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Research Article

Comparison of Hormonal Treatment Kisspeptin with GnRH and hCG on the some Reproductive Performance of Cyprus, Does during Non-Breeding Season

Maad Hasani AL-Ameri

Department of Surgery and Obstetrics, Faculty of Veterinary Medicine, University of Fallujah, 31002, Anbar, Iraq.

Abstract | The current study was conducted to investigate the influence of Kisspeptin, GnRH and hCG on some reproductive performance of Cyprus does during the non-breeding season. A total 55 Cyprus does 2-6 years old and averages 45 kg body weight. The does were randomly divided into five equal groups (11 does per group). The first group (B1) regarded as a control group, intramuscular injection with normal saline, whereas, the second (B2) and third (B3) groups were injected with 4 and 8 µg / kg body weight of Kisspeptin-10 intravenous respectively. The fourth (B4) and fifth (B5) groups were injected with hCG (250 IU / doe) and GnRH (20 µg / doe) intramuscular respectively. Bucks were introduced after 24h of the treatment in all groups, ensuring that does exhibit estrus were mated for three consecutive estrus cycles. There were significantly in kilogram kids per goats joined in group B2 (2.84±0.05 kg) and then group B5 (2.45±0.04 kg) compared with other groups. The kilograms born per goat kidding ($P< 0.05$) was lower in group B4 than other groups. Gestation length was significantly longest in group B1 as compared with other groups. Results showed that there were no significant different ($P>0.05$) male kid weight and female kid weight. In conclusion, kisspeptin-10 (4 µg/ kg/ animal) enhanced kilogram kids per goats joined and then GnRH in Cyprus goat does during non- breeding season.

Keywords | Kisspeptin-10, GnRH, hCG , Cyprus goat, Non-breeding season, Reproduction

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***Correspondence** | Maad Hasani Al-Ameri, Department of Surgery and Obstetrics, Faculty of Veterinary Medicine, University of Fallujah, 31002, Anbar, Iraq; **Email**: maad.hassani@uofallujah.edu.iq
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INTRODUCTION

Iraq has a small population of goats, it is about 1.260.481 head in 2016 (FAO, 2016). Local goat in Iraq consists of two breeds, Native goat and Meriz that are raised primarily for meat and milk production (Magid et al., 2003). Cyprus goats were introduced in Iraq and it's known as Damascus goat or Shami goats have some advantages Fertility, prolificacy as averaging 1.80 kids per doe kidding and dual purpose animal (meat and milk), however, it is considered a seasonal breeder which it starts in late August and extends through mid-December (Mavrogenis et al., 2006).The reproductive seasonality impact of variation on the price of meat and milk over the year, which affects the economy of farmers and the food industry (Gómez-Brunet et al., 2012).To solve this problem, researchers and breeders used tools to develop relevant techniques to manipulate the sexual activity of animals (Delgadillo, 2011). There are many methods for manipulation of reproduction, one method by using hormonal of these treatments (Medan et al., 2002; Husein et al., 2005; Acar et al., 2013).

Kisspeptins are the peptide product of the Kiss1 gene and act to stimulate GnRH secretion (Gottsch et al., 2004; Messager et al., 2005). Kisspeptins are located in the ovine brain in the arcuate nucleus (ARC) and the dorso-lateral preoptic area (POA) (Estrada et al., 2006; Franceschini et al., 2006; Smith et al., 2007). These ARC cells transmit sex-steroid feedback (both negative and positive) to the GnRH neurons (Smith, 2009). There is a considerable

body of evidence that this neuropeptide regulates seasonal reproduction (Revel et al., 2006; Clarke et al., 2009). The seasonal change in Kiss1 expression, the extent to which kisspeptin cells provide input to the GnRH neurons is greater during the breeding season than in the non-breeding season (Smith et al., 2008).

Nowadays, researchers are using kisspeptin which is considered gatekeeper of the hypothalamic-pituitary-gonadal (HPG) axis in which the hypothalamic GnRH plays a crucial role. Kisspeptin-10 can stimulate this axis of ewes in anestrus (Sebert et al., 2010) consequently the release of LH and FSH (Ezzat et al., 2009) at 20- 30 min after the second injection in anestrus does (Hashizume et al., 2010).

