



International Journal of Innovative Research in Science Engineering and Technology (IJIRSET)

(A Monthly, Peer Reviewed, Refereed, Scholarly Indexed, Open Access Journal)



Impact Factor: 8.699

Volume 14, Issue 8, August 2025

Effect of Postpartum Administration of PGF₂ α on Uterine Involution

Arjun Vinayan¹, C. P. Abdul Azeez², K. Promod³, Leeba Chako⁴, S. Pramod⁵

MVSc Scholar, Department of Animal Reproduction, Gynaecology and Obstetrics, College of Veterinary and Animal Sciences Pookode, Wayanad, India¹

Associate Professor, Department of Animal Reproduction, Gynaecology and Obstetrics, College of Veterinary and Animal Sciences Pookode, Wayanad, India²

Professor, Department of Animal Reproduction, Gynaecology and Obstetrics, College of Veterinary and Animal Sciences Pookode, Wayanad, India³

Associate Professor, Department of Animal Reproduction, Gynaecology and Obstetrics, College of Veterinary and Animal Sciences Pookode, Wayanad, India⁴

Assistant Professor, Livestock Research Station, Thiruvizhamkunnu, Palakkad, India⁵

ABSTRACT: This study investigated the effects of early postpartum administration of cloprostenol sodium, a prostaglandin F₂ α (PGF₂ α) analogue, on uterine involution and ovarian rebound in crossbred dairy cows. Twenty cows were randomly assigned to a treatment group receiving cloprostenol sodium on day 7 postpartum or to an untreated control group. Weekly per-rectal examinations and scheduled ultrasonographic assessments were conducted from days 7 to 60 postpartum to evaluate changes in cervical and uterine dimensions, intrauterine fluid clearance, and ovarian activity. Results revealed that cloprostenol sodium administration did not significantly hasten involution of the cervix, uterine body, or horns compared to controls. However, treated cows demonstrated earlier clearance of intrauterine fluid and a significantly earlier resumption of ovarian cyclicity, as evidenced by earlier detection of follicles and corpus luteum. In summary, while cloprostenol sodium did not markedly accelerate anatomical uterine regression, it effectively promoted uterine cleansing and enhanced ovarian rebound, supporting improved postpartum reproductive efficiency in dairy cows.

KEYWORDS: Postpartum, involution, PGF₂ α .

I. INTRODUCTION

India, home to the world's largest cattle population, ranks as the leading global producer of milk. Despite this impressive output, reproductive inefficiencies, particularly prolonged inter-calving intervals, remain a major hurdle in maximizing dairy productivity. One of the most critical phases influencing a cow's future fertility is the postpartum period, during which the uterus must involute and ovarian cyclicity must resume in a timely manner. Delayed uterine recovery or sluggish ovarian rebound can significantly prolong the calving-to-conception interval, affecting both economic returns and herd reproductive performance.

Prostaglandin F₂ α (PGF₂ α) and its analogues like cloprostenol sodium have been widely used for their uterotonic effects and their ability to modulate postpartum recovery. However, limited studies have focused on how these agents influence ultrasonographic and per-rectal findings during the early postpartum phase.

This study was designed to evaluate the impact of early postpartum administration of cloprostenol sodium on uterine involution and ovarian rebound, as assessed through weekly per-rectal and ultrasonographic examinations. By documenting the progression of uterine size reduction, resolution of intrauterine fluid, and ovarian follicular dynamics, the research aims to provide evidence-based insights into the utility of PGF₂ α treatment for improving postpartum reproductive management in dairy cows.

II. MATERIALS AND METHOD

The study was conducted between August 2024 and May 2025 at the Livestock Research Station, Thiruvazhamkunnu, under the Kerala Veterinary and Animal Sciences University. A total of 20 healthy crossbred dairy cows in their early postpartum period were selected and randomly allocated into two groups (n=10 each). Cows in Group I received cloprostenol sodium (inj. ESTRUMATE® 250 µg/ml) 500 µg, intramuscularly, in two doses 12 hours apart, on the 7th day postpartum, while Group II animals served as untreated controls. All animals were maintained under uniform feeding and management conditions throughout the study period.

