Research Report

Use of deslorelin acetate to advance ovulation in goats for timed artificial insemination

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Abstract

The objective of this study was to determine the efficacy of deslorelin in advancing ovulation for timed artificial insemination (AI) protocols in goats. We hypothesized that deslorelin treatment advances the onset of ovulation and improves AI pregnancy rates. Does were synchronized using a 5-day CIDR (controlled internal drug releasing insert) protocol with prostaglandin treatment at CIDR insertion. For Experiment 1, does received 0.2 mg of intramuscular deslorelin (n = 9) or saline (control, n = 10) at CIDR removal. Serial blood collections and transrectal ultrasonography were performed to assess ovarian dynamics and identify ovulation. For Experiment 2, does received 0.2 mg of intramuscular deslorelin (n = 42), 5 ml of PMSG (pregnant mare serum gonadotropin)/hCG (human chorionic gonadotropin) (n = 42), or were left untreated (control, n = 42) at CIDR removal, and were subsequently bred by transcervical AI with fresh semen after 48 to 56 hours. Pregnancy diagnosis was performed at 50 and 90 days after AI. In Experiment 1, compared to control does, deslorelin-treated does had an increased ($p < 0.01$) number of ovulations and increased ($p < 0.01$) serum estradiol concentrations from 48 to 72 hours after CIDR removal. Serum progesterone concentrations did not differ between treatments. In Experiment 2, there was a main effect ($p = 0.02$) of treatment on pregnancy rates, with control does tending ($p = 0.06$) to have greater pregnancy rates than those treated with deslorelin or PMSG/hCG. Deslorelin treatment also resulted in decreased ($p = 0.04$) breeding season pregnancy rates and increased ($p = 0.05$) number of cycles to achieve pregnancy compared to control does. These results demonstrated that deslorelin not only has a super-ovulatory effect but also, at the dose given, can negatively impact does' subsequent ovarian function and ability to achieve pregnancy.

Keywords: Does, estrus synchronization, deslorelin, SucroMate, breeding

Introduction

Meat goat production has increased in popularity in the United States (US) due to the growing population of ethnic and faith-based groups who consume goat meat.[1] As a result of this trend, the US has shifted from being a net exporter to a net importer of goat meat,[1] suggesting a nationwide need to increase goat productivity. One of the biggest barriers to productivity in goat herds is the increasing prevalence of antiparasitic resistance, leading to increased morbidity and mortality among herds.[2] The best strategy to combat growing antiparasitic resistance is to focus on the selection of parasite-resistant animals for breeding and dissemination of these valuable genetics.[3] The quickest and most effective way to introduce disease-resistant genetics in a goat herd is by using artificial insemination (AI) with frozen semen.

The use of fixed time AI for goats in the US is limited due to the lack of availability of commercially approved drugs.[4] Protocols using a combination of controlled internal drug releasing inserts (CIDRs or sponges) containing progesterone combined with pregnant mare serum gonadotropin (PMSG) and/or prostaglandins have been used extra-label with much success.[5] In small ruminants, PMSG is preferred for ovulation advancement due to its long half-life[6] and follicle stimulating hormone (FSH) activity that causes superovulation and increased kidding numbers.[7,8] In the US, PG600 (Merck Animal Health, Madison, NJ, USA) is the only commercially available product that contains purified PMSG, which is combined with human chorionic gonadotropin (hCG). Although the use of PG600 produces acceptable pregnancy rates with natural mating,[9] the inclusion of hCG, which has luteinizing hormone activity, may result in unpredictable ovulation

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timing and premature luteinization in small ruminants and is not ideal for use with timed insemination. Additionally, repeated use of PMSG for estrus synchronization causes anti-PMSG antibodies to form, reducing its effectiveness over time.[8,10] There is, therefore, a need to investigate alternative ovulation-stimulating products for use in goats.

