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The Effects of Oral Progestagen Administration on the Fertility of Synchronized Goats During the Breeding Season

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ABSTRACT The objective of this study was to assess the impact of oral progesterone (altrenogest) administered after mating on fertility in goats synchronized during the breeding season. A total of 47 Hair goats were included in the study. A progesterone-impregnated intravaginal sponges were administered for 12 days. On day 10 of intravaginal sponge administration, 480 IU pregnant mare serum gonadotropin (PMSG) and 0.075 mg cloprostenol were injected intramuscularly to the goats. Animals were exposed to bucks for 12 hours after detection of estrus by the foraging buck. The goats were randomly assigned to two distinct groups: Group 1 (G1, n=23) and Group 2 (G2, n=24). G1 goats were orally administrated 4.4 mg of altrenogest per day for 30 days after mating. G2 goats served as controls. Pregnancy examinations were performed by transrectal ultrasonography on the 30th and 42nd days after mating. Blood samples were taken from one day after mating to 30 days (3-day intervals). Statistical analysis comparing G1 and G2 revealed no significant differences between the groups regarding progesterone concentrations, conception rate, pregnancy rate, lambing rate, multiple birth rate, fecundity, and litter size ($p>0.05$). In conclusion, this study revealed that oral progesterone use had no impact on fertility parameters. Moreover, further research is warranted to explore the efficacy of various oral progesterone analogs.

Keywords: *Fertility, Goat, Pregnancy, Progesterone.*

ÖZ

Üreme Sezonunda Oral Progestagen Uygulamasının Senkronize Keçilerin Fertilitesi Üzerine Etkileri

Bu çalışmanın amacı, üreme mevsiminde senkronize edilen keçilerde çiftleşmeden sonra uygulanan oral progesteronun (altrenogest) fertilite üzerindeki etkisini değerlendirmektir. Çalışmada, toplam 47 Kıl keçisi kullanıldı. Hayvanlara 12 gün boyunca progesteron emdirilmiş intravajinal süngerler uygulandı. Vajinal sünger uygulamasının 10. gününde 480 IU gebe kısrak serum gonadotropin (PMSG) ve 0.075 mg kloprostenol intramüsküler olarak uygulandı. Östrüsdeki hayvanlar, arama tekesi ile tespit edildikten sonra 12 saat tekelere maruz bırakıldı. Keçiler rastgele iki ayrı gruba ayrıldı: Grup 1 (G1, n=23) ve Grup 2 (G2, n=24). G1 keçilerine çiftleşmeden sonraki 30 gün boyunca günde 4.4 mg altrenogest oral olarak uygulandı. G2 keçileri ise kontrol grubu olarak değerlendirildi. Gebelik muayeneleri çiftleşmeden sonraki 30. ve 42. günlerde transrektal ultrasonografi ile yapıldı. Kan örnekleri çiftleşmeden sonraki günden 30 güne kadar (3 günlük aralıklarla) alındı. G1 ve G2 arasında istatistiksel analiz, progesteron konsantrasyonları, konsepsiyon oranı, gebelik oranı, kuzulama oranı, çoklu doğum oranı, fekundite ve bir batındaki yavru sayısı açısından gruplar arasında anlamlı bir fark olmadığını ortaya çıkardı ($p>0.05$). Sonuç olarak, bu çalışmada oral progesteron kullanımının fertilite parametreleri üzerine herhangi bir etkisinin olmadığı tespit edildi. Ayrıca, çeşitli oral progesteron analoglarının etkinliğini araştırmak için daha fazla araştırmaya ihtiyaç vardır.

