Prostaglandins: a tool that continues to improve the **profitability** of farms

Prostaglandins are a very profitable tool to improve reproductive parameters, thanks both to their ability to synchronise farrowings and because of their postpartum uses.

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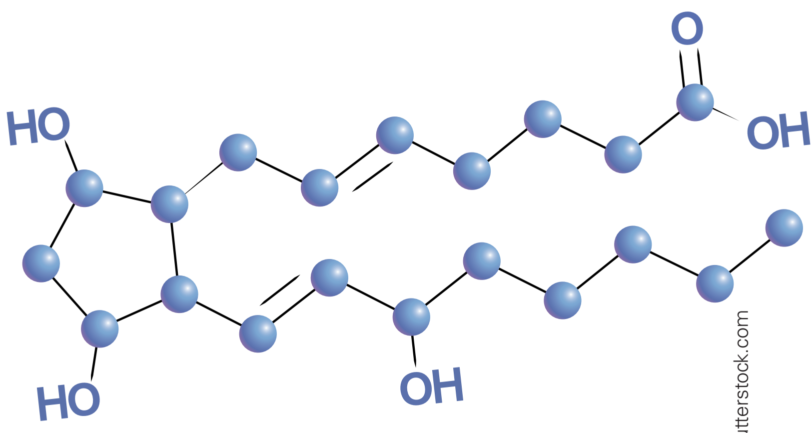

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Prostaglandins (PGs) have an important reproductive effect, especially in terms of their ovarian action, which is their most practical use; this translates into effects on the activity of the corpora lutea (CL). Among the PGs, $PGF_{2\alpha}$ has luteolytic action, and specific receptors for it can be found on the outer wall of luteal cell membranes.

During spontaneous luteolysis in sows (on day 15–16 of the oestrous cycle), $PGF_{2\alpha}$ causes a dramatic decrease in progesterone production and the structural regression of the CL.

During farrowing, PG produces a change in the foetal hypothalamus resulting in the release of foetal corticosteroids, oestrogen production, release of placental PGs, progestin synthesis inhibition, and myometrium stimulation, which initiates the contractions required for farrowing [1].

Farrowing inductions: results in hyperprolific sows

The prolificity of sows and the number of days they spend gestating per year have now increased. However, the range of farrowing days has also increased, which complicates the management of their care.

The effect of $PGF_{2\alpha}$

Two different mechanisms have been postulated to explain the effect of $PGF_{2\alpha}$:

- One is based on changes in blood flow to the corpora lutea as a result of ovarian vein vasoconstriction, which thus produces ovarian oedema with impaired luteal function.
- The second produces an immediate decrease in progestogens. $PGF_{2\alpha}$ is of extra-ovarian (uterine) origin and is delivered to the ovary by the uterine vein (arteriovenous *shunt*: uterine vein-ovarian artery).

Synthetic prostaglandins

The first synthetic $PGF_{2\alpha}$—dinoprost—was developed in 1979. After this, other $PGF_{2\alpha}$ agonists and generics appeared, some of which are chemically similar to those derived from the uterus, and others, such as cloprostenol, the same as its agonist.

Some commercial products, such as Planate®, contain a racemic mixture (DL-cloprostenol) obtained by chemical synthesis; the D-isomer has luteolytic activity and the L-isomer has uterotonic activity.

Compared to dinoprost, cloprostenol has a high affinity for $PGF_{2\alpha}$ receptors and a long half-life in circulation (three hours versus a few minutes). Furthermore, natural prostaglandin induces side effects, such as a slight increase in the frequency of defecation and in the respiratory rate, as well as tremors, agitation, erythema, and restlessness.

These synthetic analogues have been developed in order to obtain more stable, specific, and longer lasting compounds that do not produce side effects [2].

These factors have led farmers to rethink some of their operation practices, including the timing of farrowings, which brings some of the following advantages:

1. Facilitates handling and supervision

The practical purpose is to synchronise farrowings to facilitate their handling and supervision and aid them when necessary, thus resulting in an increase in piglet survival.

