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Comparison of two protocols for the treatment of retained fetal membranes in dairy cattle

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Abstract

Two protocols for the treatment of retained fetal membranes in dairy cattle were evaluated in a field trial. Cows that retained the fetal membranes for more than 12 h were assigned to two treatment groups in an alternating order. In both groups rectal temperature was measured daily for 10 days after enrollment. In Group 1 ($n = 35$) cows with a rectal temperature $\geq$39.5 °C received a systemic antibiotic treatment with 600 mg ceftiofur intramuscularly on three consecutive days. No manual removal of the fetal membranes or intrauterine treatment was conducted. In case of elevated temperature of $\geq$39.5 °C on Day 3 treatment was conducted for another 2 days. In Group 2 ($n = 35$) cows received a local antibiotic treatment (2500 mg ampicillin, 2500 mg cloxacillin) and an attempt was made to remove the fetal membranes manually. In case of a rectal temperature $\geq$39.5 °C 6000 mg of ampicillin were administered intramuscularly. Treatment was repeated on three consecutive days. If temperature did not decrease below 39.5 °C systemic treatment was extended for another 2 days.

During 10 days of observation 33 and 34 cows showed fever, i.e. a body temperature $\geq$39.5 °C in Groups 1 and 2, respectively (94.3 versus 97.1%). The proportion of cows considered as cured (temperature <39.5 °C on Day 10 after enrollment) was 65.7 and 68.6% in Groups 1 and 2, respectively. All cows showed signs of chronic inflammation of the genital tract on Day 14 after calving. Within 4 weeks postpartum three (8.6%) and four (11.4%) cows were culled in Groups 1 and 2, respectively. Days to first service and days open did not differ significantly between the groups. Proportion of cows pregnant on Day 200 postpartum was 71.4 and 54.3% for Groups 1 and 2, respectively ($P > 0.05$). Results indicate that treatment of retained fetal membranes without intrauterine manipulation and treatment can be as effective as conventional treatment including detachment and local antibiotic treatment.

Keywords: Retained fetal membranes; Antibiotic treatment; Manual removal; Reproductive performance; Dairy cattle

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1. Introduction

The retention of the fetal membranes (RFM) has been defined as the failure to expel the fetal membranes within 12–24 h after calving [1,2]. Average incidence of RFM ranges from 4 to 12% of calvings [3,4]. Predisposing factors for RFM are dystocia, abortions, length of gestation, and imbalances in nutrition [5]. The negative impact of RFM on reproductive performance of dairy cows has been documented in several studies [6–10]. Some authors, however, did not find an effect of RFM on fertility [2,11,12]. The frequent occurrence of metritis after RFM constitutes the main reason for poor fertility of affected cows [2,3,6,13]. Also, a relationship between RFM and ketosis [14] and mastitis has been described [15,16].

Manual removal of the retained membranes is still widely practiced. In a survey in 1995, more than 90% of the British cattle practitioners stated that they used this method at least occasionally [17]. However, disadvantages of manual removal are described as intrauterine trauma and interference with the uterine defense mechanisms, followed by bacterial invasion [1,18,19]. While some studies show that manual removal of the retained fetal membranes impaired fertility, others do not [1,18,20]. The treatment of RFM and toxic puerperal metritis with intrauterine application of antibiotic drugs into the uterus is very common. The use of oxytetracycline for intrauterine infusion has been recommended by several authors [21–23], but also the combination of ampicillin and cloxacillin for intrauterine treatment of RFM has been established [24]. However, the efficacy of a local antibiotic treatment is a controversial issue [1,25–28]. Furthermore, growing public concern about antibiotic residues in milk requires current studies about pharmacokinetic aspects of intrauterine applications of antibiotic drugs [29]. Negative interactions between antibiotics and the uterine environment, the inhibition of uterine defense mechanisms, and a questionable efficacy of antibiotics within the inflamed uterine wall are some reasons to reject local treatment [1,19]. The systemic use of ceftiofur for the treatment of toxic puerperal metritis has been reported recently [30,31]. In addition to the antibiotic treatment of RFM the use of ecbolic drugs, e.g. prostaglandin $F_{2\alpha}$ or oxytocin has been described. However, studies show no consistent results [27,32–34].

The objective of this study was to compare an intrauterine treatment of RFM (antibiotics and manual removal) to a protocol without manual removal or local intrauterine administration of antibiotics but with the use of ceftiofur as a systemic antibiotic treatment.

