

The Use of a Luteolytic Agent as a Treatment for Metritis

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Metritis is one of the most common pathologies faced by the practitioner. In Quebec, the cattle population is just below two million head, and Veticare statistics indicate 493,000 diagnoses and treatments on genital tract of the cow out of 933, 000 diagnoses of disease in cattle. It means that 53% of the total veterinary medical work is theriogenology. Metritis was involved in 78,000 cases or 16% of the genital tract diagnosis. These ratios did not change significantly since three years.

Treatment of post-partum metritis is well documented in the literature (3, 4). Recently, natural or synthetic Prostaglandin (PGF₂α) is claimed to be a new effective drug for uterine infections.

One of the most important and well recognized effects of PGF₂α is luteolysis. The hormonal changes initiated are as follows: CL decreases in size and activity, blood progesterone values decrease sharply within 12 hours post-injection and by 24 hours are at base-line concentration. FSH and estradiol rise gradually from 48 to 72 hours, then estrus begins (72 ± 24 hours after treatment). A surge of LH is demonstrated near the onset of estrus and ovulation occurs 24 to 30 hours later (6).

Sequin (5) has compared PGF₂α and estradiol cypionate (EC) for their luteolytic properties in clinical situations and results suggest that PGF₂α should be preferred to EC for this specific effect on CL function within 96 hours post-treatment.

There are at least two hypotheses by which PGF would be effective in treating metritis: Luteolysis and induction of estrus and direct action inducing contraction of myometrium and cervical drainage of the uterus. One might also speculate on the local inflammatory effect of PGF but more research should be done on this specific topic. This clinical trial was designed to evaluate the effect of PGF₂α in the treatment of post-partum metritis compared to conventional therapy, not on the basis of conception rate or open days but on the basis of progesterone level and CL activity, trying to state on which basis PGF will work and to compare the result with conventional treatment.

A total of 20 Holstein cows freshened less than 50 days were selected. Eleven cows received PGF analogue at a dose of 0.5 mg whatever they weighed. Nine received 100 mg of diethylstilbestrol (DES) and 80 I.U. of oxytocin 48 hours later. Metritis was diagnosed either by rectal palpation or

visualization of vaginal discharge. All uteri were enlarged, doughy, with a horn diameter greater than 8 cm. Longitudinal grooves, or enlarged caruncles or fluid content could be palpated. Ovaries were palpated to evaluate cyclic activity and serum was collected at day 0, 3 and 10 post-treatment for progesterone assay. Analysis of P₄ was achieved by specific double antibody radioimmunoassay.

Results

In the PGF₂α treated group, only three cows (3-6 and 10) were cycling at the time of treatment on the basis of ovary palpation and confirmed by the P₄ serum levels. All other cows had not shown estrus activity since parturition. The CL of the previous gestation was still palpable but not active on base of P₄ level. (Table I).

TABLE I

HISTORY, GENITAL TRACT EXAMINATION, PROGESTERONE LEVEL AND PGF₂α TREATMENT OF COWS WITH METRITIS AFTER PARTURITION

Cow no.	Days since calving	Larger uterine horn (cm)	Cervix diameter (cm)	Corpus luteum	P ₄ (ng/mL)		
					0	3d	10d
1	10	20	8	small & hard ^a	0,1	0,1	0,1
2	8	20	8	small & hard ^a	0,1	0,1	0,3
3	10	8	4	cyclic	0,9	1,5	4,1
4	7	20	5	small & hard ^a	0,4	0,2	0,7
5	13	12	6	small & hard ^a	0,1	0,2	0,2
6	14	8	4	cyclic	3,9	0,2	1,1
7	9	20	6	small & hard ^a	0,3	0,2	0,1
8	19	20	8	small & hard ^a	0,1	0,1	0,1
9	49	20	6	small & hard ^a	0,4	0,2	0,1
10	54	8	6	cyclic	9,7	0,3	2,3
11	35	15	6	hard	0,3	0,1	1,6

^aevaluated as the corpus luteum of the last gestation

In the DES-oxytocin treated group, (Table II) except cow 18 which was in post-estrus period at the time of treatment, no cows were cycling 10 days later.

TABLE II

HISTORY, GENITAL TRACT EXAMINATION, PROGESTERONE LEVEL AND D.E.S. TREATMENT OF COWS WITH METRITIS AFTER PARTURITION

Cow no.	Days since calving	Larger uterine horn (cm)	Cervix diameter (cm)	Corpus luteum	P ₄ (ng/mL)		
					0	3d	10d
12	15	8	5	small & hard ^a	0,3	0,5	0,1
13	15	20	6	not detectable	0,2	0,4	0,2
14	7	20	8	small & hard ^a	0,4	0,3	-
15	26	8	4	small & hard ^a	0,2	0,1	0,2
16	23	8	5	not detectable	0,2	0,1	0,1
17	7	20	6	not detectable	0,3	0,1	0,1
18	7	12	5	not detectable	0,7	1,5	3,3
19	7	20	8	not detectable	0,2	0,2	0,1
20	10	8	4	small & hard ^a	0,3	0,3	0,8

^aevaluated as the corpus luteum of the last gestation

The way PGF could act in the treatment of post-partum metritis was not clear. Both treatments failed to induce an estrus cycle within 10 days but an improvement of the genital tract condition was noted. No clinical difference between treatments could be detected by rectal palpation. The interval from treatment to first insemination was not recorded. Those results differed from those of Gustafsson's study (1) but the time after calving and the average progesterone level in the cows could explain the difference (Table III and IV).

