Kafkas Üniv. Vet. Fak. Derg.
2001. 7(1): 123-128

ROLE OF OXYTOCIN AND OXYTOCIN RECEPTORS IN THE SYNTHESIS OF PROSTAGLANDIN F2α IN RUMINANTS

Şevket ARIKAN* Taner PAMUKCU*

Geliş Tarihi : 14.01.2000

Swmmary: In recent years, considerable progress has been made in our understanding of the role of oxytocin receptor in the synthesis of prostaglandin F2 α (PGF2 α) and cyclic regression of the corpus luteum. In non-pregnant ruminants, PGF2α is released in a pulsatile manner from the uterus late in the oestrus cycle to cause regression of the corpus luteum. Specific oxytocin receptors are present on the endometrial cells of uterus. Binding of luteal oxytocin to the receptor stimulates the conversion of arachidonic acid to PGF2 α which has the ability to release oxytocin from the corpus luteum, and oxytocin, in turn, has the ability to release PGF2 α from the uterine endometrium. This positive feedback between luteal oxytocin and uterine PGF2α ultimately causes the regression of the corpus luteum. Concentration of oxytocin receptors in uterine tissues increase several days before oestrus, peaks at oestrus, and declines thereafter. If pregnancy occurs, both secretion of luteal oxytocin and development of endometrial oxytocin receptors are suppressed. Inhibition of oxytocin secretion and suppression of receptor development may serve to save corpus luteum for pregnancy.

Key Words: Oxytocin, receptor, progtaglandin, corpus luteum, uterus, ruminant.

Prostoglandin F2α Sentezinde Oksitosin ve Oksitosin Reseptörlerinin Ruminantlardaki Rolü

Özet: Oksitosin reseptörlerinin hem prostaglandin F2α (PGF2α)'nın sentezi ve hem de siklik korpus luteumun gerilemesi üzerine olan etkisinin anlaşılmasında, son zamanlarda önemli gelişmeler kaydedilmiştir. Gebe olmayan ruminantlarda korpus luteumun gerilemesi östrus siklusunun sonlarına doğru uterustan kısa aralıklarla salgılanan PGF2α tarafından gerçekleştirilmektedir. Uterus endometrium hücrelerinin yüzeylerinde oksitosine özgü reseptörler bulunmaktadır. Korpus luteum kaynaklı oksitosinin bu reseptörlere bağlanması arakidonik asidin PGF2α ya dönüşümünü sağlamaktadır ve oluşan PGF2α korpus luteumdan ilave oksitosin salgılanmasına ve salgılanan bu oksitosin de uterus endometriumundan daha fazla PGF2α üretilmesine neden olmaktadır. Luteal kaynaklı oksitosin ile uterus kaynaklı PGF2α arasında cereyan eden bu pozitif geri dönüşüm, sonunda korpus luteumun gerilemesine neden olmaktadır. Uterusta bulunan oksitosin reseptörlerinin miktarı östrustan birkaç gün önce artmaya başlar, östrus zamanında maksimum seviyeye ulaşır ve östrustan sonra da hızla azalır. Eger bu dönemde gebelik oluşur ise hem luteal oksitosin ve hem de endometriumdaki oksitosin reseptörü oluşumu baskılanır. Oksitosin salgılanması ve reseptör oluşumundaki bu baskılama, kalıcı gebelik korpus luteumunun oluşumunu sağlamaya yönelik olabilir.

Anahtar Sözcükler: Oksitosin, reseptör, prostaglandin, korpus luteum, uterus, ruminant.

INTRODUCTION

Oxytocin is a polypeptide hormone produced by the hypothalamus and released from the posterior pituitary known as neurohypophysis. It is also produced by the corpus luteum of ruminants. An oxytocic activity in the luteal tissue was first noticed by Ott and Scott[1] in 1910. After injection of corpus luteum extract into a cannulated goat mammary gland, they found a subsequent increase in milk secretion. This result was ignored until first radioimmunoassay measurement of oxytocin in luteal extract obtained from ovine corpus luteum by Wathes and Swann[2] in 1982. Until this date the role of oxytocin in reproductive physiology was partly established, but the effect was thought to be caused by hypophysial oxytocin. Since then, many studies have been performed to understand mechanism by which

* Kırıkkale Üniversitesi Veteriner Fakültesi, Kırıkkale-TÜRKİYE

luteal oxytocin participates in reproductive physiology.