Gonadotropin releasing hormone (GnRH) agonists are commonly used in cattle synchronization protocols but have a much shorter half-life than PMSG, which can stimulate estradiol secretion for several days in goats.[6] However, long-acting GnRH agonists were developed that may produce similar superovulation effects as PMSG without the risk of decreasing efficacy with repeated use. The incorporation of a deslorelin implant in a timed insemination protocol of lactating dairy cows with low body condition scores improved corpus luteum (CL) function and enhanced pregnancy rates.[11] The use of deslorelin implants also induced ovulation in nonlactating dairy cows and heifers[12] and tended to decrease pregnancy losses in lactating dairy cows.[13] More recently, SucroMate (Thorn Bioscience, Louisville, Kentucky, USA), a controlled release deslorelin acetate product, was developed and approved for ovulation induction in mares. When given to mares with a follicle size ≥ 35 mm, ~ 90% ovulated within 48 hours.[14] Interestingly, ovulation rates also increased from 4% to 79% when SucroMate was given to mares during the seasonal transition period.[15] Goats, like horses, are seasonal breeders; therefore, the use of deslorelin for inducing ovulation in does outside the breeding season or during seasonal transition warrants investigation. Despite its proven effectiveness for advancing ovulation onset in both transitional and cycling mares, there is no information regarding its use in small ruminants. The objective of this study was to determine whether deslorelin treatment is effective in advancing ovulation in does to synchronize estrus for timed AI. We hypothesized that deslorelin treatment advances onset of ovulation and improves AI pregnancy rates in goats.

Materials and methods

Animals

Our Institutional Animal Care and Use Committee approved (Protocol #19-078) all experimental procedures. Adult Boer or Boer-crossbred does from the Virginia Department of Corrections goat herd in Halifax, Virginia, were enrolled in this study.

Experiment 1 (deslorelin effect on ovulation)

Twenty does (10 mature does and 10 doelings) were enrolled in Experiment 1. Does were blocked by age and then randomly and equally distributed between 2 replicates for September and October 2019 (n = 5 mature does and 5 doelings per replicate) experiments. Within each replicate, does were similarly blocked by age and distributed randomly and equally between 2 treatments. All does were in good physical health prior to enrollment (FAMACHA score < 3, minimum body condition score of 2/5, and no evidence of lameness or illness).

Estrus was synchronized using a 5-day protocol as described.[5] At day -5, a CIDR insert containing 0.3 g of progesterone (Eazi-breed™ CIDR® Sheep Insert, Zoetis, Parsippany-Troy Hills, NJ, USA) was placed vaginally, and 10 mg of intramuscular dinoprost tromethamine (Lutalyse, Zoetis, USA) was administered. At CIDR removal, does were given 1 of 2 treatments: 1. 0.2 mg of intramuscular deslorelin acetate (0.1 ml; n = 10; SucroMate™, Thorn Bioscience, Louisville, Kentucky, USA) or 2. 0.1 ml of intramuscular saline (n = 10). Time 0 was designated as the time of treatment and CIDR removal. The dosage of deslorelin was extrapolated from the dosage used in mares.[14] One doe in the deslorelin-treated group was later excluded from analyses after a cystic CL was diagnosed via ultrasonography (confirmed by serum progesterone assay) that persisted throughout the duration of the sampling period.

Jugular catheters were placed in does on the day before treatment and CIDR removal (day -1) to facilitate blood sampling. Blood was collected at 0 and 12 hours and then every 4 hours from 24 to 72 hours after treatment. Serum estradiol concentrations were measured using radioimmunoassay, as described.[16,17] Interassay coefficient of variation (CV) was 9.1%, and intraassay CV was 4.5% for the estradiol assay. Serum progesterone concentrations were measured by radioimmunoassay at 0 and 72 hours and at 8 or 9 days after treatment.[16,18] Interassay CV was 8.4%, and intraassay CV was 5.5% for the progesterone assay. Does were examined for signs of estrus (immobility reflex, tail flagging, and vaginal mucus) during each sampling period after being exposed to a buck-scented item.

Transrectal ultrasonography (Exapad Mini, Universal Imaging, Bedford Hills, New York, USA) was performed to record ovarian structures, determine interval to ovulation, and identify total number of ovulations in does every 12 hours from 0 to 72 hours after treatment. Interval to ovulation was recorded at the first time point when a previously visualized dominant follicle (≥ 5 mm) was no longer visible. The number of ovulations was determined by the total number of dominant follicles that ovulated from either ovary within the 72-hour experimental period.

