

Evaluation of a Systemic Antibiotic Treatment of Toxic Puerperal Metritis in Dairy Cows

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ABSTRACT

The objective of this study was to evaluate the efficacy and economic efficiency of a systemic treatment of toxic puerperal metritis in dairy cows with ceftiofur. Cows with abnormal vaginal discharge at a postpartum examination (d 4 to 6 after calving) and a rectal temperature $\geq 39.5^{\circ}\text{C}$ were assigned to three treatment groups. Cows in group 1 (n = 70) received 600 mg of ceftiofur intramuscularly (i.m.) on 3 consecutive days. Cows in group 2 (n = 79) received an intrauterine treatment with antibiotic pills consisting of 2500 mg of ampicillin and 2500 mg of cloxacillin and an additional 6000 mg (i.m.) of ampicillin. This treatment was performed on 3 consecutive days. Cows in group 3 (n = 78) received the same intrauterine treatment as in group 2. In addition, 600 mg of ceftiofur was administered i.m. on 3 consecutive days. Body temperature was recorded daily for 6 d after first treatment.

There were no significant differences among the groups regarding clinical efficacy at d 6 after first treatment. The cure rates based on rectal temperatures declining to below 39.5°C on d 6 after treatment were 82.9, 84.8, and 84.6% for groups 1, 2, and 3, respectively. Reproductive performance did not differ significantly between group 1 and groups 2 and 3 for any of the measures tested. A financial analysis with 87 different cost scenarios demonstrated that a systemic treatment of toxic puerperal metritis in cattle with ceftiofur is an effective alternative to the combination of local and systemic treatments.

(Key words: toxic puerperal metritis, antibiotics, reproductive performance, financial analysis)

Abbreviation key: dpp = days postpartum, TPM = toxic puerperal metritis, € = Euro monetary unit ~ to \$0.85 at time of publication.

INTRODUCTION

Postpartum metritis is one of the most important disorders in dairy cattle, causing high economic losses due to prolonged days open and involuntary culling (Esslemont and Peeler, 1993). Toxic puerperal metritis (TPM) is characterized by increased rectal temperature, fetid, watery vulval discharge, and a flaccid uterus (Paisley et al., 1986; Smith et al., 1998). Incidence of TPM ranges from 18 to 37% (Bartlett et al., 1986; Etherington et al., 1984; Markusfeld, 1987; Peeler et al., 1994). Predisposing factors are dystocia, retained fetal membranes, as well as deficiencies in hygiene and metabolic imbalances around parturition (Erb et al., 1985; Gröhn et al., 1990; Markusfeld, 1984; Sandals et al., 1979). Associated bacteria are mainly *Arcanobacterium (Actinomyces) pyogenes*, coliform bacteria, and gram-negative anaerobic species such as *Fusobacterium necrophorum* and *Bacteroides* spp. (Callahan and Horstman, 1993; Miller et al., 1980; Olson et al., 1984).

A common treatment of toxic puerperal metritis is the infusion of antibiotics into the uterus (Montes and Pugh, 1993; Smith et al., 1998). However, the efficacy of a local antibiotic treatment is a controversial issue (Gilbert, 1992; Olson, 1996; Paisley et al., 1986; Whitacre, 1992). Negative interactions between antibiotic drugs and the uterine environment, the inhibition of the uterine defense mechanism by irritating drugs, e.g., oxytetracycline, and a questionable efficacy of antibiotics within the inflamed uterine wall are some reasons to reject local treatment (Paisley et al., 1986). The use of oxytetracycline for intrauterine infusion is recommended by several authors (Gustafsson, 1984; Montes and Pugh, 1993), but also the combination of ampicillin and cloxacillin for intrauterine treatment has been established (Ahlers et al., 2000). The systemic use of ceftiofur for treatment of TPM without additional intrauterine infusion of antibiotic drugs was demonstrated by Smith et al. (1998), measuring rectal temperature, daily milk yield, and serum haptoglobin concentrations for 5 d.

