B-mode and Doppler Ultrasonographic Assessment of Uterine Involution in Ewes Treated with Two Different Doses of ProstaglandinF$_{2\alpha}$

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ABSTRACT

***Background*:** Several studies consisted of *postmortem* evaluations and B-mode ultrasonography have been performed on ovine uterine involution. However, researches with Doppler ultrasonography are very limited in ewes. Doppler ultrasonography is a non-invasive method which provides information about vascular dynamics of the tissues which cannot be examined by B-mode ultrasonography. The aim of the study was to evaluate the effects of two different PGF$_{2\alpha}$ doses on uterine measurements by real time B-mode ultrasonography; and on uterine artery hemodynamics by pulsed-wave Doppler analysis during postpartum uterine involution in ewes.

***Materials, Methods & Results*:** The study was conducted with 30 primiparous Kivircik ewes which lambed singleton without any complication. The ewes were randomly divided into three groups (n= 10 for each group). A single i.m. injection of 125 μg/sheep PGF$_{2\alpha}$, 75 μg/sheep PGF$_{2\alpha}$, and 1.0 mL/sheep sterile saline solution were administered to Group 1, 2, and 3, respectively. The day of parturition was considered as the first day of the study. Examinations were performed on days 1, 2, 3, 7, 14, 21 and 28. Diameters of previously gravid horn and caruncles were measured by real time B-mod ultrasonography. Presence of lochia was also noted. Uterine artery pulsatility index (PI), resistance index (RI), systolic/diastolic ratio (S/D) values were measured by pulsed-wave Doppler ultrasonography. The one-way analysis of variance and Duncan's test were used for statistical analysis. The mean previously gravid horn diameters of ewes were 8.30 ± 0.16 cm and 1.53 ± 0.07 cm on day 1 and day 28, respectively. Previously gravid horn and caruncle diameters had a similar declining pattern in all groups as involution period proceeded. Involution was mostly completed by day 21. More than 50% reduction in uterine size was achieved in prostaglandin administered groups by day 7. Caruncles were not able to be identified after the second week postpartum. Lochia was observed for a longer period in control group. Uterine artery PI and RI showed fluctuations throughout involution period with a similar pattern among groups. S/D values progressively increased until day 14, then showed a decreasing pattern.

***Discussion*:** The effects of different PGF$_{2\alpha}$ doses on uterine measurements and uterine artery hemodynamics during postpartum period were compared in ewes for the first time. The uterine size reduction in prostaglandin administered groups suggested that both PGF$_{2\alpha}$ doses were effective in uterine involution. The last observation of lochia in uterine cavity was achieved by day 7 in prostaglandin administered groups, suggesting both PGF$_{2\alpha}$ doses trigger uterine contractions which lead to the removal of uterine content. Automatic measurements by Doppler device were taken in order to provide uniformity and to prevent operator-based bias. The significantly higher uterine artery PI value found in Group 1 on day 1 might suggest the stimulatory effect of PGF$_{2\alpha}$ administration on uterine contractility synergitically with already released endogenous PGF$_{2\alpha}$. Uterine artery PI and RI showed fluctuations throughout involution period and reached their peak values on day 14. The increasing S/D values up to day 14 indicated increasing diastolic flow, increasing resistance and decreasing blood perfusion in prostaglandin administered groups. Prostaglandin administered groups tended to show higher hemodynamic parameters throughout the study which suggested a vasoconstrictor effect of PGF$_{2\alpha}$. In conclusion, PGF$_{2\alpha}$ administration on the day of parturition might have constrictor effects both on uterine artery and myometrium which leads to a reduction in uterine blood flow and a rapid decline in uterine size especially during early puerperium even with a reduced dose.

Keywords: Doppler, involution, prostaglandin F$_{2\alpha}$, sheep, ultrasound, uterine artery.

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INTRODUCTION

Puerperium is the period starts from delivery of the placenta and continues until the genital system returns to its nonpregnant state. The morphological involution is generally completed within 20-25 days in sheep [28]. However, the duration of this period may vary between 17 to 30 days [19].

Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) administration has several indications in ovine reproduction. Prostaglandin-based protocols are one of the methods used in synchronization programs via its luteolytic effect [1,14,29]. Although exogenous prostaglandins do not induce parturition in the ewe unlike other ruminants, endogenous $PGF_{2\alpha}$ plays important role for uterine contractility during parturition [15,21,35]. Additionally, $PGF_{2\alpha}$ can be used to treat intrauterine fluid accumulation [8], or to hasten uterine involution [2].

Real-time ultrasonography is a non-invasive, safe and commonly used technique which allows visualization of internal structures in animal diagnostics and research [27]. It has become a routine method for evaluation of reproductive system in ewes [34]. However, Doppler ultrasonography provides information about vascular dynamics of the tissues which cannot be examined by B-mode ultrasonography [27,30]. To the best of authors' knowledge, any possible effect of $PGF_{2\alpha}$ administration on uterine involution enhancement has not been investigated by Doppler ultrasonography in ewes yet. It was aimed to evaluate the effects of two different $PGF_{2\alpha}$ doses on uterine measurements by real time B-mode ultrasonography; and on uterine artery hemodynamics by pulsed-wave Doppler analysis during postpartum uterine involution in ewes.

MATERIALS AND METHODS

Animals and study management

The study was conducted with thirty primiparous Kivircik ewes [2-3 years old, with a mean body condition scoring (BCS) of 3.28/5 according to Russel *et al*. [33]] in the northern hemisphere. The ewes who lambed singleton without any complication were used in the study. Parturitions took place in november. All ewes were nursing and kept with their lambs. The ewes were fed with a complete diet prepared according to their nutritional requirements. Access to water and mineral salt was *ad libitum*.

The ewes were randomly divided into three groups (n= 10 for each group). Group 1 and Group 2 received a single i.m. injection of 125 µg/sheep and 75 µg/sheep cloprostenol[1], respectively. A 1.0 mL/sheep dose of sterile saline solution was administered i.m. to Group 3 as a control group. Injections and the first ultrasonographic examination were done within first 10 h postpartum. The day of parturition was considered as the first day of the study. The ultrasonographic examinations were performed on days 1, 2, 3, 7, 14, 21 and 28.

Uterine measurements

Diameters of previously gravid horn and caruncles were measured by real time B-mode ultrasonography[2]. Ewes were examined in standing position. Ultrasonographic evaluations were performed transcutaneously from caudoabdominal region on the first week postpartum for better visualization of enlarged tissue, while the rest of the examinations were done transrectally after shrinkage of the uterus, as described by Hauser & Bostedt [19] and Ioannidi *et al*. [22]. A microconvex transducer (5-8 mHz, scanning depth: 10 cm) and a linear probe fixed to an extender rod (10 mHz, scanning depth: 7 cm) were used for transcutaneous and transrectal ultrasonography, respectively. For transrectal examination, faecal pellets were removed and 10 mL of coupling gel was introduced intrarectally. The cranial pole of the urinary bladder was used as a guide for uterus, then the probe was moved laterally around its longitudinal axis.

The previously gravid horn was identified by its larger diameter on day 1. The mean size of caruncles were determined by measurement of at least three caruncle diameters. Presence of intrauterine content was also noted.

Doppler examination of uterine artery

Doppler examination of uterine artery was performed transrectally in standing position as described by Elmetwally *et al*. [10]. The color Doppler mode was used to identify the localization of uterine artery. Uterine artery was detected craniolateral to urinary bladder, at the end of the brach of external iliac artery. Once the optimum color flow was achieved, the pulsed-wave Doppler function was activated using 6.6 mHz frequency and the sample gate was positioned inside the vessel. The insonation angle was set <60°. After observing at least three consecutive traces without

artifacts, the image was frozen and pulsatility index (PI), resistance index (RI), systolic/diastolic ratio (S/D) values were measured automatically by the device.

Statistical analysis

The SPSS 20.0 packet analysis program[3] was used for statistical analysis. The one-way analysis of variance was used to determine whether there were any statistically significant differences between study groups. Duncan's test was used to measure the significance levels for the differences between PI, RI, S/D levels; uterine and caruncle diameters. The significance level was accepted as $P < 0.05$.