Anahtar Kelimeler: *Fertilite, Gebelik, Keçi, Progesteron.*

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INTRODUCTION

Synchronization of estrus and ovulation is frequently used in reproductive management of goats. Many techniques are available for estrous synchronization in small ruminants, and progesterone-impregnated intravaginal devices are commonly used in these protocols (Kuru et al. 2018a; Erdem et al. 2021; Kaya and Kocak 2022). They cause varying degrees of vaginitis during use (Suárez et al. 2006; Manes et al. 2015) and induce discomfort while they are positioned within the vaginal canal (Kuru et al. 2016; Kuru et al. 2018b). This exogen condition and internal hormonal pattern could be one of factors negatively influencing subsequent reproductive response and fertility (Scudamore 1988; Manes et al. 2016). Fertility rates obtained from their use vary widely (Gordon 1983). Some researchers also report that pregnancy rates may be lower in ewes that received intravaginal sponges during the breeding season compared to those ewes that sponges were not applied (Manes et al. 2014).

The establishment and maintenance of pregnancy take place within a balanced system consisting of a healthy embryo, ovary, oviducts, and uterus. Any disruption within this intricate system can potentially result in a reduced embryo survival rate (Thatcher et al. 1994; Spencer 2013; Spencer et al. 2016).

For the formation and maintenance of pregnancy in ruminants, the embryo needs a uterus under the influence of progesterone (Spencer and Bazer 1996; Nava-Trujillo et al. 2008). An early increase in progesterone concentration following ovulation has been shown to enhance embryonic development and the expression of interferon-τ (IFN-τ) (Spencer 2013; Arosh et al. 2016) and promotes embryonic survival rates by improving the relationship between embryo and the uterus. The majority of embryonic losses typically occur during the critical phase of implantation, which takes place within the first few days following fertilization (Vanroose et al. 2000; Spezzigu et al. 2013). Inadequate luteal function has been identified as one of the primary factors contributing to these losses (Mann et al. 2006; Montes-Quiroza et al. 2018). The sustained secretion of progesterone by the corpus luteum is crucial for the maintenance of pregnancy (Diskin and Morris 2008). Progesterone plays a vital role in both the establishment and maintenance of pregnancy and should be on an increasing course after fertilization. Cellular divisions in the developing embryo are adversely affected when the increase in progesterone level is delayed or the progesterone level is insufficient. Since the conceptus of animals with low progesterone levels is less capable of producing interferon tau, embryonic death rates are higher in these animals. There is a positive relationship between the blood progesterone concentration and the continuation of pregnancy during the pregnancy recognition process. This shows that high progesterone concentrations are important for the maintenance of pregnancy during the pregnancy recognition process (Satterfield et al. 2006; Cetin 2021). Various approaches can be employed to achieve elevated progesterone concentrations post-insemination, aiming to mitigate or forestall embryonic losses and thereby enhance animal fertility. Among these strategies post-mating treatment with exogenous progesterone (Cetin 2021) has been shown to augment both embryo viability and pregnancy rates in ruminants (Thatcher et al. 1994; Mann and Lamming 1999; Mann et al. 2006; Alcay et al. 2022a; Koca et al. 2023a).

To our knowledge, there is no study investigating oral progesterone administiration on fertility parameters in goats. In this study, we hypothezied that oral progesterone administration may positively affect fertility parameters in synchronized goats. Therefore, this study investigated whether oral progesterone (altrenogest) administration to goats after mating during the breeding season had a potential positive effect on fertility parameters.

MATERIAL AND METHODS

Ethical Statement

Ethical approval was received for this study from Van Yuzuncu Yil University Animal Experiments Local Ethics Committee (Decision No: 2017/01) on 26.01.2017.

Location, Animals and Feeds

The current study was conducted at Van Yuzuncu Yil University Research and Application Farm, specifically during the breeding season (September-October) in Van-Türkiye. Van is situated at a high altitude of 1730 meters above sea level, precisely located at coordinates 42°40-44′30″E and 37°43-39′26″N. In this region, small ruminants show seasonal breeding characteristics most intensely in September-November.