Metritis causes severe economic losses due to costs for treatment, milk withdrawal, reduced reproductive

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performance, and premature culling (Bartlett et al., 1986; Dohoo et al., 1984; Tenhagen et al., 1998). The economic losses due to milk withdrawal depend on milk yield, milk price, and length of withdrawal period (Eslemont and Peeler, 1993).

The objective of this study was to evaluate the efficacy and financial viability of a systemic treatment of TPM in cattle with ceftiofur. Cure rates 6 d after treatment and subsequent reproductive performance were compared with two control groups treated with intrauterine and systemic application of antibiotic drugs. To determine bacteria involved, uterine swabs were taken and cultured for aerobic and anaerobic bacteria. Antibiotic susceptibilities of aerobic specimens to the used antibiotic drugs were tested. Finally, a financial analysis with 87 different cost scenarios for the three treatment groups was performed, including costs for veterinary treatments, milk withdrawal, reproductive performance and premature culling.

MATERIALS AND METHODS

The study was conducted on a commercial dairy farm in Germany with 1200 German Black Pied 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 TMR consisting of corn silage, grass silage, and concentrates. Average milk yield was 6700 kg/yr per cow (fat 4.4%, protein 3.6%).

Cows calving between January 1998 and May 1999 were included in this trial. All cows were examined by vaginal inspection between 4 and 6 d postpartum (**dpp**). Toxic puerperal metritis was defined as a fetid, reddish-brown vaginal discharge and a rectal temperature $\geq 39.5^{\circ}\text{C}$. Cows that received antiinflammatory drugs or antibiotic drugs for purposes not related to the study (e.g., acute mastitis) were excluded from the trial.

Cows diagnosed with TPM were alternately assigned to three treatment groups, i.e., first cow was assigned to group 1, second cow to group 2, and third cow to group 3. Considering the life-threatening character of TPM (Olson et al., 1986), no untreated control group was included in this trial.

Cows in group 1 were treated with 600 mg of ceftiofur (Excenel, Pharmacia & Upjohn, Erlangen, Germany) intramuscularly (i.m.) on 3 consecutive days. Cows in group 2 received an intrauterine treatment (i.ut.) with 2500 mg of ampicillin and 2500 mg of cloxacillin (Aniclox, AniMedica, Flensburg, Germany) and additionally 6000 mg of ampicillin i.m. (Ampicillin-Trihydrat 230, CP-Pharma, Burgdorf, Germany). This treatment was performed on 3 consecutive days. Cows in group 3

received the same intrauterine treatment as group 2. In addition, 600 mg of ceftiofur were administered i.m. on 3 consecutive days.

The rectal temperature of each cow was measured daily for 6 d after first treatment. Cows with body temperature $\geq 39.5^{\circ}\text{C}$ at d 6 after first treatment were considered as a treatment failure and treated with 3000 mg of oxytetracycline i.m. (Terramycin, Pfizer, Karlsruhe, Germany) on 3 consecutive days. Furthermore, uterine discharge was documented at d 6 after first treatment.

All cows of the three groups were reexamined by vaginal inspection and rectal palpation between 18 to 20 and 32 to 34 dpp. Vaginal discharge and size of the uterus were documented. All cows received two treatments of dinoprost (25 mg, i.m., Dinolytic, Pharmacia & Upjohn, Erlangen, Germany) at these examinations regardless of clinical diagnoses.

The voluntary waiting period was set at 55 dpp. Cows were inseminated by an experienced AI technician based on observed estrus. Pregnancy diagnosis was carried out by rectal palpation of the uterus and its content between d 35 and 48 postinsemination.

The cure rate for each treatment group was defined as the proportion of cows with temperature $< 39.5^{\circ}\text{C}$ at d 6 after first treatment. Reproductive performance was measured for all cows in the trial groups and for cows without TPM. The proportion of cows inseminated, days to first AI, the proportion of cows pregnant to their first service (first AI conception rate), days open, and proportions of cows pregnant and culled were recorded. Conception rate was defined as the number of cows pregnant divided by the total number of inseminations. Cows not pregnant within 200 dpp were considered as culled for infertility.