Experiment 2 (deslorelin effect on pregnancy per AI outcomes)

Does were synchronized as described in Experiment 1 using a 5-day CIDR protocol with 10 mg dinoprost tromethamine treatment at CIDR insertion in October 2019. At CIDR removal, does were stratified by body condition score and randomly allocated to 1 of 3 treatment groups: 1. 0.1 ml of intramuscular deslorelin (n = 42); 2. 5 ml of intramuscular PMSG/hCG (PG600, Merck Animal Health, Madison, NJ, USA [n = 42]); or 3. untreated (control, n = 42).

Between 48 and 56 hours after CIDR removal, transcervical AI was performed using fresh semen collected from 3 different bucks on the same day. Does were stratified by treatment group and body condition score, and randomly allocated to receive semen from 1 of 3 bucks. Does bred to Buck 1 underwent AI first (~ 48 to 50 hours after CIDR removal). The next group of does were bred to Buck 2 (~ 48 and 52 hours after CIDR removal). The last group of does were bred to Buck 3 (~ 50 to 56 hours after CIDR removal). Semen was collected from respective bucks immediately before each AI group and diluted with OptiXcell extender (Osseo, MN, USA) to achieve an appropriate volume to inseminate all does in each group. Total sperm number per dose was not determined, but a clinician examined each sample under light microscopy on farm to ensure that extended sperm concentration and motility were subjectively adequate (concentration > 100×10^6/ml; motility > 70%) before performing AI.

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All does were inseminated transcervically by a single AI technician. Each goat was manually restrained on a show stand, and the external os of the cervix was visualized using a vaginal speculum and pen light. Upon visualization of the cervix, an AI gun, preloaded with 0.5 ml of warm, fresh, extended semen, was passed through the speculum into the external os of the cervix. The gun was passed through a minimum of 2 cervical rings before semen was deposited. At ~ 18 days after AI, each group of does was turned out with their assigned buck for natural cover over a 40-day breeding season.

Transabdominal ultrasonography was performed at days 50 and 90 after AI to assess pregnancy status by AI and subsequent natural cover. Approximate gestational age, as determined by fetal size, was used to determine how many cycles the does took to achieve pregnancy by natural cover.

Data analyses

Data were analyzed using R (https://www.r-project.org/). Doe was used as the experimental unit. Interval to ovulation and number of ovulations were found to be not normally distributed by a Shapiro Wilk test and analyzed using a Kruskal-Wallis test. Interval to estrus and duration of estrus were normally distributed and analyzed using a Welch two sample t-test. ANOVA with repeated measures was used to assess the effects of treatment, time, and treatment by time interactions on serum hormone concentrations using doe ID as a random variable. Coefficient covariance was computed by heteroscedasticity-correct covariance matrices. Post-hoc tests were analyzed using a pairwise comparison with a Bonferroni adjustment. The binomial outcomes of AI and breeding season pregnancy rates were analyzed using a generalized linear mixed-effects model (glmer procedure) in R with treatment and buck included as fixed variables and doe ID included as a random variable. Significance was declared at $p \leq 0.05$ with tendencies discussed between $p = 0.06$ and 0.09.

Results

Experiment 1

The effects of deslorelin on ovulation dynamics are summarized (Table 1). There were no differences in interval to estrus ($p = 0.82$) after treatment or estrus duration ($p = 0.3$) between deslorelin-treated and control does. Similarly, interval to ovulation after treatment did not differ ($p = 0.13$) between control and deslorelin-treated does. Interestingly, there was an increase ($p = 0.007$) in the number of follicles ovulated in deslorelin-treated does compared to control does (Figure 1).

Table 1. Ovulatory dynamics, as determined by transrectal ultrasonography, in does following treatment with saline (control) or intramuscular 0.1 ml deslorelin (0.2 mg) at CIDR removal for Experiment 1

Treatment	Interval to estrus	Duration of estrus	Interval to ovulation	# Follicles ovulated
Control	39 ± 3.0	20 ± 4.0	61 ± 3.3	1.5 ± 0.2
Deslorelin	40 ± 3.9	15 ± 2.8	53 ± 3.3	2.9 ± 0.3
	p = 0.82	p = 0.3	p = 0.13	p = 0.007

Treatment with deslorelin did alter neither interval to estrus or interval to ovulation after CIDR removal nor estrus duration. However, does treated with deslorelin had an increase in the number of follicles ovulated. CIDR: controlled internal drug releasing insert.