Considerable evidence now exists indicating that pulsatile release of oxytocin from the ovary initiates a chain of events, which leads to demise of the corpus luteum at the end of the oestrous cycle. In ewe, the pulse interval for uterine oxytocin secretion at the time of the luteolysis is 2.5±0.19 pulses per 12 hour[3]. Furthermore, the presence of specific receptors for oxytocin in the ewe and bovine uterine is well established. However, receptor concentration is fluctuated throughout oestrus cycle. The concentration of endometrial oxytocin receptors rises towards the end of luteal phase and remains maximum during luteolysis, then declines in the early luteal phase (Table 1).

Receptor formation apears to be regulated by oestrogen and progesterone. Follicular oestradiol induces endometrial oxytocin receptors which lead uterine secretion of PGF2α in a pulsatile manner[4,5]. In ewes, 5 pulses of PGF2α within 24 h are necessary to cause luteal regression[6].

Table 1. Endometrial oxytocin receptor concentrations (fmol/mg protein) throughout the oestrous cycle of ewes.
Tablo 1. Koyunların östrus siklusu süresince endometrumdaki oksitosin reseptörlerinin yoğunluğu (fmol/mg protein)

Days of cycle	Oxytocin receptors	No of ewes	References
0	455.7±29	4	(13)
4	55.9±32	3	(13)
10	15.71±1.6	4	(9)
15	248.6±67	6	(14)
17	539.5±96	12	(15)

Oxytocin administration causes PGF2α secretion in the cow[7] and sheep[8]. This response increases as the luteal phase progressed and is maximal at the time of luteolysis [9]. Furthermore, oxytocin administered during the early luteal phase induces a shortening of the bovine oestrous cycle, but this do not occur if this is given in the mid-luteal phase[10]. In addition to oxytocin, administration of PGF2α causes the release of oxytocin from the corpora lutea of sheep[11]. Active and passive immunisation of ewes against oxytocin is prolonged the luteal phase of the oestrous cycle [12]. Therefore, the secretion of oxytocin from corpus luteum and expression of oxytocin receptors in the uterine endometrium are considered to be important in controlling the episodic patterns of PGF2α in both ewes and cows.

LUTEAL OXYTOCIN

The quantity of oxytocin produced in the corpus luteum varies throughout the oestrus cycle both in cow[16] and ewe[4]. The cyclic variation in the bovine ovarian oxytocin is shown in Table 2. The oxytocin concentration in the corpus luteum reaches its peak in the mid-luteal phase and then it falls as luteal regression begins. Both incubation of luteal cells in vitro[17] and immunohistochemical studies[18] have shown that the hormone resides in the large luteal cells.

Table 2. The cyclic variation in the bovine ovarian oxytocin.
Tablo 2. İneklerde ovaryum oksitosininde siklik değişim.

Days of cycle	Oxytocin	No of ewes	References
1-4	38.00±26.0		(19)
5-10	1774±125	7	(16)
10	2000±139	3	(20)
8-13	1374±908	12	(19)
11-17	986.0±223	10	(16)
18-20	55.40±20.6	6	(16)

ROLE OF PROGESTERONE AND OESTROGEN IN THE CONTROL OF UTERINE OXYTOCIN RECEPTORS

Endometrial oxytocin receptors are influenced by circulating levels of steroid hormones. The rise in oxytocin receptor

Kafkas Üniv. Vet. Fak. Derg.
2001, 7(1): 123-128

concentration coincides closely with progesterone withdrawal and the preovulatory rise in oestrogen levels[21]. Hixon and Flint[22], showed that administration of a luteolytic dose of oestradiol leads an increase in the concentration of uterine oxytocin receptors before the onset of episodic PGF2α secretion and luteolysis. Furthermore, a positive correlation between plasma oestradiol concentrations and uterine oxytocin receptors, and a negative correlation between plasma progesterone concentrations and oxytocin receptors are also reported[23].

