Reproductive and Economic Evaluation of Sexual Stimulation in Anestrus Period at a Farm Experiencing Neonatal Lamb Losses

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Abstract

Lamb deaths occurring in the neonatal phase, which covers the first four weeks after birth, cause serious economic losses for farms. This study was carried out on 140 Akkaraman-Kangal sheep that lost their lambs due to pneumonia and enteritis in the neonatal phase during the anestrus period. In the study, an intravaginal sponge containing progesterone was applied to the animals in Group 1 (n:70) on day 0, and 7 days after the application, the vaginal sponges were removed, and 263 µg PGF2α and 500 IU eCG (PMSG) hormone were applied. After removing the intravaginal sponge, rams were introduced for 7 days (between the days 8th and 14th). Without any manipulations to the animals in Group 2, the ram effect was utilized by performing simultaneous ram introduction with Group 1. To determine the reproductive response, the economic implications between the groups were compared by considering the reproductive parameters such as *oestrous* rate, pregnancy rate, multiple pregnancy rate, embryonic death rate, number of births, number of offspring, and fertility. The study group created a positive economic difference compared to the control group while analyzing the statistical differences in terms of each reproductive parameter between the study and control groups. When lamb losses are experienced in farms that build their profitability on lamb production, it was concluded that pregnancy should be achieved by sexual stimulation without waiting for the breeding season.

Introduction

Lamb deaths occurring in the neonatal phase, which covers the first four weeks after birth, cause serious economic losses for farms. To reduce labour costs in sheep farming, most farms have relinquished producing milk and dairy products. Milk, which is naturally endowed to ewes, is only used for the nutrition of the lambs through breastfeeding. In parallel to the decrease in the demand for wool in the recent years, the production of lambs has become the only factor that determines the profitability of sheep farm. Therefore, in terms of reproduction and profitability, the ewes must be immediately conceived within physiological limits in farms where lamb deaths are experienced (Gordon, 2017).

The neonatal stage, defined as the first four weeks postpartum, is a critical stage for lambs due to high morbidity and mortality. Lamb mortality in the neonatal stage is one of the most important economic losses for breeders operating in this branch of animal farming. Lamb deaths that occur in this period significantly reduce the farm inputs (Nash et al., 1997). Lamb deaths limit the development of sheep breeding globally and have still occurred at the levels of 15-20% today. It was found that the direct production losses caused by lamb deaths and the innovative strategies developed to reduce these deaths annually cost 540 million dollars in Australia (Flinn et al., 2020). More than 65% of lamb mortality in the neonatal period is multifactorial in etiology (Radostits et al., 2006). Diseases such as watery mouth disease, diarrhea, pneumonia, and umbilical cord inflammation are the leading infectious diseases that cause lamb deaths in the early postpartum (Scott PR, 2001). Today, sheep farming is one of the primary sources of economic income for countries with harsh climates and infertile lands, especially for developing countries. Reproductive performance can be increased with the effective use of oestrous

synchronization protocols, and thus by increasing lamb production, they provide direct economic gain to sheep breeders (Abecia et al., 2011; Amiridis and Cseh, 2012; Ghasemi-Panahi et al., 2016)

In sheep breeding, it is aimed to increase the fertility parameters by providing better efficiency with little expense or without increasing inputs. To achieve this, both the breeding process of sheep can be controlled, and their reproductive performance can be improved by using natural methods and various hormones (Özyurtlu and Bademkiran, 2010; Texeira et al., 2016).

This study aims to determine the effectiveness of the stimulation on reproductive and economic parameters during the early anestrus period by applying sexual stimulation to ewes that have lost their lambs in the neonatal period.

Materials And Method

Location

The study was carried out in a sheep farm – with the coordinates of 38.842174779662926, 37.28949932275392 – in Kalederesi Village of Gürün District of Sivas Province at an altitude of 1640.

Treatment Schedule

The material of this study has consisted of 140 Kangal sheep that became pregnant in autumn, gave birth in spring, and lost their lambs due to pneumonia and enteritis in about the first month (neonatal stage). At the beginning of the application, the average body weight was 44 ± 5 kg, and the BCS (Body Condition Score) was between 2.5-3.25. The animals were from 55 to 70 days postpartum. The body condition scoring method explained by Ferguson et al. (1994) was used, and the BCS values of these ewes were scored from 1 to 5.

