

Reproductive Performance of Dairy Cows After Early Detection and Oxytetracycline Treatment of Post-Partum Metritis

L. J. Dawson,¹ E. P. Aalseth,² C. H. Hawman,² T. Nalsen² and H. J. Howard³

Abstract

The effect of oxytetracycline intra-uterine infusion on reproductive performance of 20 Holstein and Ayrshire cows with retained fetal membranes (RFM), or with post-partum metritis (47 cows) was studied in comparison to 47 normal post-partum cows. Cows with post-partum metritis were those found to have an abnormal cervical and uterine involution and/or abnormal vaginal discharge, based on weekly palpation and daily appraisal. Cows with RFM were those that had not expelled the membranes by 12 hours and were treated sooner than cows with evident metritis ($P < 0.01$). Also, more treatments were given to the RFM cows ($P < 0.09$). In addition RFM cows completed treatment sooner after calving than non-RFM cows ($P < 0.03$). Palpable cervical and uterine involution (diameter) during the first 40 days was not different among normal cows, cows with RFM and post-partum metritic cows. Reproductive performance as characterized by interval to first estrus, services per conception, post-partum interval to conception and percentage cows conceiving were comparable between normal cows and those treated for metritis with or without RFM.

Introduction

Retained fetal membranes (RFM) and metritis are two common post-partum problems. It is generally accepted that the lack of dehiscence and expulsion of the fetal membranes by 12 to 24 hours post-partum constitutes retention. The incidence of RFM in various groups of cows has been reported to be from less than 2% (5) to over 50% during certain seasons (6). RFM is not necessarily associated with lowered fertility, but does predispose the post-partum uterus to overt infections (19,43). As many as 88% of RFM cows have been reported to develop metritis as compared to 8% of normal peri-partum herd mates (6). Post-partum metritis is frequently associated with a sub-

sequent increase in days open and services per conception (4,6,7,12). The goal of therapeutic regimens should be to prevent the complications that are associated with RFM. Presently accepted therapeutic approaches directed at accelerating expulsion of RFM or preventing uterine infections have produced very inconsistent results (17-25).

We attempted to maintain normal conception rates by preventing delays in uterine involution, and promoting the development of a normal uterine environment in problem cows. In this report oxytetracycline intra-uterine infusions were administered to cows with indications of post-partum complications.

Methods

From August 1983 until August 1985, 114 Holstein and Ayrshire cows were monitored for reproductive performance during the first 150 days post-partum. To do so, cows were palpated weekly beginning 7-10 days after calving until first insemination. Involution of the cervix and uterus (size), ovarian function, and pregnancy diagnosis were monitored. Pregnancy diagnosis was first conducted 35-42 days after insemination and again two weeks later to confirm the initial diagnosis. Twice daily (7 am and 9 pm), cows were specifically observed for behavioral estrus, abnormal discharge from their external genitalia, and evidence of RFM. These observations were also performed at five other times of the day during handling for feeding (3x) and milking (2x). Cows were artificially inseminated with the same freeze lot of semen (one bull) for each breed at each estrus occurring 55 or more days post-partum predominantly by one inseminator. The breeding period was continued to 149 ± 4 days (range) post-partum.

Intra-uterine therapy was done on two classes of cows. In the first class were the cows which did not expel the membranes by 12 hours after calving. Manual removal of the membranes was not attempted. Instead, cows were locally infused with 5 g of oxytetracycline (Biomycin-C) 72 hours after calving if membranes were still retained. Cows expelling membranes between 12 and 72 hours post-partum were treated when metritis became evident. All cows with RFM eventually expressed metritis. Infusions were continued every other day until membranes were expelled. The second class was cows which had normally expelled

1. *Department of Veterinary Medicine and Surgery
Boren Veterinary Medical Teaching Hospital
Oklahoma State University, Stillwater, OK 74078*
2. *Animal Science Department
Oklahoma State University, Stillwater, OK 74078*
3. *Animal Science Department
North Carolina State University, Raleigh, NC 27607*

the membranes, but on weekly palpation and visual daily appraisal, were found to have an abnormal cervical and uterine involution, and also an abnormal vaginal discharge. These cows were locally infused with 5 g of oxytetracycline and were retreated if they persisted to have uterine infections with abnormal involution and discharge.