RESULTS

Uterine measurements

The ultrasonographic examination for uterine measurements were performed transcutaneously on the first three days postpartum. On day 7, it was possible to visualize the entire uterus by transrectal ultrasonography.

The mean previously gravid horn diameters of ewes were 8.30 ± 0.16 cm and 1.53 ± 0.07 cm on day 1 and day 28, respectively. Previously gravid horn and caruncle diameters had a similar declining pattern in all groups as involution period proceeded. A significant difference in uterine measurements was existed only on day 3 ($P < 0.05$) where control group had a larger previously gravid horn diameter than prostaglandin groups (Figure 1). The results indicated that more than 50% reduction in uterine size was achieved in prostaglandin administered groups by day 7. Involution was mostly completed by day 21, as previously gravid horn diameters were measured 2.05 ± 0.19 cm, 2.23 ± 0.19 cm, and 2.33 ± 0.10 cm in Group 1, Group 2 and Group 3, respectively (Figure 1).

The mean diameter of caruncles of all animals decreased from 2.45 ± 0.06 cm (day 1) to 1.16 ± 0.03 cm (day 7). Caruncles were not able to be identified after the second week postpartum. The caruncular diameters of groups were given in Figure 2. Lochia was observed in the uterine cavity up to 7 days in prostaglandin administered groups. However, intrauterine fluid accumulation was seen up to 14 days postpartum in control group.

Figure 2. The mean diameters of caruncles of Group 1, Group 2 and Group 3 during postpartum period in ewes.

Doppler examination of uterine artery

Pulsed-wave Doppler ultrasonographic examinations were performed by transrectal scanning. An early diastolic notch in uterine artery was detected in all ewes (Figure 3). PI and RI showed fluctuations throughout involution period with a similar pattern among groups. S/D values progressively increased until day 14, then showed a decreasing pattern. Prostaglandin administered groups tended to show higher PI, RI and S/D values. Differences and statistical significance between uterine artery PI, RI, S/D values of groups were given in Table 1.
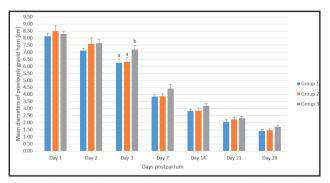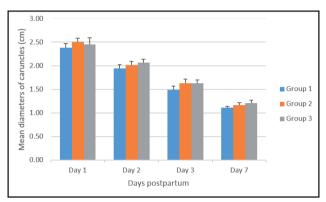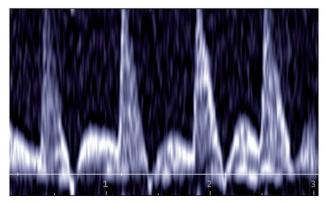

Figure 1. The mean diameters of previously gravid horn of Group 1, Group 2 and Group 3 during postpartum period in ewes. Different superscript letters indicate significant differences ($P < 0.05$).

Figure 3. Early diastolic notching in uterine artery waveform in postpartum ewes.

Table 1. The mean uterine artery Pulsatility Index (PI), Resistance Index (RI), Systolic: Diastolic Ratio (S/D) of Group 1, Group 2 and Group 3 during postpartum period in ewes.