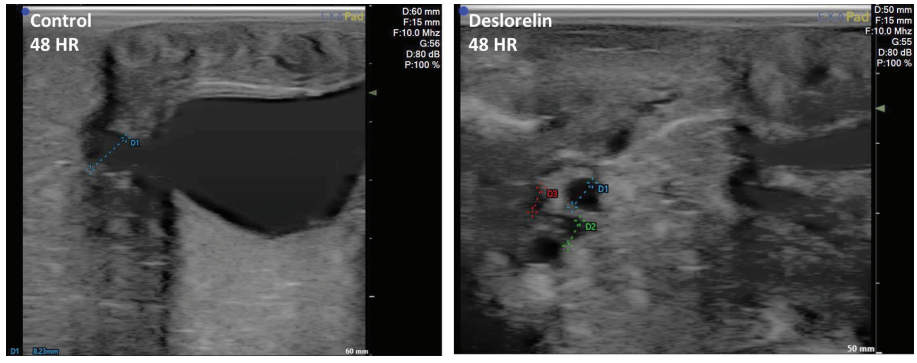

Figure 1. Representative images from serial transrectal ultrasonography of does treated with intramuscular saline (control, left) versus deslorelin (right) for Experiment 1. At 48 hours after controlled internal drug releasing insert (CIDR) removal, an average of 1.5 preovulatory follicles (ranging from 1 to 3) were observed in control does, whereas an average of 3 preovulatory follicles (ranging from 1 to 4) were observed in deslorelin-treated does. Follicles are denoted by dashed lines.

Deslorelin-treated does had increased ($p \leq 0.05$) serum estradiol concentrations from 48 to 72 hours after CIDR removal (Figure 2A) compared to control does. Serum progesterone concentrations did not differ ($p = 0.66$) between treatments (Figure 2B).

Experiment 2

There was a main effect ($p = 0.02$) of treatment on AI pregnancy rates, whereas buck tended to affect ($p = 0.06$) AI pregnancy rates (Table 2). On post-hoc analyses, control does tended to have greater ($p = 0.06$) AI pregnancy rates (26%, 11/42) compared to does treated with deslorelin (7%, 3/42) or PMSG/hCG (7%, 3/42). Does bred by Buck 1 also tended to have greater ($p = 0.09$) AI pregnancy rates (24%, 10/42) than those bred by Buck 2 (7%, 3/42), but did not differ ($p = 0.17$) from Buck 3 (9.5%, 4/42).

There was a main effect ($p = 0.05$) of treatment on breeding season pregnancy rates, but no buck effect ($p = 0.6$). Does treated with deslorelin had lower ($p = 0.04$) breeding season pregnancy rates (74%, 29/39) compared to does treated with PMSG/hCG (97.5%, 39/40) or untreated controls (100%, 36/36). Of the does that became pregnant by natural cover, deslorelin-treated does required an increased number of cycles to achieve pregnancy (1.6 ± 0.1 cycles) compared to untreated control does (1.3 ± 0.1 cycles; $p = 0.05$), but did not differ ($p = 0.53$) from PMSG/hCG-treated does (1.4 ± 0.1 cycles). There was also no difference ($p = 0.29$) in number of cycles between PMSG/hCG-treated does and untreated control does.

Discussion

The current study was the first to investigate the use of deslorelin acetate as an ovulation advancement drug in an estrus

