Impact of postpartum PGF2α treatment on reproductive performance and prevention of specific uterine disorders in dairy cows

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ABSTRACT

The aim of this study was to evaluate the impact of PGF2α treatment administered after parturition on key reproductive parameters, the incidence of postpartum pathologies, and the resumption of ovarian cyclicity in dairy cows. The study involved two groups of dairy cows: a control group (C, n=20) and an experimental group (E, n=20) that received the PGF2α treatment. Postpartum pathologies, ovarian cyclicity, and reproductive performance indicators were compared between the groups. Postpartum pathologies were observed at a higher rate in the control group, with a 30% prevalence of retained placenta, 20% for both delayed uterine involution and clinical endometritis, and 5% for pyometra. In contrast, the experimental group exhibited a lower incidence, with 10% for retained placenta, 5% for delayed uterine involution, 5% for clinical endometritis, and 0% for pyometra. Although these results suggest a trend toward lower pathology incidence in treated cows, the differences were not statistically significant ($p > 0.05$). Regarding the resumption of ovarian cyclicity, the control group showed a resumption rate of only 15%, whereas 65% of the experimental group resumed cyclicity. This yielded an odds ratio of 10.52 and a highly significant p-value (< 0.01), indicating that PGF2α treatment effectively hastened the return to normal ovarian function. Reproductive performance also improved in the experimental group, with first insemination (AI1) success rates of 45% compared to 30% in the control group (OR = 1.93). The waiting period was significantly shorter in the experimental group (73 vs. 98 days, $p < 0.001$), and calving-to-fertilization and calving-to-calving intervals were reduced by approximately 31 days ($p < 0.001$). However, the overall reduction in the breeding period remained inconclusive. While PGF2α treatment did not significantly reduce postpartum pathologies, it markedly enhanced the resumption of ovarian cyclicity and improved reproductive intervals in dairy cows, leading to enhanced reproductive efficiency.

Keywords: PGF2α, postpartum treatment, reproductive, cyclicity, dairy cows..

1. Introduction

Recent modeling studies suggest that a one-year calving interval is generally considered economically optimal for dairy cows (1). Longer intervals have been linked to a decrease in milk production per cow per year (2). To achieve this, farmers, in collaboration with veterinarians, must manage the herd's reproduction effectively to optimize performance and related parameters (3).

Achieving early, successful conception in postpartum dairy cows is crucial for maximizing reproductive efficiency and profitability in modern dairy farming. While modern dairy cows have high production potential, the added stress from peri-parturient events, along with the accompanying endocrine and metabolic changes, leads to a negative energy balance during the postpartum period (4). After calving, the uterus should return to a non-pregnant size, reshape, and reposition, a physiological process known as uterine involution. This process takes between 20 and 40 days post-calving (5).

Unfortunately, beef cows generally take longer to resume their cycles postpartum. The reasons for this delay have been identified as behavioral (6), psychological, hormonal, and nutritional factors, as well as the effects of climate change on reproduction (7). The absence of ovarian cycles postpartum is considered a survival strategy for the cow, designed to prevent pregnancy during periods of physiological or environmental stress (8).

Prostaglandins (PGF2α) are potent luteolytic agents that have been successfully used to induce estrus in cows that fail to show heat signs. They also play a significant role during the postpartum period by assisting in placental expulsion and uterine involution, mechanisms that can be compared to inflammatory responses (9). Several studies have demonstrated the effectiveness of PGF2α in treating uterine infections and improving reproductive performance (10).

This study aims to improve reproductive performance in dairy cows through a two-part approach. The first part consists of a literature review on postpartum physiology, ovarian cyclicity anomalies, and the role of prostaglandins. The second part is an experimental study evaluating PGF2α treatment in preventing and treating postpartum uterine disorders, its impact on ovarian cyclic activity, and its effect on fertility and conception rates. Data collected from various dairy farms were analyzed to track the proportion of cows that showed cyclic activity post-treatment, and the results were compared across different reproductive parameters to evaluate the overall effects of PGF2α treatment.

