

SHORT COMMUNICATION

Double cloprostenol administration during mid luteal phase of oestrus cycle does not modify the interoestrus interval in gilts

Claudio Mazzoni,¹ Roberta Saleri,²
Roy N. Kirkwood,³ Elisabetta Macchi,⁴
Techakumphu Mongkol,⁵ Fabio De Rensis¹

¹Dipartimento di Scienze degli Alimenti,
Università di Parma, Italy

²Dipartimento di Scienze Medico
Veterinarie, Università di Parma, Italy

³School of Animal and Veterinary
Sciences, University of Adelaide,
Australia

⁴Dipartimento di Morfofisiologia
Veterinaria, Università di Torino, Italy

⁵Department of Obstetrics, Gynaecology
and Reproduction, Chulalongkorn
University, Bangkok, Thailand

Abstract

The present study was undertaken to test the effect of two vulva injections of double (D)-cloprostenol on day 7, 9 and 10 of oestrous cycle on the duration of the interoestrus interval in gilts. Following a pre-treatment oestrous cycle, 87 gilts were assigned to receive vulva injections of 75 µg D-cloprostenol at 08:00 and 14:00 h on day 7 (D7; n=30), day 9 (D9; n=29) and day 10 (D10; n=28) of their second observed oestrous cycle. Across the treatments, the duration of the oestrous cycle period with D-cloprostenol treatment (19.1±0.1 d) was not different from that of the previous oestrous cycle (20.1±0.4 days). Plasma progesterone concentrations were evaluated 6 h before and 24 and 72 h after D-cloprostenol treatment in the D9 group. Compared to pre-treatment levels (9.6±0.4 ng/mL), plasma progesterone concentrations were reduced (P<0.05) at 24 h (6.3±1.0 ng/mL) and 72 h after treatment but complete luteolysis did not occur. These data indicate that in gilts double vulva administration of D-cloprostenol is not able to induce a complete luteolysis and hence the duration of the oestrous cycle is not modified.

Introduction

In pig production, the gilt replacement is about 40 to 60% into the breeding herd. The gilt replacement has a major impact on achievement of breeding targets. Typically, large groups of randomly cycling gilts are maintained in the gilt pool to ensure that sufficient females are in oestrus each breeding week. Having replacement females exhibit oestrus at predictable times would allow for a smaller gilt pool, as well as more efficient use of gestation and farrowing facilities. Methods of oestrus synchronisation include boar exposure and injection of gonadotrophins, but are effective only in pre-pubertal animals and the oestrus response can be unpredictable. In cycling gilts, an effective protocol to synchronise oestrus is oral administration of allyl trenbolone for 14 to 18 days. Oestrus responses and insemination can be made to take place about 5 to 9 d after last feeding of allyl trenbolone but this protocol requires daily treatments and is relatively expensive.

In many domestic species, prostaglandin F2α (PGF2α) administration is able to induce luteolysis during much of the luteal phase and is utilised for oestrus synchronisation and timed artificial insemination in cows (De Rensis and Peter, 1999), ewes (Menchaca *et al.*, 2004), and buffaloes (De Rensis and Lopez-Gatius, 2007). In contrast, in female pigs a single administration of PGF2α is not effective for inducing luteolysis until after day 12 of the oestrous cycle (Diehl and Day, 1974; Guthrie and Polge, 1976) and, therefore, cannot be utilised for oestrus synchronisation. The reason for the species difference in luteolytic activity of exogenous PGF2α is unclear.

As reported by Gadsby *et al.* (1990, 1993), receptors for PGF2α are present in the porcine corpora lutea (CL) by 5 d of the oestrous cycle and thus an absence of receptors is not the reason for the lack of luteolytic capacity before 12 d (De Rensis *et al.*, 2012). The pattern of PGF2α administration may have an effect since luteal regression is caused by PGF2α secreted from the endometrium in a series of discrete pulses (Kindhal *et al.*, 1981; Inskeep and Murdoch, 1980). In swine, PGF2α pulses generally occur at 6 to 8 h intervals (Gleeson *et al.*, 1974) suggesting that multiple injections of PGF2α could be more effective for inducing luteolysis than a single injection. Indeed, two PGF2α injections administered 6 h apart were more effective for farrowing induction than the traditional single injection (Kirkwood and Aherne, 1998) and in gilts, injection of 12.5 mg PGF2α every 12 h on days 5 to 10 of the oestrous cycle induced luteolysis and reduced the interoestrus interval by 6 d (Estill *et al.*, 1993, 1995). Interestingly, D-

