in parturition.

All heifers in the four treatment groups received 20 mg of dexamethasone I.M. on day 273 of gestation. Simultaneous with the dexamethasone treatment, three of the treatment groups received either 20 mg estradiol 17B in 1% methyl cellulose S.Q., 20 mg estradiol valerate in sesame oil I.M. or a combination of 100 mg estrone and 20 mg estradiol 17B in 1% methyl cellulose S.Q.

Blood samples were collected from the tail vein at the time of induction and during or within one hour after calving. The blood samples were centrifuged immediately and the plasma obtained was frozen for estrogen analysis at a later date.

The number of heifers responding, the interval from dexamethasone administration to parturition, calving difficulties, calf birth weight, calf vigor, heifer mothering ability and the incidence of retained placentas were observed and recorded. Calving difficulties were classified as unassisted, manual traction, manual repositioning and traction or Caesarean section. A calf was considered of normal vigor if it was able to stand and nurse within two hours of birth; it was classified as weak if it required any assistance for its

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TABLE I

GROUP TREATMENTS, TIME TO ONSET OF CALVING AFTER INJECTION AND INDUCTION FAILURES

Group	Number of Animals	Treatment	Mean Time to Calving (h) ± S.E.	Induction Failures
C	24	No treatment		
D	30	20 mg dexamethasone (D) I.M.	47.7±1.52	6
D + E_2	24	D + 20 mg estradiol 17B (E_2) in 1% methyl cellulose S.Q.	43.9±1.12	0
D + E_2V	25	D + 20 mg estradiol valerate (E_2V) in sesame oil I.M.	43.0±1.98	1
D + E_1E_2	24	D + 100 mg estrone (E_1) and 20 mg estradiol 17B in 1% methyl cellulose S.Q.	43.6±1.42	1

TABLE II

COMPARISON OF MOTHERING ABILITY AND CALF VIGOR IN EACH OF THE TREATMENT GROUPS

Group	Number	Did Not Accept Calf	Inadequate Milk	Calf Weak or Dead
C	24	0	0	0
D	24	1[a]	0	0
D + E_2	24	1	1	1[b]
D + E_2V	24	1	2	1
D + E_1E_2	23	1[a]	0	3[c]

[a]Very wild

[b]Premature.

[c]One cleft palate, one stillborn, one suffocated.

survival. Normal mothering ability was based on the heifer's initial acceptance of her calf and adequate milk production. Placentas were considered partially retained if they were released between 24 and 36 hours after calving; they were considered retained if they were not released by 36 hours after calving.

All heifers calved in a small corral or box stall where they were kept for one or two days after calving. They were then turned out into a 15-acre pasture and supplemented with mixed hay and rolled barley. Each heifer with a retained placenta was treated on the second day after calving with 30 cc of long-acting penicillin.[1] If a second treatment was required it was given on day 5 after calving.

The total estrogen concentrations in the plasma samples were determined by a radioimmunassay method described previously (17). The time intervals from injection to calving, birth weights and estrogen concentrations were compared by analysis of variance. Differences in the number of induction failures, calving ease, rate of placental retention and pregnancy rate were analyzed by chi square.

RESULTS

The average gestation length in control heifers was 280.3 ± 0.81 ($\bar{x}$ ± S.E.) days. Heifers treated with dexamethasone alone calved at 47.7 ± 1.52 hours after treatment; whereas heifers receiving estrogens calved at 43.5 ± 1.5 hours. This difference only approaches significance ($P > 0.1$). The group which received dexamethasone alone had a greater incidence of induction failures than the groups which also received estrogens ($P > 0.1$, Table I).

There was no clear indication that the mothering ability of the heifers or calf vigor were affected by the treatments used (Table II). The birth weights for control calves averaged 1.5 kg heavier than the treatment groups ($P > 0.05$), but this did not result in greater calving difficulties for this group as compared to the treatment groups. There were no significant differences in calving difficulties in any of the groups ($P > 0.05$, Table III).

The groups of heifers that were induced had a significantly greater frequency of retained placentas than control heifers ($P < 0.01$). The estro-

[1]Derapen A, Ayerst Laboratories.

TABLE III

COMPARISON OF BIRTH WEIGHTS AND CALVING EASE

	C	D	D + E_2	D + E_2V	D + E_1E_2
No. of animals in group	24	24	24	24	23
Mean birth weight (kg)	31.5	30.8	30.8	29.5	30.1
Unassisted	11	11	11	17	14
Manual traction	11	11	12	5	9
Positioning and traction	2	2	1	1	0
Caesarian	0	0	0	1	0

TABLE IV

TIME OF PLACENTAL EXPULSION

	<24 hours		24–36 hours		>36 hours	
Group	Number	%	Number	%	Number	%
C	22	91.7	0	—	2	8.3
D	14	58.3	2	8.3	8	33.3
D + E_2	8	33.3	0	—	16	66.6
D + E_2V	11	45.8	1	4.2	12	50.0
D + E_1E_2	12	52.2	1	4.3	10	43.4
Subtotal induced	45	47.3	4	4.2	46	48.4
Subtotal estrogen treated	31	43.6	2	2.8	38	53.5
Total	67	56.3	4	3.3	48	40.3

TABLE V

MEAN TOTAL PLASMA ESTROGENS IN CONTROL HEIFERS AT CALVING AND IN INDUCED HEIFERS AT INDUCTION AND CALVING (ng/ml ± S.E.)

