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The Effect of Naloxone on Blood Progesterone of Creole Mexican Ewes with Induced Short Luteal Phase During the Anoestrus Season

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Abstract: From an extensive sheep flock, 20 creole mexican ewes were selected, age fluctuated between 2 and 6 years, allocated at random in groups of 10. Group 1 (n = 10) received a subcutaneous implant with 15 mg naloxone HCL. Group 2 (n = 10) was sham treated on the may 30-2008. Total 7 days after receiving the implant they were treated with GnRH (250 ng iv at 2 h interval for 24 h) and one final GnRH iv injection of 125 μg. Blood samples were collected at 12 h intervals since, the beginning of the experiment and continued until 15 days after the last injection of GnRH. In 2 of the control ewes it was observed that progesterone concentrations increased since 36 h after the first dose of GnRH until a maximal of 3 ng mL^{-1} of plasma progesterone concentration was reached on day 7 and the remaining 8 control ewes showed short luteal phases with a maximum of 1 ng mL^{-1} of plasma progesterone. In ewes treated with naloxone 3 showed short luteal phases and 7 naloxone treated ewes had plasma progesterone concentrations similar to control ewes with normal luteal phases. There was a significant effect of treatment ($p<0.0019$) between control and naloxone treated ewes. This results show that endogenous opioids are important modulators of reproduction in the ewe.

Key words: Naloxone luteal phase, ewe, anestrus, GnRH, HCL, modulators of production

INTRODUCTION

When the Corpus Luteum (CL) does not develop after the display of estrus, fertility is decreased, event frequently present during early postpartum, at puberty and during the onset of the breeding season (Bramley *et al*., 2005). The ewe is an adequate experimental animal to study the occurrence of short luteal phases because they can be induced to ovulate with the administration of LH and GnRH (Hunter, 1991; Beard and Hunter, 1996). When ovulation is induced using either LH or GnRH the formed CL is smaller and secretes less progesterone (Bramley *et al*., 2005). Many are the causes for the development of a functional CL. It is possible that CL does not develop due to attenuation of the LH surge (Bartlewski *et al*., 2004).

In previous experiments, it was reported that the administration of small doses of naloxone (0.5 mg im) at 12 h intervals for several days, induce changes in behavior and changes in the plasmatic concentration of hormones related to reproduction in sheep, rams and bucks (Fuentes, 1989; Fuentes *et al*., 1997, 2001, 1998). Furthermore, it has also, being reported that the administration of naloxone in luteal phase ewes evokes large amplitude GnRH/LH pulses (Horton *et al*., 1987).

The hypothesis of this study is based on the effect of naloxone to evoke LH release, if we induce ovulation with the continuous administration of GnRH and we use naloxone to facilitate LH release, a functional Cl will be physiological able to maintain the duration of the luteal phase in the ewe during the anestrus season.

The objective of this research was to observe the effect of a subcutaneous implant with 15 mg naloxone in anestrous creole Mexican ewes with GnRH induced short luteal phases.

MATERIALS AND METHODS

For the purpose of this study, 20 creole Mexican ewes were selected at random from a range managed flock, age fluctuated between 2 and 6 years, ewes were out to pasture at 8:00 am and returned to open padocks at

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18:00 h, water was provided *at libitum*. Group 1 (n = 10) received a subcutaneous implant with 15 mg of naloxone embedded in a nitrocellulose pellet. Group 2 (n = 10) was sham treated. Seven days after both groups received the implant, ovulation was induced following the method of Beard and Hunter (1996) and both groups were injected iv with 250 ng of GnRH at 2 h intervals for 24 h with a final application of 125 μg of iv GnRH. Blood samples were collected at 12 h intervals since the beginning of the experiment and continued for 15 days after the last application of GnRH.

Progesterone plasma concentration was determined by RIA and for the statistical analysis of plasma progesterone concentrations, a student t-test was used to compare differences in the Area under the Curve (AOC).