	Day	Group 1 Mean ± SE	Group 2 Mean ± SE	Group 3 Mean ± SE	Sig
Pulsatility Index (PI)	1	1.85 ± 0.02[a]	1.79 ± 0.02[b]	1.78 ± 0.02[b]	*
	2	1.81 ± 0.01[a]	1.79 ± 0.02[a]	1.71 ± 0.02[b]	**
	3	1.79 ± 0.01	1.78 ± 0,03	1.72 ± 0.02	NS
	7	2.24 ± 0.06[a]	2.14 ± 0.04[a]	1.96 ± 0.06[b]	**
	14	2.54 ± 0.04	2.41 ± 0.05	2.50 ± 0.06	NS
	21	2.37 ± 0.07	2.29 ± 0.07	2.30 ± 0.03	NS
	28	2.17 ± 0.04	2.13 ± 0.04	2.09 ± 0.03	NS
Resistance Index (RI)	1	0.805 ± 0.003[a]	0.797 ± 0.007[ab]	0.784 ± 0.006[b]	*
	2	0.783 ± 0.007	0.777 ± 0.006	0.771 ± 0.006	NS
	3	0.777 ± 0.006	0.765 ± 0.005	0.763 ± 0.005	NS
	7	0.819 ± 0.006[a]	0.792 ± 0.008[b]	0.791 ± 0.005[b]	**
	14	0.843 ± 0.006[a]	0.829 ± 0.004[ab]	0.815 ± 0.005[b]	**
	21	0.822 ± 0.004[a]	0.81 ± 0.006[ab]	0.80 ± 0.005[b]	*
	28	0.807 ± 0.004[a]	0.787 ± 0.008[b]	0.791 ± 0.003[ab]	*
Systolic:Diastolic Ratio (S/D)	1	4.45 ± 0.21[a]	3.80 ± 0.28[ab]	3.24 ± 0.26[b]	**
	2	6.31 ± 0.24[a]	5.72 ± 0,29[a]	4.87 ± 0.31[b]	**
	3	8.40 ± 0.53[a]	7.14 ± 0.27[ab]	6.73 ± 0.48[b]	*
	7	11.62 ± 0.42	11.30 ± 0.50	10.63 ± 0.42	NS
	14	15.66 ± 0.62	15.07 ± 0.44	14.48 ± 0.50	NS
	21	12.04 ± 0.48	11.47 ± 0.51	10.54 ± 0.78	NS
	28	9.26 ± 0.30	8.25 ± 0.30	7.90 ± 0.79	NS

SE: Standard error; Sig: significance; NS: not significan ($P > 0.05$); *: $P < 0.05$; **: $P < 0.01$. Different superscript letters indicate statistical significant differences.

DISCUSSION

Ovine uterine involution has been investigated intensely by B-mode ultrasonography [13,17,19,20,26,40]. Finally, researches performed on Doppler ultrasonography in ewes have gained momentum in recent years. The most frequently used Doppler modes in sheep practice are color Doppler and pulsed-wave Doppler. Color Doppler ultrasonography allows qualitative evaluation of tissue vascularization, direction and velocity of blood flow, whereas pulsed-wave Doppler ultrasonography mode is preferred for quantitative evaluations of tissue hemodynamics via various spectral parameters [11,27,30]. Several studies have been done on pulsed-wave Doppler sonographic examinations in sheep reproduction as maternal and/or fetal blood flow characterization during pregnancy [3,4,10,12,36]; and uterine hemodynamics during perinatal-postpartum period [9,22,23,38]. Effects of PGF$_{2\alpha}$ administration were studied on uterine blood flow by invasive techniques [5,6], and on uterine involution by B-mode ultrasonography [2]. This is the first report of uterine artery hemodynamics after administration of different PGF$_{2\alpha}$ doses during uterine involution in ewes.

The complete uterine involution is determined as transversal diameter of uterine horns ≤ 2 cm and absence of any fluid accumulation in uterus [40]. The required time for the completion of uterine involution varies between studies. Mc Entee [25] reported that it takes a long period of time, even up to 49 days in ewes according to his histological findings. On the contrary, involution process was reported to be ended between 14-21 days in native Pantanal sheep [13]. Many variables like breed, lambing season, parity and suckling may affect the duration of postpartum period. For instance, the uterine involution was completed by day 35 in primiparous ewes, whereas it took longer time in pluriparous ones [40]. The time span for the completion of uterine involution was found 29.4 ± 1.2 days in ewes which lambed in february, while this process took 33.9 ± 1.1 days in ewes that lambed in june [20]. In Barbary ewes, animals which lambed in march completed involution earlier than in ones lambed in january and february (28 vs. 35 days, respectively) [26]. In the present study, uterine involution was mostly completed by day 21 in primiparous Kivircik ewes that lambed in november.