Problems during farrowing that lead to long intervals between piglet births (for example, more than 45 min) can mean that piglets go without oxygen (anoxia). This can lead to the death of these piglets or diminish their viability, which predisposes them to neonatal mortality.

2. Colostrum management and fostering

Piglets that were born weak, got cold, or are from very large litters may not consume enough colostrum and consequently, their passive immunity may be reduced.

Furthermore, these piglets can become more easily infected and may become disease carriers that can infect other transition piglets as their passive immunity decreases over time [3].

Studies in the field

Here we present the results from a recent study carried out in 2016 at a commercial farm in northeast Spain which works with Danbred genetics.

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Materials and Methods

This study followed a total of 875 farrowings in sows randomly divided into two groups: group A (444 farrowings) and group B (431 farrowings).

The farrowings were induced in group B sows by administering **2 ml** (175 µg) of intramuscular cloprostenol (Planate) on the farrowing day, but **only** in those who had undergone four or more cycles.

The farrowing process was carefully supervised.

The differences between the induced group and the control group were compared for the following parameters:

- Farrowing duration.
- Percentage of farrowings at each time of the day.
- Total number of piglets born.
- Number of stillbirths.

Results

- Reproductive data was compared using the ANOVA statistical method (*table 1*).
- The average total number of births was 16.64 in the control group and 17.03 in the induced group ($p < 0.05$).
- The percentage of morning farrowings was 22.2% in the control group compared to 54% in the induced group ($p < 0.001$; *figure 1*).

Cycle	5	6	7	8	Mean
Control group farrowings	4.45	2.68	2.76	1.90	2.95
Induced farrowings	1.70	2.00	1.82	1.27	1.70

Table 1. Number of stillbirths per farrowing.