Gonadotropin releasing hormone (GnRH) or human chorionic gonadotropin (hCG) injections are applied to improve the reproductive performance in anestrus goats (Medan et al., 2002; Rodríguez-Martínez et al., 2018). A strategy of reproductive performance included inducing estrus and ovulation (Cameron et al., 1988; Khan et al., 2003; González-Álvarez et al 2016).The hCG has an activity similar to luteinizing hormone (LH), while the GnRH acts on the pituitary gland, stimulates the release of LH and FSH and subsequently the secretion of steroid hormones from the gonads. These hormones when administrated in the luteal phase act indirectly or directly on the ovary generating the formation of an accessory corpus luteum and increasing the serum progesterone concentration (Ishida et al.,1999; Lankford et al., 2010). Increased the progesterone concentration (Moeini et al., 2013) led to improve the embryo survival (Lashari and Tasawar, 2010) and accelerate embryonic development and improve pregnancy rates (Nephew et al., 1994).

There is no available information about the effect of kisspeptin-10, hCG and GnRH on some reproductive performance of Cyprus does in non- breeding season.

MATERIALS AND METHODS

Animals

The present study was conducted in Ruminant Research in the Department of Agricultural Research Station / Ministry of Agriculture, Abu Ghraib /Baghdad (latitude 33 20 ‘° N). A total of 55 Cyprus does 2-6 old and averages 45 kg body weight. Goats were kept indoors at night, and allowed field grazing pasture near the station on day. Indoors, the goats were fed hay and concentrated diet. All does have free access to water and trace mineral salt blocks.

Experimental Design

During the non-breeding season in 22 June does were divided randomly into five groups (11 does per group). Before starting the hormonal treatment were does weight. The first group (47.6 ± 1.24 kg) control (B1) 0.9% NaCl intramuscular injections are divided into two doses (2 ml / animal / dose). A second group 43.0 ± 2.86 kg (B2) injected kisspeptin-10 intravenous (AnaSpec, Inc., USA) 4 µg / kg/ animal. A third group (46.6 ± 3.77 kg) (B3) injected kisspeptin-10 intravenous 8 µg / kg/ animal. Divided doses based on preliminary results (Hashizume et al., 2010). Fourth group 43.04 ± 3.00 kg (B4) hCG intramuscular injection (Chorulon, Intervet International BV, Boxmeer, Holland) 250 IU/ animal, divided two doses. A fifth group 44.7 ± 2.49 kg (B5) GnRH intramuscular injection (Receptal, Intervet International BV, Boxmeer, Holland) 20 µg/ animal and divided two doses. All goats received all the treatments and carried out two doses at 2-h intervals. Ten fertile bucks introduced to the does of all groups, two bucks for each group for estrus detection and mating; started 24 hours after treatments and left to ten days. Estrus checked continuously by observation. The kidding performance of the does in all groups assessed by kidding data including kilogram kids per goats joined, kilograms born per goat kidding, gestation length, birth type, kid weight and sex which recorded.

Statistical Analysis

Statistical analysis was performed with the SPSS Statistics 24.0 (2016). Statistical significance was declared at $P<0.05$.

RESULTS

In the present study, the effect of hormonal treatments on some reproductive performance of Cyprus goat does in non- breeding season summarized in Table 1. There were significant differences ($P< 0.05$) among treated groups on kilogram kids per goats joined. The results revealed that the mean kilogram kids per goats joined increased in group B2 (2.84±0.05 kg) than other groups. As shown in the Table 1 kilograms born per goat kidding had lower ($P< 0.05$) in group B4 than other groups. Additionally the mean gestation length was significantly ($P< 0.05$). However, the gestation length increased in group B1 compared to other groups. No significant differences were detected in male kid weight and female kid weight (Table 1). The significantly ($P<0.05$) higher in overall kids weight (kg) in groups (B2, B1, B3 and B5) than B4 group.

The percent of Cyprus goat does showing different birth type based on treatments is presented in Table 2. Birth type proportions for twinning were higher ($P<0.05$) (80%) and (72.73%) in B5 and B3 groups respectively followed by in single ($P<0.05$) (40%) in B4 group and triplet ($P<0.05$) in B1 group. The sex ratio of kids was higher 60% male in B1 group and 70% female in B4 group (Table 2).

Table 1: Effect of hormonal treatments on the some reproductive performance of Cyprus does during non-breeding season (Mean ±SE).