2. Material and methods

The study was conducted on a commercial dairy farm in Germany with 1200 Holstein–Frisian cows. Animals were housed in free stall facilities with cubicles, rubber mats and slotted floors. One week before expected calving cows were housed in a free stall barn with straw bedding. Cows were fed a total mixed ration (TMR), consisting of corn silage, grass silage and concentrates. Average milk yield was 8500 kg/year per cow (fat 4.3%, protein 3.6%).

Cows calving between June 1999 and November 1999 and between May 2000 and March 2001 were included in the trial. Retention of the fetal membranes (REM) was defined as the

failure to expel all or part of the placenta from the uterus within 24 h. All cows were examined after calving by adspection and in case of doubt by vaginal inspection. Cows that received anti-inflammatory drugs or antibiotic drugs for purposes not related to the study (e.g. acute mastitis, surgical correction of displaced abomasum) were excluded from the trial.

Cows with retained fetal membranes were assigned alternately to two treatment groups. Rectal temperature of each cow was measured daily for 10 days after enrollment. In Group 1 cows with a rectal temperature $\geq$39.5 °C received a systemic antibiotic treatment with 600 mg of ceftiofur (Excenel®, Pharmacia, Erlangen, Germany) intramuscularly (i.m.) on three consecutive days. No manual removal of the fetal membranes or intrauterine treatment was conducted. In order to prevent detrimental effects on milking hygiene, the shortening of visible parts of the membranes with a clean knife was allowed. In case of elevated temperature on Day 3 treatment was conducted for a total of 5 days. In Group 2 manual removal of the fetal membranes was attempted on three consecutive days. Cows received an intrauterine treatment (i.u.) with 2500 mg of ampicillin and 2500 mg of cloxacillin (Aniclox®, AniMedica, Flensburg, Germany). In case of a rectal temperature $\geq$39.5 °C 6000 mg of ampicillin (Ampicillin-Trihydrat 230®, CP-Pharma, Burgdorf, Germany) were administered i.m. Treatment was repeated on three consecutive days. If temperature did not decrease below 39.5 °C on Day 3 the systemic treatment was extended for another 2 days. In both groups cows with body temperature $\geq$39.5 °C after 5 days of systemic treatment were considered as a treatment failure. These cows received 3000 mg of oxytetracycline (Terramycin®, Pfizer, Karlsruhe, Germany) i.m. on three consecutive days as an escape therapy.

All cows in the two groups were examined by vaginal inspection and palpated per rectum between 18–20 and 32–34 days postpartum. Vaginal discharge and size of the uterus were documented. All cows received two treatments of dinoprost (25 mg, i.m., Dinolytic®, Pharmacia, Erlangen, Germany) at these examinations regardless of clinical diagnoses. The voluntary waiting period was set at 50 days postpartum. Cows were inseminated by an AI-technician based on observed estrus. Pregnancy diagnosis was carried out by palpation of the uterus and its content between Days 35 and 48 after insemination.

Cure rate for each treatment group was defined as the proportion of cows with a temperature <39.5 °C on Day 10 after enrollment and no escape therapy applied. Reproductive performance was measured for all cows in the trial groups. The proportion of cows inseminated, days to first service, proportion of cows pregnant to first service (first-service conception rate), days open, and proportions of cows pregnant and culled were recorded. Total conception rate was defined as the number of cows pregnant divided by the total number of inseminations. Cows not pregnant within 200 days postpartum were considered as culled for infertility.

Data were analyzed using SPSS® for Windows (Version 9.0, SPSS Inc., Munich, Germany) and Excel® (Version 2000, Microsoft). Cure rate, proportion of cows inseminated, conception rates, proportions of cows pregnant and culled were analyzed by chi-square analysis [35]. Days to first service and days open were compared by using Mann–Whitney *U*-test. Temperature at treatment days was compared using the repeated measurement procedure of SPSS. Level of significance was set at $\alpha = 0.05$. The risk of removal from the herd was analyzed using logistic regression including treatment group, treatment outcome and parity as covariates.

3. Results

During the two study periods a total of 1651 cows calved. Retention of the fetal membranes occurred in 78 cows. The lactational incidence rate of RFM was 4.7%. In the first study period 29 cows were enrolled, 14 cows in Group 1, 15 cows in Group 2. In the second study period 21 and 20 cows were enrolled additionally in Groups 1 and 2, respectively. A total of eight cows were not eligible for the final evaluation. In Group 1, three cows were excluded for displaced abomasum and one cow for acute mastitis. In Group 2, three cows were excluded for acute mastitis and one cow for displaced abomasum. Finally, 35 cows were eligible for analysis in each group. Number of primiparous cows was 16 (45.7%) and 11 (31.4%) in Groups 1 and 2, respectively.