To determine the bacteria involved, we collected uterine swabs from 15 randomly selected cows with TPM before the first treatment. Swabs were cultured for aerobic and anaerobic bacteria within 4 h after sampling. Swabs were sampled by inserting a sterile insemination catheter via the cervix into the cavity of the uterus. Fluid was withdrawn with a sterile syringe into the catheter. To prevent false-positive findings, fluid for inoculation was taken from the middle of the catheter.

To isolate aerobes, we inoculated sheep blood agar (nutrient agar base supplemented with 5% defibrinated sheep blood) and Gassner agar plates (SIFIN, Berlin, Germany). The plates were incubated at 37.0°C aerobically and examined at 24 and 48 h.

To isolate anaerobic bacteria, we plated specimens onto both Columbia agar (Columbia agar base supplemented with 5% defibrinated sheep blood, 0.5% laked sheep blood, 0.005% hemin, 0.0001% vitamin K1, and 0.03% L-cysteine hydrochloride monohydrate; bioMérieux, Marcy l'Etoile, France) and Columbia agar supple-

mented with 0.004% gentamicin. After inoculation, plates were incubated at 37.0°C in anaerobic jars using the AnaeroGen atmosphere generation system (Oxoid, Basingstoke, UK). Examinations followed at 48 and 96 h. Aerobic and anaerobic bacteria were further identified by techniques described previously (Murray et al., 1995; Summanen et al., 1993). Antibiotic susceptibility of aerobic bacteria to ceftiofur (30 µg), ampicillin (10 µg), oxacillin (5 µg), and tetracycline (30 µg) was determined by the agar diffusion method on Mueller Hinton agar (SIFIN, Berlin, Germany). DIN values (Deutsches Institut für Normung, 1998) or manufacturer recommendations were used to evaluate inhibition zone diameters.

Data were analysed using SPSS for Windows (version 9.0, SPSS Inc. Munich, Germany) and Excel (version 2000, Microsoft, Redmond, WA). Cure rate, proportion of cows inseminated, first AI conception rate, and proportions of cows pregnant and culled were analyzed by chi-square analysis (Sachs, 1993). Days to first AI and days open were compared by using Kruskal-Wallis H-Test. Temperature at treatment days was compared using the repeated measurement procedure of SPSS. The level of significance was set at $\alpha = 0.05$. The risk of removal from the herd was analyzed using logistic regression including treatment group, diagnosis at third examination (32 to 34 dpp), temperature at d 1, and treatment outcome as covariates.

To evaluate the financial outcome of the three treatment protocols, we considered two aspects, i.e., the costs for treatments and the costs per pregnancy. This evaluation was performed for this particular trial and the dairy farm involved. Analysis was calculated with the raw data of this trial, regardless of statistically significant differences.

Costs for treatments are presented as direct costs, i.e., drugs and applications, and indirect costs, i.e., costs for milk withdrawal. Costs for each treatment episode (three consecutive treatments, including fee for applica-

tion of drugs) and costs for milk withdrawal are shown in Table 4. In case of a treatment failure, costs for additional treatment with oxytetracycline were included. Average milk yield was 23 kg per cow per day. In Germany, the withdrawal period for milk is 1 d for ceftiofur, 3 d for intrauterine antibiotics, 4 d for oxytetracycline, and 6 d for ampicillin given i.m. Average day of first treatment was d 4 after calving. Milk delivery is allowed from d 6 after calving (German milk ordinance, 1995). Thus, the effective withdrawal period for each treatment episode in group 1 was 1 d, in group 2 6 d, and group 3 3 d, respectively. Effective withdrawal period for oxytetracycline was 6 d.

Costs per pregnancy were calculated for 87 different scenarios. Cost factors included in this evaluation were drugs and applications, milk price, days open, AI, and replacements. For each cost factor, a standard, minimum, and maximum price was set. These prices were derived from different large animal veterinarians and the German schedule of fees for veterinarians (Gebührenordnung für Tierärzte, 1999). Total costs for each group were added and divided by the number of cows pregnant or replaced. Different scenarios resulted from varying one cost factor in several increments between the minimum and maximum price, while other cost factors were held constant at their standard price level. Cost factors, price levels and increments are shown in Table 5.

