THERIOGENOLOGY

INDUCTION OF PARTURITION

IN CASES OF PATHOLOGICAL GESTATION IN CATTLE

By

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ABSTRACT

One or two injections of 20 to 40 mg dexamethasone (i.m.) induced parturition in 17 out of 21 cows (81%) with dropsy in the 7th to 9th month of gestation. Although the doses employed were high, induction was slow and relaxation of the genital tract was frequently insufficient. Ten cows with mummified fetuses, which were unresponsive to dexamethasone, delivered between Days 3 to 11 after repeated i.m. injection of DES, in doses ranging from 60 to 800 mg. As a rule, the corpus luteum regressed in all cases prior to the onset of parturition. Rapid regression of the corpus luteum also preceded expulsion of mummified fetuses treated with PGF$_{2\alpha}$ by intrauterine infusion of 10.5 to 45 mg. In cows carrying a macerated fetus, estrogen induced parturition only if regression of the corpus luteum was obtained. However, prostaglandins always caused regression of corpora lutea. The assumption is made that estrogens stimulate prostaglandin production in intact endometrium, causing luteolysis and, subsequently, parturition. Since with mummification the uterine lining remains unimpaired, while it is severely damaged with maceration, estrogens work in the former, but not in the latter situation, in which PGs can be used with success.
INTRODUCTION

In pathological gestations in cattle, induction of abortion or parturition is often indicated. Different methods, such as abdominal or cervical puncture of the fetal sacs, injections of estrogens, and even caesarean sections have been employed. Recently, the development of new methods for the induction of premature or early parturitions by hormones, certain corticosteroids (for review: see 2) and prostaglandins (5) as well, has been reported. The goal of this study was to apply these methods for the determination of the most efficient hormonal regime for the induction of parturition in cases of dropsy of the fetal sacs, of mummified and of macerated fetuses. It was hoped that the results obtained would contribute to a better understanding of the mechanism of action employed in the different hormonal treatments for artificially induced termination of pregnancy.

I. Dropsy of the fetal sacs

1. Material and methods

From June 1970 until May 1973, 21 cows with dropsy of the fetal sacs (all patients of our hospital) have been treated. The age of the animals ranged between 2 and 10 years, the period of gestation between 6 and 10 months. The amount of fetal fluid fluctuated from 100 to 230 litres. In all cases, except two (one hydramnios, one mixed case) hydroallantois was diagnosed. All patients were non-lactating and in poor physical condition at arrival. Animals were injected (i.m.) either with a single or (2 or 3) repeated dose of 20 to 40 mg of dexamethasone.

2. Results

Of the 21 animals treated, 17 (81 %) came into birth (Table 1). However, the time required for induction and the number of injections needed varied markedly. Eleven cows responded to a single injection and seven of them came into birth within two days following the application of dexamethasone. In four animals, parturition was delayed for 3 (2 animals), 4 and 9 days after the injection of the drug. Repeated injections were effective in 6 of 9 animals on Day 2 (3 animals), 3, 4 and 6 following the last injection. Most of the animals needed obstetrical help (massage, foetotomy or even caesarean section) since relaxation of the birth canal frequently was insufficient.
TABLE 1

INDUCED PARTURITION WITH SINGLE OR REPEATED INJECTIONS (i.m.) OF DEXAMETHASONE IN 19 CASES OF HYDROALLANTOIS, ONE CASE OF HYDRAMNIOS AND ONE MIXED CASE

<table>
<thead>
<tr>
<th>Injections of Dexamethasone</th>
<th>Number of Cows</th>
<th>Parturitions Induced</th>
<th>Period to Parturition</th>
<th>Retained Placenta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single^a</td>
<td>12</td>
<td>11</td>
<td>3 4 4 4</td>
<td>7</td>
</tr>
<tr>
<td>Repeated^b</td>
<td>9</td>
<td>6^c</td>
<td>0 3 3</td>
<td>2^d</td>
</tr>
</tbody>
</table>

^a 20 to 40 mg.
^b Two or 3 injections of 20 to 40 mg at 1- or 2-day intervals.
^c Two of the cows which failed were the only ones treated before the 7th month of gestation.
^d No information on 3 cows.