Group	Induction	Calving
C	—	4.3±0.40
D	2.7±0.13	5.3±0.47
D + E_2	2.9±0.23	5.3±0.35
D + E_2V	2.5±0.15	5.1±0.49
D + E_1E_2	3.0±0.15	6.9±0.70
Subtotal induced	2.7±0.17	5.7±0.50
Subtotal induced + estrogens	2.8±0.18	5.8±0.51

gen treated groups had a higher frequency of retained placentas than the group induced with dexamethasone alone, but this difference was significant only for the D + E_2 group ($P < 0.05$, Table IV).

Forty-eight heifers had retained placentas and were treated once with long-acting penicillin on the second day after calving; three of these heifers required a second treatment on day 5 after calving.

The groups of heifers that were induced tended to have higher total plasma estrogen concentrations at calving than the control group ($P = 0.06$). The estrogen treated heifers had plasma concentrations of total estrogen similar to the dexamethasone group; however, the D + E_1E_2 group tended to have higher concentrations than any of the groups ($P > 0.05$, Table V). The circulating estrogen concentrations at the time of calving were similar in heifers which retained placentas and those which did not retain the placenta (Table VI).

After the 1976 breeding season, of the entire experimental herd, 12 heifers were not pregnant. Six of the 12 were heifers that had not retained placentas (Table VII). The treatments did not appear to adversely affect the pregnancy rate (Table VIII).

DISCUSSION

The simultaneous use of estrogens and dexamethasone for inducing parturition in cattle does not appear to significantly affect the time from

TABLE VI

MEAN TOTAL PLASMA ESTROGENS AT INDUCTION AND CALVING FOR HEIFERS RETAINING MEMBRANES LESS THAN 24 HOURS, 24–36 HOURS AND GREATER THAN 36 HOURS AFTER CALVING (ng/ml ± S.E.)

	<24 hours		24–36 hours		>36 hours	
Group	Induction	Calving	Induction	Calving	Induction	Calving
C	—	4.3±0.40	—	—	—	—[a]
D	2.8±0.19	6.0±0.64	2.1±0.05	4.3±0.25	2.5±0.19	4.5±0.66
D + E_2	2.7±0.35	5.0±0.37	—	—	2.9±0.29	5.6±0.50
D + E_2V	2.5±0.16	5.6±0.92	3.4	5.3	2.4±0.26	4.5±0.42
D + E_1E_2	3.4±0.21	6.7±0.67	3.1	11.5	2.8±0.27	6.9±1.29
Subtotal induced	2.8±0.23	5.8±0.65	2.8±0.05	7.0±0.25	2.7±0.25	5.3±0.71
Subtotal induced + estrogens	2.8±0.24	5.8±0.65	3.3	8.4	2.7±0.27	5.6±0.73

[a]Two animals had retained placentas but blood samples were not taken.

injection to calving, calving difficulties, mothering ability or calf vigor. Animals treated with estrogens tended to have a slightly shorter interval from induction to parturition ($P > 0.1$). Previous workers (14) showed that when E_2 was used in conjunction with dexamethasone, this interval was significantly shorter ($P < 0.05$) than when dexamethasone alone was used; however, a higher dose and a different vehicle for E_2 was used (25 mg in absolute ethanol subcutaneously).

TABLE VII

COMPARISON OF PREGNANCY RATE IN HEIFERS WHICH DID NOT RETAIN THE PLACENTA TO THOSE WHICH RETAINED THE PLACENTA

	Normal Placental Expulsion	Partial or Complete Retention
No. of heifers	67	52
No. not pregnant	6	6
% not pregnant	8.9	11.5

Fewer induction failures occurred in the estrogen treated groups; this tendency was observed by other workers (16) but it was not found to be statistically significant. At calving, groups D + E_2 and D + E_2V had plasma concentrations of total estrogens similar to group D; whereas, the D + E_1E_2 group had higher concentrations. This may indicate that the doses of estrogens used in groups D + E_2 and D + E_2V were not large enough to add significantly to the levels of endogenous circulating estrogens.

There is evidence from this study that dexamethasone will result in total plasma estrogen concentrations at calving similar to or slightly higher than is seen at a normal parturition. It has been suggested that dexamethasone may cause the release of placental estrogens which reach highest concentrations in the fetal cotyledons during late pregnancy (14). This would indicate that it is not necessary to use exogenous estrogens to mimic, in dexamethasone induced cattle, the normal prepartum rise in estrogen concentrations. In this experiment a higher frequency of retained placenta occurred in the estrogen treated groups. This may indicate that elevated levels of estrogens exacerbate rather than alleviate placental retention. Previous studies have shown that in cows which calved normally but had retained placentas, there had been a marked increase in plasma estrogens within 12 hours before parturition; whereas, in cows which expelled the placenta, the plasma estrogen concentrations had reached a plateau during the last three days of gestation (3, 8). By contrast, other workers found that total plasma estrogens increased daily up to the time of parturition in animals which expelled the placenta as well as those which did not (6).