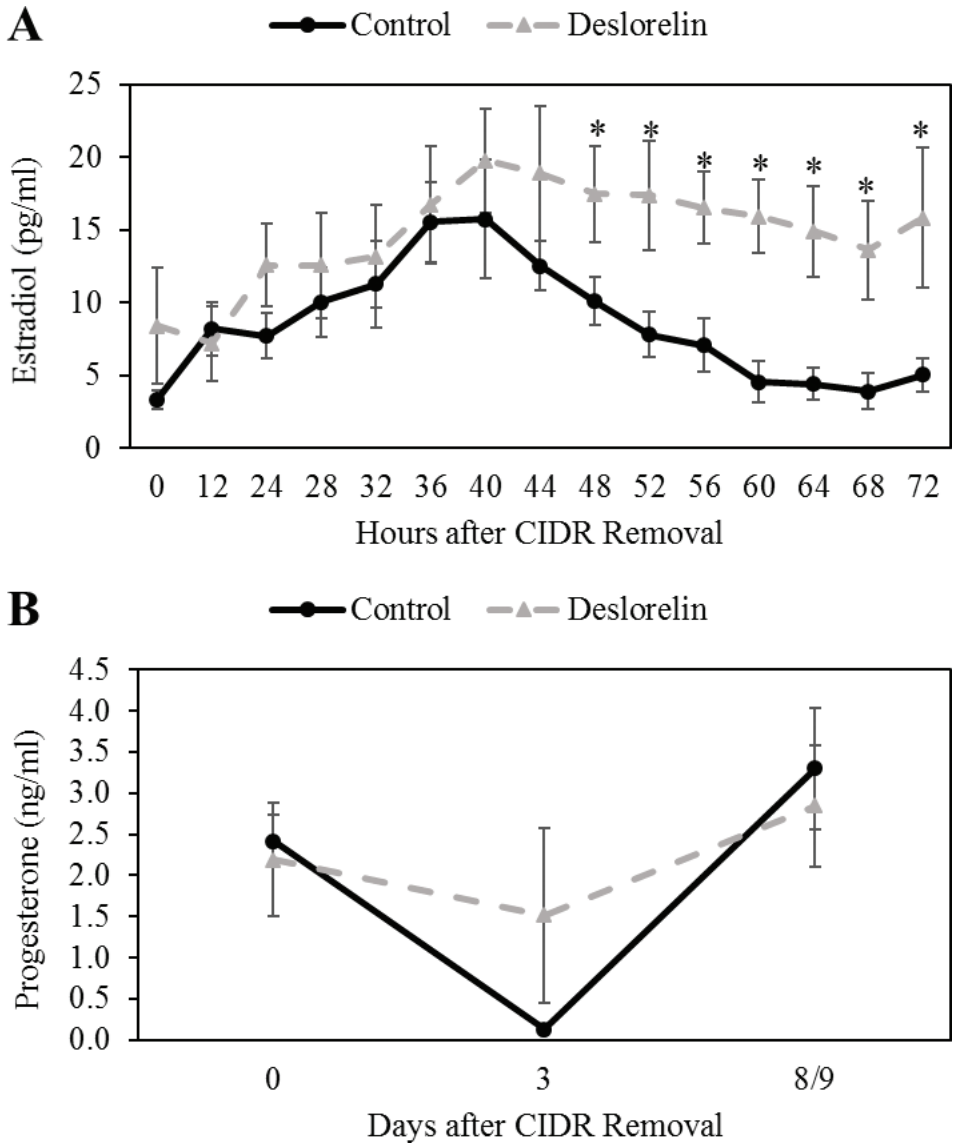

Figure 2. Serum hormone concentrations of does following treatment with 0.1 ml intramuscular saline (control) or deslorelin (0.2 mg) at controlled internal drug releasing insert (CIDR) removal for Experiment 1. A. Serum estradiol concentrations increased ($p \leq 0.05$) in does from 48 to 72 hours after treatment and CIDR removal (denoted by asterisks); B. Serum progesterone concentrations did not differ ($p = 0.66$) between treatments.

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Table 2. AI pregnancy rates in does untreated (control) or treated with deslorelin or PMSG/hCG and subjected to transcervical AI for Experiment 2

	Control (%)	Deslorelin (%)	PMSG/hCG (%)
Buck 1	50 (7/14)	7 (1/14)	14 (2/14)
Buck 2	7 (1/14)	7 (1/14)	7 (1/14)
Buck 3	21 (3/14)	7 (1/14)	0 (0/14)
Total	26 (11/42)	7 (3/42)	7 (3/42)

There was a main effect (p = 0.02) of treatment on AI pregnancy rates, whereas buck tended (p = 0.06) to affect AI pregnancy rates. On post-hoc analyses, control does tended (p = 0.06) to have greater AI pregnancy rates compared to does treated with deslorelin or PMSG/hCG. Does bred by Buck 1 also tended (p = 0.09) to have greater AI pregnancy rates than those bred by Buck 2; however, they did not differ (p = 0.17) from Buck 3. PMSG/hCG: pregnant mare serum gonadotropin/human chorionic gonadotropin; AI: artificial insemination.