14 Kangal rams were also used to perform mating by sexual stimulation since the study was conducted *in anestrus*. When the farm records were examined, it was found that no pregnancy was achieved, although the sheep were with rams during anoestrous period in previous years. Progesterone (P4) measurements were made in the blood samples taken before the applications. The P4 value of animals in both groups was < 1 ng/ml. 140 sheep experiencing neonatal lamb losses were divided into two equal groups within each group. By starting synchronization 1 month before (-30th day), the animals were grazed only at nights for 45 days, and by keeping the animals in their barns during daylight hours, exposure to daylight was reduced. Thus, we waited for the postpartum physiological process during this period, including uterine involution, endometrial regeneration, and bacterial elimination of the uterus.

In the study, the animals in Group 1 (n:70) were administered an intravaginal sponge (20 mg fluorogestone acetate, Chronogest®, MSD) containing progesterone on day 0. 7 days after the application, the vaginal sponges were removed, and 263 µg PGF2α (d-cloprostenol, Estrumate®, MSD) and 600 IU equine chorionic gonadotropin (eCG) (Chorono-Gest/PMSG, Intervet International B.V., Boxmeer, Netherlands) were administered. The rams were introduced 1 day after the intravaginal sponge

had been removed. On the 8th day of the study, the rams were separated from the herd. The animals in Group 2 were not manipulated, but they were just simultaneously introduced to the rams with the ones in Group 1 to benefit from the effect of ram.

Pregnancy examination

Following the rams were introduced, two pregnancy examinations were performed via trans-rectal on the 38th day and the transabdominal ultra-sonographic method on the 68th day. The trans-rectal and transabdominal examinations were achieved by using B-mode, linear-array ultrasonography device containing a 5.0-7.5 MHz rectal probe (Mindray DP50/Vet/US). The trans-rectal examinations were performed in the supine position. For the transabdominal examinations, the hairless area of the ventral abdominal wall just in front of the udder preferred for the placement of the probes. In the dorso-caudal direction of the udder, this area was thoroughly examined depending on whether pregnancy-related findings could be obtained or not. According to the gestation period in the ultrasonographic examination, after the detection of the gestational sac, the embryo/fetus, fluids, heartbeat, and placentomas, it was observed that the animal was pregnant. Lambing were followed and recorded.

Blood Analysis/assay

10 ml blood samples were taken from the vena jugularis to determine the progesterone level on the specified days of administration. After waiting for half an hour at room temperature, the blood samples were centrifuged at 3,000 revolutions/5 minutes in a cooled centrifuge, from each sample, blood was taken to Eppendorf tubes of 2 pieces of 1 ml and was stored at -80 °C until the measurement time. Progesterone measurement with analytical sensitivity ≤ 0.1 ng/ml and measurement range: 0.1 ng/ml-36.0 ng/ml progesterone was made by using the ARCHITECT Progesterone Chemiluminescence (7K77) Abbott assay and the fully automated ARCHITECT -i2000SR (Abbott) instrument via the Chemiluminescence Microparticle Immunoassay (CMIA)) method. The intra-assay coefficient of variation (CV) ranged from 3.4-5.5% to 1.6-2.2% for low and high progesterone concentrations respectively. Analyses were validated for Serum (in serum and blood collected in serum separator tubes) and Plasma (with Na heparin, Li heparin, and K EDTA anticoagulants) samples. Validation was not performed with other anticoagulants other than the specified anticoagulants.

Method to be Used for Economic Analysis

Findings from the animals included in the study will be analyzed by using the formula below. As a result of the formula, it will be checked whether the method applied is "more economical" according to the findings obtained from the animals in the control group.

Economic Difference;
$$EF = \sum M_1 - \sum M_2$$

Total Income of the Experimental Group;
$$\sum M_1 = (\sum Kg_1 - \sum P_1)$$

Total Income of the Control Group; $\sum M_2 = (\sum Kg_2 - \sum P_2)$

EF: income differences

M₁: The total economic income obtained as a result of the method applied to the animals in the experimental group

M₂: Total income from animals in the control group

$\sum Kg$: (Total lamb obtained x Market value*) / Current Dollar Rate**

$\sum P$: (Applied Treatment Cost*** + Travel Fee + Veterinarian Practice Fee + Labour Cost****) / Current Dollar Rate

* The current market price for lambs is included in the calculation separately for males and females.

** (TCMB, 2021).

*** The costs such as Progesterone sponge + 500 IU (international unit) eCG + 263 µg PGF2α + the consumable costs (injectors, cotton, alcohol, etc.) per animal were included in the account.

.**** Calculation was made based on the total working hours over the minimum wage for 2020 (Aile Calisma, 2020).