Septicemic and fibrile cows were given a parenteral injections of Procaine Penicillin G (Crystacillin) 20,000 I.U. in the muscle once a day for four days, and also infused with 5 g of oxytetracycline (Biomycin-C). Those cows treated for septicemia were not included in these data.

Statistical inferences were based on analysis of variance considering classes of uterine therapy as the main effect. Percentages were compared with chi square analysis. Cervical and gravid uterine horn involution were evaluated by comparing the average response of normal cows with both classes of uterine therapy at 95% confidence intervals for each day post-partum.

Cows involved in this research were part of a larger experiment studying the influence of dietary protein on reproductive performance (41). The objective of these antibiotic treatments was to maintain normal reproductive performance in cows by facilitating normal post-partum recovery of the reproductive tract. Thus, it was not advantageous to treat normal cows with oxytetracycline nor avoid treatment of infected cows.

Results

The relationship between class of cows given intra-uterine antibiotics and treatment logistics is shown in Table 1. Cows with RFM were treated sooner than cows with evident post-partum metritis ($P < 0.01$). While the number of days cows were treated did not differ, more treatments were given to the RFM cows ($P < 0.09$). RFM cows also completed treatment sooner after calving than non RFM treated cows ($P < 0.03$).

TABLE 1: Treatment logistics of cows requiring post-partum uterine therapy.

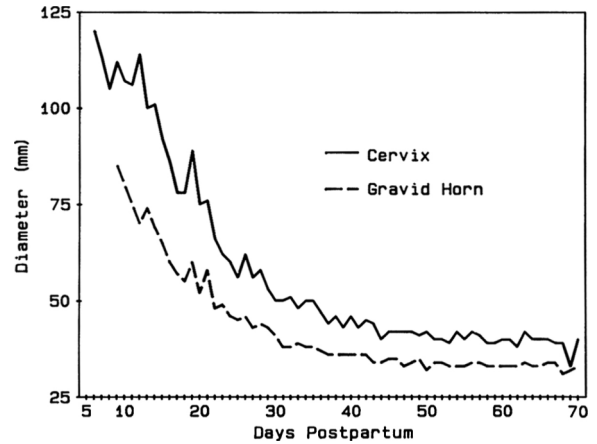
	Post-partum metritis	Post-partum metritis plus retained placenta
	Mean ^a SEM	Mean ^a SEM
Number of cows	47	20
Days post-partum to ^b first treatment	19.9±1.9	7.2±2.8
Days treated	9.4±11.9	11.6±3.3
Number of treatments ^c	2.7±0.4	3.8±0.6
Days post-partum to ^d last treatment	29.4±2.6	18.9±3.9

^aLeast squares means ^bMeans are different $P < 0.09$

^bMeans are different $P < 0.01$ ^dMeans are different $P < 0.03$

Cervical and gravid uterine horn diameter decreased rapidly in the first 30 days post-partum (Figure 1) and was essentially complete by 40 days. Comparisons were made between normal cows and both classes of antibiotic treated cows for either cervix or gravid horn diameter over the post-partum interval, and found to be not different for either tract region. While not significantly different, there was a tendency for involution to be slower for both RFM and metritic cows.

Figure 1. Palpable diameter of cervix and largest uterine horn after calving. Means are of those cows on all treatments at a post-partum day at each regular weekly palpation.



Indicators of reproductive performance (Table 2); interval to first estrus, services per conception, post-partum interval to conception and percentage cows conceiving were comparable between normal cows and those treated for metritis with or without RFM (Table 2). Services per conception on pregnant cows is perhaps the best indicator of fertility. These criteria compensated for those cows predisposed not to conceive, as these cows had ample opportunity to do so during the three month breeding period

TABLE 2: Reproductive performance of dairy cattle without post-partum complications, treatment for post-partum metritis and treated for retained placenta plus post-partum metritis.

	Antibiotic Therapy								
	Without Metritis		Post-Partum Metritis		Retained Placenta + Post-Partum Metritis				
	Mean ^a	SEM	n	Mean ^a	SEM	n	Mean ^a	SEM	n
Days post-partum ^b first estrus	36.9	3.3	44	40.3	3.2	45	43.7	4.9	18
Services/conceptions of all cows	1.58	0.14	47	1.87	0.14	47	1.40	0.21	20
Services/conceptions of pregnant cows	1.43	0.14	43	1.62	0.14	38	1.36	0.19	19
Days post-partum ^b to conception	81.8	3.8	38	83.9	4.1	33	73.5	6.2	14
Percent cows conceiving	91%			81%			95%		

^aLeast squares means.