Changes in uterine secretory responsiveness to oxytocin that occur during the oestrus cycle may arise due to ovarian steroids. Oestradiol from ovarian follicles and progesterone from corpus luteum have a controlling influence on the oxytocin receptor concentration and the uterine PGF2α resonse to oxytocin[24]. The increase in the concentration of oxytocin receptors around luteolysis coincides with a fall in the concentrations of progesterone in plasma in ewes[21,25]. In ovariectomized ewes, administration of progesterone initially decreases the receptor concentrations, but if treatment is continued progesterone loses its inhibitory effect after 10 to 14 days and receptors reappear[24,26]. However, administration of progesterone during the first 3 days of the oestrous cycle results in the premature release of ovarian oxytocin and uterine PGF2α[27]. Administration of oestrogen alone to anoestrous animal increases the number of oxytocin receptors on the uterine endometrium and myometrium[28]. However, administration of oestrogen and progesterone together initially depress endometrial oxytocin receptors in ovariectomized ewes, but the presence of oestrogen after prolonged progesterone treatment or progesterone withdrawal enhances both the oxytocin receptors and the PGF2α response to an oxytocin challenge[29]. In the ovarian auto-transplanted ewe, administration of exogenous oestrogen provides a positive stimulus for the release of ovarian oxytocin and uterine PGF2α[30]. It is also suggested that chronic treatment of ewes with oestradiol during the cycle (for 20 days, beginning on day 4 of the cycle) can prolong the inter-oestrus interval by reducing uterine concentration of oxytocin receptors and hence oxytocin-induced secretion of prostaglandin[31].

PROSTAGLANDIN F2α SECRETION IN RESPONSE TO OXYTOCIN

Administration of oxytocin was first shown to stimulate endometrial PGF2α secretion in anoestrous ewes by Sharma and Fitzpatrick[32] and subsequently in cycling ewes by Roberts et al.[25]. For much of the oestrous cycle, the uterus cannot secrete PGF2α in response to oxytocin[33]. Effects of progesterone withdrawal on uterine secretion of PGF2α in response to oxytocin in ewes were investigated by Kaminski et al.[34]. They demonstrated that the increase in uterine secretory responsiveness to oxytocin is dependent on oestradiol replacement in ovariectomized ewes.

The human oxytocin receptor has been cloned and shown to encode a 388-aminoacid polypeptide[35]. Binding of oxytocin to its endometrial receptors activates a G protein[35] which mobilises intercellular calcium and activates protein kinase C to catalyse the hydrolysis of phosphoinositide[36,37]. This in turn activates the synthesis of arachidonic acid from which prostaglandins are derived. Thus, the administration of oxytocin into the peripheral circulation by jugular vein will only result an increases in plasma concentrations of PGF2α metabolite, 13, 14-dihydro 15-keto-PGF2α, in venous blood if endometrial oxytocin receptors are present. Hence, an indirect measure of uterine oxytocin receptor function can be obtained by determining the sensitivity to oxytocin by measuring the release of PGF2α from uterus in response to parenteral injection of oxytocin.

Uterine oxytocin receptor concentrations are low between days 3 and 13 of the cycle, but rapidly increase between days 14 and 16 post oestrous and reach maximum level on the day of oestrous in sheep[21,25]. The presence of receptors on uterine endometrium allows exogenous oxytocin to cause rapid secretion of endometrial PGF2α. Thus, the peripheral injection of a bolus of oxytocin during the early and mid-luteal phase has no effect on plasma PGFM, Whereas treatment between days 14 and 16 result in an increase to reach maximum level on day of oestrous[33].

Kafkas Univ. Vet. Med. J.
2001, 7(1): 123-128

INHIBITION OF OXYTOCIN RECEPTORS IN EARLY PREGNANCY

Normal pregnancy depends on a process called early embryonic signalling. This process is termed maternal recognition of pregnancy. Failure in the embryonic signalling leads to loss of the pregnancy and return to oestrous cycle as a result of luteolysis of corpus luteum and loss of progesterone secretion[41]. Therefore, it seems essential that, in ruminant, the formation of the uterine oxytocin receptors and the pulsatile release of PGF2α must be inhibited for the establishment of pregnancy. Uterine endometrial oxytocin receptors and plasma progesterone concentrations on day 18, in cyclic and pregnant cows are shown in Figure 3.

The expression of oxytocin receptor in the uterine endometrium plays an important role in the initiation of luteolysis. During early pregnancy, the conceptus secrets trophoblast interferon that inhibits oxytocin receptor up-regulation and luteolysis[38]. In ewes, the endometrial receptors for oxytocin are present early in oestrous cycle (days 0-3) decline and remain low until day 13 and then increase to their highest numbers at oestrous[25,29].