Although it is probable that endogenous estrogens play some role in normal placental delivery (10, 11, 12), it appears that the administration of exogenous natural estrogens are of no benefit in reducing the frequency of placental retention in dexamethasone induced parturitions in cattle. A significant reduction in the frequency of placental retention, in dexamethasone-induced cattle, was observed when a synthetic estrogen (diethylstil-

TABLE VIII

EFFECT OF TREATMENTS ON PREGNANCY RATE

	C	D	D + E_2	D + E_2V	D + E_1E_2
No. pregnant	19	21	23	24	20
No. not pregnant	5	3	1	0	3
% of group pregnant	79.2	87.5	95.8	100	86.9

bestrol) and calcium borogluconate were used in the induction regime (12).

SUMMARY

The use of exogenous estrogens with dexamethasone for the induction of parturition in cattle had no significant effect on the time interval from injection to calving, calving difficulty, mothering ability or calf vigor when compared to inductions using dexamethasone alone. The total plasma estrogen concentrations at parturition were higher in heifers which were induced with dexamethasone than in the control heifers but similar in estrogen treated heifers and heifers receiving only dexamethasone. This may indicate that dexamethasone results in estrogen concentrations at parturition equal to or higher than is seen normally. Estrogen administration at induction appeared to increase the frequency of placental retention; however, placental retention had no adverse effect on the pregnancy rate in the following breeding season.

RÉSUMÉ

L'injection simultanée d'oestrogènes exogènes et de dexaméthasone, dans le but de provoquer le vêlage, ne produisit aucun effet appréciable sur l'intervalle entre l'injection de ces substances et la parturition, ni sur les dystocies, l'instinct maternel ou la vigueur des veaux, comparativement à l'injection exclusive de dexaméthasone. Au moment du vêlage, la teneur du plasma en oestrogènes s'avéra plus élevée chez les taures auxquelles on avait injecté de la dexaméthasone que chez les témoins; elle se comparait cependant à celles des taures qui avaient aussi reçu des oestrogènes. Ces résultats révélèrent que l'injection de dexaméthasone résulte, au moment du vêlage, en une teneur du sérum en oestrogènes qui égale ou dépasse la normale. L'injection d'oestrogènes exogènes sembla toutefois augmenter le nombre de rétentions placentaires; ces dernières n'affectèrent pas défavorablement le taux de fécondation, au cours de la période suivante de reproduction.

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LETTER TO THE EDITOR

The Canadian Veterinary Medical Association – Democracy or Oligarchy: A Member Comments

DEAR SIR:

Re the letter from the London, Ontario veterinarians which appeared in the February issue of the Journal.

There are very valid pro's and con's in their letter. There is absolutely no doubt that if one looks at the board of Editors over the past twenty-five or more years, one cannot help but feel that there has been an oligarchy based on O.V.C. – with members pretty well hand picked by senior members of O.V.C. – "mais, c'est la vie". But do not forget that there are people like James Archibald and Cliff Barker that really got things rolling. Now its up to veterinarians in the field to nominate people to the board.

For you to sit back in your havens in Ontario, and declare that there is no need for a school of veterinary medicine in the Maritimes – is to represent yourselves as racing trotters with blinds on. Simply because everyone in small animal practice wants to drive a Cadillac.

Education, is a provincial matter. The opportunities for motivated English speaking students from Quebec to Newfoundland are nil. Secondly, from New Jersey to Maine, New York excepted, there is no school of veterinary medicine. Consequently there is a dearth of veterinarians in this entire area. The state of Connecticut has an arrangement with Cornell, whereby they would pay Cornell for 12 places in the clinical years – whether they have students to offer or not. The Connecticut students are given their pre-vet training at the U. of C. at Storrs. But getting into Cornell depends upon academic standards, and a ticket to Storrs – does not guarantee admittance to Cornell.

The University of Tufts in Medford, Maine is about to start a similar program to accept students at the beginning of their clinical studies, to start in the fall of 1980. Since the total student body at Tufts is now 7,500 you will realize that the new faculty will be small.

All of the hundreds of students I have talked to from this part of the continent over the past fourteen years are highly motivated, farm-oriented students – there is a vast number of them – there is a tremendous need for them, and most important a Maritime school of veterinary medicine is essential.

On the other hand I cannot see the use of schools of agriculture in every province with two in Quebec – to serve the nation, when you know that the vast majority of graduates do not serve in any agricultural discipline. One final example: Macdonald College of McGill University. A huge campus, with innumerable buildings and acres of lawn. Total student population? 457! In other words this institution is graduating English speaking graduates who will never serve or work in this province, at a cost in excess of producing a medical specialist.

So, you see, you must look at both sides of the coin.

Yours sincerely

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