

Termination of Pregnancy with Cloprostenol and Dexamethasone in Intact or Ovariectomized Cows

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SUMMARY

Termination of pregnancy in cows was investigated using sham-operated (SH) or ovariectomized (OV) cows treated with either a saline vehicle (V), cloprostenol (PG), dexamethasone (DEX) or dexamethasone and cloprostenol (DEX+PG). Surgery was done at 210 days of pregnancy and treatment was administered 72 hours later.

Days (mean±S.E.) from treatment to termination of pregnancy for the treatment groups were: sham-operated+vehicle (SH+V): 61.5±11.3; ovariectomized+vehicle (OV+V): 53.4±15.7; sham-operated+cloprostenol (SH+PG): 61.8±1.7; ovariectomized+cloprostenol (OV+PG): 54.5±13.1; sham-operated+dexamethasone (SH+DEX): 74.8±4.8; ovariectomized+dexamethasone (OV+DEX): 2.8±0.4; sham-operated+dexamethasone+cloprostenol (SH+DEX+PG) 26.0±23.0; ovariectomized+dexamethasone+cloprostenol (OV+DEX+PG): 7.2±4.9. Pregnancies in the OV+DEX and OV+DEX+PG groups were terminated significantly earlier than in all other groups ($P<0.05$) except the SH+DEX+PG group. These findings suggest that dexamethasone will terminate pregnancy in cows near seven months of gestation after the ovarian source of progesterone has been removed by either an injection of prostaglandin or by ovariectomy.

RÉSUMÉ

Interruption de la gestation, à l'aide de cloprosténol et de dexaméthasone, chez des vaches intactes et chez d'autres qui avaient subi une ovariectomie
Cette expérience consistait à étudier la

possibilité d'interrompre la gestation, chez des vaches auxquelles on avait fait subir une ovariectomie simulée ou réelle, avant de leur administrer, par la voie intramusculaire, l'une ou l'autre des substances suivantes: eau physiologique, cloprosténol, dexaméthasone, ou un mélange de dexaméthasone et de cloprosténol. On pratiqua les interventions chirurgicales, aux environs du 210^e jour de la gestation, et on administra le traitement, 72 heures plus tard.

Le nombre moyen de jours, ± E.S., entre le traitement et l'interruption de la gestation, s'établit ainsi: 61,5±11,3, chez les vaches qui avaient subi une ovariectomie simulée et une injection d'eau physiologique; 53,4±15,7, chez les vaches qui avaient subi une ovariectomie réelle et une injection d'eau physiologique; 61,8±1,7, chez les vaches qui avaient subi une ovariectomie simulée et une injection de cloprosténol; 54,5±13,1, chez les vaches qui avaient subi une ovariectomie réelle et une injection de cloprosténol; 74,8±4,8, chez les vaches qui avaient subi une ovariectomie simulée et une injection de dexaméthasone; 2,8±0,4, chez les vaches qui avaient subi une ovariectomie réelle et une injection de dexaméthasone; 26±23, chez les vaches qui avaient subi une ovariectomie simulée et l'injection d'un mélange de dexaméthasone et de cloprosténol; 7,2±4,9, chez les vaches qui avaient subi une ovariectomie réelle et l'injection d'un mélange de dexaméthasone et de cloprosténol. L'interruption de la gestation, chez les vaches qui avaient subi une ovariectomie réelle et une injection de dexaméthasone, ainsi que chez celles qui

avaient subi la même intervention et l'injection d'un mélange de dexaméthasone et de cloprosténol, se produisit plus rapidement ($P<0,05$) que chez les vaches des autres groupes, à l'exception de celles du groupe qui avait subi une ovariectomie simulée et l'injection d'un mélange de dexaméthasone et de cloprosténol.

Ces constatations révélèrent que la dexaméthasone pouvait provoquer l'interruption de la gestation, chez des vaches qui en avaient complété environ sept mois, après l'enlèvement de la source ovarienne de progesterone, soit par l'injection de prostaglandine ou par l'ovariectomie.

INTRODUCTION

Pregnant heifers in a commercial feedlot operation are undesirable as they have poor feed efficiency, are discounted at slaughter and cause management problems if they calve in the feedlot. Thus, there is considerable interest in finding a safe, reliable method to terminate pregnancy in feedlot cattle.