Parameters / Treatments	No of goats	Kgs kids per goats joined	Kgs born per goat kidding	Gestation length (days)	kids weight (kg)		
					Male	Female	Overall
B1	11	1.70±0.06 cd	3.11±0.12 a	153.17±0.83 a	2.24±0.31 a	2.50±0.43 a	3.11±0.48 a
B2	11	2.84±0.05 a	3.12±0.06 a	150.70±0.66 b	2.11±0.19 a	2.38±0.40 a	3.12±0.37 a
B3	11	1.95±0.05 b	3.07±0.08 a	150.29±0.64 b	2.05±0.12 a	2.25±0.44 a	3.07±0.33 a
B4	11	1.63±0.03 cd	2.55±0.05 b	150.29±0.68 b	1.78±0.03 a	2.51±0.38 a	2.55±0.32 b
B5	11	2.45±0.04 ab	3.03±0.07 a	150.22±0.61 b	2.27±0.37 a	1.95±0.26 a	3.03±0.30 a

Means within the column with different letters are significantly different ($p < 0.05$).
B1 = 2ml (0.9% NaCl) (control), B2 (4 µg / kg/ animal) kisspeptin, B3 (8 µg / kg/ animal) kisspeptin , B4 (250 IU hCG / animal) and B5 (20 µg/ animal GnRH).

Table 2: Birth type and sex ratio

Treatments	Birth type			Overall	No. of Male	%	No. of Female	%
	Single	Twin	Triplets					
B1	3 (30%)b	2(4) (40%)d	1(3) (30%) a	10	6	60	4	40
B2	4 (23.53%)c	5(10) (58.82%)c	1(3) (17.65%)b	17	9	52.95	8	47.05
B3	3 (27.27%)b	4(8) (72.73%) b	-	11	5	45.45	6	54.55
B4	4 (40%)a	3(6) (60%)c	-	10	3	30	7	70
B5	3 (20%)d	6(12) (80%) a	-	15	7	46.66	8	53.34

Means within the column with different letters are significantly different ($p < 0.05$).
B1 = 2ml (0.9% NaCl) (control), B2 (4 µg / kg/ animal) kisspeptin, B3 (8 µg / kg/ animal) kisspeptin , B4 (250 IU hCG / animal) and B5 (20 µg/ animal GnRH).

DISCUSSION

New strategies for the manipulation of reproduction in seasonal breeders by kisspeptin system. Kisspeptin changed in reproductive function during seasonality acyclic females which it reduced expression in the arcuate nucleus during non-breeding season as results increased negative feedback of estrogen on GnRH secretion (Clarke et al., 2009). Therefore, the process of correcting lower levels of kisspeptin in anestrous by infusion of kisspeptin (Smith, 2012) led to change gonadotropin secretion and ovaries that responses to synchronize LH surges and cause ovulation (Caraty et al., 2007).

The effect of exogenous kisspeptin-10 to stimulate LH and FSH-release in goats has been reviewed by Hashizume et al. (2010) who indicated that it given 1, 5 or 10 µg/ kg/ animal at 2-h intervals of i.v. injection of kisspeptin-10 led to stimulate LH at 20- 30 min after the second injection.

In the present study, the effect of hormonal treatments on some reproductive performance of Cyprus goat does in non- breeding season. There were significant differences ($P< 0.05$) among treated groups on kilogram kids per goats joined. The results illustrated that the mean kilogram kids per goats joined increased in group B2 (2.84±0.05 kg) than other groups. These results agreed with findings (Hashizume et al., 2010) in the present study that injection of Kisspeptin-10 (4 µg/ kg/ animal) and (8 µg/ kg/ animal) at 2-h intervals. In contrast, injection single dose (1 µg/ kg/ animal) of Kisspeptin-10 did not stimulate the release of LH during the anestrous in female goats (Arjmand et al., 2014).

The results of the present study showed that hormonal treatments caused the significant increase in kilogram kids

per goats joined. Kisspeptin-10 can stimulate the quiescent hypothalamo- hypophyseal-ovarian axis in anestrus. Caraty et al. (2007) reported that infusion of Kisspeptin-10 led to elevate plasma LH levels and caused to synchronize LH surges in progesterone-primed and ovulation. In addition, Sebert et al.(2010) reported that kisspeptin increase LH surge in 75% of treated animals within 24h after initiation of kisspeptin-10. Caraty et al. (2012) observed that kisspeptin stimulate to activate ovarian function, increase ovarian steroidogenesis andovulation.