Corresponding author: Dr. Fabio De Rensis,
Dipartimento di Scienze degli Alimenti,
Università di Parma, Parco Area delle Scienze
59/A, Parma, Italy.
Tel. +39.0521.902659 - Fax: +39.0521.902798.
E-mail: fabio.derensis@unipr.it

Key words: Gilts, Prostaglandin, Luteolysis,
Progesterone.

Acknowledgments: the authors thank Dr. Carlo
Gazza (FATRO, Ozzano dell'Emilia, Italy) for the D-
cloprostenol and Dr. A. Negri for technical support.

Received for publication: 18 February 2014.

Accepted for publication: 20 May 2014.

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Italian Journal of Animal Science 2014; 13:3318
doi:10.4081/ijas.2014.

cloprostenol, a PGF2α analogue with a 10-fold potency compared to the commercial racemic mixture of DL-cloprostenol (Re *et al.*, 1994), induces luteal PGF2α production but this auto-amplification occurred only in CL with luteolytic capacity. However, in miniature pigs, two vulvar injections of a high dose (3.0 mg) of cloprostenol with a 12 h interval on day 7 of their oestrous cycle induced luteolysis and a return to oestrus on day 12 (Kuge *et al.*, 2006), suggesting that administration of high doses may eliminate the need for auto-amplification. Further, this early luteolytic effect was not evident following intramuscular injection which supports the earlier observation that vulva injections are effective at 25% of the label luteolytic dose (Kirkwood *et al.*, 1996) with the corollary that any dose injected into the vulva will be equivalent to a higher dose injected intramuscular. Taken together, it is evident that the luteolytic effect of PGF2α in pigs is dependent on the day of the oestrous cycle administered, as well as dose and frequency of injection. The present study was undertaken to test the effect of two vulva injections of double (D)-cloprostenol on day 7, 9 or 10 of oestrous cycle on the duration of the interoestrus interval in gilts.

Materials and methods

The experiment was conducted on a commercial swine farm located in Parma province,

Italy, in compliance with the requirements of the University of Parma Animal Care Committee.

A total of 87 white crossbred gilts were housed in groups of approximately 5 per pen and were fed a commercial ration formulated to provide 15% crude protein. Water was available *ad libitum*. At the start of the study, gilts were 138.0 ± 8.6 kg body weight and 232.0 ± 3.8 days of age and had exhibited an oestrous cycle of normal length. The duration of the previous oestrous cycles served as the control comparison for the duration of the subsequent treatment oestrous cycle. Gilts received vulva injections of 75 μ g D-cloprostenol (Dalmazin®; FATRO, Ozzano dell'Emilia, Italy) at 08:00 h and again at 14:00 h on day 7 (D7; n=30), day 9 (D9; n=29) and day 10 (D10; n=28). After D-cloprostenol administration, gilts were subject to twice daily contact with a mature boar to facilitate detection of oestrus. Oestrus detection was performed daily until

oestrus occurred or until day 16 if gilts remained anoestrus.

Blood samples were collected via jugular venipuncture from ten D9 gilts 6 h before the first cloprostenol injection and at 24 h and 72 h after the second cloprostenol injection for determination of plasma progesterone concentrations using a commercial radioimmunoassay kit (DSL 3900; Diagnostic System Laboratories, Webster, TX, USA) previously validated for pigs (Macchi *et al.*, 2010). Assay sensitivity and intra-assay coefficient of variation were 0.09 ng/mL and 5%, respectively.

Statistical analysis

Differences within groups for the duration of the oestrous cycles were compared using Wilcoxon test. As data of plasma progesterone concentration were normally distributed (Kolmogorov-Smirnov test), statistical analysis was performed by the parametric t test for paired data.