synchronization protocol for timed AI in goats. In the US, there are currently no approved drugs for ovulation advancement in small ruminants. Historically, the use of PMSG or a combination PMSG/hCG product (PG600) that is labeled for the induction of estrus in peri-pubertal gilts has been used extra-label in goats with varying success rates. These drugs are purified from mammalian tissue, rather than being generated in a recombinant form. Therefore, issues with antibody formation following repeated use of PMSG have been reported, which may diminish its effectiveness in superovulation and ovulation advancement in small ruminants.[8,10] Additionally, the inconsistent availability of these drugs in the US justifies the need to evaluate alternative options for ovulation advancement in small ruminants.

In cattle, GnRH agonists have been widely used for decades within estrus synchronization protocols. These products are small, recombinant proteins that do not appear to generate an immune response after administration. However, their half-life is much less than that of PMSG due to the ease that they can be degraded by endopeptidases and nonspecific exopeptidases present in the pituitary gland, liver, and kidney.[19] In goats, the long half-life of PMSG aids in allowing for selection of multiple dominant follicles, resulting in a superovulation effect that increases kidding rates. The use of nano-delivered drugs has been proposed as an alternative way of delivering synchronization drugs, with the use of nano-GnRH having improved luteal function in pregnant goats.[19,20] Unfortunately, nano-drugs are not commercially available, so their current usefulness to producers is minimal. We utilized a commercially available GnRH agonist (deslorelin) that is suspended in sucrose acetate isobutyrate (SAIB) and is labeled for estrus advancement in horses (SucroMate). The SAIB vehicle is a highly viscous and hydrophobic polymer that allows for a sustained and prolonged release of a drug. Authors in a recent study reported that supplementing SucroMate with sulpiride and estradiol resulted in their long-term delivery after a single treatment in horses.[21] To the authors' knowledge, the current study is the first to evaluate the use of SAIB for sustained-delivery of a synchronization drug in goats.

Neither the interval to estrus, duration of estrus, or interval to ovulation differed between deslorelin and saline-treated control does in Experiment 1. The interval to estrus reported herein (39 to 40 hours after CIDR removal) is consistent with that reported in Boer goats synchronized with progesterone sponges and PMSG (500 IU) outside the natural breeding season.[22] On the contrary, we noted the estrus duration to be 15 to 20 hours, which is significantly shorter than that reported in an earlier study (38 to 40 hours).[22] However, that study utilized vasectomized bucks to visualize behavioral estrus, whereas we did not have access to a buck and relied on a buck-scented item that may have diminished the observed estrual behavior over time. In contrast to these findings, interval to estrus was decreased in dairy goats treated with either PMSG (33 hours; single dose of 750 IU at norgestomet implant removal) or FSH administration (32 hours; twice daily injections of descending doses of 4 to 1 mg over 4 days, starting 48 hours before implant removal) compared to untreated controls (48 hours).[23] The discrepancy in findings highlights the vast differences that can be observed among different breeds of goats, especially among those intended for meat versus dairy. Further studies assessing the onset and duration of estrus after deslorelin treatment in several breeds of goats and with alternative dosages are, therefore, warranted to best determine its potential usage.