Within the 10 days of observation the total number of cows with elevated temperature was 33 (94.3%) and 34 (97.1%) in Groups 1 and 2, respectively. Fig. 1 shows the distribution of the first day of fever. In Group 1, 27 cows (77.1%) showed fever at the first examination (Day 1). Another six cows showed fever on Day 2 (17.1%) while two cows (5.7%) had a temperature lower than 39.5 °C during the observation period. In Group 2, 24 cows (68.6%) and 2 cows (5.7%) had a temperature ≥39.5 °C on Day 1 and Day 2, respectively. Eight cows (22.6%) showed an elevated temperature for the first time after Day 2.

Daily temperatures from Day 1 to Day 10 after the first examination for both groups are presented as box plots in Fig. 2. On Day 2 the mean temperature was significantly lower in Group 2 than in Group 1. However, analysis of the decrease of rectal temperature using the repeated measurement procedure showed no significant differences between the groups.

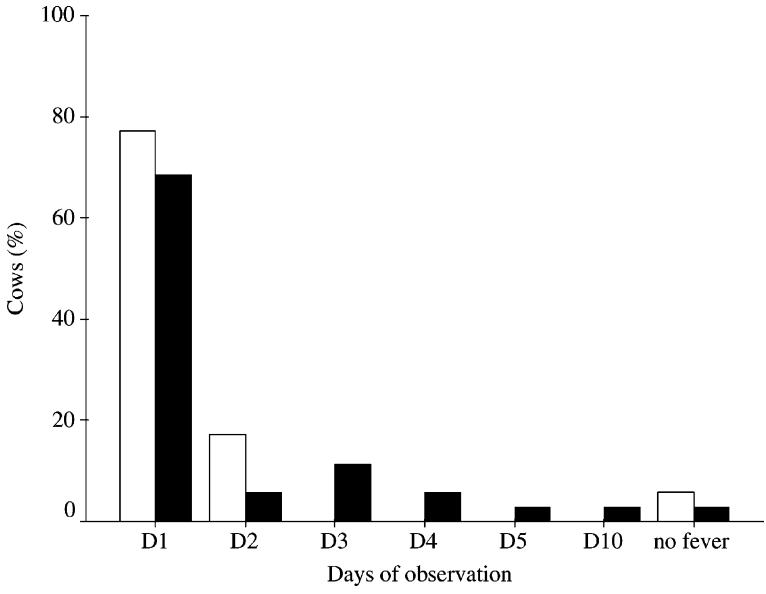

Fig. 1. First day (Day 1) of temperature ≥39.5 °C for Group 1 (□) and Group 2 (■). Day 1 (D1) = day of first examination.

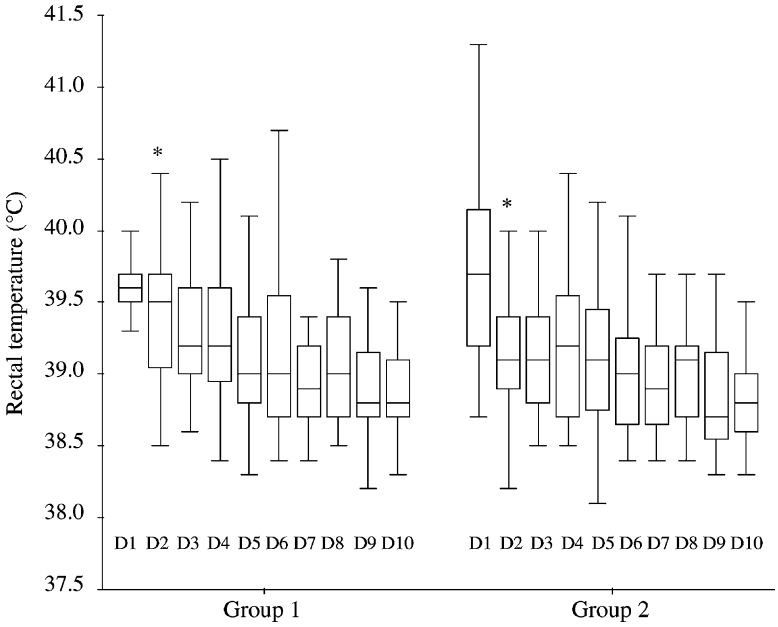

Fig. 2. Box plots indicating rectal temperature on Day 1 (D1) to Day 10 (D10) after first treatment (outliers and extremes not shown; $^{*}P < 0.05$).