Singh's study (7) on tissue strips from uterus of pregnant and non pregnant cows shows sharp increase in tension of uterine tissues from pregnant cows treated with PGF₂ whereas tension in tissues from non pregnant cows increased moderately. Literature results (2) suggest that contraction of smooth muscle induced by PGF₂ might depend on both an increase in calcium influx and on an intra-cellular release of calcium.

TABLE III

AVERAGE PROGESTERONE LEVEL (NG/ML)
IN PGF AND D.E.S. TREATED GROUPS

Day	0	3	10
Treatment			
PGF	1,63	0,32	1,10
D.E.S.	0,30	0,40	0,55
\bar{X}	0,95	0,34	0,80

TABLE IV

PYOMETRIA VS PGF₂α TREATMENT

Total no. of animals	No. of cows emptying uterus	P ₄ before treatment (N = 24)
26	22	3.1 ng (1.4-7.5)

Gustafsson, Therio.: 1976

Such disappointing results force us to adapt post-partum treatment of metritis to clinical examination. The genital tract was then graded as follows:

- Grade A: flaccid, large volume, not retractable in the pelvic inlet, fluid or necrotic placenta, cow depressed + fair condition.
- Grade B: flaccid uterus, retractable in the pelvic inlet, fluid contents were palpable, no systemic effect was noted.
- Grade C: good tonus, retractable thick wall, groove or caruncles might be palpable.
- Grade D: about normal in size & volume, no contents palpable but abnormal discharge.

Treatment included uterine infusions and hormonal injections.

Infusions Grade A and B

1. Furacin 100 mL (.2%)
2. Furacin 100 mL + 250 mL dextrose 50%
3. Furacin 100 mL + neomycin 2 gm
4. Dextrose 250 mL (50%)
5. Tetracycline 5 gm + 250 mL H₂O

Infusions used in Grade C and D

1. Tetracyclines (2 gm in 50 mL)
2. Gentamycin (200 mg in 100 mL)
3. Ampicillin (2 gm in 50 mL)
4. Lugol (2% vol/vol in 50 mL)

Hormonal treatment was one of the following:

- A - Estrogen (E.C.P.) (D.E.S.)
- B - PGF₂α
- C - Oxytocin
- D - Ergonovine

Some of those cases were primary metritis but most were concurrent with other pathologies such as left or right displaced abomasum, fatty liver syndrome or others.

Results

Preliminary results seem to demonstrate that Grade A uterus found in post-partum period responds to drugs acting strongly on uterine muscle such as ergonovine or oxytocin. Estrogen (estradiol cypionate or D.E.S.) added to the treatment do not improve the uterine response based on clinical examination. If the cow was not cycling (mainly Grade A), PGF₂ α did not initiate uterine drainage. A vigorous uterine message, preferably with the cow on her back and daily uterine infusion with dextrose and furacin is of good help in treating those problems as far as the uterus could be classified as type C.

Grade B uterus was easier to treat and even the large uterus responded well to PGF when CL was active. Drainage of the genital tract was detectable within 48 hours.

Type C and D were never treated with a large volume of infusion: 50 to 100 ml of antibiotic or antiseptic solution was infused (tetracycline, gentocin, lugol) with satisfying results. PGF₂ α effect was closely related to the presence of functional CL on the ovary.

Bacteriological findings were as reported in the literature: *C. pyogenes*, *E. coli*, *Proteus* or other. One of the most surprising findings was the isolation of PI₃ in five out of seventeen samples submitted for viral culture. All cases, positive to PI₃ culture, were also positive to FA.

The significance of this finding is not clearly understood. PI₃ was found with *E. coli* or *C. pyogenes*, and in any type of uterus (Table 5). Mycoplasma was not found in any of those individual problems.

PGF₂ α has also been used in five cases of macerated foetus where we had septic necrosis during the first half of pregnancy. Expulsion of the foetus failed in all those cases even after repeated injections. Treatment of macerated foetus is still by caesarean or slaughtering, as it is reported in the literature, and metritis following those pathologies is extensive, with in-depth lesions, as demonstrated by uterine biopsy. None of them conceived following such condition.

Many literature reports concerning PGF₂ α used in cases of mummified foetus have been published with very good results, and our experience just emphasizes the efficacy of PGF which should be considered as the drug of choice in treating those pregnancy pathologies.

To conclude, it is important to stress on the clinical examination of the genital tract and to be selective in the choice of the treatment. PGF does not initiate good drainage of a large uterus in the post-partum period if a CL is not active. It failed to induce estrus within 10 days in clinical situations. Myocontractants such as ergonovine or oxytocin seem to be more active, based on clinical examination, to drain the uterus, then PGF therapy will complete the treatment.

TABLE V

CULTURE RESULTS OF 17 UTERUS - AEROBIC BACTERIOLOGY +
VIROLOGY FOR HERPES, B.V.D. and PI₃

<i>C. pyogenes</i>	8
<i>E. coli</i>	6
PI ₃	5
<i>Proteus</i>	2
<i>Acinetobacter</i>	1
Neg.	2

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