^bCows treated for ovarian cysts prior to first estrus or conception were not included.

While there was a tendency for fewer of the treated cows, especially those without RFM to conceive during the breeding period, these percentages were not different.

Discussion

Many factors contribute to the diminished efficiency of most of the commonly used I.U. drugs (22,23,38). The post-partum bovine uterus is an anaerobic environment making the aminoglycoside group of antibiotics ineffective. Also, during the early post-partum period, many organisms in the uterus are capable of producing enzymes that inactivate or degrade antibiotics (penicillinase) (22). In addition, the presence of pus and organic debris in the uterine fluids could potentially inhibit drugs such as sulfonamides, aminoglycosides and nitrofurazone (22). Sulfonamides compete for essential metabolites needed by the bacteria. However, the post-partum uterus has enough necrotic tissue debris to supply most of the metabolites necessary for bacterial growth. Thus sulfonamides are ineffective antibacterial agents in the post-partum uterus (22).

Oxytetracycline was chosen for intra-uterine therapy because it is effective in the treatment of many mixed infections of the uterus (22). Oxytetracycline inhibits protein synthesis at the level of the bacterial ribosome. However, resistance to oxytetracycline occurs due to decreased absorption of the antibiotic by the bacteria, which is a gradual process. Resistance is an individual cell phenomenon that does not affect adjacent susceptible cells. Oxytetracyclines are inhibited only slightly by purulent exudate and do not require oxygen to be active. Hence, oxytetracyclines are effective in local therapy of early postpartum uterus (22).

Pharmacokinetics, rate of administration, and minimum inhibitory concentrations (MIC) for *C. pyogenes* and other pathogenic bacteria need to be considered in selection of oxytetracyclines dosages for intra-uterine use. The average MIC of oxytetracycline for *C. pyogenes* isolated from the uterus is 20.4 microgram/ml of media. *Fusobacterium* and *Bacteriodes* spp. are both fairly susceptible to it. Pharmacokinetic studies show a need for 11 mg/kg of oxytetracycline to be administered twice daily by intravenous injections to maintain a serum level of 5 micrograms/ml in cattle. Five micrograms/ml is well below the average MIC of oxytetracycline for *C. pyogenes* isolated from the uterus. Therefore, systemic therapy would likely be ineffective, since plasma to uterine tissue concentration ratios are slightly greater than 1:1. However, effective levels can be easily achieved within the uterine lumen by once daily infusion with four to five grams of oxytetracycline (22,35).

Cows which do not expel the membranes by 12 hours were classified as cows with RFM. Manual removal of the fetal membranes was not attempted because most of the literature supports the conclusion that it may cause impairment rather than improvement of fertility

(17,23,24,35,42,43,44). Delaying intra-uterine therapy with oxytetracycline until 72 hours reportedly enables the placenta to (42) undergo progressive liquifactive putrefaction which facilitates discharge. Few of the cows with RFM actually discharged their placenta before 72 hours. However, on visual examination and weekly palpation, if they had evident metritis antibiotic therapy was initiated at that time rather than 72 hours post-partum.

Basically our antibiotic therapy with oxytetracyclines was done to reduce subsequent bacterial colonization and complications. Normal cervical and uterine involution was achieved with both treated groups of cows. The indicators of reproductive performance were comparable between normal cows and those treated with oxytetracycline for metritis with or without RFM. Early detection of metritis by frequent observation of vaginal discharge supplemented with palpable signs likely contributed to early recovery of the reproductive tract and maintenance of reproductive performance. While non-significant, there does appear to be a trend for lower fertility in the non-RFM treated cows. Perhaps this is due to the delay in detection of metritis, compared to immediate indication of potential metritis in RFM cows. Since RFM cows started and completed treatment sooner in the post-partum period, the recovery period before breeding was longer. This would allow for a more normal reproductive tract and could enhance their fertility.