II. Fetal mummification

1. Material and methods

Between January 1970 and June 1973, 15 cows carrying mummified fetuses have been subjected to one of the following treatments or to a combination of these treatments at our hospital:

(a) dexamethasone, 20 to 80 mg, given in 1 to 3 i.m. injections at daily intervals (6 animals);

(b) diethylstilbestrol (DES) in a total dose of 60 to 800 mg (i.m.) spread over 2-6 injections at daily intervals (10 animals, including 6 animals which did not respond to dexamethasone treatment);

(c) prostaglandins (PGF₂α), 10.5 to 45 mg (i.u.), given in 1 to 6 injections with 1- or 2-day intervals (5 animals). PG was infused into the uterine horn ipsilateral to the ovary with the CL pseudograviditatis. Palpation of the ovaries was facilitated by the use of a cervical forceps. The mean length of gestation at the moment of intervention was 9.2 months (6-14 months).

Uterine biopsies were taken and processed for histological examination within 3 to 6 days following the expulsion of the mummy.

2. Results

(a) Corticosteroids, even in large and repeated i.m. doses, failed to induce regression of the corpus luteum (CL) and
expulsion of the mummy in all 6 animals (Table II).

(b) Estrogens were effective in all 10 animals; they pro-
voked regression of the CL and expulsion of the mummy-
fied fetus even in the 6 animals where the initial treat-
ment with dexamethasone had failed. Obvious regression
of the CL was palpable 3 to 8 days following the injection
of DES and expulsion occurred between Days 3 and 11.

(c) PGF$_{2\alpha}$ induced parturition in 3 out of 5 cases. In the
animals responding to PG$_{2\alpha}$-treatment, regression of the
CL and expulsion occurred rapidly and almost simultaneous-
ly (3-4 days). The two animals which did not react were
injected i.m. with DES. One animal delivered the mummy
30 hours following the application of 50 mg DES in a single
dose. The second cow was refractory to 500 mg DES given
in 10 doses at 2-day intervals.

TABLE II

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of Cows$^a$</th>
<th>Regression of CL</th>
<th>Parturition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone, 20-80 mg, 1-3 injections, daily intervals</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>DES, 60-800 mg, 2-6 injections, daily intervals</td>
<td>10$^b$</td>
<td>10 (3-8 days)</td>
<td>10 (3-11 days)</td>
</tr>
<tr>
<td>PGF$_{2\alpha}$, 10.5-45 mg, 1-6 injections</td>
<td>5$^c$</td>
<td>3 (3-4 days)</td>
<td>3 (3-4 days)</td>
</tr>
</tbody>
</table>

$^a$ Cows 6 to 14 months pregnant; fetuses died at 4 to 8 months.
$^b$ Includes 6 cows which did not respond to dexamethasone.
$^c$ Of 2 cows not responding to PGF$_{2\alpha}$, one expelled the mummy after subsequent DES treatment.

Following the expulsion of the mummified fetus, placental
structures were well preserved and the uterine wall looked
macroscopically normal. The histological picture of the
uterine wall showed a greatly intact epithelium, a hyper-
trophic compacta, well preserved uterine glands and very little
infiltration.
III. Maceration

1. Material and methods

Between April 1968 and February 1973, 5 cows having macerated fetuses were treated with various hormonal preparations:

(a) dexamethasone (i.m.), 3 injections of 20, 80 and 80 mg;
(b) DES (i.m.), 120 to 1400 mg, given in 4 to 6 injections with a 2-day interval;
(c) prostaglandins (PGF$_{2\alpha}$), 22.5 or 35 mg, given in 3 or 4 injections with 1- to 2-day intervals.

PGF$_{2\alpha}$ was injected into the horn ipsilateral to the ovary carrying the CL pseudograviditatis. Following parturition, or at slaughter, uterine specimens were sampled for histological examination. All cases were severely infected, mainly with Corynebacterium pyogenes bovis. Therefore, hormonal treatments were supplemented with intrauterine infusions of broad spectrum antibiotics.

2. Results

(a) Dexamethasone, given to only one animal, was ineffective in reducing the life span of the CL pseudograviditatis, nor did it induce parturition (Table III).

**TABLE III**

EFFECT OF DEXAMETHASONE (i.m.), DES (i.m.) and PGF$_{2\alpha}$ (i.u.) IN COWS CARRYING A MACERATED FETUS

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of Cows$^a$</th>
<th>Regression of CL</th>
<th>Parturition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone, 3 injections: 20, 80, 80 mg</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>DES, 120-1400 mg, 4-6 injections, 2-day intervals</td>
<td>$^b$5</td>
<td>2 (4 &amp; 5 days)</td>
<td>2 (6 &amp; 7 days)</td>
</tr>
<tr>
<td>PGF$_{2\alpha}$, 22.5 and 35 mg, 3 and 4 injections, 1- to 2-day intervals</td>
<td>$^c$2</td>
<td>2 (4 &amp; 5 days)</td>
<td>$^d$0</td>
</tr>
</tbody>
</table>

$^a$ Cows 6 to 9 months pregnant; fetuses died at 4 to 6 months.
$^b$ Including 1 cow which did not respond to dexamethasone.
$^c$ Both cows did not respond to DES.
$^d$ Ovulatory estrus at 6 and 7 days.
(b) Injections of estrogens resulted in an intensified vaginal discharge of pus but provoked regression of the CL and expulsion of the macerated fetus in only two of five animals treated. In the remaining three cases, no obvious regression of the CL could be palpated and no parturition was induced.