In the study, 47 clinically healthy Hair goats between 3-5 years of age that had given birth at least once were used. In addition, 7 fertile bucks that have no reproductive problems were used for mating. Animals were housed under semi-extensive conditions during the study. In addition to grazing, the animals were fed with 0.5 kg of concentrated feed (1300 kcal/goat/day metabolizable energy, 60 g/goat/day crude protein) daily. No heat, light, feed, or water restrictions were applied.

Estrus Synchronization Protocol

Goats were randomly divided into two groups considering age, body weight, and body condition scores (BCS). The BCS values of these goats were scored from 1 to 5 (Ferguson et al. 1994; Cizmeci et al. 2022).

Flugestone acetate-impregnated intravaginal sponge (FGA, 20 mg, Chronogest-CR®, MSD Animal Health, France) was administered to all goats. For each goat, on day 10 of intravaginal sponge (VS) application, 480 IU (PMSG) (Chrono-Gest/PMSG®, MSD Animal Health, Germany) and 0.075 mg cloprostenol (Estropur®, Bioveta, Czech Republic) were injected intramuscularly. Sponges were removed from the vagina on the 12th day (Figure 1).

Estrus Detection (ED) and Mating

After the sponges were removed, estrus was detected daily (morning-evening) for 3 days with the foraging buck. Goats in estrus were exposed to bucks for 12 hours.

Oral Progesterone Administrations

Goats were randomly divided into two groups considering age, body weight, and body condition scores (BCS). To the best of our knowledge, this is the first report investigating the effect of oral progesterone (altrenogest) administration on fertility parameters in goats considering different doses, durations, and routes of administration. In the study, animals in G1 were treated with 4.4 mg (2 ml) of altrenogest (Regumate®-MSD Animal Health, France) orally per day for 30 days, starting 24 hours after mating. No hormone supplementation was given to G2.

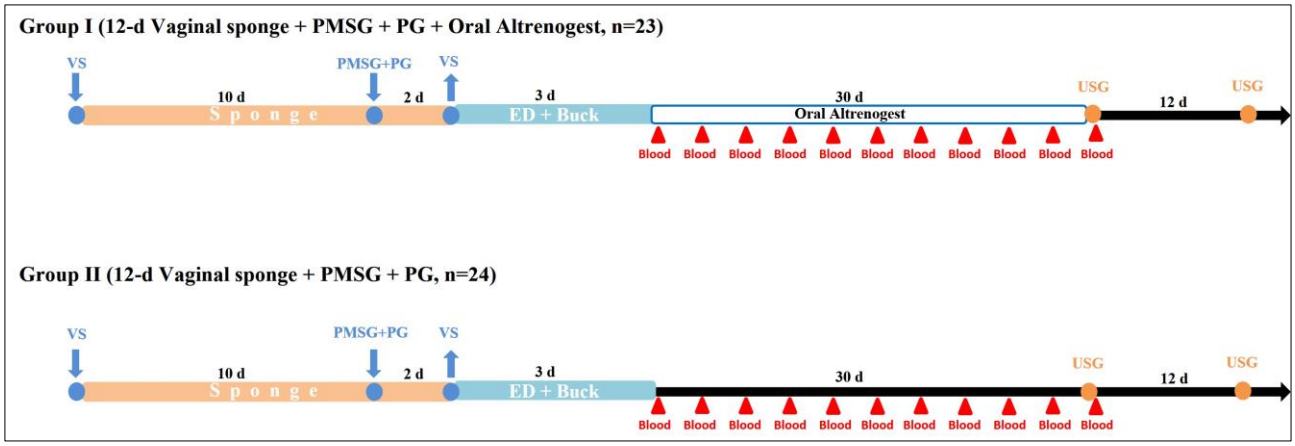

Figure 1: Schematic representation of the experimental design in G1 and G2. PMSG: Pregnant mare serum gonadotropin, PG: Prostaglandin F2 alpha, USG: Ultrasonography, d: Day, ED: Estrus detection, VS: Vaginal sponge.

