

# Effect of the Combined Usage of Ceftiofur with Buserelin and Beta-cloprostenol During Puerperium in Dairy Heifers

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## Abstract

The aim of this study was to test the effect of combined usage of ceftiofur with beta-cloprostenol and busereline for puerperal endometritis treatment in dairy heifers. The results received suggest that combined usage of ceftiofur with cloprostenol and buserelin successfully treats puerperal endometritis and significantly improves reproductive performance.

**Key words:** ceftiofur, buserelin, cloprostenol, puerperal endometritis, reproductive performance

## Introduction

The effect of reproductive performance is defined by the maximum coincidence of the limits for the desired and the economically effective calving interval. Since after calving the only period that can be manipulated is the service period, current guidelines in reproductive science are directed towards trials for its shortening to an acceptable level.

At present, the desired service period is widely approved to be around 85 days – depending on local conditions.

Widely accepted is also the statement that puerperium – being a period succeeding the calving and included in the service period – must also be shortened to a maximum. In practice this is the only period that can be medically manipulated – to improve the duration of the service period.

The usage of a combination of antibiotics and hormones – in puerperium – has its specific advantages, because of uterine involution stimulation which is established by lowering or total cleaning of infection in utero. (1,2,3,4,5). Prostaglandin F<sub>2</sub> positively affects uterine involution and induces estrus in cows with active luteal tissue. (6,7,8).

The examination of different combinations of GnRH-analogues and cloprostenol with ceftiofur – has received heightened attention over the last years. (5,9,10) Scientists receive clearly good results by applying treatment with a combination of ceftiofur with one or both hormones. They advise that this scheme be tested on a larger number of animals in different conditions.

Intrauterine ceftiofur treatment has been tested by Jermejeva et al. (9) in highly yielding dairy cows in Estonia. They note the seriousness of puerperium problems in their country and conclude that future tests are needed in the field of combined usage of antibiotics and hormones during puerperium. Jermejeva et al. (10) state also that in the cases with acute puerperal endometritis parenteral antibiotics are a must, independently of other supportive or hormonal therapy.

Janowski et al. (5), on the other hand compare the activity of ampicillin and ceftiofur – in combination with cloprostenol and buserelin. Their results and conclusions confirm the good effect on uterine sanitation on day 12 after calving.

The facts above gave us grounds to widen the examination of combined usage of ceftiofur with hormones in industrial farming groups of animals.

The aim of this study was to define the effect of combined usage of ceftiofur (1.1 mg/kg) with buserelin (50 µg/kg) and -cloprostenol (500 µg/kg) during puerperium, on its shortening, hence shortening of the service period.

## Material and Methods

The study was carried out on a total of 578 calving dairy Holstein heifers in Scotland. The animals were kept and treated in full compliance with EU animal welfare legislation. The animals were managed in cubicles with free choice of TMR food, and additional concentrate top-up in automatic feeders. After finishing of the fetus expulsion animals were subdivided into 6 groups:

Group 1A – 78 animals with normal fetal membrane release, treated with 1,1 mg/kg ceftiofur (Naxcell® - Pfizer, UK) on third day post partum.

Group 1B – 74 animals with normal fetal membrane release, treated with 50 µg Buserelin (Receptal® Intervet, Holland) on day 11, and 500 µg/head Cloprostenol (Estrumate® - Shering Plough Animal Health) on day 21.

Group 1C – 91 animals with normal fetal membrane release, treated with 1,1 mg/kg ceftiofur (Naxcell® - Pfizer, UK) on the third day, 50 µg Buserelin (Receptal® Intervet, Holland) on day 11, and 500 µg/head Cloprostenol (Estrumate® - Shering Plough Animal Health) on day 21 post partum.

\*Group 2A – 81 animals with retained fetal membranes (RFM) treated with 1,1 mg/kg ceftiofur (Naxcell® - Pfizer, UK) on the third day post partum.

\*Group 2B – 77 animals with RFM treated with 50 µg Buserelin (Receptal® Intervet, Holland) on day 11, and 500 µg/head Cloprostenol (Estrumate® - Shering Plough Animal Health) on day 21.