2. Materials and methods

2.1. Study area and protocol

The present study was conducted in the Wilaya of Tizi-Ouzou from August 2020 to August 2021, across several farms. A total of 40 multiparous Holstein black-and-white dairy cows, aged between 3 and 5 years, were included.

The cows were divided into two groups: Control Group (n=20), which did not receive any treatment and Experimental Group (n=20) which received intramuscular injections of Dinolytic prostaglandin (PGF2α, Zoetis) at a dosage of 5 ml. These injections were administered on the day of calving and again 26 days postpartum. The study began with the measurement of the cows' live weights, followed by an assessment of their body condition scores (BCS). A qualitative analysis of the feed provided to the animals was also conducted. Artificial insemination was performed during observed estrus, with all procedures carried out by the same inseminator to ensure consistency. Inclusion criteria required the cows to have a BCS of 3, while exclusion criteria eliminated cows with a history of dystocia, pathologies during the dry period, a BCS lower than 2.5, or those older than 5 years.

2.2. Body Condition Score Evaluation

Body condition score (BCS) was assessed using a 5-point scale (1 = emaciated; 5 = obese), with a precision of ½ point. All cows included in the study had a BCS of 3.

2.3. Clinical examination

A thorough general examination was conducted to ensure that only clinically healthy cows were included in the study. Systematic evaluations were carried out on days 0, 26, and 35 postpartum:

- **Day 0**: The first PGF2α injection was administered, accompanied by a clinical examination to detect febrile metritis, acute mastitis, or retained placenta (RP).
- **Day 26**: The second PGF2α injection was administered, followed by an examination of the vulvovaginal area to assess clinical endometritis, detect estrus, and evaluate fertility parameters.
- **Day 35**: A transrectal examination was performed to monitor uterine involution, identify pyometra, and confirm the resumption of postpartum cyclicity.

2.4. Diagnosis of postpartum diseases

- **Retained Placenta**: Diagnosed when fetal membranes were not expelled within 12 to 24 hours postpartum.
- **Delayed Uterine Involution**: Assessed around day 30 postpartum through transrectal palpation, confirmed by ultrasound using a "DRAMINSKY" device with a 7.5 MHz probe. Delayed uterine involution was diagnosed when one or both uterine horns exceeded 5 cm in diameter.
- **Clinical Endometritis**: Diagnosed in cows that showed no systemic symptoms after 21 days postpartum. The presence of purulent or mucopurulent discharge was observed using a vaginoscope.
- **Pyometra**: Diagnosed via transrectal examination, revealing an enlarged uterus with an abnormally large volume of uterine fluid, a closed cervix, and the presence of a corpus luteum on one of the ovaries.
- **Resumption of Ovarian Cyclicity**: Detected by palpation and confirmed via ultrasound, identifying the presence of a corpus luteum.

2.5. Data analysis

Statistical analysis was performed using R software. The differences between groups were evaluated using the Student's t-test for independent samples, with a significance level set at 0.05.

3. Results

The table 1 presents the postpartum pathologies in the control and experimental groups. For retained placenta, the control group had a higher incidence, with 30% (6/20) of animals affected, compared to 10% (2/20) in the experimental group. The odds ratio (OR) of 3 suggests the control group had three times the odds of having retained placenta, but the p-value of 0.235 indicates no statistically significant difference. For delayed uterine involution, 20% (4/20) of animals in the control group were affected, while only 5% (1/20) in the experimental group showed this condition. The OR of 4 suggests the control group had a higher risk, but again, the p-value of 0.342 indicates no significant difference. The incidence of clinical endometritis was also higher in the control group (20%, 4/20) compared to the experimental group (5%, 1/20), with an OR of 4, yet the p-value of 0.342 confirms no statistical significance. Lastly, for pyometra, 5% (1/20) of the control group animals were affected, while there were no cases in the experimental group. The absence of cases in the experimental group means no OR or p-value could be calculated.