(c) Two of these animals, refractory to injections of DES, were treated with PGF\(_{2\alpha}\) (1.0). Although rapid regression of the CL was noted (after 4 and 5 days), followed by an ovulatory estrus (after 6 and 7 days), the fetus was not expelled in these two animals.

Maceration invariably provoked a hypertrophy of the uterine wall. Histologically, the presence of exudate in the uterine lumen, destruction of the endometrial epithelium and accumulation of lymphocytes and neutrophiles in the thickened compacta were noted.

**DISCUSSION**

The use of a highly potent corticosteroid, dexamethasone, for the induction of parturition in the presence of dropsy of the fetal sacs has given encouraging results (Table I). This is in agreement with a case reported by Carter, Butler and Valli (1), and the well-described effects of dexamethasone in induction of parturition during the last trimester of gestation in cattle (2). Of the four remaining cases, two were unresponsive with pregnancies which had not advanced beyond the second trimester, while two animals were lost by emergency slaughter. The great variation in time needed for induction might partly be due to different stages of pregnancy, the degree of dropsy and the pituitary dysfunctions in fetuses, which is a common finding in such cases (3, 4). In spite of a disturbed puerperium, 13 out of the 17 cows recovered and were put up for fattening. These results are clearly superior to those reported earlier following the use of DES in the same indication (4).

The failure of corticosteroids to induce parturition in cows carrying mummified fetuses (Table II) was not an unexpected finding since the corticoid effect is thought to be mediated by an estrogen and prostaglandin release from the fetal-placental unit (for review: see 2). In absence of an active fetal-placental unit, failure of this therapy could be anticipated. The highly successful use of DES is in agreement with our earlier trials in 40 cows carrying a mummified fetus, all of which came into parturition following DES administration. Repeated rectal examinations revealed that rapid expulsion can occur even before detectable regression of the corpus luteum has started. Delayed expulsion is preceded by luteal regression.

The mechanisms of DES action are unknown. The assumption can be made that they are, in part, direct anti-progestogenic effects at the myometrium, but more likely they result in a stimulation of prostaglandin production and release from the endometrium.
Local application of prostaglandins caused rapid regression of corpora lutea, but induced parturition only in three out of five animals. In all five animals, relaxation of the birth canal was satisfactory but expulsion mechanisms were obviously defective in two patients. In those animals, PG caused development of a new corpus luteum which, however, was reduced in size at palpation.

From results obtained in cows carrying a macerated fetus (Table III), it can be surmised that the first condition for any hormone effect is corpus luteum regression. Luteolysis can be achieved by estrogens, provided the endometrium is not too severely damaged and its capability of prostaglandin production is not markedly reduced. In animals refractory to DES, luteolysis can be induced by prostaglandin injection. Again, in some animals, regression of the corpus luteum is not followed by expulsion of the macerated fetus. It seems that the overall conditions for parturition are underdeveloped or inadequate in these cases, resulting in failure to relax the birth canal and to increase uterine activity or fetal expulsion. Furthermore, subsequent fertility will be highly problematic even after complete evacuation of the uterus, due to the damaged uterine structures. From an economical point of view, the recommendation can be made that induction of parturition by the above-mentioned hormonal means and methods is indicated in cases of dropsy of the fetal sacs and in cases of mummification, but is contraindicated in cows carrying a macerated fetus.

We offer the following conclusions concerning induction of parturition in normal or pathological gestations in the bovine species: Certain corticoids are effective only if a living fetus is present, which is at least 7 months old (2); estrogens are effective when a dead and mummified fetus is present (4), but the uterine structures remain mostly undamaged from the pathological gestation; prostaglandins are effective for termination of normal (5), delayed (5) and pathological gestations primarily by enforcement of corpus luteum regression, but only as long as the uterine and genital tract structures are undamaged enough to go through with normal physiological procedures for initiation of parturition in delivery of the dead fetus.

REFERENCES