RESULTS

It was observed (Fig. 1) that in 2 of the control ewes plasma progesterone increased since 36 h after the first GnRH injection and reached the highest concentration of >3 ng mL^{-1} on day 7th, in the remaining 8 control ewes short luteal phases were observed with plasmatic concentrations of Progesterone concentrations were in the order of 1 ng mL^{-1}. In ewes of group 2 treated with naloxone (Fig. 2) 2 ewes showed concentration of plasma progesterone as observed in the control ewes with short luteal phase. The 8 remaining ewes showed plasma progesterone concentrations similar to the observed concentrations of progesterone of control ewes with normal luteal phase. The statistical analysis indicated a highly significant effect of treatment between control and treated ewes ($p<0.0019$).

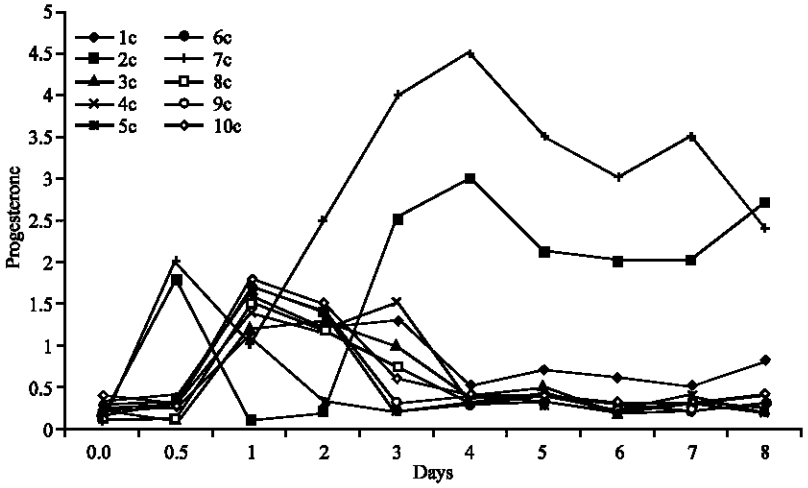

Fig. 1: Control ewes with induced short luteal phase during the anestrous season. Progesterone in ng mL^{-1}

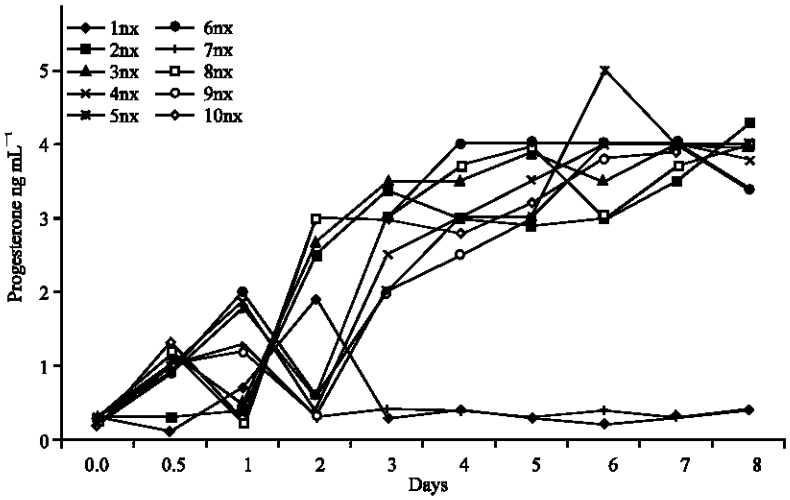

Fig. 2: The effect of naloxone on the induced short luteal phase of creole ewes during enestrus