Table 1: Frequencies of pathologies in the control (n=20) and experimental group (n=20)

Post-partum pathologies	**Control group (Number, (%), [CI, 95%])**	**Experimental group (Number, (%), [CI, 95%])**
Retained Placenta	6 (30) [14.5, 51.9]	2 (10) [2.79, 30.10]
Delayed Uterine Involution	4 (20) [8.1, 41.6]	1 (5) [0.89, 23.61]
Clinical Endometritis	4 (20) [8.1, 41.6]	1 (5) [0.89, 23.61]
Pyometra	1 (5) [0.9, 23.6]	0 (-) -

The table 2 presents the frequency of resumption of ovarian cyclicity in the control and experimental groups. In the control group, only 15% (3/20) of animals resumed ovarian cyclicity, with a 95% confidence interval (CI) of [3.2-37.9]. In contrast, the experimental group had a significantly higher rate of 65% (13/20), with a CI of [40.8-84.6] ($p<0.01$), suggesting that the experimental group had a significantly higher frequency of resumption of ovarian cyclicity compared to the control group.

Table 2: Frequency of resumption of ovarian cyclicity in the control and experimental groups

Group	**Frequency (n, %)**	**95% CI**	**P value**
Control group (n=20)	3 (15)	[3.2-37.9]	< 0.01
Experimental group (n=20)	13 (65)	[40.8-84.6]	

The table 3 presents the success rates for the first, second, and third or more artificial inseminations (AI1, AI2, ≥AI3) in the control and experimental groups. For AI1, the control group had a success rate of 30% (6/20) compared to 45% (9/20) in the experimental group, with an odds ratio (OR) of 1.93, suggesting the experimental group had almost twice the chance of success. However, the p-value of 0.51 indicates no statistically significant difference. For AI2, both groups had similar success rates—50% (10/20) in the control group and 45% (9/20) in the experimental group. The OR of 0.82 shows a slight disadvantage for the experimental group, but the p-value of 1.00 confirms no significant difference. For AI ≥3, the control group had a success rate of 20% (4/20) while the experimental group had a lower rate of 10% (2/20), with an OR of 0.44 indicating lower chances for the experimental group, but again, the p-value of 0.66 shows no significant statistical difference.

Table 3: Success rates for the first, second and third or more artificial inseminations (AI1, AI2, ≥AI3) in the control (n=20) and experimental (n=20) group

Parameters	Control group (Number, (%), [CI, 95%])	Experimental group (Number, (%), [CI, 95%])	Odds Ratio (OR)	P value
AI_1	6 (30) [11.9- 54.3]	9 (45) [23.1 - 68.5]	1.93	0.51
AI_2	10 (50) [27.2 - 72.8]	9 (45) [23.1 - 68.5]	0.82	1.00
AI ≥3	4 (20) [5.7 - 43.7]	2 (10) [1.2 - 31.7]	0.44	0.66

The table 4 highlights a notable improvement in reproductive parameters in the experimental group compared to the control group. The table summarizes the statistical analysis comparing the control group and the experimental group across four reproductive parameters. It shows that the waiting period (WP) is significantly reduced in the experimental group (73 ± 10.7 days) compared to the control group (98 ± 18.8 days), with a difference of 25 days ($p < 0.001$), indicating a faster return to cyclicity. Similarly, both the calving-to-fertilization insemination interval (ICFI) and the calving-to-calving interval (ICC) are reduced by approximately 31 days in the experimental group, each with p-value less than 0.001, which suggests a significant improvement in overall reproductive efficiency. In contrast, the breeding period (PR) is only reduced by 6 days (from 19 ± 11.5 to 13 ± 12.7 days) ($p > 0.05$), meaning this change is not statistically significant. Overall, the table indicates that the intervention implemented in the experimental group has led to significant enhancements in key reproductive parameters (WP, ICFI, and ICC), potentially improving production efficiency and economic outcomes in animal production, while the change in PR remains inconclusive.