Prostaglandin $F_{2\mu}$ and its analogues have been shown to be reliable abortifacients when administered in the first 150 days of pregnancy (7,8,10,17) and were effective in the induction of parturition after 255 days of gestation (6,9,14). The efficacy of prostaglandin as an abortifacient was poor between 150 and 240 days of pregnancy although it resulted in a precipitous drop in serum progesterone and often signs of estrus (10).

The use of glucocorticoids such as dexamethasone to induce parturition after 255 days of gestation is well documented (1,2,3,5,16,21). Dexametha-

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some and flumethasone have been reported to cause abortion in cows at earlier stages of pregnancy but results have not been sufficiently consistent to consider them as a reliable abortifacients (3,16).

Ovariectomy of cows prior to 163 days of pregnancy resulted in abortions four to 11 days later (11,18,19). However, pregnancy was maintained when progesterone was administered to cows ovariectomized prior to 143 days of gestation (11,15,18). Response to ovariectomy between 170 and 200 days of gestation was variable with abortions occurring seven to 101 days later (11,19). Pregnant cows ovariectomized after 200 days maintained pregnancy but had shortened gestations, uterine inertia, partial cervical dilation and fetal membrane retention (11,15,18).

A reliable, practical method to terminate pregnancy between 150 and 255 days of gestation is obviously required.

The present experiment was designed to investigate the combined effects of ovariectomy, cloprostenol and dexamethasone treatment as a method to terminate pregnancy in cows at 210 days gestation. It was hypothesized that dexamethasone would induce abortion after removal of the ovarian source of progesterone.

MATERIALS AND METHODS

Thirty-two crossbred cows estimated by rectal palpation to be 40-60 days pregnant were purchased. The day of pregnancy was determined independently by three veterinarians and was assumed to be accurate within ± 10 days. The cows were housed in feedlot conditions at the University of Saskatchewan Goodale Farm and fed a ration of chopped hay and grain.

The experiment was a two by four factorial design. One-half of the cows were sham-operated and the other half were ovariectomized. The four treatments consisted of: (a) 2 mL of a saline vehicle (V), (b) 500 μ g cloprostenol¹ (PG), (c) 25 mg dexamethasone² (DEX) or (d) 25 mg dexamethasone plus 500 μ g cloprostenol (DEX+PG). All treatments were administered intramuscularly. Four cows were

assigned at random to each of the eight experimental groups.

Surgery, either sham-operation or ovariectomy, was performed at approximately 210 days of gestation. A flank laparotomy was done ipsilaterally to the corpus luteum (CL) with the cow standing. Palpation of the uterine artery per rectum was used to determine the ovary bearing the CL. Prior to ovariectomy care was taken to ligate the vessels to the ovary with the CL. The contralateral ovary was removed without ligation of vessels. Treatments were administered 72 hours post-surgery and the cows were observed three times daily for signs of impending abortions.

Days from treatment to termination of pregnancy were analysed statistically by analysis of variance using a two by four factorial design. Mean \pm S.E. for each of the treatment groups were compared by the protected 1sd test for multiple comparisons.

RESULTS

All calves, whether aborted, premature or term, were born alive. The aborted calves were very weak and lived only a few minutes. There was no death loss of term calves. Results are summarized in Table I.

Ovariectomized cows treated with either dexamethasone (OV+DEX) or dexamethasone+prostaglandin (OV + DEX + PG) calved significantly earlier ($P < 0.05$) than all other groups except those in the sham-operated+dexamethasone+prostaglandin treated (SH+DEX+PG) group (Table I). Time from treatment to parturition in the SH+DEX+PG group was significantly shorter ($P < 0.05$) than in the sham-operated + dexamethasone-treated

(SH+DEX) group but was not different from all other groups.

The vehicle-treated animals that were sham-operated (SH+V) calved 61.5 ± 11.3 days following treatment and those that were ovariectomized (OV+V) calved 53.4 ± 15.7 days following treatment. All calves were born at term with the exception of one calf in the OV+V group which was born approximately one month premature.

The prostaglandin-treated animals that were sham-operated (SH+PG) calved 61.8 ± 1.7 days following treatment while the ovariectomized animals (OV+PG) calved 54.5 ± 13.3 days following treatment. One calf in the OV+PG group was born approximately one month premature while all others were born at term.