DISCUSSION

The administration of GnRH with out the priming effect of progesterone in the ewe during the anestrous season promotes the development of a CL that regresses in about 4 days (Southbee *et al*., 1988). This effect is also, present during puberty and at the beginning of he oestrus season (Lamming *et al*., 1981; Beard and Hunter, 1996). The prompt regression of the CL when it is the outcome of the exogenous administration of GnRH, might be due to an early luteolisis from prostaglandins produced by the uterus (Hunter, 1991). In this research, it is observed that the effect of GnRH on the physiological function of the uterus is similar with reports of other workers (Southbee *et al*., 1988). When, the ewes with induced CL are simultaneously treated with naloxone, it was observed that the duration of the luteal phase was significantly increased, this latter effect can be related to the facilitating effect of naloxone on the release of LH (Fuentes *et al*., 2001). If we consider that the functional duration of the CL is in direct relation to the pulsatile secretion of LH and if we also consider that endogenous opioids are important modulators of the endocrine mechanisms that control LH release (Piva *et al*., 1985; Fuentes *et al*., 2001). Furthermore, when naloxone is administered in low doses facilitates the pulsatile release of LH (Fuentes *et al*., 2001). This latter effects give way to postulate that ewes with induced short luteal phase and treated with low doses of naloxone maintained normal luteal phases, accumulating further evidence related to the importance of endogenous opioids as modulators of the neuroendocrine mechanisms that control estrous cycles in the ewe.

REFERENCES

Bartlewski, P.M., J. Aravinakshan, A.P. Beard, M.L. Nelson, M. Batista-Arteaga, S.J. Cook and N.C. Rawlings, 2004. Effects of Medroxyprogesterone Acetate (MAP) on ovarian antral follicle development, gonadotrophin secretion and response to ovulation induction with Gonadotrophin-Releasing Hormone (GnRH) in seasonally anoestrous ewes. Anim. Reprod. Sci., 81: 63-75. NLM ID: 7807205.

Beard, A.P. and M.G. Hunter, 1996. Effects of exogenous oxytocin and progesterone on GnRH induced short luteal phases in anoestrous ewes. J. Reprod. Fertil., 106: 55-61. NLM ID: 0376367.

Bramley, T.A., D. Stirling, G.S. Menzies and D.T. Baird, 2005. Corpora lutea induced by gonadotrophin-releasing hormone treatment of anoestrous Welsh Mountain ewes: Reduced sensitivity to luteinizing hormone *in vivo* and to chorionic gonadotrophin *in vitro*. Reproduction, 129: 61-73. NLM ID: 10096 6036.

Fuentes, V.O., 1989. Effect of naloxone, nalbuphine, progesterone and pmsg on the sexual behaviour of ewes. Vet. Rec., 14: 274-276. NLM ID: 0031164.

Fuentes, V.O., P.I. Fuentes and A. Garcia, 1998. The effect of naloxone on plasma concentrations of testosterone in male goats. Small Rum. Res., 27: 173-176. NLM ID: 9885624.

Fuentes, V.O., V. Sanchez, H. Gonzalez, P.I. Fuentes, A. Garcia and R. Rosiles, 1997. La funcion endocrina del testiculo en el carnero criollo mexicano durante las diferentes epocas del ano y su control opioidergico durante el anestro. J. Vet. Med. A., 44: 259-263.

Fuentes, V., R. Sanchez, Rosiles and P.I. Fuentes, 2001. The Effect of Low doses of Naloxone on the preovulatory surge of LH and on the onset and duration of oestrus in the Ewe with induced oestrus during the nonbreeding season. Anim. Reprod. Sci., 65: 225-230. NLM ID: 7807205.

Horton, R.J.E., J.T. Cummins and I.J. Clarke, 1987. Naloxone evokes large amplitude GnRH pulses in luteal phase ewes. J. Reprod. Fertil., 81: 277-286. NLM ID: 0376367.

Hunter, M.G., 1991. Characteristics and causes of the inadequate corpus luteum. J. Reprod. Fertil., 43: 91-99. NLM ID: 8808774.

Lamming, G.E., D.C. Wathes and A.R. Peters, 1981. Endocrine patterns of the postpartum cow. J. Reprod. Fertil. Sup., 30: 155-170. NLM ID: 8808774.

Piva, F., R. Maggo, P. Limonta, M. Motta and L. Martin, 1985. Effect of naloxone on Luteinizing Hormona, Follicule Stimulating Hormona and Prolactin secretion in the different phases of the Estrous Cycle. Endocrinology, 117: 766-772. NLM ID: 0375040.

Southbee, J.A., M.G. Hunter and W. Haresing, 1988. Function of abnormal corpora lutea *in vivo* after GnRH-induced ovulation in the anoestrous ewe. J. Reprod. Fertil., 84: 131-137. NLM ID: 8808774.