The suppression of the oxytocin receptors in the late luteal phase is a major component of the maternal recognition of pregnancy in domestic ruminants[10,40,41]. Both receptor binding[8] and autoradiographical studies[14] have shown that endometrial oxytocin receptors are considerably reduced in early pregnancy. During the early pregnancy, a specific class of trophoblast interferon is released by the developing blastocyst[42] and this interferon inhibits the formation of uterine oxytocin receptors[10]. Hence, in vivo oxytocin injection fails to induce PGF2α production between days 13 and 20 of pregnancy[33].

The response to oxytocin administration in pregnancy apparently reappears by day 24, at the time when the endogenous interferon production falls[33]. Therefore, the ability of the trophoblast interferon to inhibit uterine secretory responsiveness may be a transient phenomenon. Nevertheless, levels of oxytocin receptor genes (mRNA) are also two-fold lower in the endometrium of day 15 cyclic ewes receiving intrauterine injections of recombinant ovine trophoblast interferon from day 11 to day 14 compared to control ewes[43]. The concentration of oxytocin levels is decreased after 18 day of pregnancy[20]. After this period luteal oxytocin secretion is absent. Hence, episodic secretion of PGF2α fails.

Table 3. Endometrial oxytocin receptor (fmol/mg protein) and plasma progesterone concentrations (ng/ml/ on day 18, in cyclic and pregnant cows (44).
Tablo 3. Siklusun 18. gününde gebe ve gebe olmayan ineklerde, endometrium oksitosin reseptörü (fmol/mg protein) ve plasma progesteron (ng/ml) konsantrasyonu

	Cycle	Pregnant
Oxytocin receptors	563.4±117	18.1±4.6
Progesterone	0.93±0.4	8.37±0.7
No of cows	4	6

CONCLUSIONS

In this review, the interaction among prostaglandin, oxytocin and oxytocin receptors at luteolysis and at the time of maternal recognition has been discussed. It has been suggested that a better understanding of these interactions could lead to advances in the control of cyclic activity and to decrease in early embryonic loss in ruminants. There is no doubt that real, authentic oxytocin, is present in the ruminant ovary and indeed, is synthesed there. It is now clear from work in ruminants that oxytocin and oxytocin receptors play a key role in reproductive processes. In the ruminants, the majority of luteal oxytocin is secreted during the early and mid-luteal phases at a time when receptors are not apparently present in the uterine endometrium. Thus, it seems that the endometrial response to oxytocin in vivo is regulated at the receptor level, rather than by circulating oxytocin concentrations. On the other hand, has to be stated that there is a lack of knowledge about relationship among oxytocin, oestrogen and progesterone receptors. Therefore, further studies are required to elucidate interrelationship between two steroid

hormones and between steroid and oxytocin receptors. Furthermore, additional studies regarding to oxytocin receptor gene (mRNA) might lead to a greater understanding of the mechanism of action of ovarian oxytocin in the future.

REFERENCES

1. Ott I, Scott JC: The galactogen action of the thymus and corpus luteum. *Proc Soc Exp Biol Med*, 8: 49-51, 1910.

2. Wathes DC, Swann BW: Is oxytocin an ovarian hormone? *Nature*, 297: 225-227, 1982.

3. Jenkin G: Interaction between oxytocin and prostaglandin F2α during luteal regression and early pregnancy in sheep. *Reprod Fertil Devel*, 4: 321-328, 1992.

4. Flint APF, Sheldrick EL: Evidence for a systemic role for ovarian oxytocin in luteal regression in sheep. *J Reprod Fertil*, 67: 215-225, 1983.

5. Hooper SB, Watkins WB, Thorburn GD: Oxytocin, oxytocin-associated neurophysin and prostaglandin F2α concentrations in the utero-ovarian vein of pregnant and non-pregnant sheep. *Endocrinology*, 119: 2590-2597, 1986.

6. Schramm W, Boviard L, Glew ME, Schramm G, McCacken BM: Corpus luteum regression induced by ultra low pulses of prostaglandin F2α. *Prostaglandins*, 26: 347-364, 1983.

7. Lamming GE, Mann GE: Control of endometrial oxytocin receptors and prostaglandin F2α production in cows by progesterone and oestradiol. *J Reprod Fertil*, 103: 69-73, 1995.