Starting from day 7 postpartum, cows in both groups were subjected to weekly per-rectal examinations until day 56 postpartum and ultrasonographic examinations on 20, 30, 40, 50 and 60 day postpartum (dpp), to monitor uterine involution. Per-rectal palpation was used to assess cervical diameter, uterine size and consistency using uterine score (1 to 3) while transrectal ultrasonography (5–7.5 MHz linear-array probe) was performed to record cervical, uterine body, uterine horn diameter, presence of intrauterine fluid.

Uterine score considered the size and tonicity of the uterus at the greater curvature of the uterine horn (3 = flaccid uterus larger than one hand, 2 = uterus with moderate tonicity and smaller than one hand, and 1 = high tonicity and less than 3 fingers width; Melendez et al. (2004).

The data obtained were analysed using SPSS version 24.0 statistical software package. Data collected were analyzed using repeated measures ANOVA and independent t-tests to compare mean uterine diameters and ovarian activity parameters between the two groups over time. A p-value of <0.05 was considered statistically significant.

III. RESULT AND DISCUSSION

Cows belonged to both group I and group II were subjected to per-rectal examination of reproductive tract commencing from day 7 until day 56 postpartum and cervical, uterine, and ovarian changes during different postpartum days were studied.

Table 1. Comparison of cervical diameter (Mean ± SE) between group I and group II (n=10) in cows during different postpartum days assessed by per-rectal palpation

Postpartum days	Cervical diameter (mm)		t-value (p-value)
	Group I	Group II	
7	7.57 ^a ± 0.91	6.65 ^a ± 0.59	0.785 ^(ns) (0.390)
14	4.77 ^b ± 0.37	4.90 ^b ± 0.40	0.052 ^(ns) (0.823)
21	3.72 ^c ± 0.19	3.80 ^c ± 0.22	0.063 ^(ns) (0.806)
28	3.27 ^d ± 0.19	3.52 ^d ± 0.16	1.778 ^(ns) (0.203)
35	3.07 ^d ± 0.13	3.25 ^e ± 0.11	1.778 ^(ns) (0.203)
42	3.07 ^d ± 0.13	3.15 ^e ± 0.11	0.250 ^(ns) (0.625)
49	3.07 ^d ± 0.13	2.83 ^e ± 0.29	0.785 ^(ns) (0.390)
56	3.05 ^d ± 0.13	2.82 ^e ± 0.29	0.785 ^(ns) (0.390)
F-value (P-value)	29.264** (<0.001)	32.374** (<0.001)	

** Significant at 0.01 level; Means having different letters as superscript differ significantly within a column

The mean cervical diameter was observed to be highest on day seven postpartum with a diameter of 7.57 ± 0.91 mm and 6.65 ± 0.59 mm in Group I and Group II respectively, there from the size of cervix decreases rapidly to 4.77 ± 0.37 mm and 4.90 ± 0.40 mm in Group I and Group II, respectively, during day 14 postpartum. Thereafter the reduction of the size was gradual, reaching 3.72 ± 0.18 mm and 3.80 ± 0.22 mm on day 21. The reduction of the size was statistically significant till the day 28 (3.27 ± 0.19 mm) and 35 (3.25 ± 0.11 mm) within Group I and Group II respectively, thereafter there was no significant reduction in size of cervix.

When comparing cervical diameter between groups at any given postpartum day, the effect of $\text{PGF}_{2\alpha}$ did not produce statistically significant changes, even though it caused an earlier completion of cervical involution within groups (by 21–28 dpp in Group I vs. 28–35 dpp in Group II). This implies that $\text{PGF}_{2\alpha}$ has no discernible effect on cervical regression.

However, in the study of Abdel-Khalek et al. (2013), the mean cervical diameter was 3.74 ± 0.26 , 3.18 ± 0.17 , 2.84 ± 0.13 , 2.60 ± 0.21 , and 2.60 ± 0.21 cm on postpartum days 7, 14, 21, 28, and 35, respectively, on $\text{PGF}_{2\alpha}$ -treated (6-12 h after calving) animals, and thereafter there was no significant reduction in the cervical size. And suggested that the $\text{PGF}_{2\alpha}$ -treated animals completed cervical involution by 21 dpp compared to 28 dpp in non-treated animals. This was contrary to the current study, where the group I and group II animals have no significant difference on cervical involution.