Apart from this Calculation, that the economic value of the new lambs included may add to the farm will approximately be calculated using the formula below.

$$\sum MA^* = A_d + A_{ey} + D_s + E_s + E_d$$

A_d: It was predicted that 80% of the female lambs could reach the ewe quality. The economic value of ewes was obtained by multiplying their number and market fair value.

A_{ey}: It is predicted that the females who reach the brood-level can give birth to one lamb within the first year and two lambs in the other year, and half of those born will be male and the other half will be female. It is also predicted that all of the lambs obtained will be sold at the age of 6 months and they will provide an income for the farm. The income value is obtained by multiplying the market sales value of the female and male animals in this category with the number of the lambs sold. The income values of the currently born ones were ignored while calculating A_{ey}.

D_s: It is predicted that 20% of the female lambs will be sold at the age of 6 months. Its economic value is obtained by multiplying the number of the sold ones and the market fair value.

E_s: It is predicted that 80% of the males will be sold to the market. Its economic value is obtained by multiplying the males sold and the market fair value.

E_d: It is predicted that 20% of the males can reach breeding qualification. The economic value of breeding males was obtained by multiplying them and market fair value.

* While calculating the value of A, the costs of all animals included in the formula (such as feeding, maintenance, electricity, water, veterinary/health) are calculated and subtracted from the economic value.

Statistical analysis

Statistical analysis of all the data obtained in the study was evaluated using SPSS 25 (IBM Corp. Released 2017, IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) statistical package program. First, it was checked whether the variables met the assumptions of normality and homogeneity with Shapiro Wilk and Levene tests, respectively. The single effect of the treatments on oestrous rate, pregnancy, fertility, and multiple pregnancy rates were analyzed using the chi-square test. Fisher's exact test was used when one of the expected cell values was less than 5. Litter size data were log-transformed to attain normal distribution and analyzed with the independent sample t-test. In all analyses, $P < 0.05$ was considered statistically significant.

Results

When the progesterone levels were examined, it was determined that there were no sheep with a P4 value above the luteal level (≥ 1 ng/ml) in both the experimental and control groups and that the P4 value of the animals in both groups was at the Subbase Level (< 1 ng/ml).

After completing the procedure of applications, reproductive parameters such as oestrus rate, pregnancy rate, multiple pregnancy rate, embryonic death rate, number of births, number of offspring, and fertility were compared to determine the reproductive response to the applications.

The parameters used in the interpretation of reproductive results were established as follows.

Oestrous rate: Number of animals showing oestrous in the group/Total number of animals in the group

Pregnancy rate: Number of pregnant animals in the group/Total number of animals in the group

Multiple pregnancy rate: Number of multiple pregnant animals in the group/ Total number of pregnant animals in the group

Births realized: Number of pregnant animals that completed pregnancy and gave birth

Offspring number: Number of offspring born from pregnant animals in the group

While a total of 46 lambs, 24 females and 22 males, were obtained in 32 births of pregnant animals in Group 1, a total of 5 lambs, 3 males and 2 females, were obtained in 5 births of pregnant animals in Group 2.

When the findings obtained in the study were evaluated, $\sum M_1$ was calculated as 33.271,40 TL (4.471,96 \$) and $\sum M_2$ was calculated as 4.575,7 TL (615,01 \$). The group with the treatment protocol earned an extra 28695.70 TL (\$3856.95) compared to the control group. In the light of the Calculation results, it was determined that the treated group achieved 88.15% better economic results than the control group. Considering the economic sustainability of livestock farms, this value seems to be significantly meaningful.

The effect of synchronization protocol on oestrous rates, pregnancy and fertility rates is presented in Table 1. oestrous rate and pregnancy rate in the first group were significantly higher than the second group. The fertility rate differences between groups were not significant due to the reduced number of lambing in the second group. Litter size in the first group was $1,42 \pm (0,11539)$, and similar to the fertility rate, there were no significant differences between the groups (Table 2).

Table 1

Oestrous response rate, pregnancy rates ewes on the day 30 post-mating, number of embryonic death and number of lambs following synchronization

Group Name	The number of animals in the group	The number of oestrous	The number of pregnancies (30th Day)	The number of multiple pregnancies	The number of births	The number of embryonic deaths	The number of offspring
Study (Group1)	70	51	33	11	32	1	46
Control (Group2)	70	7	5	-	5	0	5

Table 2. Oestrous (Mated / All), pregnancy (Pregnancies / All) and fertility rates (Pregnant / Mated) and number of pregnant versus non-pregnant ewes on the day 30 post-mating (pregnant/non-pregnant) a,b: Varied characters in the same row are different (P < 0.05).