Cure rate was 65.7 and 68.6% in Groups 1 and 2, respectively ($P > 0.05$). A total of 23 cows received an escape therapy during the observation period. Seven of those (30.4%) showed a rectal temperature $\geq$39.5 °C on Day 10. All cows in both groups showed clinical signs of chronic inflammation of the genital tract (purulent vaginal discharge) 18–20 days postpartum. Fourteen days later (i.e. 32–34 days postpartum) 83.9 and 74.2% of cows examined showed purulent vaginal discharge in Groups 1 and 2, respectively ($P > 0.05$).

Reproductive performance measures are summarized in Table 1. The results are presented for all cows enrolled and for cows regarded as cured on Day 10. Days to first service were similar for both groups. First-service conception rate was higher in Group 1 ($P > 0.05$). The difference between Groups 1 and 2 was more pronounced in the total conception rate. For cows regarded as cured the difference between the groups was significant even at the $P < 0.1$ level. Days open was slightly lower in Group 2 than in Group 1. However, the differences were not significant. On the other hand, the proportion of cows pregnant was higher in Group 1 compared to Group 2. This difference was significant for cows regarded as cured ($P < 0.05$).

The percentage of cows pregnant during the course of lactation is shown in Fig. 3. During the first 100 days postpartum the percentage of cows pregnant was similar for both groups. After 100 days, more cows became pregnant earlier in lactation in Group 1.

During the 10 days of observation, none of the cows included in the study was culled or died. Within 4 weeks postpartum three (8.4%) and four (11.4%) cows left the herd in Groups 1 and 2, respectively. Due to the higher percentage of cows pregnant in Group 1, the percentage of cows culled was lower in Group 1 than in Group 2 (Table 1). Reasons for

Table 1
Reproductive performance measures for cows in Groups 1 and 2

Parameter	Group 1		Group 2	
	All cows ($n = 35$)	Cows cured ($n = 23$)	All cows ($n = 35$)	Cows cured ($n = 23$)
Cows inseminated (%)	82.9	82.6	82.9	75.0
Days to first service	75.2 ± 21.0	69.2 ± 16.2	81.0 ± 25.8	79.8 ± 26.4
No. of inseminations	58	37	60	40
First service conception rate (%)	37.9	42.1	34.5	33.3
Total conception rate[1] (%)	43.1	43.2[a]	31.7	22.5[b]
Days open	107.4 ± 38.6	97.6 ± 38.2	98.1 ± 36.4	87.0 ± 36.8
Cows pregnant (<200 dpp[2]) (%)	71.4	69.6[c]	54.3	37.5[d]
Cows culled (%)	28.6	30.4[c]	45.7	62.5[d]

Rows with different superscripts (a, b) differ $P < 0.1$. Rows with different superscripts (c, d) differ $P < 0.05$.
[1] No. of cows pregnant × 100/no. of AI.
[2] Days postpartum.

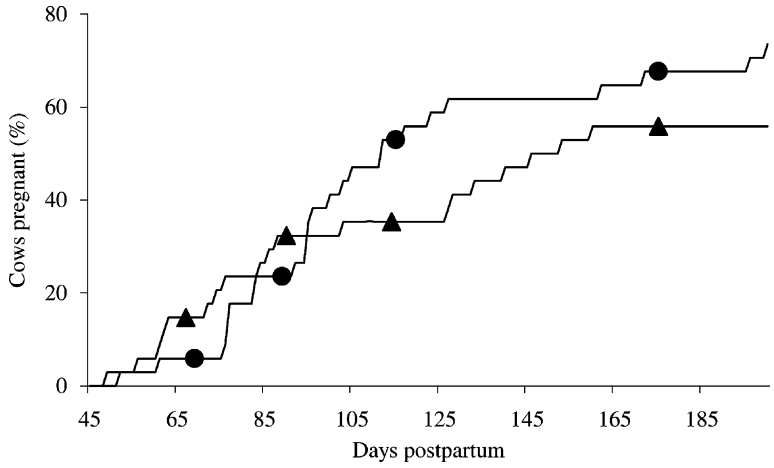

Fig. 3. Percentage of cows pregnant for Group 1 (●) and Group 2 (▲), respectively.

culling within 200 days after calving included infertility (two cows), low milk yield (nine cows), mastitis (one cow) and other diseases (ten cows). The logistic regression model revealed that treatment group had no significant effect on the risk of removal from the herd. Primiparous cows with RFM were less likely to be culled than older cows. Surprisingly, cows regarded as cured had a higher risk to be culled than cows regarded as treatment failures.