In the study of Stephan (2010) on the postpartum effect of oxytocin and $\text{PGF}_{2\alpha}$, it is stated that these ecobolics administered on the seventh day postpartum in crossbred cows had no effect on involution of the cervix. This was in accordance with the present study.

These differences in the observations of various authors might be due to the difference in dosage and time of administration of $\text{PGF}_{2\alpha}$, as well as the difference in breed and other management conditions.

Uterine size and consistency

Table 2. Comparison of uterine scores attained by group I and group II cows during postpartum period assessed by per-rectal examination

Postpartum days	Uterine score (3 to 1)	Group I (n=10)		Group II (n=10)	
		No. of animals	Per cent	No. of animals	Per cent
7	3	4	40	1	10
	2	6	60	9	90
	1	0	0	0	0
14	3	0	0	0	0
	2	8	80	10	100
	1	2	20	0	0
21	3	0	0	0	0
	2	2	20	8	80
	1	8	80	2	20
28	3	0	0	0	0
	2	0	0	1	10
	1	10	100	9	90
35	3	0	0	0	0
	2	0	0	0	0
	1	10	100	10	100

The uterine size and consistency in both groups were assessed using a standardized uterine scoring system. On the 7th day postpartum, uterine scores of 1, 2, and 3 were observed in 0%, 60%, and 40% of animals in Group I, respectively, and 0%, 90%, and 10% of animals in Group II, respectively. Notably, none of the animals in either group exhibited a uterine score of 1, indicating that the uterus was still undergoing involution and the process was not yet complete.

By 14 days postpartum, In Group I, 80% of animals exhibited moderate involution (score 2), while 20% had progressed to complete involution (score 1). In contrast, all animals in Group II (100%) remained at score 2, with none showing complete involution at this stage. These findings suggest a faster rate of uterine recovery in the treated group.

Melendez et al. (2004) reported that postpartum cows treated with PGF_{2α} (25 mg Lutalyse, on 8 d postpartum, 8 h apart) exhibited lower uterine scores compared to untreated cows. On day 12 postpartum, the percentages of animals attaining uterine scores of 1, 2, and 3 in the treated group were 16%, 48%, and 36%, respectively, while in the untreated group, the corresponding percentages were 13.04%, 52.17%, and 34.78%. Comparing to the current study this was late. However, these findings support the observation that PGF_{2α} can enhance the progression of uterine involution.

According to Yu et al. (2016), animals treated with PGF_{2α} on day 14 postpartum attained an average uterine score of 2.0, compared to 2.5 in untreated cows. A comparable trend was observed in the current study, although with a slight difference in average scores: 1.8 in the treated group and 2.0 in the non-treated group, further reinforcing the positive effect of PGF_{2α} on uterine involution.

By 21 days postpartum, 80% of animals in Group I exhibited a uterine score of 1, indicating a near complete uterine involution, while 20% remained at score 2. In contrast, 80% of animals in Group II still showed a score of 2, and only 20% had achieved score 1. This further underscores the relatively slower involution in the untreated group.

On day 28 postpartum, all animals in Group I (100%) exhibited a uterine score of 1, indicating completion of uterine involution. In Group II, 90% of animals had also reached a score of 1 by this time. By day 35 postpartum, all animals in both groups (100%) had attained a uterine score of 1, confirming that uterine involution in Group II was completed by this point.

Praveen (2016) reported the cloprostenol sodium treated cows completed the uterine involution by 28.33 ± 1.67 days postpartum, which closely aligns with the findings of the present study. Additionally, Guilbault et al. (1987) observed that uterine involution was completed by 35 days postpartum in untreated cows, which is consistent with the timeline observed in Group II.

The faster uterine involution in animals treated with PGF_{2α} during early puerperium has also been supported by Iqbal et al. (2003). However, contrasting results were reported by Elsheikh and Ahmed (2005), who found no significant benefit of PGF_{2α} treatment on uterine involution. The accelerated uterine recovery observed in the treated group of the present study may be attributed to the enhanced myometrial contractions stimulated by exogenous PGF_{2α}, described by Pandey et al. (2007).