PGF$_{2\alpha}$ and its analogues are quite favorable and ethical agents due to their pulmonary metabo-

lism [24,29]. As fertility parameters of PGF$_{2\alpha}$-treated ewes are low, several studies were performed to determine the appropriate luteolytic dose of prostaglandins [7,29,31,32,39]. The luteolytic effect of PGF$_{2\alpha}$ treatment may vary depending on the day, dosage, frequency and route of administration in ewes [31]. The commonly used PG analogues are cloporostenol and luprostiol. The recommended doses of these PG analogues are 125 µg cloprostenol and 7.5 mg luprostiol in sheep [1]. Pope & Cardenas [31] obtained similar luteolytic results from 5 and 10 mg dinoprost, a PG analogue, on days 3.5 and 4 of estrous cycle. A dose of 6 mg/sheep PGF$_{2\alpha}$ was reported to be effective for luteolysis in ewes, nevertheless, any PG analogue was not specified [7]. Endogenous PGF$_{2\alpha}$ has crucial role during parturition. As the fetal cortisol increases after maturation of hypothalamo-pituitary-adrenal axis, placental progesterone converts into estrogen. One of the roles of estrogen is the uterine release of PGF$_{2\alpha}$. Endogenous PGF$_{2\alpha}$ plays important role at the onset of parturion by leading to relaxin release, luteolysis and finally increase in responsiveness of myometrium to oxytocin [21]. It was reported that the lower plasma PGF metabolite concentrations started to increase 3 days prior to lambing, and peaked during parturition. Although these levels decreased gradually during the first 3 postpartum days, they were maintained for three weeks. Finally a decreasing model was observed again during the 4th week postpartum. The author suggested the stimulatory effect of prostaglandins on uterine involution [15]. Another researcher reported that the high postpartum plasma PGF metabolite profiles were decreased to basal values by day 9 [35]. Interestingly, Wade & Lewis [39] drew attention to the stimulating effect of exogenous PGF$_{2\alpha}$ administration on utero-ovarian release of PGF$_{2\alpha}$. The effects of PGF$_{2\alpha}$ and oxytocin treatment on uterine involution was compared in a study. A dose of 7.5 mg/sheep PGF$_{2\alpha}$ was accomplished more rapid involution than oxytocin administered group with a decrease of uterine diameter from 6.50 ± 0.45 cm to 1.1 2 ± 0.12 cm within 4 weeks postpartum [2]. In the presented study, in the light of information mentioned above, it was supposed that exogenous PGF$_{2\alpha}$ administration on the day of parturition may facilitate uterine contractility synergitically with highly released endogenous PGF$_{2\alpha}$, and a reduced dose of PGF$_{2\alpha}$ may exert similar effect on uterine involution. Therefore, it was aimed to compare the effects of two different doses of cloprostenol on uterine measurements and uterine artery hemodynamics which reflect the tissue perfusion during postpartum period in ewes.

Ultrasonographic evaluation of postpartum uterus reflects the real-time status of the tissue. The method enables interpretation of involution process by diameter measurements and intrauterine content visualization. The mean previously gravid horn diameter of all ewes were measured 8.30 ± 0.16 cm on day 1 postpartum. The reduction in uterine size was more than 50% by day 7 in prostaglandin administered groups, suggesting both PGF$_{2\alpha}$ doses were effective in uterine shrinkage during early puerperium. Transcutaneous approach allows better ultrasonographic evaluation of uterus during first week of postpartum period; and transrectal technique is recommended for subsequent days, especially after the 11th day postpartum [19]. In the presented study, it was possible to visualize the entire uterus transrectally on day 7. According to Hauser & Bostedt's [19] findings, 50% of uterine size was rapidly regressed within first 5 days, subsequently the uterine involution was completed by day 17 postpartum. However, 50% reduction of postpartum uterus was also reported by day 9 [9], and by day 14 [2]. The previously gravid horn diameters on day 7 were 3.85 ± 0.15 cm, 3.87 ± 0.20 cm, and 4.42 ± 0.28 cm in Group 1, 2, and 3, respectively (Figure 1). Diameter of previously gravid horn was found 4.02 ± 0.19 cm on day 7 postpartum in a study conducted on Tuj ewes lambed in winter. The measurements were performed on the bases of the anechoic lines along the endometrium, regardless of the uterine wall layers [17]. The differences in uterine size reduction between studies may arise from not only diversities in breeds, seasons, treatment protocols, but methodologies as well.

