Songklanakarin J. Sci. Technol.
40 (4), 904-908, Jul. - Aug. 2018

http://www.sjst.psu.ac.th

Original Article

Effect of controlled internal drug release device and progesterone sponge on short-term estrus synchronization in *Zandi* ewes during the breeding season

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Received: 23 August 2016; Revised: 16 April 2017; Accepted: 16 May 2017

Abstract

The aim of this study was to investigate the effect of a controlled internal drug release (CIDR) device and progesterone sponge on the short-term estrus synchronization in *Zandi* ewes during the breeding season. Sixty *Zandi* ewes were selected and divided into 3 groups at the beginning of breeding season. The first group was the control group. The second group received insertion of a CIDR device and 1.5 ml of gonadotropin-releasing hormone on day 0, 1.5 ml of natural prostaglandin on day 6, and 2.5 mg of pregnant mare serum gonadotropin with removal of the CIDR device on day 7. In a third group, the same treatment was used, but a medroxyprogesterone acetate-impregnated sponge was inserted instead of the CIDR device. All of the ewes mated naturally. There were significant differences in estrus, fertility, and pregnancy rates between the second group and the control group ($P<0.05$). The CIDR device is recommended due to relative improvement of some reproductive parameters.

Keywords: CIDR, intravaginal sponge, sheep, estrus synchronization, breeding season

1. Introduction

Estrus synchronization allows us to manipulate time of parturition so that we can have a better time of delivery in a year. Better management of the market, easy access to feed, and lower amount of allocated work and costs are the other advantages (Whitley & Jackson, 2004).

The most common method of estrus synchronization in ewe is the use of intravaginal devices with a synthetic progesterone or progestogen such as flurogestone acetate (FGA) or medroxyprogesterone acetate (MPA) (Fukui, *et al.*, 1999). The intravaginal sponges containing MPA or FGA are usually inserted into the vagina for 10-14 days and combined with a dose of equine chorionic gonadotropin (eCG) about 24 hours before removing the progesterone sponge (Zeleke *et al.*, 2005). In addition, prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) can be injected 48 hours before or at the time of removal of sponge (Ali, 2007; Beck *et al.*, 1993; Dogan & Nur, 2006).

The traditional treatment for estrus synchronization in ewe and goats was developed over 30 years ago and is still recommended (Menchaca *et al.*, 2007). The treatment consists of a long progestogen insertion associated with an intramuscular injection of eCG given at the end of the treatment

Due to the negative effect of long-term progesterone treatment on the subsequent fertility of ewes (Vinoles *et al.*, 2001), a functional alternative short-term treatment has

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recently been proposed for estrus synchronization in ewes (Ali, 2007; Husein *et al.,* 2007). Short-term periods (5-7 days) of treatment with progesterone sponges have been used successfully for synchronization of estrus in ewes within or out of the breeding season (Ataman & Akoz, 2006; Beck *et al.,* 1993; Vinoles *et al.,* 2001). In 2009, the efficacy of using an intravaginal controlled internal drug release (CIDR) device for estrus synchronization was also approved by the FDA (Food and Drug Administration of America) and it is now used for estrus induction in anestrus ewes for 5 to 7 days (Jackson *et al.,* 2014). In addition, a dose of gonadotropin-releasing hormone (GnRH) has been widely used in cattle to manipulate patterns of follicular development in the ovaries (Macmillan *et al.,* 2003). Administration of GnRH causes ovulation of the dominant follicles in the atresian phase and induces a new wave of follicular growth within 3 to 4 days after treatment in every stage of the reproductive cycle in cattle (Twagiramungu *et al.,* 1995). An alternative method is the use of a simultaneous injection of GnRH and $PGF_{2\alpha}$ that has also been used in sheep during the breeding season (Beck *et al.,* 1996). The effective treatment of ewes in the synchronization of estrus using the combination of GnRH and $PGF_{2\alpha}$ has been reported in the study conducted by Ataman *et al.* (2006).

The aim of this study was to investigate the effect of a CIDR device and progesterone sponge on the short-term estrus synchronization in *Zandi* ewes during the breeding season.

2. Materials and Methods

Islamic Azad University animal health and breeding department approved all protocols and procedures used in this study. Sixty heads of 3-4 year old *Zandi* ewes with the average weight of 44-48 kg were selected. All were physically and reproductively healthy and pastured with mixed grass. The experiment was carried out in the countryside in the city of Baladeh situated in Mazandaran Province (36/2014° northern & 51/8083° eastern) of Iran in early September of 2015 which is the beginning of breeding season in this region. The ewes fed freely from pasturage, and salt and water were available for them. All rams were separated from the herd. After determining the age of the ewes and numbering them, the ewes were moved to dry lot and divided into 3 groups of 20 head each. The first group was the control group that received no treatment.