Palpable structures on the ovaries

The mean day of first palpable corpus luteum (CL) formation was significantly earlier in PGF_{2α}-treated cows (Group I) at 28.00 ± 1.48 days postpartum compared to untreated controls (Group II), which showed first CL palpation at 37.80 ± 2.14 days. Similarly, the detection of the first follicle was observed much earlier in Group I (14.70 ± 0.70 days) than in Group II (22.40 ± 1.40 days). These findings suggest a pronounced effect of PGF_{2α} administration in enhancing the postpartum ovarian rebound in treated cows.

The mean day of first follicular detection in the untreated group of the present study (22.40 ± 1.40 days) was notably later than the 15 ± 2.0 days reported by Webb et al. (1980). This discrepancy may be due to breed differences, nutritional status, or varying environmental and management conditions between the two studies. Such factors are known to influence the timing of postpartum ovarian rebound. In contrast, the treated group in the present study exhibited earlier follicular development (14.70 ± 0.70 days), further highlighting the potential role of PGF_{2α} in facilitating earlier resumption of ovarian activity.

Gitonga (2010) reported that the presence of either a corpus luteum (CL) or a large follicle can be considered an indication of the resumption of ovarian activity.

IV. ULTRASONOGRAPHIC EXAMINATION OF THE REPRODUCTIVE TRACT

Diameter of cervix and uterus (mm)

Table 4. Comparison on diameter of cervix between group I and group II (Mean \pm SE) in postpartum cows assessed by ultrasonographic examination (n=10)

Postpartum days	Diameter of cervix (mm)		t-value (P-value)
	Group I	Group II	
20	37.38 ^a \pm 1.84	38.56 ^a \pm 2.24	0.407 ^{ns} (0.689)
30	32.31 ^b \pm 2.02	34.73 ^b \pm 1.43	0.168 ^{ns} (0.868)
40	32.20 ^c \pm 1.86	32.39 ^c \pm 1.28	0.361 ^{ns} (0.722)
50	31.67 ^c \pm 1.91	29.47 ^d \pm 1.11	0.092 ^{ns} (0.927)
60	31.39 ^c \pm 1.69	28.38 ^d \pm 1.01	1.538 ^{ns} (0.142)
F-value (P-value)	18.953** (<0.001)	14.568** (<0.001)	

** Significant at 0.01 level; ns non-significant; Means having different letter as superscript differ significantly within a column

In group I and group II cows, the largest cervical diameters were observed on day 20 postpartum (37.38 \pm 1.84 and 38.56 \pm 2.24 mm, respectively) which were significantly higher ($p < 0.001$) than that of all other observations in respective groups. In group I cows, there was a significant ($p < 0.001$) reduction in cervical diameters from day 30 (32.31 \pm 2.02 mm) to day 40 (32.20 \pm 1.86 mm) and after that the measurements up to day 60 did not vary significantly ($p > 0.05$). However, in group II, a significant ($p < 0.001$) reduction in cervical diameters continued from day 30 (34.73 \pm 1.43 mm) till day 50 (29.47 \pm 1.11 mm) and nonsignificant ($p > 0.05$) reduction was observed till day 60 postpartum. In both the groups, the reduction in cervical diameter followed a decreasing logarithmic pattern in the initial weeks followed by a gradual decline. While comparing the cervical diameters of both the groups during different postpartum days, no significant variation could be obtained ($p > 0.05$). This suggests that cloprostenol sodium had no effect on hastening the cervical involution. This was agreed by Stephan (2010) stating that the diameter of the cervix reduced similarly in PGF₂ α treated and non-treated postpartum cow. In contrast Abdel-khalek et al. (2015) suggested that the involution of cervix in PGF₂ α treated postpartum cow happened in a faster rate.

LeBlanc et al. (2002) observed that the reduction in uterine diameter follows a pattern similar to that of the cervix, although cervical involution typically occurs at a slower rate. Consistently, Morrow et al. (1966) reported that in purebred cows, both the uterus and cervix generally regress to a diameter of less than 5 cm by approximately 25 days postpartum. Supporting this, Poyam and Tiwari (2015) noted that by day 40 postpartum, healthy Sahiwal cows exhibited uterine and cervical diameters below 5 cm, even though complete involution may not be achieved until around 50 days postpartum.