8. Burges KM, Raip MM, Jenkin G, Thorburn GD: Effect of oxytocin and oestradiol on uterine prostaglandin release in non-pregnant and early-pregnant ewes. *Biol Reprod*, 42: 822 -833, 1990.

9. Beard AP, Lamming GE: Oestradiol concentrations and the development of the uterine oxytocin receptor and oytocin-induced PGF2 release in ewes. *J Reprod Fertil*, 100: 469-475, 1994.

10. Flint APF, Stewart HJ, Lamming GE, Payne JH: The role of the oxytocin receptor in the choice between cyclicity and gestation. *J Reprod Fertil Suppl*, 45: 53-58, 1992.

11. Flint APF, Sheldrick EL: Ovarian secretion of oxytocin is stimulated by prostaglandin. *Nature* (London) 297: 587-588, 1982.

12. Schams D, Prokopp S, Barth D: The effect of active and passive immunisation against oxytocin on ovarian cyclicity in ewes. *Acta Endocrinologica*, 103: 337-344, 1983.

13. Ayad VJ, Wathes DC: Characterisation of endometrial and myometrial oxytocin receptors in the non-pregnant ewe. *J Endocrinol*, 123: 11-18, 1989.

14. Ayad WJ, Parkinson TJ, Matthews EL, Wild ML: The effects of pregnancy and systemic or intrauterine oxytocin infusion on the distribution of endometrial oxytocin receptors in the ewe: An autoradiographic study. *J Endocrinol*, 137: 423-431, 1993.

15. Sheldrick EL: Effect of continuous infusion of oxytocin on ovarian function and uterine oxytocin receptor concentration in the cyclic ewe. *Reprod Fertil Dev*, 4: 505-513, 1992.

16. Wathes DC, Swann BW, Pickering BT: Variations in oxytocin, vasopressin and neurophysin concentrations in the bovine ovary during the oestrus cycle and pregnancy. *J Reprod Fertil*, 71: 551-557, 1984.

17. Rodgers BJ, O'Shea JD, Findly JK, Flint APF, Shekdrick EL: Large luteal cells the source of luteal oxytocin in the sheep. *Endocrinology*, 113: 2302-2304, 1983.

18. Watkins WB: Immunohistochemical localisation of neurophysin and oxytocin in the sheep corpora luteal. *Neuropeptides*, 4: 51-54, 1983.

19. Schams D, Schallenberger E, Mayer HHD, Bullerman B, Breitinger HJ, Enzenhofeer G, Koll R, Kruip TAM, Walters DL, Karg H: Ovarian oxytocin during the oestrous cycle in cattle. In: Amigo JA and Robinson AG (eds), *Oxytocin: Clinical and laboratory studies*, 317-334, 1985.

20. Parkinson TJ, Wathes DC, Jenner LJ, Lamming G: Plasma and luteal concentrations of oxytocin in cyclic and early-pregnant cattle. *J Reprod Fertil*, 94: 161-167, 1992.

21. Sheldrick EL, Flint APF: Endocrine control of uterine oxytocin receptors in the ewe. *J Endocrinol*, 106:249-258,1985.

22. Hixon JE, Flint APF: Effect of a luteolytic dose of oestradiol benzoate on uterine oxytocin receptor concentrations phosphoinositide turnover and prostaglandin F2α secretion in sheep. *J Reprod Fertil*, 79: 457-467, 1987.

23. Parkinson TJ, Jenner LJ, Lamming GE: Comparison of oxytocin/PF2α interrelationship in cyclic and pregnant cows. *J Reprod Fertil*, 90: 337-345, 1990

24. Vallet JL, Lamming GE, Batten M: Control of endometrial oxytocin receptor and uterine response to oxytocin by progesterone and oestradiol in the ewes. *J Reprod Fertil*, 90: 635-644, 1990.

25. Roberts JS, McCracken JA, Gavagan JE, Soloff MS: Oxytocin-stimulated release of prostaglandin F2α from ovine endometrium in vitro: Correlation with oestrous cycle and oxytocin receptor binding. *Endocrinology*, 99: 1107-1114, 1976.

26. Lau TM, Gow CB, Fairchough BJ: Increase in the oxytocin-induced prostaglandin F2α response and reduction in the concentrations of endometrial oxytocin receptors in ewes in response to progesterone. *J Reprod Fertil*, 95: 11-18, 1992.

