Effect of Dopamine Antagonist (Resperdal)® on Ovarian Activity of Egyptian Baladi Goats Out-Off Breeding Season

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Abstract: The present investigation aimed to treat the female goats out – off breeding season by means of one of dopamine antagonist preparation which block dopamine receptors in the reproductive system. Two groups of mature non cyclic Baladi does (experimental and control) fed and managed under the natural Egyptian environmental conditions were used at the end of the breeding season. The experimental animals were treated orally by 16 mg. dopamine receptor antagonist drug (Resperdal)® / doe divided into two doses with three days interval. The estrous signs and ovarian activity were investigated by ultra- sonography and the results were confirmed by blood plasma progesterone assay. The results indicated more number of does showing estrus signs and improvement in the ovarian activity as well as blood plasma progesterone in experimental animals than in control ones. It was concluded that administration of dopamine receptor antagonist (Resperdal)® can be used for treating more than 50% of does out – off breeding season which reflect positively on the kidding crop.

Key words: (Resperdal)®, ovarian activity; goats; dopamine antagonist

1. Introduction
Seasonal breading in sheep, goat and horse is governed by photoperiod. The signal requires a euro-endocrine transduction (Herbison, 1995). Dopamine, opioids and melatonin are the wide known mediators between brain and gonadal functions (Parvizi, 2000). Dopamine is a hormone, derived from amino acid tyrosine, synthesized from hypothalamus and ventrolateral medulla, act as a neurotransmitter signal for reproduction in seasonal breeding animals (Simonian et al., 1998). Its function in male differ than in female animals, however, it was recorded that, central dopamine is a neurotransmitter in the control of the sexual function in male, its stimulation enhances erection, increases testosterone level and increases sexual desire (Francois and Juleen, 2001 and Juan et al., 2005). In female, cerebrospinal dopamine, inversely correlated with plasma LH (Besognet et al., 1996), inhibits gonadotropin releasing hormones and or luteinizing hormone (GnRH/LH) in an anoestrus ewes (Anderson et al., 2001). Moreover, dopamine inhibits the release of prolactin and interferes with mammary gland development and lactation (Serafim and Felicio, 2001).

Dopamine antagonists are drugs which blocks dopamine receptors. In this respect, it was demonstrated that, the application of dopamine receptors antagonists (Sulpride, Resperdal,…®) can be used for improving reproductive performances of seasonal breeding animals and treating the animals out-off season. Dopamine D2 antagonist was used to induce ovarian activity in seasonal anoestrus mare, increase prolactin, FSH and LH concentrations, the estrous cycle length, ovulation and luteal progesterone were as normal estrus animals (Besognet et al., 1996). In ewe, dopamine antagonists enhance the amplitude of LH pulses during non breeding season (Gallegos et al., 1998). On the other hand, administration of dopamine antagonist (sulpride) to seasonally anovulatory mares increased daily prolactin levels but did not stimulate gonadotropin secretion or ovarian activity (Donadeu and Thompson, 2002). Moreover, it was postulated that dopamine D2 antagonist had been used for induction of lactation in intact mares during birth season with the presence of gonadal hormones but not in ovarictomized animals (Guillaume et al., 2003). In goats, Luis et al. (2011) Stated that dopamine antagonist increased LH secretion under high plane of nutrition during short day light. Therefore, the aim of the present investigation was a trial to improve the ovarian activity of Egyptian Baladi goats out-off breeding season by administration of dopamine antagonist (Resperdal)®.

2. Materials and Methods
A total number of 14 mature non-cyclic Baladi goats (14 -16 months age and 26±2.5 kg. life body weight.) were used during June (The end of the breeding season) after ultrasonic (U, 1000, scanning probe, 3.5 M.Hz) examination of their ovaries. The animals were divided into 2 groups (experimental and control) and were fed on concentrated mixture
The animals were housed and managed under Egyptian environmental conditions. The experimental animals were orally administered 16 mg dopamine receptor antagonist drug (Risperdal® 4 mg/capsule manufactured by Janssen-cilag pharm – Beerse, Belgium.) divided into 2 doses with 3 days interval. The estrus signs were detected by vasectomized buck. The ovarian activity was examined weekly by ultrasonography for three weeks as well as heparin blood samples were collected. Plasma of the blood samples were separated by centrifugation (3000 g/15 min. 4°C) then kept at – 20°C till progesterone assay. Progesterone assay was carried out in order to confirm the functional corpus luteum. The assay was run by radioimmunoassay (Abraham, 1981) with using kits from diagnostic product corporation (Los Angeles, USA). Sensitivity of assay was 0.02 ng/ml. the results were analyzed statistically according to Snedecor and Cochran (1980) using "t" test.