Previously gravid uterine horn diameter was measured 7.72 ± 0.3 cm on the day of parturition, and decreased to 1.87 ± 0.1 cm on day 18 postpartum in German Merino ewes [9]. Uterine secretions were gradually decreased within two weeks in the same study. After seperation of the placenta, a caruncular tissue degeneration occurs. Autolysis and liquefaction in the superficial layers of caruncles lead to lochia [28]. Despite the lochia was observed ultrasonographically up to 14 days in control animals, intrauterine content

was not detected after the 7th day of the study in prostaglandin administered groups. This finding reveals that PGF$_{2\alpha}$ administration triggers uterine contractions which lead to the removal of uterine content and facilitates involution during early postpartum period even with a reduced dose.

According to postmortem evaluations, degenerated caruncles have similar -but less edematous- appearance on day 14 postpartum. Caruncles resume a clean, glistening surface following the necrosis of their whole superficial surface by day 16, or sometimes necrotic caruncular tissue might still attached until day 21. Finally, regeneration of the caruncles are completed by reepithelization on day 28 postpartum [25,28]. Ahmed *et al.* [2] visualised caruncles until 10 days postpartum in Awassi ewes. In another study, caruncle diameters were measured as 2.02 ± 0.16 cm on the first day postpartum and regressed to 1.24 ± 0.17 cm on day 8 [19]. Although caruncles were not able to be identified after the 8th day of postpartum in the mentioned study, Ioannidi *et al.* [23] reported the last ultrasonographic observation of caruncles on day 20. Caruncle diameters did not exhibit significant differences between groups in the presented study. The mean caruncular diameter of all ewes was 2.45 ± 0.06 cm on day 1 and reduced to 1.16 ± 0.03 cm on day 7. Caruncles could not be identified ultrasonographically on day 14. Although any other examination was not performed between day 7 and day 14, the findings of the presented study are compatible with Hauser & Bostedt's [19] observations.

PGF$_{2\alpha}$ was reported to have dose dependent effects on uterus as reduction in uterine blood flow; increase in uterine tonus and contractile activity after its local intra-arterial infusion in pregnant and nonpregnant ewes [5,6]. PGF$_{2\alpha}$ had a vasoconstrictor effect on uterine artery which suggested an increase in vascular resistance [5]. Electromagnetic flow probes were used to measure uterine blood blow in the mentioned studies [5,6]. Eventually, Doppler ultrasonography enables to get information about blood flow without need for invasive methods.

PI, RI and S/D values evaluated in the presented study are the frequently used parameters for semi-quantitative evaluation of arterial blood flow velocity waveforms. PI defines the degree of pulse waveform damping, while RI is the resistance indicator of the vascular bed [27]. In other words, increased RI indicates a decreased blood perfusion in addition to an increased resistance in the examined artery, whereas increased PI reflects a decreased perfusion of the distal tissues [16]. S/D indicates the ratio of systolic and diastolic phases of the blood flow [30]. These Doppler parameters are especially important for gynecological evaluations as they are angle-independent. The increase in these parameters indicates decreased vascular perfusion and vice versa [11,30]. Several discrepancies have been reported between automatic and manual evaluation of Doppler velocity measurements. Beltrame *et al.* [4] reported underestimated PI and S/D values of ovine uterine artery in manual method and suggested that the overestimation of end diastole and underestimation of systolic peak resulted in differences in S/D ratio. On the contrary, Unal *et al.* [37] reported underestimation of systolic peak and RI; and overestimation of end diastole in automatic calculation compared to manual method. Their results also showed interobserver variability. Automatic measurements by Doppler device were taken in order to provide uniformity and to prevent operator-based bias in the presented study.