Collection of Blood Samples and Progesterone Analysis

Blood samples were obtained from the jugular vein (vena jugularis) into tubes for serum progesterone analysis from day 1 after mating until day 30 (3-day intervals). During the procedure, the collected blood samples were centrifuged at 3000 rpm for 10 minutes to separate the serum. Then, serum samples were stored at -20 °C for further analyses. Serum progesterone concentrations were measured by immunoanalyzer method using automated commercial kit (Elecsys®, Roche Diagnostics, Mannheim, Germany).

Pregnancy Examinations

Pregnancy examinations were performed on the 30th after mating with trans-rectal ultrasonography (7.5 MHz Linear Probe, Honda HS 1500, Japan). In addition, in the previous examination, the goats diagnosed as pregnant were re-examined again on the 42nd day to confirm pregnancy.

Fertility Parameters

Fertility parameters, including estrus rate, onset of estrus, conception rate, pregnancy rate, kidding rate, multiple birth rate, fecundation rate, and litter size in goats, were determined using the formulas previously reported (Kuru et al. 2017).

Statistical Analysis

In our study, the sample size calculation considered a minimum power of 80% and a type 1 error of 5% for each variable. The Shapiro-Wilk test (for n<50) was utilized to assess the normal distribution of continuous measurements in the study. Since the timed measurements were found to deviate from normal distribution, nonparametric tests were employed. Descriptive statistics for continuous variables were expressed as mean, standard error, number, and percentage. The Mann-Whitney U test was utilized to compare continuous measurements based on categorical groups. The relationships between categorical variables were determined using the Chi-square (Fisher's exact) test. A statistical significance level (α) of 5% was considered in the calculations, and the SPSS (IBM SPSS for Windows, ver.26) statistical package program was employed for the analysis.

RESULTS

None of the intravaginally inserted sponges fell out, and there were no abortions, preterm births, or stillbirths during the study.

According to the data presented in Table 1, estrus was observed in 85.1% (40/47) of all animals included in the study. The mean onset time of estrus was recorded as 28.5±1.59 SEM hours after the removal of the sponges.

Between G1 and G2 based on the findings presented in Table 1, no significant difference was observed regarding the pregnancy rate, conception rate, lambing rate, multiple birth rate, fecundity, and litter size (p>0.05).

Table 1: Fertility parameters of Hair goats following treatment with oral progestagen (G1 altrenogest: 4.4 mg/day x 30 days, G2: control) after mating.

Parameters	G1 (n=23)	G2 (n=24)	Total (n=47)
Estrus rate (%)	87 (20/23)	83.3 (20/24)	85.1 (40/47)
Estrus onset (h) (mean±SEM)	29.8±1.75	27.2±1.63	28.5±1.59
Conception rate (%)	60 (12/20)	60 (12/20)	60 (24/40)
Pregnancy rate (%)	52.1 (12/23)	50 (12/24)	51.1 (24/47)
Lambing rate (%)	100 (12/12)	100 (12/12)	100 (24/24)
Multiple birth rate (%)	50 (6/12)	50 (6/12)	50 (12/24)
Fecundity (n)	1.05 (21/20)	1.15 (23/20)	1.1 (44/40)
Litter size (n)	1.75 (21/12)	1.92 (23/12)	1.83 (44/24)

Multiple birth rates were 50% in both groups, 1.75 and 1.92 in litter size for G1 and G2 groups, respectively (p>0.05). Birth types were found to be similar (p>0.05) in both groups (Table 2).

Table 2: Type of birth of Hair goats following treatment with oral progestagen (G1 altrenogest: 4.4 mg/day x 30 days, G2: control) after mating.