RESULTS AND DISCUSSION

Cows Included in the Study

During the study period a total of 1756 cows calved and 325 cases of toxic puerperal metritis were recorded (18.5%). The incidence rate is in accordance with Etherington et al. (1984) and Bartlett et al. (1986), but less than the rate of 37% reported by Markusfeld (1987). After a retrospective review of the inclusion criteria 227 cases were eligible for the final evaluation (group

Table 1. Cure rate at d 6 after first treatment and reproductive performance measures for cows treated with ceftiofur (group 1), antibiotic pills and ampicillin (group 2), antibiotic pills and ceftiofur (group 3), including cows considered as failures.

| Measure | Group 1 n = 70 | Group 2 n = 79 | Group 3 n = 78 |
|-------------------------------|---------------------|-------------------|-------------------|
| Cure rate % | 82.9 | 84.8 | 84.6 |
| Cows inseminated % | 77.1 | 87.3 | 76.9 |
| Days to first AI ¹ | 87.1 ± 3.5 | 87.1 ± 2.4 | 82.3 ± 2.9 |
| First AI conception % | 40.7 | 50.7 | 41.7 |
| Cows pregnant % | 52.9 ^{a,b} | 68.4 ^a | 46.2 ^b |
| Days open ¹ | 99.3 ± 4.8 | 103.5 ± 4.3 | 101.3 ± 6.0 |
| Conception rate % | 35.2 | 48.2 | 30.3 |
| Cows culled % | 47.1 ^{a,b} | 31.6 ^b | 53.8 ^a |

^{a,b}Numbers within the same row with different superscripts differ ($P < 0.05$).

¹Means ± SE.

Table 2. Reasons for culling for cows treated with ceftiofur (group 1), antibiotic pills and ampicillin (group 2), and antibiotic pills and ceftiofur (group 3).

| Culled for | Group 1 | Group 2 | Group 3 |
|---------------|-------------------------|-----------------------|---------------------------|
| Infertility | 15 (21.4%) ^a | 5 (6.3%) ^b | 10 (12.8%) ^{a,b} |
| Udder | 7 (10.0%) | 8 (10.1%) | 16 (20.5%) |
| Milk yield | 3 (4.3%) | 4 (5.1%) | 6 (7.7%) |
| Other reasons | 8 (11.4%) | 8 (10.1%) | 10 (12.8%) |
| Total | 33 (47.1%) | 25 (31.6%) | 42 (53.3%) |

^{a,b}Numbers within the same row with different superscripts differ ($P < 0.05$).

1, $n = 70$; group 2, $n = 79$; and group 3, $n = 78$). No escape therapy was applied to any of these cows during 6 d after first treatment. Ninety-eight cases had to be removed from analysis because of other acute diseases or treatments not according to the study protocol. Retained placental membranes, a predisposing factor for TPM, had been diagnosed in 63 of 227 cows (27.8%) included in the trial (group 1: 27.1%, group 2: 25.3%, group 3: 30.8%).

Clinical Findings and Reproductive Performance

The cure rates at d 6 after first treatment and reproductive performance measures for the three groups are shown in Table 1. Cure rates were 82.9, 84.8, and 84.6% for groups 1, 2, and 3, respectively. Differences among the groups were not significant. An equally successful treatment response for different systemic and local antibiotic treatments was recently reported by Smith et al. (1998), who administered (i.m.) a dosage of 2.2 mg/kg of ceftiofur sodium. The label instructions for the dosage of ceftiofur in Germany is 1.1 mg/kg, i.e., the dosage in our study was lower. Control groups in the publication by Smith et al. (1998) were treated with procain penicillin G i.m. and procain penicillin G i.m. in addition to oxytetracycline as an intrauterine infusion,