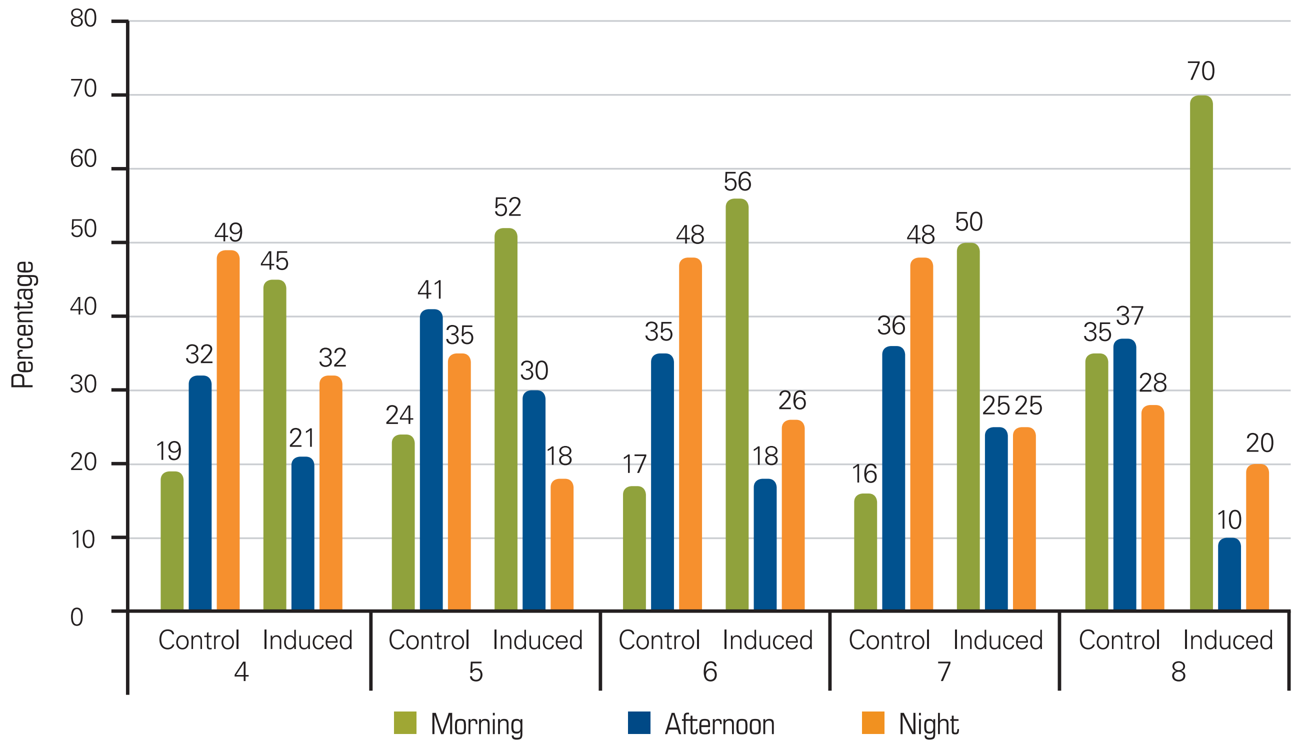

Figure 1. Number of farrowings in the morning, afternoon, or at night, according to the group.

Discussion

Inducing farrowings allows producers to manage their breeding stock more effectively by synchronising them, facilitating monitoring, and increasing the possibility of matching litter sizes by implementing adoption techniques such as*cross-fostering.*

Induced farrowings in hyperprolific sows is a management tool that can reduce piglet mortality and help increase the percentage of farrowings at times of the day when they can be supervised by staff, resulting in decreased stillbirths, even in very prolific sows [4].

Porcine endometritis (dirty sow syndrome)

This syndrome has serious economic consequences because of the increase in the percentage of repetitions above the normal rate for each farm. In addition, any alteration that compromises the milk production of the sows will have a negative impact on the productive parameters of the piglets, and can even produce a direct economic loss due to perinatal mortality.

Sometimes vulvar discharges are not seen on some farms but can be identified when the urogenital apparatus is checked in breeding sows sent to the slaughterhouse.

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How can this problem be controlled?

This problem causes significant economic losses, but it can be controlled by:

- Prevention and vigilance of management measures: maintaining a cleanliness vacuum, environmental hygiene, and avoiding moisture and dirt.
- Treatment using antibiotics, nonsteroidal anti-inflammatory drugs, or PGs.

Vulvar discharges

These sporadically appear on all Spanish farms and do not actively require measures to prevent them as long as only 1%–2% of sows show this symptom [5].

On some farms this problem is more serious and affects a higher percentage of breeders and significantly lowers the fertility rates and overall productivity of the farm.

Causes

- Not all vulvar discharges are caused by a pathology.
- It is also common to observe normal postpartum discharges as part of uterine cleaning and, therefore, these must be discriminated from abnormal discharges (*table 2*).
- From the 4th–5th day postpartum, these discharges should be considered abnormal and should be specifically treated.
- They may be the result of a metritis or endometritis process (*figure 2*) resulting from bacteria entering the uterus during farrowing; such microorganisms can come from faeces, the environment, or the hands of the operator attending the farrowing.

Discharge type	Significance
1–4 days postpartum	Normal
> 5 days of lactation	Abnormal
At covering	Normal
Up to 5 days post-coverage	Normal
14–21 days post-coverage	Abnormal
During pregnancy	Abnormal

Adapted from Muirhead and Alexander (1997).

Table 2. Discharge types depending on the time of their appearance and their extent.