The dexamethasone-treated, sham-operated animals (SH+DEX) calved 74.8 ± 4.8 days following treatment. However, the dexamethasone-treated, ovariectomized animals (OV+DEX) calved 2.8 ± 0.4 days following treatment. All calves in the SH+DEX treatment group were born at term while those in the OV+DEX treatment group were born at approximately seven months gestation, were very weak and lived for only a short time.

The dexamethasone+prostaglandin-treated animals that were sham-operated (SH+DEX+PG) calved 26.0 ± 23.0 days following treatment. Three of the four cows in this group aborted within 3.0 ± 0.4 days following treatment, while one cow calved 95 days following treatment. The three aborted feti were of approximately seven months gestation and lived for only a short time, while the fourth calf was born at term. The dexamethasone + prostaglandin-treated animals that

TABLE I
TIME FROM TREATMENT TO TERMINATION OF PREGNANCY IN COWS TREATED WITH VEHICLE, PROSTAGLANDIN, DEXAMETHASONE OR PROSTAGLANDIN + DEXAMETHASONE 72 HOURS AFTER SHAM-SURGERY OR OVARIECTOMY

Treatments	Sham Surgery		Ovariectomy	
	Days (\pm S.E.)	No. of Abortions	Days (\pm S.E.)	No. of Abortions
Vehicle (V)	$61.5 \pm 11.3^{ab*}$	0/4	53.4 ± 15.7^{ab}	0/4
Prostaglandin (PG)	61.8 ± 1.7^{ab}	0/4	54.5 ± 13.1^{ab}	0/4
Dexamethasone (DEX)	74.8 ± 4.8^a	0/4	2.8 ± 0.4^c	4/4
DEX+PG	26.0 ± 23.0^{bc}	3/4	7.2 ± 4.9^c	4/4

*Means with superscripts not in common are significantly different ($P < 0.05$).

¹Estrumate, ICI Pharmaceuticals, Mississauga, Ontario.

²Dexamone '2', Rogar/STB, Div. of BTI Products Inc., London, Ontario.

were ovariectomized (OV+DEX+PG) calved 7.2 ± 4.9 days following treatment. Three cows aborted 2.3 ± 0.3 days following treatment while one cow aborted 22 days following treatment. All calves lived for only a short time.

Of the 12 cows in the OV+DEX, OV+DEX+PG, SH+DEX+PG groups, ten aborted within four days following treatment. One cow in the SH+DEX+PG group calved 95 days post treatment and one cow in the OV+DEX+PG group aborted an eight-month fetus 22 days posttreatment.

DISCUSSION

The CL is the main source of progesterone during pregnancy in the cow, although the placenta and the adrenal gland have also been shown to produce progesterone (4,12,20). The stage of gestation at which ovariectomy will result in abortion corresponds with the period when prostaglandin is a reliable abortifacient. The stage between 150 and 200 days may be a transitional period from a time of primarily ovarian progesterone production to a time when the placenta and adrenal gland produce sufficient progesterone to maintain pregnancy in the absence of the CL. As pregnancy may be maintained in the absence of ovarian progesterone after 200 days of gestation (11,15,18), it may be presumed that extraovarian progesterone production is adequate to maintain pregnancy at this time. Although the amount of progesterone produced by the placenta has been shown to be small (20), it may be sufficient when acting locally in the uterus.

In the experiment, removal of the CL, either by ovariectomy or cloprostenol, plus treatment with dexamethasone resulted in the termination of pregnancy in 11 of 12 cows. These results suggest that dexamethasone did reduce extraovarian progesterone production to a level incompatible with the maintenance of pregnancy.

Dexamethasone may reduce adrenal production of progesterone through the negative feedback effect on the hypothalamus-anterior pituitary-adrenal axis, or it may have a direct

effect on the placenta causing a reduction in placental progesterone production. It is possible that dexamethasone has an effect on both adrenal and placental progesterone production.

It is not clear from this study whether adrenal or placental progesterone production alone is sufficient to maintain pregnancy in the absence of ovarian progesterone. The placental source of progesterone is probably more important in that the placenta is likely to change its metabolic function during the transition period of mid-pregnancy. Evidence does exist which suggests that dexamethasone will reduce placental progesterone near term (13). Regardless of its site of action, dexamethasone did terminate pregnancy once the ovarian source of progesterone was removed. Therefore, prostaglandin and dexamethasone used together may constitute a reliable method to terminate pregnancy in cows between 150 and 255 days gestation.

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