respectively. Smith et al. (1998) included in each group 17 cows with a body temperature $>39.2^{\circ}\text{C}$, while in our trial the inclusion criterion was a temperature $>39.5^{\circ}\text{C}$. That could have resulted in more cows with a severe TPM included in our trial. However, the decrease in temperature was comparable for the treatment groups within both studies, indicating a successful treatment. Decreases of mean body temperatures from d 1 to 6 after first treatment in the current study are presented in Figure 1. Body temperature was significantly higher at d 1 (LSM $39.95^{\circ}\text{C} \pm 0.03$) than at d 6 (LSM $39.05^{\circ}\text{C} \pm 0.03$). No significant differences were found among the three groups. Because of concerns about animal welfare, no cows with TPM were left untreated to be able to ascertain a spontaneous cure rate.

Uterine discharge was documented at d 6 after first treatment. In group 1 a total of 65.7% showed fetid, reddish-brown discharge. In groups 2 and 3, the proportions were 48.7 and 47.4%, respectively. The difference between group 1 and group 3 was significant ($P < 0.05$), but not the difference between group 1 and group 2. Within the class of cows considered as cured on d 6, the proportion of cows with fetid discharge was 49.7% (group 1: 63.2%, group 2: 44.8%, group 3: 43.1%; group 1 vs. group 3 $P < 0.05$). The quality of the uterine discharge was not regarded as a criterion for treatment

Table 3. Frequency and susceptibility of the isolated bacteria.

| Species | Frequency | Susceptibility (n) to | | | |
|----------------------------------------|-----------|-----------------------|------------|-------------|--------------|
| | | Ceftiofur | Ampicillin | Cloxacillin | Tetracycline |
| Aerobic | | | | | |
| <i>Arcanobacterium pyogenes</i> | 5 (33%) | 5 | 5 | 4 | 4 |
| <i>Escherichia coli</i> | 8 (53%) | 8 | 2 | 1 | 4 |
| <i>Streptococcus</i> spp. ¹ | 8 (53%) | 2 | 3 | 2 | 1 |
| <i>Citrobacter</i> spp. | 3 (20%) | 2 | 0 | 0 | 3 |
| <i>Proteus</i> spp. | 2 (13%) | n.t. ² | n.t. | n.t. | n.t. |
| Anaerobic | | | | | |
| <i>Fusobacterium</i> spp. | 10 (67%) | n.t. | n.t. | n.t. | n.t. |
| <i>Bacteroides</i> spp. | 5 (33%) | n.t. | n.t. | n.t. | n.t. |
| <i>Clostridium perfringens</i> | 3 (20%) | n.t. | n.t. | n.t. | n.t. |
| <i>Porphyromonas levii</i> | 10 (67%) | n.t. | n.t. | n.t. | n.t. |

¹Three isolates were not tested for susceptibility.

²n.t. = Not tested.

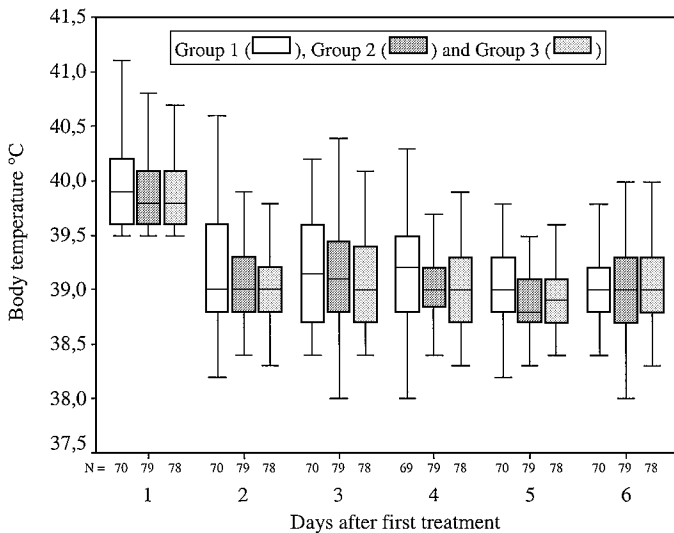


Figure 1. Boxplots indicating body temperature at d 1 to d 6 after first treatment in group 1 (ceftiofur), group 2 (antibiotic pills and ampicillin) and group 3 (antibiotic pills and ceftiofur). Outliers and extremes not shown.