These differences in the results observed by various authors might be due to the difference in dosage and time of administration of PGF₂ α , as well as difference in breed and other management conditions.

Table 5. Comparison on diameter of uterine body (Mean \pm SE) in group I and group II during postpartum cows assessed by ultrasonographic examination (n=10)

Postpartum days	Diameter of uterine body (mm)		t-value (P-value)
	Group 1	Group 2	
20	34.58 ^a \pm 2.02	34.99 ^a \pm 1.25	0.171 ^{ns} (0.866)
30	31.06 ^b \pm 1.07	32.49 ^b \pm 1.24	0.876 ^{ns} (0.392)
40	30.43 ^b \pm 1.07	28.94 ^c \pm 0.80	1.116 ^{ns} (0.279)
50	30.10 ^b \pm 1.09	28.65 ^c \pm 0.68	1.122 ^{ns} (0.277)
60	29.57 ^b \pm 1.14	27.58 ^c \pm 0.43	1.627 ^{ns} (0.131)
F-value (P-value)	9.354** (0.006)	23.754** (<0.001)	

** Significant at 0.01 level; ns non-significant

Means having different letter as superscript differ significantly within a column

The ultrasonographic examination of the uterine body revealed that uterine involution was completed between 20–30 days postpartum within Group I and 30–40 days postpartum in Group II. However there no statistically significant difference between Group I and II, indicates that the administration of PGF₂ α on day seven postpartum have no significant effect on uterine involution. This was similar with Stephan (2010), stating that the administration of PGF₂ α on seventh day postpartum have no effect on hastening uterine involution and suggested that this might be due to the downregulation of PGF₂ α target cells after continuous exposure to the endogenous PGF₂ α during calving.

On the other hand, Abdel-Khalek et al. (2015) reported a significant reduction ($P<0.05$) in uterine body diameter in PGF₂ α -treated cows by day 21 postpartum, compared to day 28 in untreated cows. This accelerated involution observed in the PGF₂ α group may be attributed to enhanced myometrial contractions stimulated by the exogenous administration of PGF₂ α .

These differences on the observation of various authors might be due to the difference in dosage and time of administration of PGF₂ α , as well as difference in breed and other management conditions.

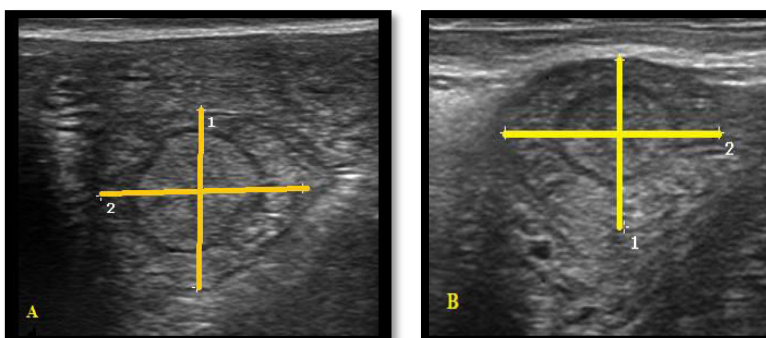


Figure 1. uterine body diameter on 20 dpp (A=31.43mm) and 60 dpp(B=26.71mm)

Diameter of uterine horns

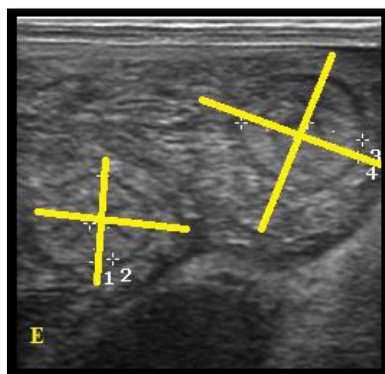


Figure 2 Uterine lumen: previously gravid and previously non gravid

Table 6. Comparison on diameter of previously gravid and non-gravid uterine horns (mean \pm SE) in postpartum cows (n=10, between groups)