These studies illustrate the ability of kisspeptin to stimulate hypothalamo- hypophyseal-ovarian axis during non-breeding season in Cyprus does led to induce ovaries function , secretion E2 , higher ovulation rate, high conception rate and production of embryos. These hypotheses support data result in the present study to increase kilogram kids per goats joined in group B2 and less in group B3. On the other hand, increased serum concentration of P4 as result induced the formation of accessary corpus luteum (Fernandez et al., 2018). It has been reported that (Bazer et al., 1998) there were interactions between the conceptus, uterus and ovaries that require the continued actions of progesterone. Lankford et al. (2010) provide evidence that increased serum P4 concentrations as result increased the number of corpus luteum that reduces embryonic mortality.

In the present study, increase kilogram kids per goats joined in groups B2 and B5 than other groups indicated maintenance of pregnancy that is require elevated progesterone and protect the corpus luteum during early pregnancy and inhibition prostaglandin F2α from uterine by interferon-tau (IFNT) from the elongating embryo (Wiltbank et al., 2018) and accelerate embryonic development and improve pregnancy rates (Nephew et al., 1994). However, the results obtained in this study in group B5 agreement with (Medan et al., 2002; Husein et al., 2005; Zonturlu et al., 2018). In contrast, decrease kilogram kids per goats joined in group B4 was similar to other studies reported (Fonseca et al., 2005; Dias et al., 2018) hCG treated to improve ovulation synchronization and in contrast decrease in the pregnancy rate. Provide evidence that decrease kilograms born per goat kidding in group B4 as compared with other groups.

The breeding season in Cyprus goat onset in late August (Mavrogenis et al., 2006). Goats in group B1 showed estrus when breeding season starts in this time. However, decrease kilogram kids per goats joined in group B1 than other groups that indicate provide evidence that the effect of hormonal treatments increase kilogram kids per goats joined and distinguish goats treated kisspeptin-10 (4 µg / kg/ animal) group B2 and GnRH group B5 during non-breeding season.

From the results of the present study, gestation length in group B1 was the longest compare with groups due to external and internal factors such as breeds, breeding season, litter weight and parity (Mellado et al 2000). On the other hand, Ruvuna et al. (1988) reported that differences in the gestation length due to season of kidding and litter size. Mellado et al. (2000); Haldar and Ghosh. (2015) pointed out that gestation length was longer one day if goats mated in summer compare to mate in autumn. However, gestation length within an acceptable ranges (Haldar and Ghosh, 2015).

In the current study, the effect of hormonal treatments produced a higher proportion of twins in B5 and B3 groups. However, Cameron et al. (1988) reported that increased ovulation rate of goats treated with GnRH. Caraty et al. (2012) pointed out that kisspeptin increase ovarian steroidogenesis and ovulation. In addition, there were differences between B2 and B3 groups as results increase ovulation rate in B2 group than B3 group due to use dose kisspeptin-10 (4 µg / kg/ animal) vs. (8 µg / kg/ animal) lead to obtain 1 Triplets in B2 group. These results provide evidence that lower levels of kisspeptin in anestrous (Smith, 2012) led to change gonadotropin secretion and ovaries that response to synchronize LH surges and cause ovulation (Caraty et al., 2007). On the other hand, birth type difference among groups as results the number of ovulations and time of ovulation (Simoes et al., 2008; Ince, 2010).

In the present study, sex ratio of kids was higher 60% male in B1 group. These results agreement with Sivakumar and Soundararajan, (2006) reported that the percentage of male was higher all the seasons except during summer. In contrast, it has been reported that Abecia et al. (2017) there were not differ significantly affect lunar phase and season on offspring sex ratio in goats. On the other hand, sex ratio of kids was higher 70% female in B4 group may be there were factors such as timing of hormonal treatments and mating which related to change sex ratio of kids. However, decreased female weight in B4 group due to most kids born to female's agreement with Al-Shaikh and Mogawer, (2001) who found that birth weight of male kid was higher than that of the female kid.

CONCLUSION

It can be concluded that the use of hormonal treatments kisspeptin-10, GnRH and hCG are very effective for stimulating hypothalamo- hypophyseal-ovarian axis in Cyprus does during the non-breeding season. The results of this study indicate that kisspeptin-10 (4 µg/ kg/ animal) enhanced kilogram kids per goats joined and then GnRH, increased proportions for twinning by using GnRH and kisspeptin-10 (8 µg/ kg/ animal) and increased number of

kids by using kisspeptin-10 (4 µg/ kg/ animal) in Cyprus does during the non- breeding season.

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