response in this study. The consequence of considering cows with fetid discharge as a treatment failure would have been to treat these cows with oxytetracycline i.m. But, for prudent use of antibiotic drugs in farm animals (Ungemach, 1999), a systemic antibiotic treatment of cows without signs of systemic disorders has to be rejected (Montes and Pugh, 1993). It is questionable whether the quality of the vaginal discharge within the early postpartum period, i.e., at d 6 in this trial, is a solid parameter for uterine disorders. On the other hand several authors (Brooks, 2000; Dohmen et al., 1995; Murray et al., 1990) described the uterine discharge score as a useful method to evaluate uterine disorders, especially chronic endometritis.

The relationship between TPM and chronic endometritis is well known (Leslie, 1983), but data of follow-up investigations are rarely reported. The proportion of cows showing signs of chronic endometritis, i.e., enlarged uterus and purulent discharge at the third examination was 44.8% in group 1 and 50.0% in both groups 2 and 3. Even though the number of cows with pathological discharge at d 6 after first treatment was significantly higher in group 1, the proportion of cows with signs of chronic endometritis was similar for all groups.

There were no significant differences in reproductive performance measures among the three groups (Table 1). Days to first AI in the three groups (87.1, 87.1, and 82.3 d in groups 1, 2, and 3, respectively) were similar to cows without TPM, calving during the study period (82.8 ± 0.7 ; $n = 1050$). First AI conception rate was

highest in group 2 (50.7%), but the difference compared to group 1 (40.7%) and group 3 (41.7%) was not significant. In comparison to cows without TPM first AI conception rate (36.6%) was significantly lower compared with group 2 ($P < 0.05$). Surprisingly, days open were not longer in cows with TPM (99.3, 103.5, and 101.3 d in groups 1, 2, and 3, respectively) than in cows without TPM (99.7 ± 1.4 ; $n = 681$). Sandals et al. (1979), Oltenacu et al. (1983), and Lee et al. (1989) found prolonged days to first AI, lower conception rates, and prolonged days open for cows with postpartum metritis. One possible explanation for the results of our trial, beside the effect of the antibiotic treatments, is the positive effect of prostaglandin $F_{2\alpha}$ given twice in the postpartum period (Benmrad and Stevenson, 1986; Etherington et al., 1994).

The proportion of cows pregnant was highest in group 2 (68.4%), but the difference to group 1 (52.9%) was not significant. However, the difference between group 2 and group 3 (46.2%) was significant ($P < 0.05$). Figure 2 demonstrates the proportion of cows pregnant within 200 dpp. No major differences can be observed until d 100 after calving. After 100 dpp, group 3, and after 120 dpp, group 1 had slower increases in proportions of pregnant cows than group 2. This suggests that in group 2 the number of cows with reproductive disorders was less than in group 1 and group 3. The difference in proportion of cows removed for reproductive reasons was significant between groups 1 and 2 (Table 2). However, reporting and analyzing reasons for culling is a complex issue (Erb et al., 1985; Monti et al., 1999). Regarding the risk of removal from the herd, the logistic regression model did not reveal significant differences