Day	Previously gravid		
	Group I	Group II	t-value (P-value)
20d	28.84 ^a \pm 0.76	30.08 ^a \pm 1.21	0.144 ^{ns} (0.887)
30d	26.76 ^b \pm 0.77	26.88 ^b \pm 1.34	0.144 ^{ns} (0.887)
40d	26.32 ^b \pm 0.97	25.07 ^c \pm 0.86	0.965 ^{ns} (0.347)
50d	25.86 ^b \pm 1.04	24.77 ^c \pm 0.85	0.808 ^{ns} (0.43)
60d	25.77 ^b \pm 0.95	24.01 ^c \pm 0.59	1.574 ^{ns} (0.133)
F-value (P-value)	9.087** (<0.001)	15.072** (<0.001)	

** Significant at 0.01 level; ns non-significant; Means having different letter as superscript differ significantly within a column

Comparison between the diameter of previously gravid horns and non-gravid horns of group I and II were depicted in table 6. From the comparative data on diameter of uterine horns, it is inferred that the administration of PGF₂ α have no significant effect on hastening the involution of previously gravid as well as in previously non-gravid horns. This was similar in the study of Hendricks et al. (2006) stating that PGF₂ α treatment twice on days 7 and 14 post-partum and once daily on days 22 and 35 post-partum did not yield any faster uterine horn involution. Also, according to Hirsbrunner et al. (2006), there was no positive impact on hastening the involution of uterine horns after administration of PGF₂ α or a combination of PGF₂ α and PGE₂ α between 21 and 35 days after calving.

According to Iqbal et al. (2003), Elsheikh and Ahmed (2005) and various other authors suggested that the PGF₂ α had a significant effect on the uterine body involution, this was dissimilar in current study. This might be due to the difference in dosage and postpartum day on which the PGF₂ α was administered. Stephan et al. (2019) similarly suggested that the postpartum administration of PGF₂ α on seven day postpartum had no effect on the uterine horn involution and also suggested that this might be due to the downregulation of PGF₂ α target cells after continuous exposure to the endogenous PGF₂ α during calving.

Uterine lumen

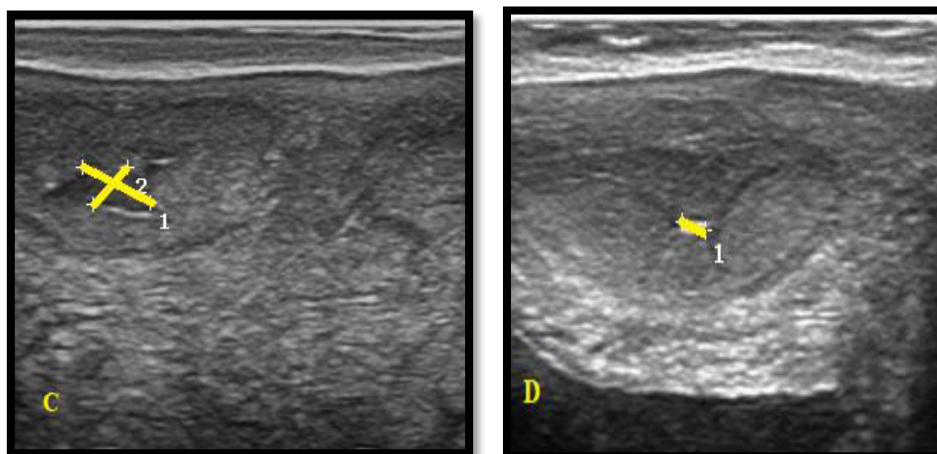


Figure 3 Uterine lumen on 20 dpp (C=6mm) and 30 dpp (D=1.3mm)

Three out of ten animals (30%) in group II had a uterine lumen more than 2 mm in diameter containing echogenic fluid during day 20 postpartum. None of the animals had fluid in the uterine lumen in group I during the study, and none of the animals in group II had fluid in the uterine lumen after 30 dpp. This was suggestive of early cleansing of the uterine debris in cloprostenol sodium-treated cows.

This was in accordance with Carbonari et al., (2024), administration of $\text{PGF}_{2\alpha}$ during early postpartum enhanced the uterine contraction and resulted in early clearance of fluid in the uterus. According to Jyoti et al. (2012), excess fluid during the postpartum period denoted inadequate uterine clearing and uterine pathology.