Type of birth	G1 (n=23)	G2 (n=24)	Total (n=47)
Single, %	50 (6/12)	50 (6/12)	50 (12/24)
Twin, %	33.4 (4/12)	25 (3/12)	29.2 (7/24)
Triplets, %	8.3 (1/12)	8.3 (1/12)	8.3 (2/24)
Quadruplet, %	8.3 (1/12)	16.7 (2/12)	12.5 (3/24)

The blood progesterone level in pregnant goats was found to be below 1 ng/ml (G1 0.38±0.27 ng/ml and G2 0.46±0.33 ng/ml) in both groups on the 1st day after the mating. The highest progesterone level was respectively detected in G1 on the 10th day after mating (13.19±6.18 ng/ml) and in G2 on the 7th day (14.59±5.58 ng/ml). After the highest measurement, a downward trend was recorded until the 13th day and after this day it remained almost stable at about 7-8 ng/ml. It was determined that the blood progesterone concentration was not statistically different between the groups for all times (Figure 2).

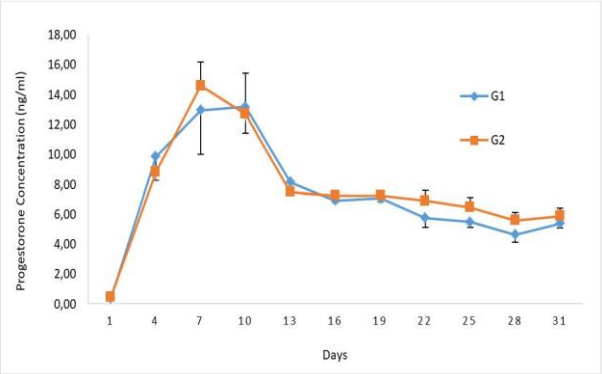

Figure 2: Serum progesterone levels in G1 and G2.
G1: Altrenogest, 4.4 mg/day x 30 days, G2: Control .

DISCUSSION AND CONCLUSION

Improvement of production traits in ruminants are important for sustainability of animal production (Koca et al. 2023b; Turgut et al. 2023). And recent studies in ruminants focus on production traits such as milk traits, fertility traits, and reproductive parameters (Alcay et al. 2022b; Koca et al. 2024a; Koca et al. 2024b). In this context, reproductive hormones are commonly used for diagnosis of congenital diseases and evaluation of reproductive performance in ruminant species (Koca et al. 2024a; Koca et al. 2024b; Turgut and Koca 2024).

Progesterone supplementation has been shown to have positive effects on fertility in ruminants (Lopez-Gatius et al. 2004; Villaroel et al. 2004; Kenyon et al. 2005). Therefore, we investigated whether oral progesterone administration following synchronization enhanced fertility in goats. The expectation was that such administration would confer advantages in fertility parameters, including pregnancy/conception/lambing rates, multiple birth rates, fertility, and litter size.

Intravaginal devices have been used successfully for estrus synchronization in small ruminants (Kuru et al. 2020; Cetin et al. 2021). In our study, the estrus rate (85.1%) and estrus onset time (28.5±1.59 hours) were determined, which corroborate with the results reported by findings of Omontese et al. (2013).

There are studies on progesterone supplementation after mating aiming to increase pregnancy rates in ruminants (Robinson et al. 1989; Lopez-Gatius et al. 2004; Villaroel et al. 2004; Kenyon et al. 2005; Nava-Trujillo et al. 2008; Arndt et al. 2009; Montes-Quiroza et al. 2018). Intravaginal devices were used for progesterone supplementation after mating in these studies. However, it was stated that intravaginal devices cause varying degrees of inflammation in the vagina during synchronization (Suárez et al. 2006; Manes et al. 2015) and can cause stress in animals during the application (Kuru et al. 2016; Kuru et al. 2018b). These changes have a negative effect on fertility (Scudamore 1988; Manes et al. 2016). While these methods aim to increase the pregnancy rate, pregnancy rates may be negatively affected indirectly due to the reasons mentioned above. In our study, progesterone (altrenogest) supplementation was administered orally to animals in a non-invasive way for the first time.