Table 4: Comparison of reproductive parameters between control and experimental groups

Parameters	Control group (n=20)	Experimental group E (n=20)	Differences (days)	p-value
WP (days)	98±18.8	73±10.7	**25**	**<0.001**
BP (days)	19±11.5	13±12.7	**6**	**>0.05**

ICFI (days)	117±17.2	86±14.5	**31**	**<0.001**
ICC (days)	397±17.2	366±14.5	**31**	**<0.001**

WP: waiting period, BP: breeding period, ICFI: interval: calving - fertilizing insemination, ICC: interval calving-calving

4. Discussion

Postpartum intervention via the administration of $PGF_2\alpha$ has proven promising by simultaneously improving uterine health and the resumption of ovarian activity. Indeed, although the differences observed for conditions such as retained placenta, delayed uterine involution, and clinical endometritis did not reach statistical significance ($p > 0.05$), the trends indicate high odds ratios (around 3 to 4), with, for example, a reduced rate of retained placenta (10% vs. 30%) and a lower incidence of clinical endometritis (5% vs. 20%), thus corroborating the findings of LeBlanc (11), who link these conditions to decreased fertility. This benefit is explained by the mechanism of action of $PGF_2\alpha$, which stimulates uterine contractions, thereby promoting the rapid expulsion of debris, placental residues, and lochia, and consequently contributing to an accelerated uterine involution and a reduction in subclinical infections (12).

Our study indicates that $PGF_2\alpha$ administration during the postpartum period positively impacted the reproductive parameters of treated cows. Specifically, it promoted early resumption of ovarian activity and reduced the interval between calving and fertilizing insemination by 31 days compared to the control group, ultimately improving reproductive efficiency. We found that 90% of cows in the experimental group did not present retained placenta, compared to 70% in the control group, aligning with numerous studies that highlight the efficacy of $PGF_2\alpha$ injections during the postpartum period (13). In cases of delayed uterine involution, 95% of cows in our experimental group showed normal involution, compared to 80% in the control group, exceeding results reported by Zidane (14), who observed 30% of untreated animals exhibiting normal uterine involution, versus 50% in the treated group.

Uterine involution, which involves the return of the uterus to its normal size and function, depends on factors such as myometrial contractions, bacterial infection clearance, and endometrial regeneration (15). Hirsbrunner (16) and Hanzen (17) both observed the beneficial effects of $PGF_2\alpha$ on uterine involution, with Hanzen specifically noting that repeated $PGF_2\alpha$ administration at 10-day intervals postpartum facilitated uterine involution. Masoumi et al. (12) found that Dinoprost (a $PGF_2\alpha$ analog) significantly reduced uterine diameter and improved fertility, while Elsheikh and Ahmed (18) reported that $PGF_2\alpha$ injections accelerated uterine involution and improved reproductive performance. Furthermore, our study demonstrated a 5% incidence of endometritis in the treated group compared to 20% in the control group, which is consistent with Sheldon et al. (19), who found a 29% frequency of uterine infections in a Belgian study. Although some studies report mixed results on the effectiveness of $PGF_2\alpha$ for treating endometritis, with Lewis et al. (20) suggesting potential benefits in non-cyclic females, our findings support the idea that $PGF_2\alpha$ can help reduce uterine infections. Despite these mixed results, the luteolytic effect of $PGF_2\alpha$ remains its primary indication for treating clinical endometritis in cows (11). Finally, we observed that the use of $PGF_2\alpha$ in our study accelerated uterine involution and reduced the incidence of infection, which likely contributed to the improved reproductive outcomes in the experimental group.