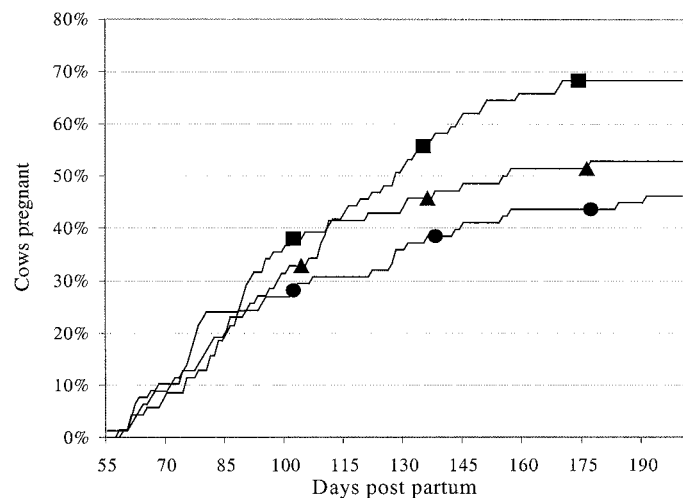


Figure 2. Proportion of cows pregnant within 200 d postpartum for group 1 (▲ ceftiofur), group 2 (■ antibiotic pills and ampicillin), and group 3 (● antibiotic pills and ceftiofur).

Table 4. Direct costs in Euro (€) units (drugs and applications) and indirect costs (milk withdrawal) for cows treated with ceftiofur (group 1), antibiotic pills and ampicillin (group 2), antibiotic pills and ceftiofur (group 3), and oxytetracycline (failures).

| Group | Costs factors in € | | | Costs per cow ¹ in € | | |
|-----------------------|--------------------|-----------------------------|-----------------------------|---------------------------------|----------------|-------|
| | Direct costs | | Indirect costs ⁴ | Direct costs | Indirect costs | Total |
| | Drugs ² | Applications ^{2,3} | | | | |
| 1 | 22.50 | 9.20 | 6.90 | 36.36 | 14.00 | 50.36 |
| 2 | 23.50 | 24.50 | 41.40 | 52.13 | 47.69 | 99.82 |
| 3 | 36.00 | 24.50 | 20.70 | 64.69 | 27.07 | 91.76 |
| Failures ⁵ | 18.00 | 9.20 | 41.40 | | | |

¹Including costs for failures.

²Three treatments.

³According to the German schedule of fees for veterinarians.

⁴Estimated costs for milk withdrawal.

⁵Costs for additional treatment with oxytetracycline in case of treatment failure.

between group 1 and either groups 2 or 3. Overall culling or not being pregnant within 200 dpp, respectively, for cows with TMP was 44.1% compared with 53.0% for cows without diagnosed TMP. However, it should be noted that a comparison of cows culled with and without TMP is not completely valid because it was not determined how many cows in the group without TMP were already considered as “do not breed” cows after calving. Some studies have shown a positive correlation between metritis and culling (Bartlett et al., 1986; Pugh et al., 1994), but others have not (Dohoo et al., 1984). One explanation for the controversial findings is that the risk of culling is different for toxic puerperal metritis and chronic endometritis. Also the severity of metritis influences cure rate, reproductive performance and thus the risk of culling (Miller et al., 1980; Pepper and Dobson, 1987; Tenhagen and Heuwieser, 1999). However, the logistic regression in this study revealed that in cows with TPM temperature at d 1 and treatment response had no significant influence on the risk of removal from the herd.

Bacteria Isolated

The majority of aerobic isolates were *Escherichia coli* and *Arcanobacterium pyogenes*. Anaerobic species were most commonly *Fusobacterium* spp., *Porphyromonas levii* and *Bacteroides* spp. *Arcanobacterium pyogenes* was not found as often as described by other researchers (Miller et al., 1980; Olson et al., 1984), but this might result from the small number of samples. Also, it is difficult to determine distinct pathogenic and nonpathogenic bacteria involved in metritis and endometritis (Ball et al., 1984). Frequency of the isolated species and susceptibility of aerobic bacteria to the antibiotics used are summarized in Table 3. The majority of isolated aerobic bacteria were susceptible to ceftiofur in vitro. Susceptibility of *E. coli* to ampicillin, cloxacillin and oxytetracycline was not as pronounced as to ceftiofur. However, the small number of samples does not allow a confident general conclusion on susceptibility patterns. Susceptibility of anaerobic bacteria was not tested in this study. Samitz et al. (1996) recommended ceftiofur

Table 5. Cost factors in Euro (€) units, price levels (standard, minimum, and maximum), and number of increments between minimum and maximum used for an economic evaluation.