Table 1. The effects of D-cloprostenol injection on days 7, 9 or 10 of the oestrous cycle on interestrous interval length in gilts (mean \pm standard deviation).

Administration day	Gilts, n	Duration of the treatment oestrous cycle, d	Duration of the preceding oestrous cycle, d	P
7	30	20.6 \pm 0.7	20.1 \pm 0.2	0.45
9	29	19.2 \pm 0.4	20.2 \pm 0.4	0.35
10	28	18.9 \pm 0.5	20.0 \pm 0.5	0.07

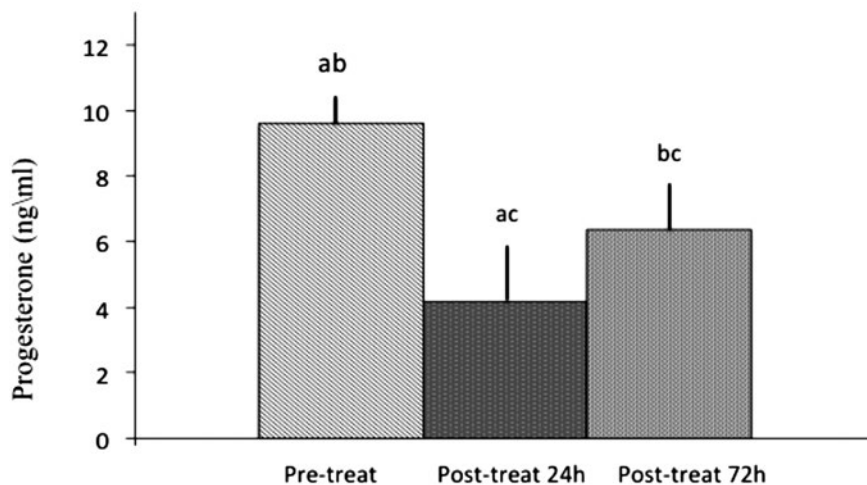


Figure 1. Mean (\pm standard error) plasma progesterone concentrations at 24 and 72 h after two vulva injections of D-cloprostenol 6 h apart on day 9 of their oestrous cycle. Pre-treatment values are also provided. Means with the same letter are significantly different from one another ($P < 0.05$).

Results and discussion

To our knowledge, this is the first study to evaluate the effect of two vulva injections of a high dose of the PGF 2α analogue D-cloprostenol on plasma progesterone levels before day 12 of their oestrous cycle in commercial gilts; a time when the CL are considered insensitive to single prostaglandin injection. The results show that there was no significant effect of the day of injection on oestrous responses (Table 1). Across the treatments, the duration of the oestrous cycle with D-cloprostenol treatment (19.1 ± 0.1 d) was not different from the preceding oestrous cycle (20.1 ± 0.4 d). These results were contradictory with data previously reported for miniature pigs, where the duration of oestrous cycles were reduced after D-cloprostenol administration at day 7 of the oestrous cycle (Kuge *et al.*, 2006).

Compared to pre-treatment concentrations (9.6 ± 0.4 ng/mL), plasma progesterone concentrations were reduced (4.17 ± 1.0 ng/mL; $P < 0.05$) at 24 and 72 h (6.3 ± 1.0 ng/mL) following D-cloprostenol injection (Figure 1) but, differently from the mini pig (Kuge *et al.*, 2006) a complete luteolysis was not observed. The reason for this difference between commercial gilts and mini pigs is unknown, although an association between the dose of cloprostenol and the metabolism of the animal may be involved. Although speculative, the absence of a complete luteolytic effect may be related to the number of CL, with a larger number of CL requiring a higher cloprostenol dose to ensure a complete luteolysis.

Conclusions

In conclusion, the data of this study indicate that in commercial gilts a double vulvar high dose D-cloprostenol administration at day 7, 9 and 10 of the oestrous cycle decreases plasma progesterone levels but complete luteolysis does not occur. Future development of a longer lasting potent analogue of PGF 2α may allow a more consistent luteolytic effect permitting the development of protocols for oestrus synchronisation.

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