This study is the first to report a superovulation effect of a GnRH agonist in goats. Using ultrasonography, we directly observed an ovulation rate of 3 in deslorelin-treated does versus an ovulation rate of 1.5 in saline-treated control does in Experiment 1. Ovulation rates can vary among goat breeds[24] but have been reported similarly in Boer does at 1.7.[25] Similar superovulation effects were reported in ewes treated with PMSG/hCG within the breeding season. In that study, the ovulation rate increased to 3.25 in ewes treated with 5 ml PMSG/hCG compared to 2.17 in those treated with 5 ml saline and 2.29 in those treated with 1.5 ml PMSG/hCG.[26] Consistent with ultrasonography findings, we observed an overall increase in serum estradiol concentrations in deslorelin-treated does compared to control does. Serum estradiol concentrations peaked at ~ 40 hours after CIDR removal in both deslorelin-treated and control does, which is consistent with other synchronization studies in goats.[27] In goats treated with a single superovulation dose of PMSG (1,000 IU), the duration of elevated estradiol was 3.6 days, compared to 0.5 day in those treated with twice daily FSH injections (8 mg on day 12, 4 mg on day 13, 2 mg on day 14, and 1 mg on day 15).[27] We observed a similar trend, where the estradiol concentrations in control does began to decline after peaking at 40 hours, reaching baseline values at ~ 52 hours after CIDR removal (a total duration of 12 hours or 0.5 day). On the contrary, the deslorelin-treated does experienced a prolonged elevation of estradiol throughout the remaining experimental period of 72 hours after CIDR removal (32+ hours duration). Unfortunately, samples were not collected beyond this time point, so we were unable to determine the duration of estradiol elevation in these animals. Further studies that extend sample collection beyond 72 hours after CIDR removal would be needed to determine the exact duration of elevated estradiol after deslorelin treatment. It would also be worthwhile to explore the timing of deslorelin treatment within this synchronization protocol, its use within other synchronization protocols, or its use in conjunction with an alternative prostaglandin source (e.g. cloprostenol) to best assess its effects on estradiol concentrations and estrus duration.

Despite the observed superovulation effect in the current study, postovulatory progesterone concentrations did not differ between deslorelin and saline-treated control does in Experiment 1. Biodegradable implants that release deslorelin in vitro over a 4-day period have been previously investigated in cattle[28] and can both suppress ovarian activity at a high

dosage (2,100 µg) or increase plasma progesterone and luteinizing hormone concentrations at a lower dosage (700 µg).[29] The use of a deslorelin implant (700 µg) in a timed insemination protocol for nonlactating Holstein cows had a greater rate of increase of plasma progesterone up to 15 days after ovulation due to accessory CL formation compared to untreated or buserelin (8 µg)-treated cows.[11,29] On the contrary, another study in nonlactating dairy cows and heifers identified minimal to no difference in plasma progesterone concentrations in cows given either 750 or 1,000 µg deslorelin implants during estrus synchronization.[12] They did, however, report a significant increase near day 10 in cows, given a 450 µg deslorelin implant compared to gonadorelin-treated controls.[12] These studies highlighted important dose- and time-dependent effects of deslorelin treatment on CL formation and function. Though no differences in progesterone were detected in the current study, we were limited by only acquiring 1 sample after ovulation to measure progesterone. Follow-up studies with serial ultrasonography and blood collections during the diestrus period would be needed to better measure the potential luteotrophic effect of deslorelin treatment in does after ovulation.

Although Experiment 1 discovered a superovulation effect with deslorelin treatment, the results of Experiment 2 identified its deleterious effect on fertility in does. One potential issue with fertility rates may have been the timing of AI. Although not statistically significant, interval to ovulation in deslorelin-treated does in Experiment 1 was numerically decreased (53 hours) compared to untreated controls (61 hours). The high variability in interval to ovulation may account for the lack of significance, and a difference may have been detected if we had increased the frequency of ultrasonography examinations. Overall, the greatest AI pregnancy rates were achieved in does bred to Buck 1, followed by Buck 3 and then Buck 2. Due to logistical limitations, we had to breed each of the stratified groups to 1 male at a time. Therefore, does bred to Buck 1 underwent AI first at ~ 48–50 hours after CIDR removal, which may have contributed to improved overall AI rates. Within this group bred by Buck 1, 50% of control does became pregnant versus 7% of deslorelin-treated does and 14% of PMSG/hCG-treated does. There is also a likelihood that sperm quality or concentration was better for certain bucks, since this was not extensively evaluated on site and may explain why AI pregnancy rates were intermediate for Buck 3 (AI interval from 50 to 56 hours after CIDR removal) and worst for Buck 2 (AI interval from 48 to 52 hours). Within the group bred by Buck 3, 21% of control does became pregnant versus 7% of deslorelin-treated does and 0% of PMSG/hCG-treated does. There were no differences in AI pregnancy rates among the does bred to Buck 2 (7% for all treatment groups). Based on these findings, it is possible that a hastened onset to ovulation could have caused decreased AI pregnancy rates in both of the treatment groups compared to the control group. Further studies are warranted to better determine an appropriate interval to AI when using deslorelin within a doe estrus synchronization protocol.