| Factor | Standard (€) | Minimum (€) | Maximum (€) | Increments (€) |
|----------------------------------------|--------------|-------------|-------------|----------------|
| Ceftiofur ¹ | 22.50 | 14.50 | 32.50 | 2.00 |
| Ampicillin ¹ | 10.00 | 6.00 | 15.00 | 1.00 |
| Uterine pills ¹ | 13.50 | 8.50 | 17.50 | 1.00 |
| Oxytetracycline ¹ | 18.00 | 10.00 | 24.00 | 2.00 |
| Injection intramuscularly ¹ | 9.00 | 3.00 | 9.00 | 0.75 |
| Application intrauterine ¹ | 15.00 | 5.00 | 15.00 | 1.50 |
| Milk price/liter | 0.30 | 0.25 | 0.35 | 0.01 |
| Day open > 85 | 2.50 | 0.50 | 5.00 | 0.50 |
| Artificial insemination ² | 15.00 | 5.00 | 27.50 | 2.50 |
| Replacements | 400.00 | 250.00 | 750.00 | 50.00 |

¹Per treatment episode.

²Including semen and fees.

Table 6. Costs in Euro units (€)¹ per pregnancy per cow for cows treated with ceftiofur (group 1), antibiotic pills and ampicillin (group 2), antibiotic pills and ceftiofur (group 3). Mean, median, minimum and maximum costs in 87 scenarios.

| Costs per pregnancy | Group 1 | Group 2 | Group 3 |
|---------------------|---------------|---------------|---------------|
| Mean ± SE) | 292.22 ± 3.39 | 291.19 ± 2.44 | 362.09 ± 3.87 |
| Median | 286.02 | 287.26 | 355.45 |
| Minimum | 215.30 | 239.80 | 274.68 |
| Maximum | 451.02 | 398.02 | 543.92 |

¹Euro monetary unit = ~\$0.85.

as the drug of choice for infections caused by *F. necrophorum*, but reported of poor activity against *Bacteroides* spp.

Financial Aspects

To evaluate the financial efficiency, the costs for treatments and the costs per pregnancy for the three treatment protocols were compared.

Costs for treatment per cow were lower in group 1 than in groups 2 and 3, respectively. The advantage of group 1 over group 2 is mainly a result of a reduced milk withdrawal period (Table 4).

Costs per pregnancy were calculated for 87 different scenarios. Mean, median, minimum and maximum costs, respectively, are shown in Table 6. In all scenarios analyzed costs in group 3 were higher than in group 1 [up to €92.90] (€ Euro monetary unit = ~\$0.85.) and in group 2 (up to € 145.90). The differences between group 1 and group 2 varied between € 24.49 in favor of group 1 and € 52.99 in favor of group 2. Although the difference in proportion of cows culled was not significant between group 1 and group 2, culling had the greatest influence on relative costs of the groups in this trial. Britt (1985) and Dijkhuizen et al. (1985) reported prolonged days open and involuntary culling as the predominant reproductive cost factors in dairy herd management. These findings were confirmed by Tenhagen et al. (1998) and are supported by our analysis. Because cows in this study were affected by toxic puerperal metritis, it is not surprising that costs for treatments were also important to the total costs per pregnancy. Mean costs for treatments (drugs and applications) ranged from 12.4% (group 1) to 17.6% (groups 2 and 3) but costs for culling were the predominant factor (mean: 66.3, 44.7, and 61.1% for groups 1, 2, and 3, respectively) in determining total costs per pregnancy. However, this financial evaluation is a herd specific and trial specific approach to economic aspects of reproductive management.

CONCLUSIONS

The systemic treatment of toxic puerperal metritis in cattle with ceftiofur is an effective alternative to protocols based on combined intrauterine and systemic antibiotic treatment. Cure rates as well as reproductive performance measures in group 1 were similar to two control groups. Further research is required to compare the clinical findings of our study with pharmacological data, i.e., intrauterine concentration of ceftiofur and susceptibility of bacteria to ceftiofur in vivo. Costs for treatments were reduced in group 1. Costs per pregnancy were mainly influenced by the proportion of cows culled.

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