\*Group 2C – 79 animals with RFM, treated with 1,1 mg/kg ceftiofur (Naxcell® - Pfizer, UK) on the third day, 50 µg Buserelin (Receptal® Intervet, Holland)- on day 11, and 500 µg/head Cloprostenol (Estrumate® - Shering Plough Animal Health) on day 21 post partum.

Group 3 – 61 control animals with normal released fetal membranes.

Group 4 – 37 control animals with retained fetal membranes.

\*In groups 2A, 2B, and 2C the retained fetal membranes were not detached manually.

The following parameters were monitored: tracking completion of uterine involution by day 42, by the method of rectal palpation and ultrasound examination described by ocamuftuoglu and Vural (11); uterine discharge scoring with the method METRICHECK® - SIMCROTECH Inc., New Zealand described by McDougall (12); first service conception rate; total conception rate; duration of service period.

Results were evaluated statistically with MS Office Excel 2013. They are presented as percentage or Mean.

## Aim

The aim of this study was to test the effect of combined usage of ceftiofur with beta-cloprostenol and busereline for puerperal endometritis treatment in dairy heifers.

## Results

**Results are presented in tables 1 and 2.**

Table 1 presents the average score for uterine discharge - first to seventh week post partum. The result is given as mean of the average.

**Table 1. Uterine discharge score in first to seventh week interval**

RFM condition	Subgroup	Weeks p.p.						
		1	2	3	4	5	6	7
		<b>Uterine discharge score (Mean)</b>						
<b>RFM negative</b>	1A Ceftiofur 1.1 mg/kg	3,92	2,24	2,08	1	0	0	0
	1B Buserelin (50µg/kg) + Cloprostenol (500 µg/kg)	4,11	3,64	1,88	1,08	0,96	0,44	0
	1C Ceftiofur 1.1 mg/kg + Buserelin (50µg/kg) + Cloprostenol (500 µg/kg)	3,12	2,02	0,77	0,44	0	0	0
<b>RFM positive</b>	2A Ceftiofur 1.1 mg/kg	3,64	3,13	2,66	1	1	1	1
	2B Buserelin (50µg/kg) + Cloprostenol (500 µg/kg)	4,02	3,86	3,21	1,86	1,04	0,86	0,61
	2C Ceftiofur 1.1 mg/kg + Buserelin (50µg/kg) + Cloprostenol (500 µg/kg)	3,38	2,62	1,11	0,94	0,46	0	0
<b>RFM negative</b>	3 Control	3,88	3,03	1,63	1,04	0	0	0
<b>RFM positive</b>	4 Control	3,96	3,81	3,23	2,79	1,9	1,1	1,4

Table 2 presents the characteristics of reproductive performance in dairy heifers treated with ceftiofur, buserelin and cloprostenol. Results are given as percentage – for uterine involution completion and pregnancy rate, and as days for the service period. Pregnancy AI index is given as number.

**Table 2. Reproductive performance in dairy heifers treated with ceftiofur, buserelin and cloprostenol**

RFM condition	Group	Completion of uterine involution at day 42 p.p. (%)	First service pregnancy rate (%)	Total pregnancy rate (%)	P/AI index	Service period (days)
RFM negative	1A Ceftiofur 1.1 mg/kg	89.1***	37.7	72.3	2.1	97.3
	1B Buserelin (50µg/kg) + Cloprostenol (500 µg/kg)	84.4***	41.4	74.4	1.9	101.4
	1C Ceftiofur 1.1 mg/kg + Buserelin (50µg/kg) + Cloprostenol (500 µg/kg)	97.8***	57.7	93.3**	1.6	86.6**
RFM positive	2A Ceftiofur 1.1 mg/kg	82.8	44.6	67.3	2.3	112.9
	2B Buserelin (50µg/kg) + Cloprostenol (500 µg/kg)	77.3	46.2	63.9	2.3	128.2
	2C Ceftiofur 1.1 mg/kg + Buserelin (50µg/kg) + Cloprostenol (500 µg/kg)	84.8***	48.4	74.6	1.9	104.4
RFM negative	3 Control	81.1	42.8	71.7	1.8	98.4
RFM positive	4 Control	70.2	32.8	57.2	2.6	144.9