A more likely explanation for decreased fertility in the current study is an overstimulation of the ovaries with both deslorelin and PMSG/hCG treatment. Several outcomes observed in the deslorelin-treated does of the study support this theory: the prolonged estradiol secretion in Experiment 1; the increased number of cycles to breed back with bucks in Experiment 2; and the decreased overall pregnancy rates in Experiment 2. Consistent with our findings, pregnancy rates decreased to 37.5% in ewes treated with 5 ml PMSG/hCG compared to those treated with 1.5 ml PMSG/hCG (87.5%) or 5 ml saline (75%) within the breeding season.[26] Also similar to our findings with deslorelin-treated does, serum estradiol concentrations increased in ewes treated with 5 ml PMSG/hCG compared to those treated with 1.5 ml PMSG/hCG or control.[26] In lactating dairy cows, a deslorelin dose of 750 µg resulted in decreased AI pregnancy rates (28%) compared to 450 µg deslorelin dose (41%) or gonadorelin-treated control cows (39%), suggesting a dose-dependent effect.[13] After resynchronization of nonpregnant cows in that study, only 9.6% of cows treated with the 750 µg deslorelin dose and 17% of cows treated with the 450 µg deslorelin dose became pregnant at the second AI compared to 25% of gonadorelin-treated control cows.[13] Not surprisingly, the decrease in second AI pregnancy rates was due to a result of suppressed ovarian activity in both deslorelin-treated groups, regardless of dose.[13] Delayed follicular growth, the development of follicular cysts, and failed ovulations in subsequent estrous cycles were also reported in lactating and nonlactating cows treated with deslorelin implant dosages ranging from 450 µg to 2,100 µg.[11–13,28,29] These findings are in line with the results of the current study that suggest the deslorelin-treated does experienced a disruption in their cycles, likely due to suppressed ovarian activity. Future studies are needed to determine an ideal dosage of deslorelin for ovulation advancement in goats without altering subsequent ovarian activity.

In mares, a single intramuscular injection of 1.8 mg of deslorelin acetate, suspended in SAIB (SucroMate), was sufficient for inducing ovulation when a dominant follicle was present.[30] On average, this would equate to a dosage of ~ 2 µg/kg. We extrapolated this dosage to a ~ 68-kg goat, which would be 136 µg. SucroMate has a concentration of 1.8 mg (1,800 µg) per ml, so the extrapolated volume for a goat is 0.076 ml. Due to the low volume and high viscosity of the solution, we elected to round up the volume to 0.1 ml (200 µg) to facilitate its administration. Compared to other GnRH agonists, this dosage is high. In general, 50 µg of the GnRH agonist gonadorelin diacetate tetrahydrate is commonly given to goats undergoing estrus synchronization in the US.[31] In other countries, 25 µg lecirelin is used for synchronizing ovulation in does.[32] The reported dosage for buserelin is even lower at 4 µg per doe.[33,34] In lactating dairy cows, both 450 µg (~ 0.7 µg/kg) and 750 µg (~ 1.2 µg/kg) deslorelin dosages have been investigated, with the larger dose causing a decrease in pregnancy rates, but both doses causing subsequent ovarian suppression.[13] These previous studies, combined with the results presented herein, provide a starting point for determining adequate dosing and timing for the use of deslorelin in SAIB for estrus synchronization in goats and require further investigation. If investigated, the feasibility of diluting SucroMate with another carrier (e.g. saline) also needs assessment since dosing below the 200 µg used in the current study would not be feasible without being able to adjust the volume and concentration.

In conclusion, the results did not support the use of the commercially available deslorelin product, SucroMate, for synchronization of estrus in goats at the dose of 200 µg per doe. The findings presented herein suggest that, at the dose given (200 µg), deslorelin exerted a superovulation effect on ovaries of treated does. This effect overstimulated the ovaries and caused subsequent ovarian suppression, altering the doe's ability to be rebred. Further research is needed to investigate alternative dosing regimens on ovulation and subsequent CL

function in small ruminants. Additionally, there is a need to thoroughly evaluate its use in synchronization protocols to ensure that the best time for AI is determined.

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Conflict of interest

None.

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