Other investigations have achieved different degrees of success following treatment of RFM and metritis with tetracycline drugs. Mutiga and Kimberling (24) infused tetracyclines in cows with RFM longer than 48 hours post-partum, treatment was repeated at 48 hour intervals until the fetal membranes were expelled. Average days to post-partum estrus, interval from parturition to conception, and average number of services per conception between treated cows and cows with no obvious post-partum problem were not different. It was concluded that RFM along with other post-partum complications were prevented from suppressing future reproductive performance by the tetracycline infusions.

In other research Banerjee (42) divided RFM cows less than 72 hours post-calving into four groups; group I were infused with 1 g of terramycin and the placenta was not manually removed, group II cows were infused with 1 g of terramycin and the placenta was manually removed, group III cows were not treated parenterally or locally and the placenta was not manually removed, group IV cows were not treated parenterally or locally, but the placenta was manually removed. The percentage of cows conceiving after the first service were 70%, 39%, 50% and 39% in I, II, III and IV groups respectively. This demonstrated the value of letting the placenta pass on its own and the effectiveness of oxytetracycline treatment.

Chlortetracycline and oxytetracycline were used on RFM cows 3-4 days after calving by Gould (44). While there was

no difference in their reproductive performance, most (90%) of the cows showed clinical improvement. Such was defined as a decrease in septicemia, hastened placental expulsion and decreased incidence of chronic metritis.

Easterbrooks (10) gave 500 mg of aureomycin bolus IU to RFM cows every day or every other day, if they had not expelled their placenta by 12 hours post-calving. Manual removal was not attempted. For every day versus every other day treatment of cows, services per conception were 1.6 and 1.4, with the calving interval 392 and 377 days respectively. The overall average treatment period was 5 days. This suggested that treatment every 48 hours is sufficient to control RFM related metritis.

However, in contrast to these reports other investigators have not perceived any beneficial effects of post-partum uterine therapy with drugs of the tetracycline group. Cows with dystocia and/or RFM, or cows with post-partum metritis were treated with 5 g of tetracycline powder IU on day 1 of treatment plus 10.5 million units Procaine Penicillin G (IM) on day 1, 2 and 3; or received four sulfa urea boluses IU on day 1 (19). Bretzlaff, et al, concluded neither treatment was effective, due to inappropriate dosages or regimens.

Moller (5) examined the effects of various degrees of placental removal, in conjunction with intra-uterine antibiotic therapy consisting of chlortetracycline (500 mg) or chloramphenicol (500 mg) with or without 15-30 mg of Stilbestrol.

His conclusion was that subsequent fertility may not be depressed if no form of medication was used. Lowered fertility may be due to low dosage of antibiotic infused, which could have predisposed the uterus to secondary metritis caused from the formation of bacterial resistance within the uterus.

Conclusion

From our research and others (10,24,42,44), it appears that oxytetracycline is the drug of choice for control of metritis. With prompt detection of post-partum uterine infections, aggressive treatment resulted in normal involution of the reproductive tract and subsequent reproductive performance.

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Residue Prevention

AVMA Urges Cooperation

AVMA stressed the need for cooperative efforts to prevent residues at a recent FDA meeting on sulfamethazine (SMZ). The session gave various groups an opportunity to provide updates on their current residue prevention programs with a particular focus on dairy products. Dr. Arnold Hentschl, speaking on behalf of AVMA, emphasized the need to minimize the incidence of harmful residues in dairy products, namely those created due to the use of SMZ. Hentschl had previously called for a temporary moratorium on the use of SMZ (*see News from Washington*, June 1, 1988). The meeting was chaired by Dr. Gerald Guest, director of FDA's Center for Veterinary Medicine (CVM).

After highlighting segments of AVMA's May testimony and stating that SMZ should be used only under the direct supervision of a veterinarian if, and when, the moratorium is lifted, Hentschl offered additional guidelines to help alleviate the residue problem and stated that AVMA will take the following actions:

- * encourage food animal practitioners to offer on-farm assistance to producers to plan and evaluate their drug use programs and to identify areas of potential concern;
- * support veterinary assistance in residue testing to assure that human food derived from animals is free from harmful residues;
- * urge that a study be undertaken to determine the feasibility of a sound certification program whereby only certified producers will be authorized to obtain and administer over-the-counter animal drugs;
- * promote the use and further development of diagnostic test kits to screen for residue violations at the farm level; and
- * maintain that residue detection methodologies undergo an official governmental process to assure their validity, accuracy and limitations.

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