		Groups		Total
		1	2	
Oestrous Rate	Positive	51 ^a (72,9%)	7 ^b 10,0%	58
	Negative	19 ^a (27,1%)	63 ^b (90,0%)	82
Total		70	70	140
Pregnancy Rate	Positive	33 ^a (47,1%)	5 ^b (7,1%)	38
	Negative	37 ^a (52,9%)	65 ^b (92,9%)	102
Total		70	70	140
Fertility Rate	Positive	32 ^a (62,7%)	5 ^a (71,4%)	38
	Negative	18 ^a (37,3%)	2 ^a (28,6%)	20
Total		51	7	58

Discussion

Lamb losses in the neonatal stage are substantial economic losses for sheep breeders worldwide (Nash et al., 1997).

The fact that sheep are not productively active in the anoestrous period is the most important problem of operating efficiency and profitability (Knights et al., 2001). It is aimed to get offspring twice a year or 3 times in 2 years by using various hormones to increase fertility and obtain more offspring in sheep (Kivrak et al., 2021; Lewis et al., 1996). It is known that the ovaries of sheep are not completely stagnant in terms of follicular dynamism; in other words, they are dynamic during the anoestrous period. It is known that Follicle-stimulating hormone (FSH) synthesis continues during this period and that there are fluctuations in follicular development in parallel with these FSH fluctuations (Bartlewski et al., 1998), and besides the continuation of follicular activity during the anoestrous period, it is possible to reach the production system in which pregnancies can be obtained by interventions to ovulation (Simões, 2015). Off-season oestrous induction methods are carried out based on the use of progesterone and its analogues with eCG. It is known that the pregnancies obtained with the use of P4 in aneestrous are less than the pregnancies in the synchronizations created with the use of P4 in the season (Wildeus, 2000). With the use of progesterone in sexual synchronization, the negative feedback effect of progesterone on gonadotrophin releasing hormone (GnRH) and luteinizing hormone (LH) is utilized, and when the P4 concentration drops suddenly, the LH concentration increases 30 times, and the dominant follicle becomes sensitive to LH. Thus, ovulation occurs (Kaçar et al., 2016). In this study, it was aimed to stimulate oestrous and create ovulation in the early anoestrous period by utilizing the effectiveness of progesterone on GnRH and LH, or to provide ovulation in a shorter period by combining it with

gonadotropins and PGF2 α . Thus, without wasting time, sexual stimulation was performed for the ewes that lost their lambs for various reasons. Reflections of the study in terms of reproductive and economic aspects were evaluated.

The use of progesterone and its analogues in synchronization protocols depends on keeping LH secretion under control by releasing progesterone like the corpus luteum in the oestrous cycle, and thus it is based on the principle of being able to dominate the formations of oestrous and ovulation (Abecia et al., 2012). For progesterone administrations to be more effective, it is necessary to have sufficient gonadotropins to initiate the pre-ovulation process and to increase 'exogenous' FSH and endogenous gonadotropins. For this, eCG, which is obtained from pregnant mare serum and has LH and FSH-like effects, should be administered when progesterone-containing materials are removed (Powell et al., 1996).

To minimize exposure to progesterone, it was determined that oestrous and ovulation can be synchronized by keeping the duration of progesterone-containing devices in the vagina short (Knights et al., 2001). Therefore, in this study, an intravaginal device (sponge) containing progesterone was kept as much as possible in the vagina for at least 7 days. For the sexual stimulation to be successful, it was aimed to ensure that ovulations occur in a shorter period by combining the eCG and the PGF2 α while removing the sponge. In a study investigating the effectiveness of eCG applied at different doses on ovarian functions, it was found that eCG applied at doses higher than 750 IU increased the ovulation rate but decreased the pregnancy rate. In addition, regarding the use of PGF2 α , D-cloprostenol, a synthetic form of PGF2 α , is used very effectively in oestrous induction and its synchronization in sheep, and it provides an exquisite stimulation by terminating progesterone activity (Ramírez et al., 2018).

When eCG was administered at doses of 550-650 IU, pregnancy rates were found to be high apart from multiple pregnancies (Kermani Moakhar et al., 2012). In the light of this piece of information, in this study, at the time of removing the vaginal sponge, 600 IU of eCG and D-cloprostenol form 263 μ g of PGF2 α were administered. Moakhar et al. (2012) achieved 75% pregnancy by applying 550 IU and 650 IU eCG, while 47% pregnancy rate and 33% (11/33) multiple pregnancies were achieved in the application group of this study. It was thought that the difference occurred was since the sheep in the studies were carried out on prolific and non-prolific breeds (Kermani Moakhar et al., 2012).