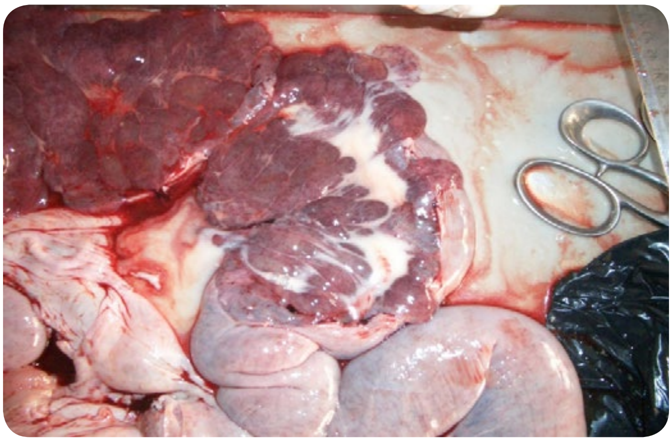

Figure 2. Uterus with sow endometritis after farrowing.

However, farms that, in the producer's view, do not present this problem, usually suffer from subclinical presentations that worsen the reproductive parameters over time because suitable preventive measures are not applied.

Endometrial regeneration and uterine involution

After farrowing, endometrial regeneration and uterine involution will occur in the 15 and 21 subsequent days [6].

Inadequate uterine involution and low natural PG production, due to different circumstances, results in slow and incomplete CL regression and continued progesterone secretion [7] which will have a suppressive effect on the innate immune system of the endometrium and make the uterus more susceptible to infection.

Using PG 24–36 hours after farrowing increases fertility and the total number of piglets born in the following cycle [8]. This is more likely to happen to sows that have had more than four parturitions because uterine defences tend to decrease with age.

Short lactations also predispose them to the appearance of these problems because they prevent complete uterine involution.

Postpartum use of prostaglandins

Improvements have been reported including [8]:

- A reduction in the weaning-heat interval.
- An increase in the number of piglets born live in the next cycle.
- An increase in fertility at farrowing.
- An increase in the weight of piglets at weaning.
- Lower neonatal mortality.

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In addition, PGs promote the release of oxytocin and prolactin after farrowing, which facilitates lactogenesis and milk expression. A failure in this phase causes the sows to become hypogalactic or agalactic and, consequently, reduces the viability of the newborn piglets.

In conjunction with luteolysis, PGs cause uterine smooth muscle contraction by reducing intracellular levels of cyclic AMP and raising intracellular levels of calcium. PG levels remain elevated during the first two days postpartum, which favours rapid uterine involution.

Exogenous PGs in pig production are especially useful for their luteolytic effect (ability to lyse LCs), and racemic cloprostenol and some natural PGs also have a uterotonic effect (they act on smooth muscle to increase its tonicity and produce contractions).

In the case of the smooth musculature of the sow's uterus, these contractions can be useful to favour the elimination of uterine secretions after farrowing or weaning and to prevent frequent 'dirty sow syndrome' (porcine endometritis). PG should be injected 24–48 hours postpartum in order to prolong their physiological peak.

The use of synthetic prostaglandins in the field

One of these studies [10] used Planate® 24–48 hours after farrowing and, compared to an untreated control group, showed an improvement in the percentages of sows returning to oestrus and undergoing their first covers within 10 days after weaning, as well as an increase in litter sizes at the next farrowing. This effect occurred even in situations where there was a low incidence of vaginal discharge.

Other work went further to compare the use of cloprostenol postpartum or natural $PGF_{2\alpha}$ (dinoprost tromethamine) to a control group on a farm with a history of a high prevalence of vaginal discharge at farrowing.

Compared to the control, significantly more piglets were born alive in the following cycle to both the treated groups (with no differences between the two) [17].

Effects of cloprostenol

Two other experiences of the effects of cloprostenol (Planate®) were published in 2009:

- *In vitro*: its effect on uterine smooth muscle.
- *In vivo*: to try to reproduce the improvements in the reproductive parameters observed in previous work.

In vitro study

The first study was carried out to analyse the effects of cloprostenol on the smooth muscles of the sow's uterus *in vitro*, compared to dinoprost, a product commonly used on farms postpartum.