In this study, no statistically significant difference was observed between the fertility parameters such as pregnancy/conception/lambing/multiple birth rates, fecundity, litter size, and serum progesterone level. Nava-Trujillo et al. (2008) and Montes-Quiroz et al. (2018) reported the findings between the experimental and control groups of oral progesterone supplementation after mating using intravaginal devices in goats. In these studies, Nava-Trujillo et al. (2008) reported 55.5% in the control group and 44.4% in the experimental group, while Montes-Quiroz et al. (2018) found a similar pregnancy rate in both groups. In our study, we have observed a total pregnancy rate that aligns closely with the results reported by Nava-Trujillo et al. (2008). However, it is worth noting that Montes-Quiroz et al. (2018) reported a higher pregnancy rate compared to the one we have obtained. In our study, progesterone levels were similar between the experimental and control groups. The fertility outcomes achieved through progesterone supplementation after mating or insemination in other species exhibit variability. Arndt et al. (2009) stated that the pregnancy rate was not affected in cows after the application of an intravaginal device containing progesterone from day 4 to day 18 insemination. Kenyon et al. (2005) reported that the application of intravaginal materials containing progesterone at different times after mating in sheep had no effect on reproductive performance. Larson et al. (2007) reported that the pregnancy rate has been increased with intravaginal device application containing progesterone between day 3.5 and day 10 after insemination in cows. The results obtained in our study are also consistent with other reported studies (Nava-Trujillo et al. 2008; Arndt et al. 2009). Progesterone supplementation after mating/insemination may help prevent pregnancy losses in animals with luteal deficiency, but it does not seem effective in increasing fertility after synchronization.

Different findings have been obtained in studies using progesterone supplements to increase fertility in ruminants. Montes-Quiroza et al. (2018) reported that the blood progesterone level was higher after reinsertion of the CIDR devices after post-insemination synchronization compared to the group that did not undergo reinsertion. Likewise, Kenyon et al. (2005) reported that application of

the intravaginal devices containing progesterone after mating in sheep, causes increased plasma progesterone concentrations in sheep compared to the group that did not receive the inserts. Larson et al. (2007) reported that blood progesterone concentrations increased in cows in which they applied progesterone supplementation with intravaginal devices after insemination. In another study, Walton et al. (1990) employed a combination of intravaginal devices, human chorionic gonadotropin (hCG) injections, and progesterone injections after insemination in repeat breeder cows. Their findings indicated that following these interventions, plasma progesterone concentrations increased in cows that received intravaginal devices and hCG injections. However, there was no observed change in animals that received progesterone injections. Arndt et al. (2009) found that the administration of an intravaginal device containing progesterone after insemination did not increase blood progesterone concentration in cows. In our study, there was no statistically significant difference detected between the groups in blood progesterone levels at all times after the administration of exogenous oral progesterone after mating. The observed phenomenon is believed to be attributed to several potential factors. One possible reason could be that the dosage of the administered hormone is insufficient to significantly impact hormone levels. Additionally, it's conceivable that the administered hormone might be absorbed inefficiently through the digestive system, affecting its overall effectiveness.

In conclusion, exogenous oral progestagen administration after mating had no effect on fertility parameters in synchronized Hair-goats during the breeding season. Nevertheless, compherensive investigations should be conducted across different breeding seasons and management systems using various progesterone analogues and different dosage regimens. These studies can help advance our understanding of how to optimize fertility outcomes in Hair goats and may provide valuable insights into improving reproductive success in this context.

CONFLICTS OF INTEREST

The authors report no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Idea / Concept: NÇ, SŞ
Supervision / Consultancy: AW, SŞ
Data Collection and / or Processing: NÇ, FE, DK
Analysis and / or Interpretation: MK, BAU
Writing the Article: NÇ, MK, DK
Critical Review: NÇ, MK, DK

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