The second group received CIDR treatment that consisted of three steps. On day zero, the CIDR device was inserted intravaginally. Each CIDR contained 300 mg of natural progesterone (Pfizer® Animal Health, New Zealand), 1.5 ml of GnRH (each ml contains 0.0042 IU of buserelin acetate, Rooyan Darou®, Iran, I.M.). On the sixth day, 1.5 ml of $PGF_{2\alpha}$ (Vetalyse® [5 mg/ml dinoprost tromethamine], Aburaihan® Co., Iran) was given intramuscularly. On the seventh day, the CIDR was removed and 500 IU of pregnant mare serum gonadotropin (PMSG) (Folligon®, 200 IU/ml, Intervet, Boxmeer, The Netherlands) was injected intra-muscularly into each of the ewes.

The third group received the same treatment as the second group, but instead of the CIDR device, sponges impregnated with 60 mg of medroxyprogesterone acetate (Esponjavet 60 mg, Hipra-lab, Spain) were inserted intra-vaginally in the ewes. The treatments used on the three groups are presented in Table 1 and Figure 1. After removal of the CIDR and sponge on the seventh day, clinically healthy rams

Table 1. Average age and weight and the treatment used for the groups of ewes.

Groups	Number (head)	Average Age (year)	Average Weight (kg)	Treatment
Control	20	3.45	45.95	No treatment
CIDR	20	3.50	46.06	Day 0: insertion of CIDR and injection of 1.5 mg GnRH simultaneously + 6th day: injection of 1.5 mg $PGF_{2\alpha}$ + 7th day: removal of CIDR and injection of 2.5 mg PMSG, simultaneously
Sponge	20	3.40	45.82	1st day: insertion of sponge and injection of 1.5 mg GnRH simultaneously + 6th day: injection of 1.5 mg $PGF_{2\alpha}$ + 7th day: removal of sponge and injection of 2.5 mg PMSG, simultaneously

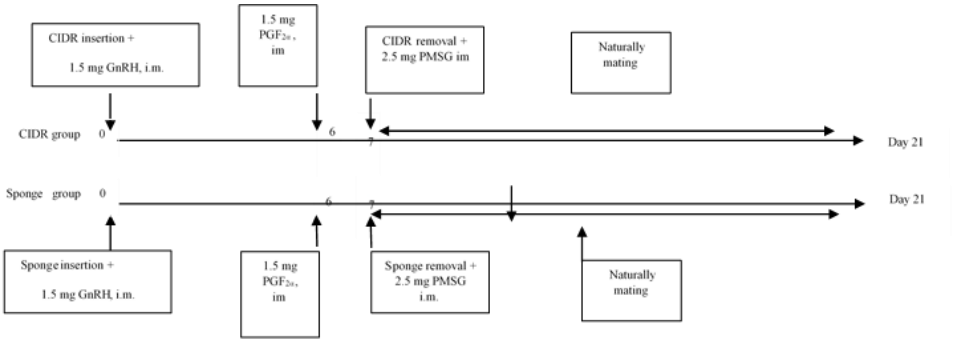

Figure 1. Treatments used for CIDR and sponge groups.

with a good reproductive history in the previous breeding season were allowed to enter into the three groups of ewes for mating. One 2-4 year-old ram for every 5 heads of ewes entered for 2 weeks for all groups.

Data on the herd of ewes were collected. The number of lambs born per ewe (single or twins), sex, and birth weight were recorded. Also calculated and compared between the three groups were i) estrus rate (number of ewes showing estrus/total number of ewes in each group × 100), ii) pregnancy rate (number of pregnant ewes/number of mated ewes in each group × 100), iii) fertility rate (number of ewes lambing/number of mated ewes in each group × 100), iv) litter size (number of lambs born in each group/total number of mated ewes in each group × 100), and v) multiple birth rate (number of multiple lambing/total lambing in each group × 100).

For the statistical analysis, initially the mean squares of reproductive parameters were compared with each other between the three groups. The coefficients of variation (CV) of the reproductive parameters were then compared individually in each of the groups. Analysis of variance of reproductive parameters including the estrus rate, pregnancy rate, fertility rate, litter size, and multiple birth rates in ewes were done using SPSS (ver.20) and the Dunnett and Duncan methods. A comparison of the means was performed using the Chi-square test at the probability level of 5%.

3. Results and Discussion

There were significant differences (P<0.05) between the CIDR group and the control group in the estrus rate, pregnancy rate, and fertility rate, but there were no significant differences (P>0.05) between the CIDR group and the sponge group in reproductive parameters (Table 2). Furthermore, no significant differences (P>0.05) were observed between the sponge group and the control group in terms of reproductive parameters. Moreover, no significant differences (P>0.05) were found between the treatment groups and the control group in litter size, average birth weight or multiple birth rates. Based on the results of variance analysis, the highest variations are related to estrus rate, pregnancy rate, and fertility rate (Table 3).