Endometrial thickness

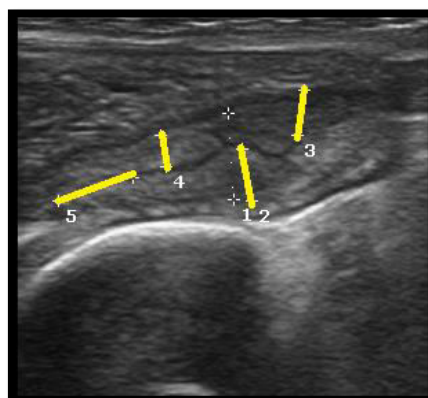


Figure 4 Endometrial thickness 20 dpp

Table 7. Endometrial thickness between group I and group II (ME \pm SE)

Postpartum day	Endometrial thickness (mm)		t-value (P-value)
	Group I	Group II	
20	10.88 ^a \pm 0.33	10.40 ^a \pm 0.30	1.078 ^{ns} (0.295)
30	8.65 ^b \pm 0.26	8.29 ^b \pm 0.27	0.973 ^{ns} (0.344)
40	6.68 ^c \pm 0.14	7.08 ^c \pm 0.25	1.414 ^{ns} (0.174)
50	6.42 ^c \pm 0.22	6.42 ^d \pm 0.13	0.012 ^{ns} (0.991)
60	6.77 ^c \pm 0.48	6.19 ^d \pm 0.16	1.146 ^{ns} (0.276)
F-value (P-value)	44.838** (<0.001)	107.13** (<0.001)	

** Significant at 0.01 level; ns non-significant

Means having different letter as superscript differ significantly within a column

A progressive decline in uterine wall thickness was observed from day 20 to day 60 postpartum in both PGF₂ α -treated (Group I) and untreated (Group II) cows. The highest thickness was recorded on day 20 in both groups (10.88 \pm 0.33 mm in Group I and 10.40 \pm 0.30 mm in Group II), followed by a gradual reduction through day 30 (8.65 \pm 0.26 mm and 8.29 \pm 0.27 mm), day 40 (6.68 \pm 0.14 mm and 7.08 \pm 0.25 mm), and day 50 (both 6.42 mm), reaching the lowest values on day 60 (6.77 \pm 0.48 mm in Group I and 6.19 \pm 0.16 mm in Group II).

However, statistical analysis revealed no significant differences between the groups on any of the days examined, indicating that PGF₂ α administration had no apparent effect on endometrial thickness during the postpartum period. Despite numerical differences, the similarity in patterns between the two groups suggests that the natural course of uterine involution proceeded independently of treatment.

Within group analysis showed a significant reduction in uterine wall thickness up to day 30 in Group I and up to day 40 in Group II (P <0.001). This indicates a marginal effect of treatment within both groups. Nevertheless, the lack of intergroup significance implies that PGF₂ α did not influence the overall endometrial regression pattern.

On day 40, uterine wall thickness observed in Group I (6.68 \pm 0.14 mm) was similar to the 6.01 \pm 0.24 mm reported by Praveen (2016) in PGF₂ α -treated cows on the same day postpartum. The values observed in the present study fall below the range of those reported by Mochow and Olds (1966), who found an average uterine thickness of 7.32 \pm 1.8 mm. Cengic et al. (2012) reported even higher values (8.42–9.02 mm) during 38–45 days postpartum, these differences possibly due to breed variation, management practices, or undetected subclinical conditions.

V. CONCLUSION

This study assessed the impact of early postpartum cloprostenol sodium (PGF₂ α analogue) administration on uterine involution and ovarian rebound in crossbred dairy cows. Results showed that while treatment did not significantly accelerate the involution of the cervix, uterine body, or uterine horns, as measured by per-rectal examination and ultrasonography, it did promote earlier clearance of intrauterine fluid and significantly hasten the resumption of ovarian activity. Thus, cloprostenol sodium primarily benefited postpartum recovery by supporting uterine cleansing and earlier return to ovarian cyclicity, rather than markedly affecting anatomical uterine regression. These findings suggest PGF₂ α analogues can enhance reproductive efficiency mainly through improved uterine health and fertility restoration, rather than by speeding up overall uterine involution. Adoption should consider herd conditions and economic viability.

Additional research with larger groups and varied protocols is recommended to further optimise postpartum reproductive management in dairy cows.

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