27. Al-Matubsi HY, Downing J, Jenkin G, Fairclough RJ: Stimulation of ovarian oxytocin secretion and uterine prostaglandin release by exogenous progesterone early in the cycle of the ovarian autotransplanted ewe. *J Reprod Fertil*, 112: 279-288, 1998.

28. Matthews EL, Ayad VJ, Wathes DC: The effect of oestradiol-17β on oxytocin receptor concentrations in the reproductive tract of the anoestrous ewe. *J Reprod Fertil* (Abstr Ser) 8: 81, 1991.

29. Zhang JP, Weston PG, Hixon JE: Role of progesterone and oestrodiol in the regulation of uterine oxytocin receptors in ewes. *J Reprod Fertil*, 94: 395-404, 1992.

30. Al-Matubsi HY, Downing J, Jenkin G, Fairclough BJ: Effect of oestradiol on ovarian oxytocin secretion rate and luteolysis in the ewe after ovarian autotransplantation. *Reprod Fertil Dev*, 9(7): 683-688, 1997.

31. Hazzard TM, Stormshak F: Down-regulation of oxytocin receptors and secretion of prostaglandin F2α after chronic treatment of ewes with estradiol 17-β. *Biol Reprod*, 56(6): 1576-1581, 1997.

32. Sharma SC, Fitzpatrick BJ: Effect of oestradiol 17β and oxytocin treatment on prostaglandin F2α release in the oestrous ewe. *Prostaglandins*, 6: 97-105, 1974.

33. Silvia WJ, Raw BE, Aldrich SL, Hayes HS: Uterine secretion of prostaglandin F2α in response to oxytocin in ewes: Changes during the oestrous and early pregnancy. *Biol Reprod*, 46: 1007-1010, 1992.

34. Kaminski MA, Hayes SH, Silvia WJ: Effects of progesterone witdrawal on uterine secretion of prostaglandin F2 alpha in response to oxytocin in ewes. *Reprod Fertil Dev*, 9(2): 255-262, 1997.

35. Kimura T, Tanizawa O, Mori K, Brownstein MJ, Okayama H: Structure and expression of a human oxytocin receptor. *Nature*, 356: 526-529, 1992.

36. Flint APF, Leat WMF, Sheldrick EL, Stewart HJ: Stimulation of phosphoinositide hydrolysis by oxytocin and the mechanisms by which oxytocin controls prostaglandin synthesis in the ovine endometrium. *Biochem J*, 237: 797-805, 1986.

37. Tysseling KA, Thatcher WW, Bazer FW, Hansen PJ, Mirando MA: Mechanisms regulating prostaglandin F2 alpha secretion from the bovine endometrium. *J Dairy Sci*, 81: 382-389, 1998.

38. Asselin E, Bazer FW, Fortier MA: Recombinant ovine and bovine interferons tau regulate prostaglandin production and oxytocin response in cultured bovine endometrial cells. *Biol Reprod*, 56: 402-408, 1997.

39. Flint APF, Sheldrick EL: Ovarian oxytocin and maternal recognition of pregnancy. *J Reprod Fertil*, 76: 831-839, 1986.

40. McCracken JA, Schramm W, Okulicz WC: Hormone receptor control of pulsatile secretion of PGF2α from the ovine uterus during luteolysis and its abrogation in early pregnancy. In: Edqvist LE and Kindahl H (Eds): *Prostaglandin in Animal Reroduction*, II. 31-56, 1984.

41. Bazer FV, Thatcher WW, Hansen PJ, Mirando MA, Ott TL, Plante C: Physiological mechanisms of pregnancy recognition in ruminants. *J Reprod Fertil Suppl*, 43: 39-47, 1991.

42. Flint APF, Parkinson TJ, Stewart HJ, Vallet JL, Lamming GE: Molecular biology of trophoblast interferons and studies on their effects in vivo. *J Raprod Fertil Suppl*, 43: 13-25, 1991.

43. Spencer TE, Bazer FW: Ovine interferon tau suppresses transcription of the oestrogen receptor and oxytocin receptor genes in the ovine endometrium. *Endocrinology*, 1144-1147, 1996.

44. Jenner LJ, Parkinson TJ, Lamming GE: Uterine oxytocin receptors in cyclic and pregnant cow. *J Reprod Fertil*, 91: 49-58, 1991.