Various sources of exogenous progesterone (CIDR and sponge) are used to induce estrus and estrus synchronization in seven days. This pattern of estrus synchronization was used in a study conducted by Jackson *et al.* (2014). They used CIDR and PG injection and only CIDR insertion for 7 days and tested the reproductive parameters between the two treatment groups and a control group. They found no significant differences (P≥0.28) between the treatments in lambing rate and multiple birth rates, but the CIDR treated ewes had fewer days to estrus and lambing (P≤0.05) than the control ewes (Jackson, *et al.*, 2014). Furthermore, this pattern of estrus synchronization was applied in a study carried out by Wheaton *et al.* (1992). They reported that the interval between the transitional phase and estrus in ewes treated with CIDR lasted for 2 days after CIDR withdrawal on average, but in the control group that received no treatment, this interval lasted for 21 days on average (Wheaton *et al.*, 1992). However, Titi *et al.* (2010) found no difference between the control group and the CIDR group that was treated for 5 days regarding the average lambing days. In fact, the days of lambing were similar for all groups and as in this current study they found no significant differences (P>0.05) between the treatment groups and the control group in the estrus rate. But they reported increases in the fertility rate in the ewes treated with CIDR for 5 days in combination with GnRH and $PGF_{2\alpha}$ which was in agreement with the present study. This was probably because the ewes did not have synchronous follicular developments or active corpus luteum. Furthermore, the ewes may have shown a false estrus or a complete estrus cycle at the time of $PGF_{2\alpha}$ injection.

In agreement with the present study (short-term treatment with exogenous progesterone), Karaca *et al.* (2008) used progestogen sponges in combination with GnRH, $PGF_{2\alpha}$, and eCG for synchronization of estrus with two methods of short-term and long-term treatments. With the exception of fertility rate, there were no significant differences (P>0.05) between the other reproductive parameters in their study. The results showed a higher fertility rate in the short-term treatment (6 days) than in the long-term treatment (12 days) with progestogen at the beginning of the mating season (P<0.05). Vinoles *et al.* (2001) concluded that the lower pregnancy rate observed after long-term progestogen treatment was related to a slower follicular turnover that promoted the ovulation of persistent dominant follicles, and short-term treatment resulted in a higher pregnancy rate probably due to the ovulation of newly recruited growing follicles. Further, Barrett *et al.* (2004) declared that the injection of 500 IU of

Table 2. Assessment of changes in reproductive traits in the different experimental groups.

Parameters	Control group	Sponge group	CIDR group
Number of ewes (head)	20	20	20
Male lamb (head)	9	15	15
Female lamb (head)	8	7	7
Total number of lambs (head)	17	22	22
Average weight of male lambs (kg)	3.63	3.73	3.71
Average weight of female lambs (kg)	3.47	3.16	3.53
Total average weight of lambs (kg)	3.55	3.45	3.62
Number of delivery (birth)	16	19	20
Estrus rate (%)	80 [b]	95 [ab]	100 [a]
Number of twins	1	3	2
Litter size (%)	6.25	15.79	10
Pregnancy rate (%)	80 [b]	95 [ab]	100 [a]
Fertility rate (%)	80 [b]	95 [ab]	100 [a]
Multiple birth rates (%)	106.25	115.79	110

[a b] represent a significant difference between the groups (P<0.05)

Table 3. Analysis of variance and coefficient of variation.

Sources of Variation	Degree of freedom	Mean Squares				
		Estrus rate	Multiple birth rate	Pregnancy rate	Fertility rate	Litter size
Treatment	2	*433.33	70.75	*433.33	*433.33	70.75
Experimental Error	9	122.22	176.16	122.22	122.22	176.16
Coefficient of Variation (%)	-	12.1	11.9	12.1	12.1	11.9

* represents significant differences at a level of 5%

eCG after 12 days of progestogen treatment had limited effects on the dynamics of ovarian follicular waves.

In the present study, although a high dose of PMSG (2.5 mg) was used in short-term treatment with progestogen (7 days), no significant differences were observed in multiple birth rate or litter size. This is probably due to the different protocol of using $PGF_{2\alpha}$ and GnRH dosage in the *Zandi* breed which naturally has a lower multiple birth rate. However Menchaca and Rubianes (2004) reported the lysis of the corpus luteum with the injection of $PGF_{2\alpha}$ that increased estrus rate and pregnancy percentage during the treatment with progestogen in the breeding season of sheep.

Husein and Kridli (2003) have reported that seasonal anestrus ewes treated with GnRH-$PGF_{2\alpha}$ showed an increase in estrus responses and pregnancy rates. Also, the use of GnRH in the current study improved the estrus rate, pregnancy rate, and fertility rate.

Disagreements observed among the various studies may be due to the increase in the number of follicles, follicular synchronization, and starting a new recruitment of follicular growth for ovulation at the time of starting a treatment protocol.

4. Conclusions

Based on the results, it can be concluded that both CIDR and sponge can be used for estrus synchronization. However, due to the ease of CIDR insertion, fewer side effects, and the improvement in the estrus, pregnancy, and fertility rates in comparison with the sponge, the CIDR is recommended for short-term treatment in the breeding season for estrus synchronization.

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