In a study of PMSG injections applied at different times, it was found that pregnancy occurs better 24 hours before (78%) and at the time of the removal of sponge (75%) (24 hours before the sponge was removed, when the sponge was removed, 24 hours after the removal of the sponge, and when nothing was done) than in eCG applied groups with (70%) 24 hours after removal of the sponge and the groups with no application of eCG with (%60) (Zelege et al 2005). In the study, eCG was applied to the animals in the treatment group when the sponge was removed, and 47% pregnancy was achieved. Compared to the study of Zelege et al. (2005), the reason why we had a lower pregnancy rate in our study was thought to be because the infections that caused neonatal losses in the farm where we carried out our study also affected the ewes of the farm. Besides that, Zelege et al (2005) carried out their studies on a prolific breed during the transition period from breeding season to anestrous. Kangal sheep is a non-prolific breed and

has a short breeding period (Zelege et al., 2005). Above all, our study was conducted in the early anestrous period.

In the study, in which the effectiveness of the postpartum stage on reproductive performance was evaluated by synchronizing in the early, middle, and late puerperal periods in the postpartum period, pregnancy rates were obtained at a rate of 43.8%, 29.7%, and 47.1%, respectively (Ungerfeld and Sanchez-Davila, 2012). In our current study, which we performed in the late postpartum stage, reproductive results similar to that study were obtained.

When the economic effects of the study were examined, it was found that the group that received the treatment protocol earned an extra 28695.70 TL (\$3856.95) income compared to the control group. The income per sheep was 409.94 TL (\$55.09). According to the calculations, it was found that the treated group achieved 88.15% better economic results than the control group did. It has been determined that hormonal therapy increases reproductive performance and provides better economic results. Swellum et al. (2018) mention that hormonal synchronization is a profitable initiative in increasing reproductive performance and consequently increasing economic profit (Swellum et al., 2015). At this point, our study and their results are similar.

In their study, Al-Karablieh and Abdelrahman (2000) found the mean fertility for the treated groups is 22.1% which is better than the one for the control group. They reported that the lambing rate increased from 64.9–111.0%, and the twinning rate increased from 3.13–29.9% as a result of treatment. In the study, the increased net profit thanks to hormone therapy was found as 8.91 JD (12.5\$) / sheep (Al-Karablieh and Abdelrahman, 2000). The results of our study were found to be better than the results of Al-Karablieh and Abdelrahman's study in terms of economic efficiency.

In the study of Gizaw and Tegegne in 2017, in breeding practices, in females synchronized by applying hormones once and twice, it was determined that the annual profit increased by 78.6% and 101.5%, respectively when compared to the females who were not administered hormones.

The application provided a profit of 188.8% and 223.7% more than the improvement works in the village (Gizaw and Tegegne, 2018). The percentage profit values found by Gizaw and Tegegne are higher than the values in our study. This was associated with the fact that the ewes were affected by respiratory infections that caused the death of neonatal lambs. Swellum et al., in their study conducted in 2019, determined that the net profit was obtained in CIDR applied animals was 17.6% higher than the profit obtained from the animals in the control group, which is lower than our findings.

It is thought that the difference in productivity and profit rates is due to many variables such as geography, sheep breed, differences in breeding characteristics, and the difference in protocols used by practitioners.

Conclusion

It has been concluded how vital it is in terms of reproduction and economy to perform sexual stimulation as soon as possible without waiting for the breeding season in farms where lamb deaths occur in the postpartum period. For the formation of ovulating oestrus in Kangal sheep during the anoestrus period, intravaginal devices containing progesterone, sexual stimulation methods including gonadotropin and PGF2 α are needed.

Declarations

STATEMENTS AND DECLARATIONS

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

DATA AVAILABILITY

Not applicable.

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STATEMENT OF ANIMAL RIGHTS

The presented study was carried out with the approval and permission of Cumhuriyet University Veterinary Faculty Experimental Animal Production and Research Center Ethics Committee (Date: 06.02.2021 No: 392).

CONFLICT OF INTEREST STATEMENT

The authors report no declarations of interest.

CRedit AUTHORSHIP CONTRIBUTION STATEMENT

Abdurrahman TAKCI: Conceptualization, Funding acquisition, Methodology, Writing – original draft, Investigation **Mehmet Buğra KIVRAK:** Writing – original draft, Formal analysis **Hakan MURAT:** Methodology, Writing – original draft, Investigation **Sakine Ulkum CIZMECI:** Conceptualization, Methodology

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