\*\* p 0.01; \*\*\*p 0.001

## Discussion

*Uterine involution/puerperium duration*

In groups 1A, B and C the involution of the reproductive tract was accomplished earlier than in Group 3 controls ( $P < 0,01$ ). In all the three subgroups the uterus was palpated and visualized in the pelvic cavity on day  $32,8 \pm 4,4$  ( $P < 0,001$ ). In the animals of control Group 3 this event happened on day  $41,4 \pm 7,1$ . Involution completed by day 42 was noted in subgroups 1C and 2C ( $P < 0,001$ ) – Table 2. We accept that these results come from uterine environment improvement caused by antibiotic and follicular wave stimulation by hormones. Uterine involution and cyclicity are the milestones of reproductive tract improvement during puerperium, hence the service period. Similar data for hormone usage have been discussed in Bulgaria for decades (13, 14, 15). They also support the use of hormonal therapy during puerperium.

Similar results were reported (11), but with the note that they used matured cows in their trial. We accept that the latter fact can explain the difference between our and their results. P cal et al. (8) reported results close to ours, without noting puerperium duration, but they report completed involution and normal cyclicity on day  $34,09 \pm 0,312$  – in animals treated with cloprostenol. In their trial cloprostenol treatment was carried out in the first week post partum and the number of animals in the study is not enough – only 14.

#### *Uterine discharge score*

The obtained results reveal that in all six experimental subgroups the uterine discharge score (UDS) was improved (less pus and odor) in comparison with the two control groups.

In our trial the earliest improvement and yielding of discharge with UDS = 1 was on day  $11 \pm 3,8$  in group 1C in the third week. The latest improvement we received on day  $29 \pm 2,2$  in subgroup 2A on the fifth week. The overall average of UDS improvement was on day  $17 \pm 4,4$  (third week) for experimental animals of group 1, and  $24 \pm 4,1$  (fourth week) for group 2. The result of control groups 3 and four was  $22 \pm 7,2$  days (fourth week) and  $31,1 \pm 6,7$  days (fifth week) respectively.

The results we explain with sanitation of the uterine cavity by ceftiofur exactly on the day of buserelin injection, i.e. day 11. The clean uterine environment establishes normal endocrine and solinocrine hormonal secretion by the endometrium, hence better rebound of cyclicity. In confirmation, the activity of ceftiofur was checked by UDS in a large number of animals with puerperal metritis (16). They reported effect of 85 % clean uterine culture exactly on day 12 post partum, a fact which we also confirm in our trial. For UDS, we can make comparisons only with the results reported in New Zealand by McDougall (11), because his method although considered precise is not widely accepted yet. Our final results for the pregnancy rate – 93.3 % is very close to that of McDougall (11) – 92.7% which confirms the precision of the 'metrheck' test.

Our result is also in the line of shortening the puerperium in comparison with results reported in Poland, Estonia, Turkey and Romania (5,10,11,8). At the same time this result is not statistically confident ( $P < 0,05$ ), a fact that we explain with the usage of heifers in our trial and of matured cows in research reported elsewhere.

#### *First service pregnancy rate and overall pregnancy rate*

The percentage of first service pregnancy rate in our experimental groups does not differ significantly from that in the literature cited. Since we use similar treatment protocols we find this coincidence normal.

The significant difference is in the overall pregnancy rate. In our trial it varies between groups from 63.9 to 93.3% (Table 2). We note this fact because this parameter is the final result of the service period. Significant is the difference inside groups. In both experimental main groups it is in favour of combined ceftiofur, cloprostenol and buserelin treatment ( $P < 0,01$ ).

#### *Service period duration*

For this parameter we received statistically significant shortening in comparison with controls. Similar results in matured cows were reported in Poland (5).