3. Results

The present results (Table 1) showed that administration of dopamine receptors antagonists (Risperdal®) to does with smooth ovaries activated them in the form of increase the number of does showing estrus signs (71.43 vs. 14.28% in non treated does). The sonographic examination showed more does number with mature Graffian follicles (71.43 vs. 14.28%) and functional corpus luteum (57.14 vs. 0.0%) in experimental does than in control ones. Moreover, Risperdal® treatment induced regular estrus cycle length averaged 19 ± 2.27 days in comparing to more than 21 days in control non-cyclic does.

The present results in table(2) showed that the level of progesterone in experimental does was significantly higher than in the control ones, the highest level was during 2nd week (4.89±1.08 ng/ml) however, the level was below 1 ng/ml in control does. The ultrasonographic examination showed the state of the ovaries (Figs. 1,2 and 3).

Table 1: Effect of dopamine receptors antagonist (Risperdal®) on estrus activity in Baladi does

<table>
<thead>
<tr>
<th></th>
<th>Experimental</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of does used</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>No of does exhibited estrus signs</td>
<td>5/7 (71.43%)</td>
<td>1/7 (14.28%)</td>
</tr>
<tr>
<td>No of does showed smooth ovaries</td>
<td>2/7 (28.58%)</td>
<td>6/7 (85.27%)</td>
</tr>
<tr>
<td>No of does showed follicles</td>
<td>5/7 (71.43%)</td>
<td>1/7 (14.28%)</td>
</tr>
<tr>
<td>No of does showed corpus luteum</td>
<td>4/7 (57.14%)</td>
<td>-</td>
</tr>
<tr>
<td>Estrus cycle length (days)</td>
<td>19±2.27</td>
<td>&lt; 21</td>
</tr>
</tbody>
</table>

Figure 1: Ovary of doe showing mature follicle.
Figure 2: Smooth Ovary of doe.

<table>
<thead>
<tr>
<th>Table (2) Effect of dopamine receptor antagonist (Resperdal)® on progesterone levels of Baladi does</th>
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<tbody>
<tr>
<td>Progesterone (ng/ml)</td>
</tr>
<tr>
<td>1st week</td>
</tr>
<tr>
<td>2nd week</td>
</tr>
<tr>
<td>3rd week</td>
</tr>
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Mean ± S.D   * P < 0.05   ** P < 0.01

Figure 3: Ovary of doe showing corpus luteum.
4. Discussion
The present results (Table 1) showed that the treatment of smooth ovaries of does out-of-the breeding season with dopamine receptor antagonist (Resperdal)® was associated with higher incidence of estrus and their ovaries showed higher shedding of both mature, Graffian follicles and corpus luteum. It can be suggested that Resperdal inhibit / antagonize the release of dopamine hormone which inhibit the synthesis and release of gonadotropins (Anderson et al., 2001). Resperdal may be act directly on the ovarian function (Besognet et al., 1996) or directly on the hypothalamus and pituitary gland to increase prolactin, FSH and LH concentration (Besognet et al., 1997). Moreover, Resperdal may be act by blocking the receptors of dopamine hormone on reproductive system, however, it was recorded that in ewes and goats, the seasonal changes in the hormonal LH pattern mainly reflect an increase in the negative feedback exerted by estradiol under long days on the frequency of pulsatile LH secretion. However, the resulting seasonal inhibition of LH secretion involves the activation of monoaminergic and specially dopaminergic systems by estradiol (Thiery et al., 2002).

The present investigation resulted (Table 2 and Figs,1,2 and 3) in regular regimen of progesterone level and estrus cycle in does treated with Resperdal with mature functional corpus luteum, may be due to the positive effect of Resperdal on LH release and ovulation, however, it was recorded that dopamine antagonists increased LH secretion in goats under high plane of nutrition during short day light (Luis et al., 2011).

Therefore, it can be concluded that administration of dopamine receptor antagonist (Resperdal)® can be used for treating more than 50 % of does out-off the breeding season which reflect positively on the kidding crop.

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