Our study demonstrates that $PGF_2\alpha$ administration during the postpartum period exerts multiple beneficial effects on reproductive performance. In our experimental group, 90% of the cows did not present retained placenta compared to 70% in the control group, and in cases of delayed uterine involution, 95% of treated cows showed normal involution versus 80% in untreated cows—findings that align with the efficacy of $PGF_2\alpha$ reported by Abuelhamd et al. (13). Uterine involution, which depends on myometrial contractions, bacterial clearance, and endometrial regeneration (15), is accelerated by $PGF_2\alpha$; Hirsbrunner (16) observed that repeated administration twice daily from days 3 to 13 postpartum shortened involution time by

6 days. Moreover, Ingawale and Bakshi (21) reported that $PGF_2\alpha$ injections on day 14 postpartum reduced the interval from calving to first estrus, while Hanzen (17) noted that a single injection of Cloprostenol on day 26 postpartum decreased abnormal discharges and uterine infection signs. Supporting these findings, Masoumi et al. (12) found that Dinoprost—a $PGF_2\alpha$ analog—significantly reduced uterine diameter, improved fertility by increasing pregnancy rates, shortening the time to first mating, and reducing days open, and Elsheikh and Ahmed (18) confirmed that both single and double $PGF_2\alpha$ injections during the postpartum period accelerated uterine involution and enhanced reproductive performance.

The mechanism underlying these benefits appears to be related to the uterotonic effect of $PGF_2\alpha$, which stimulates uterine contractions to promote the rapid expulsion of retained placenta, debris, and lochia. Exogenous $PGF_2\alpha$ increases uterine secretion of endogenous $PGF_2\alpha$ and luteal leukotriene B4 (LTB4), thereby facilitating uterine involution and reducing infection risks, even in the absence of a corpus luteum (20). Furthermore, our study recorded a 5% incidence of endometritis in the treated group compared to 20% in the control group, a result consistent with Sheldon et al. (19). However, the literature remains divided on this point: while Lewis (20) suggests that $PGF_2\alpha$ may help treat endometritis in non-cyclic females. Other authors (11) have also reported conflicting results regarding the impact of $PGF_2\alpha$ on uterine involution, bacterial clearance, and overall fertility.

Our results are in overall agreement with studies that have evaluated the effect of $PGF_2\alpha$ administered at the time of insemination. For example, the study by López-Gatius et al. (22) shows that an intravenous injection of cloprostenol in primiparous cows increases pregnancy rate (odds ratio = 3.60). These results suggest that, regardless of the time of administration, $PGF_2\alpha$ promotes complete regression of the corpus luteum and creates a hormonal environment (low in progesterone) favorable to ovulation and optimal gamete transfer (23). Furthermore, several works (24) indicate that $PGF_2\alpha$ administration increases the ovulation rate in cows and heifers, corroborating our finding of a faster recovery of ovarian cyclicity.

The mechanistic effect, independent of luteolysis, whereby the $PGF_2\alpha$ analogue increases pituitary sensitivity to GnRH and enhances LH release, as well as Cruz et al. (25) observation of increased LH release when $PGF_2\alpha$ is administered before GnRH, are consistent with the idea that $PGF_2\alpha$ acts favorably on the ovulatory process.

In conclusion, our study, focusing on $PGF_2\alpha$ administration in the postpartum period, demonstrated a significant improvement in reproductive performance either through improved uterine health (reduced placental retention, accelerated uterine involution and reduced incidence of endometritis) and early resumption of ovarian activity and postpartum cyclicity, or through optimization of ovulatory conditions and conception during insemination.

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Authors' Contribution

Study concept and design: K.H.O. and M.N.

Conducting the experiment: A.K. and A.B.

Analysis and interpretation of data: N.O. and N.A.K.T.

Drafting of the manuscript: T.K., O.S. and A.L.

Critical revision of the manuscript: K.H.O., M.N., N.O. and N.A.K.T.

Ethical approval

Experimental procedures approved by the Institutional Committee for the Protection of Animals of the National Administration of Higher Education and Scientific Research of Algeria (98-11, Act of 22 August 1998).

Conflict of interests

The authors declare that they have no known conflict of interest in the conduction of the current study.

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No finding.

Data Availability

Not applicable.

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