As metabolic requirements of placenta and foetus are ceased after parturition, the blood flow to uterus changes significantly [9]. An early diastolic notch is a normal finding in non-pregnant uterine artery [18]. The spectral analysis of uterine blood flow identified a marked systolic peak which was followed by an early diastolic reversed flow in the presented study (Figure 3). Although both PI and RI are closely related to the hemodynamics of examined tissue, PI is more suitable when a part or full of diastolic flow is absent [16]. Uterine artery PI values increased on the 7th day of postpartum period, and peaked on day 14. PI values showed a decreasing pattern on subsequent examinations. Similarly, uterine artery PI values showed an increasing pattern after the 6th day of postpartum period, however this index was decreased on day 21 postpartum. Alterations in PI value were attributed to the changes in blood flow volume [9]. The significantly higher PI value of Group 1 on the day of parturition ($P < 0.05$) may reveal the stimulatory effect of PGF$_{2\alpha}$ administration on uterine contractility together with endogenous PGF$_{2\alpha}$. Although control group had lower PI values than prostaglandin administered ewes throughout the study, the differences was significant also on days 2 and 7 ($P < 0.01$) [Table 1]. According

to the findings of the presented study, administration of $PGF_{2\alpha}$ was suggested to exhibit constrictor effects both on uterine artery and myometrium which leads to a rapid decline in uterine size especially during early puerperium.

Hemodynamics of uterine artey was investigated from mid-gestation through postpartum 30 days in ewes [38]. Although several spectral parameters were recorded, there were no statistical differences for uterine artery PI, RI and S/D parameters until postpartum period. These parameters showed an increasing pattern after parturition. PI and RI reached their peak value on day 15 postpartum. Additionally, the uterine artery diameter and blood volume were decreased, and finally stabilized by day 15 postpartum. The uterine artery blood flow was found to be negatively correlated with PI, RI and S/D values. Hemodynamic parameters of uterine artery in the presented study were compatible with results of Veiga *et al*. [38]. Uterine artery PI and RI showed fluctuations throughout involution period and reached their peak values on day 14. The increasing S/D values up to day 14 indicated increasing diastolic flow, increasing resistance and decreasing blood perfusion in prostaglandin administered groups. Significant differences occured in PI, RI and S/D values between groups, as mentioned in Table 1. Prostaglandin administered groups tended to show higher hemodynamic parameters throughout the study which clarifies increasing resistance and decreasing perfusion in uterine artery. Although uterine artery diameters were not measured in the presented study, these higher values reflect vasoconstrictor effect of $PGF_{2\alpha}$ administration which leads to the reduction in uterine blood flow. The rapid uterine size reduction observed in $PGF_{2\alpha}$ administered groups also proved the efficacy of exogenous $PGF_{2\alpha}$ on uterine involution. Veiga *et al*. [38] noted the vasodilatory effect on uterine artery was ceased after expulsion of placenta - the main source of hormones regulating pregnancy-, which leads to a marked decrase in uterine blood supply during the initial postpartum period. They suggested that the increase in PI, RI and S/D values during postpartum period reflects the morphological regression of the uterine tissue; and the reduction in uterine blood flow is essential for achieving its nonpregnant state.

$PGF_{2\alpha}$ administration after parturition may have beneficial effects from different perspectives too. The economical pressure on having three parturition within two years in sheep management necessitates the postpartum periods as short as possible [20]. Additionally, ewes with pregnancy toxaemia have larger caruncular diameter, endometrium thickness and uterine lumen diameter than healthy ewes [23]. In such conditions, postpartum $PGF_{2\alpha}$ administration may help uterine involution process and provide participation of all ewes to synchronization programs at the same time, considering the similar effect of reduced dosage found in the presented study.

CONCLUSIONS

In conclusion, the effects of different $PGF_{2\alpha}$ doses on uterine measurements and uterine artery hemodynamics during postpartum period were compared in ewes for the first time. The involution was mostly completed by day 21, however, more than 50% reduction in uterine size, and the last observation of lochia in uterine cavity were achieved by day 7 in prostaglandin administered groups. It has been suggested that both $PGF_{2\alpha}$ doses were able to trigger uterine contractions which lead to the removal of uterine content and facilitate involution process. Automatic measurements by Doppler device revealed higher uterine artery PI, RI, S/D values in prostaglandin administered groups, reflecting an increased resistance and a decreased perfusion in uterine artery. It has been suggested that $PGF_{2\alpha}$ causes vasoconstriction which decreases uterine blood supply. It has been concluded that exogenous $PGF_{2\alpha}$ administration on the day of parturition may exhibit constrictor effects both on uterine artery and myometrium which leads to a rapid decline in uterine size especially during early puerperium even with a reduced dose.

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