4. Discussion

The incidence of retained fetal membranes in the current study was within the reported range [3,4]. Most of the cows showed an elevated rectal temperature within the 10-day

observation period. Fever as an effect of RFM has been described by several authors [27,36]. Dinsmore et al. [29] and Hernandez et al. [37] found 60 and 55% of cows with RFM had temperatures greater than 39.7 and 39.5 °C, respectively. However, it is noteworthy that the number of cows with fever in Group 2 increased after enrollment, i.e. after the first local antibiotic treatment. One explanation might be the release of toxins from bacteria after antibiotic induced killing of bacteria. Another hypothesis is that manual removal caused lesions in the mucosa followed by a systemic infection or depression of the uterine defense mechanisms [1,18,19]. This observation might also explain the different distribution in the first days of fever in the two groups. In Group 1, the first day of fever occurred only on Day 1 or Day 2 of the observation period. Even though on Day 2 the mean rectal temperature was significantly higher in Group 1, the comparable decrease of temperature indicates an equally successful treatment response for both groups. This is confirmed by similar cure rates on Day 10 for both groups. Successful local treatment of RFM with ampicillin and cloxacillin has been reported recently [24]. The use of ceftiofur for systemic treatment of toxic puerperal metritis (TPM) has been described by Smith et al. [31] and Drillich et al. [30]. The latter reported a cure rate of 82.9% for cows with TPM. However, about one third of the cows in this study received oxytetracycline as an escape therapy. Of those 30.4% were considered as treatment failures. This shows the limited efficacy of antibiotic treatment and the severity of the disease [19,20,27].

The frequent occurrence of puerperal metritis after RFM has been described by several authors [1–3,31,36]. Two recent studies reported 92% of cows with RFM showed abnormal discharge 14 days postpartum [36,38]. This is in agreement with 100% found in this study. While Dohmen et al. [36] found 14 of 15 cows with normal discharge on Day 30 postpartum, the percentage of cows with purulent discharge as a sign of chronic endometritis [39] on Day 32 postpartum was much higher in our study. In a study of TPM an endometritis prevalence of 45–50% was found on Day 32 postpartum [30].

Reproductive performance measures for all cows enrolled showed no statistically significant differences between the groups. Fig. 1 shows that after 100 days postpartum the percentage of cows pregnant increased faster in Group 1 than in Group 2. The reason for this remains speculative. Probably the high percentage of cows with purulent discharge in the postpartum period, which was assumed to be a sign of endometritis, was the main reason that only a few cows became pregnant within the first weeks after the voluntary waiting period of 50 days. The intrauterine treatments could have led to a sustained inhibition of the uterine defense mechanism [1,19]. An impaired reproductive performance for cows with RFM in combination with postpartum metritis has been reported by several authors [2,7,40]. According to Bolinder et al. [18] the manual removal of retained membranes can delay the postpartum return to normal reproductive status. However, most differences in reproductive performance in our study were statistically not significant. Furthermore, the logistic regression model showed that treatment group had no statistically significant effect on the risk of removal from the herd. The percentage of cows culled in Group 1 (28.6%) is in accordance with the percentage (27%) published recently for cows with RFM after different intrauterine treatments [38]. Dohmen et al. [36] reported a pregnancy rate of 55%. However, only 15 cows were investigated. In our study cows not pregnant within 200 days postpartum were regarded as culled. This procedure increases the number of cows ‘‘culled’’. However, reproductive data are more comparable between the

groups because extremes and outliers are excluded. We did not compare cows with RFM to cows without RFM. However, with regard to the voluntary waiting period of 50 days, a calving to conception interval of about 100 days is acceptable. Stevens et al. [27] reported 120 days open for cows with RFM treated with intrauterine antibiotics and prostaglandin $F_{2\alpha}$. The total conception rate in Group 1 (43.1%) was in an average range for German dairy herds, while total conception rate for Group 2 (31.7%) was lower [30,41].

The cure rates and reproductive performance measures for both groups indicate that the systemic treatment of cows with RFM and elevated temperature with ceftiofur is at least as successful as a common therapy including manual removal, local and systemic antibiotic treatment. These findings support authors who have questioned the use of intrauterine antibiotics and manual removal of the retained membranes [1,18,28]. Stevens et al. [27] have reported no differences in days open, and percentages of cows pregnant and culled between an untreated control group and an antibiotic treatment group. Considering the life-threatening character of toxic puerperal metritis [19] following RFM, no untreated control group was included in this trial. However, with regard to the public concern about the use of antibiotics for food producing animals further research is required to identify effective and prudent treatment protocols for RFM.

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