In our trial we have  $95,1 \pm 16,1$  days overall average duration, and 86.6 days in subgroup 1C. This result is significantly better ( $p < 0,01$ ) than that reported by Janowski (5) – 89,9 days – in the study with the same treatment. We accept that the difference comes from the different dose of buserelin we used - 50  $\mu\text{g}$ , compared to 20  $\mu\text{g}$  in the study in Poland (5). We suspect that in our case at the moment of cloprostenol injection on day 21 there was a responsive active luteal tissue and a dominant follicle as a consequence of the buserelin injection administered on day 11, in both groups with or without RFM.

## Conclusions

The combined usage of ceftiofur with buserelin and cloprostenol generates significant shortening of the puerperium and service periods.

The combination generates significant shortening of the period for uterine discharge score improvement, up to the third week.

The combination generates higher percentage of first service pregnancy rate, and overall pregnancy rate, 57.7 and 93.3 % respectively.

## References

1. Bosted H, Peche E, Strobl K. Zur Auswirkung fröhzeitig post partum verabreichter GnRh-Gaben auf Puerperalverlauf und Konzeptionsergebnis bei Kühen nach Retentiosecundinarum. *Berl Munch Tierarztl Wschr* 1980; 93:184-188.
2. Bostedt H. Zur Fertilitätslage nach Puerperalerkrankungen des Rindes. *Berl Munch Tierarztl Wschr* 1979; 89: 24-28.
3. Leslie KE, Dooig PA, Bosu WTK, et al. Effects of gonadrophin releasing hormone on reproductive performance of dairy cows with retained placenta. *Can J Comp Med* 1984; 48: 354-359.
4. Zdunaczyk S, Zebracki A.: Versuch einer metaphylaktischen Anwendung des GnRH-Analogons Buserelin in einer Problemherde mit Berücksichtigung der hormonanalytischen und histologischen Untersuchungen. *Wien Tierarztl Mschr* 1986; 73: 314-319.
5. Janowski T, Zdunaczyk S, Mwaanga ES. Combined GnRH and PGF2a application in cows with endometritis puerperalis treated with antibiotics. *Reprod Dom Anim* 2001; 36, 244-246.
6. Lindell JO, Kindahl H. Exogenous prostaglandin F2a promotes uterine involution in the cow. *Acta Vet Scand* 1983; 24: 269-274.
7. Young JM, Anderson DB. First service conception rate in dairy cows treated with dinoprost trimethamine early post partum. *Vet Rec* 1986; 18: 112-213.
8. Pical N, Şipeşan C, Bencsik I, et al. The influence of synthetic analogues of PgF2 on the evolution of puerperal period and the duration of the interval from calving to the first estrus in cows. *Animal Science and Biotechnologies* 2014; 47:1: 57-59.
9. Jermejeva J, Orro T, Waldman A, et al. Treatment of dairy cows with PGF2a or NSAID, in combination with antibiotics, in cases of postpartum uterine inflammation. *Acta Veterinaria Scandinavica* 2012; 54: 45.
10. Jermejeva J, Orro T, Waldman A, et al. Effect of two different treatments on the clinical signs and inflammatory parameters in case of experimental induced acute puerperal metritis in dairy cows. *Veterinarija ir Zootechnika* 2010; 52:74: 49-58.

11. Kocamuftuoglu M, Vural R. The evaluation of postpartum period in dairy cows with normal and periparturient problems. *Acta Veterinaria* 2008; 58:1: 75-87.
12. McDougall S, Macaulay R, Compton C. Association between endometritis diagnosis using a novel intravaginal device and reproductive performance in dairy cattle. *Animal Reproduction Science* 2007; 99: 9–23.
13. Dimitrov M. Research and field trials for puerperium management in cows under different management conditions (In Bulgarian). PhD Thesis 1982.
14. Kanchev L. Biology and biotechnology of reproduction in domestic animals. (In Bulgarian) Publisher: Bulgarian Academy of Sciences 1989 book.
15. Kanchev L, Baychev Z. Reproductive endocrinology. Publisher: Videnov and Son 2008.
16. Lima FS, Vieira-neto A, Vasconcellos G, et al. Efficacy of ampicillin trihydrate or ceftiofur hydrochloride for treatment of metritis and subsequent fertility in dairy cows. *J. Dairy Sci* 2014; 97: 5401–5414.

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