Materials and Methods

An *in vitro* organ bath technique was used in this study which involves placing small portions of the organ under study into culture dishes containing Ringer Krebs solution. This technique has previously been used in intestinal motility studies. These dishes are maintained in a constant CO_2/O_2 atmosphere and the tissue is attached to an isometric transducer. The preparation is then put under tension to assess its spontaneous motility and then, the different products being studied are added to the dishes to compare the contractions they produce in the tissue.

Myometrial segments from different sows (always the same size from the same uterine location) were used in this particular study. First, the spontaneous motility of the longitudinal and circular smooth muscles of the uterus was studied, and then the longitudinal and circular smooth muscle motility was examined in response to dinoprost and cloprostenol.

Data on the amplitude, frequency, and area under the curve of the uterine contraction motility generated per unit time were recorded for the interval/time/surface area, and maximum, minimum, and time intervals.

Results

According to the results obtained for uterine motility, cloprostenol generated the same effect in sow uterine smooth muscle contractions as dinoprost did, both in circular (*table 3*) and longitudinal (*table 4*) fibres.

The fact that no significant differences were found between the sows being studied indicates the repeatability of the results for both treatments [12].

	Interv/t/superf	Max–Min	Interv./time
Cloprostenol	0.023 ± 0.006	0.99 ± 0.19	0.99 ± 0.17
Dinoprost	0.023 ± 0.004	1.18 ± 0.25	1.09 ± 0.145
	p = 0.804	p = 0.548	p = 0.666

Table 3. Average value (± SD) of motility in circular fibres.

	Interv/t/superf	Max–Min	Interv./time
Cloprostenol	0.059 ± 0.011	3.89 ± 1.03	2.7 ± 0.46
Dinoprost	0.044 ± 0.006	3.29 ± 0.76	2.14 ± 0.36
	p = 0.548	p = 0.603	p = 0.58

Table 4. Average value (± SD) of motility in longitudinal fibres.

In vitro *study*

The second study was carried out *in vivo* on a PRRS-negative, 1,400-head breeding farm in north Spain, with a history of a return to oestrus in 25% of sows and abnormal vulvar discharges post-farrowing in 8%–10% of sows.

Materials and Methods

The farm carried out early weanings (between 19–21 days) which worsened the problem of sows with possible insufficient uterine involution.

A total of 452 sows were included in this study: half were treated with cloprostenol and the other half with dinoprost as a positive control, both 24–36 hours after farrowing.

The farm's history was used as a negative control because this study was completed using a referenced product.

Results

The reproductive results obtained with both treatments on this farm significantly improved compared to previous results [13] (*tables 5* and *6*):

- Fertility: improved by more than ten points.
- The weaning-to-first-fertile-service interval.
- The weaning-to-oestrus interval (WEI).
- The presentation of vulvar discharges practically disappeared.

	Dinoprost	Cloprostenol	
N° weaned	11.31 ± 0.34	10.97 ± 0.2	$p = 0.63$
Lactation days	19.08	18.98	
% fertility	96	96.6	$p = 0.93$
% with vulvar discharge	4	0	$p > 0.05$
Fertile WEI	6.4	6	$p = 0.31$

Table 5. Comparative results for primiparas.

	Dinoprost	Cloprostenol	
N° weaned	11.14 ± 0.2	11.24 ± 0.1	$p = 0.102$
Lactation days	19.08	18.98	
% fertility	87.9	88.1	$p = 0.19$
% with vulvar discharge	2.5	1.7	$p = 0.73$
Fertile WEI	12.7	11.9	$p = 0.18$

Table 6. Comparative results for multiparas.

Conclusions

PGs are a very profitable tool for producers when it comes to improving the reproductive parameters of their farms. PGs are used in protocols to synchronise the timing of farrowings as well as after farrowings and can help organise farm work and reduce problems such as porcine endometritis. PGs continue to be extremely useful tool in increasingly prolific sows.

These uterotonic effects can be achieved by natural prostaglandins ($PGF_{2\alpha}$) as well as synthetic prostaglandin analogues, specifically, racemic cloprostenol (Planate®), and the use of the latter can also minimise the appearance of side effects.

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