

Synchronization of oestrus in sheep: The use of controlled internal drug release (CIDR) dispensers

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The use of the CIDR (controlled internal drug release) dispenser as a progestagen-synchronizing agent was evaluated in 37 Karakul ewes during the breeding season, using the intravaginal progestagen sponge as a control (30 ewes). Although there was no significant differences in oestrous response, following intravaginal insertion for 14 days, between these two progestagen devices, the time from device withdrawal to the onset of the induced oestrous period (31,2 vs 62,5 h) and the duration of the induced oestrous period (32,7 vs 47,4 h) was significantly ($P < 0,01$) shorter in the CIDR dispenser group. The mean time from device withdrawal to the serum pre-ovulatory LH peak and the interval from the onset of oestrus to the pre-ovulatory LH peak was significantly ($P < 0,01$) earlier in the CIDR dispenser group (28,0 vs 78,0 h and 5,3 vs 17,3 h respectively). No significant difference in the serum progesterone concentrations was noted between the two groups. No significant difference in reproductive performance was obtained with conception, lambing rates and fecundities of 72,2 vs 79,3%; 75,0 vs 89% and 103,8 vs 113,0% for the dispenser and sponge treatment groups respectively. Results confirm the potential of the CIDR dispenser as an efficient synchronizing agent and the more concentrated synchrony obtained makes it ideal for fixed-time insemination.

Die gebruik van die CIDR-dispensor as 'n progestoogeen-sinkronisasiemiddel is in 37 Karakoelooie tydens die teelseisoen geëvalueer, met die intravaginale progestoogeenimpregneerde spons as kontrole (30 oöie). Alhoewel daar geen betekenisvolle verskil in estrusrespons na intravaginale toediening vir 14 dae tussen die twee progestoogeenbehandelings was nie, was die tydsduur vanaf die einde van behandeling tot die aanvang van estrus (31,2 vs 62,5 h) en die tydsduur van die geïnduseerde estrusperiode (32,7 vs 47,4 h) betekenisvol ($P < 0,01$) korter in die CIDR-dispensorgroep. Die gemiddelde tydsduur vanaf onttrekking tot die voor-ovulasie LH-piek en die interval vanaf die aanvang van estrus en die voor-ovulasie LH-piek was betekenisvol ($P < 0,01$) vroeër in die CIDR-dispensorgroep (28,0 vs 78,0 h en 5,3 vs 17,3 h respektiewelik). Geen betekenisvolle verskil in die serum-progesteroonkonsentrasies is waargeneem tussen die twee groepe nie. Geen betekenisvolle verskil in vrugbaarheidsresultate is verkry met konsepisie, lampersentasie en fekunditeite van 72,2 vs 79,3%; 75,0 vs 89,7% en 103,8 vs 113,0% vir die CIDR-dispensor- en sponsbehandelingsgroepe respektiewelik. Resultate dui op die potensiaal van die CIDR-dispensor as 'n effektiewe sinkronisasiemiddel en die meer gekonsentreerde sinkronisasie verkry, maak dit ideaal vir uitvoering van KI op 'n vasgestelde tyd.

Keywords: Synchronization, oestrus, sheep, progestagen, progesterone, LH

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Introduction

The control of oestrus and ovulation in sheep with progesterone and its analogues has been extensively evaluated, applied and accepted in sheep breeding programmes (Robinson, 1967; van Niekerk & Belonje, 1970; Boshoff, van Niekerk & Morgenthal, 1973; Harsign, 1978; Hunter, 1980).

As the synchronization of oestrus with progestagens commonly results in reduced fertility at the induced oestrous period (van der Westhuysen & van Niekerk, 1971), mainly due to the timing of the LH release and the magnitude of the LH release being affected by the progestagen treatment (Baumgartner, Lishman, Louw & Botha, 1974; van der Westhuysen, Malan & Dierkse, 1977), it is understandable that all synchronization techniques warrant investigation.

The intravaginal CIDR (controlled internal drug release) dispenser (Hoechst, SA) is based on progestagen administration, very much the same as the conventional progestagen intravaginal sponge and consists of a plastic core and an outer surface of an elastomer impregnated with progestagen. Research has found the CIDR dispenser to have a much less foul-smelling discharge

(mucus) on removal, a lower rate of loss during treatment and a quicker reaction time, i.e. earlier and more compact synchronization, when compared to the intravaginal progestagen sponge in sheep (Welch, 1984). Factors that could make it a more efficient synchronizing agent, especially for fixed-time insemination in sheep.

This investigation was therefore undertaken to evaluate the efficiency of synchronization and fertility of the CIDR device with the intravaginal progestagen sponge (MAP — 60 mg; Upjohn) as control in the synchronization of oestrus in Karakul sheep.

Procedure

Sixty-seven mature Karakul ewes were randomly allotted to the following two treatment groups during the breeding season (March, 1985). Group 1 (control) contained 30 ewes, each receiving an intravaginal (MAP; 60 mg) sponge for a period of 14 days. Group 2 contained 37 ewes, each receiving an intravaginal CIDR dispenser for a period of 14 days.

Following the termination of progestagen treatment all ewes were tested six-hourly (06h00, 12h00, 18h00 and 24h00) for oestrus with the aid of vasectomized rams.

From 10 ewes in each group, venous blood (10 ml) was sampled three times per week (days 0, 3, 6, 9, 12 and 14) during device insertion and at eight-hourly intervals (coinciding with the testing for oestrus), starting at device withdrawal until the end of the subsequent induced oestrous period or for an observation period of 130 hours. Serum was recovered and stored at -20°C until assayed for serum progesterone and LH concentrations by radio-immunoassay. The serum progesterone concentration was determined using the technique of Youssefnejadian, Florensa, Collins & Sommerville (1972) as basis and modifications as described by Faure (1975). The anti-sera were prepared and made available by Dr J.C. Morgenthal (University of Stellenbosch). Inter- and intra-assay coefficients of variation were 15,6% and 8,9% respectively. The serum LH concentrations were performed according to the double-antibody technique as described by Niswender, Reichert, Midgley & Nalbandov (1969) and anti-LH (ovine) supplied by Dr J.C. Morgenthal (University of Stellenbosch) was used. The inter- and intra-assay coefficients of variation for LH were 15,0% and 9,1% respectively. The LH labelling was done according to Hunter & Greenwood (1962).

Ewes in oestrus were hand-mated (using Karakul rams) 12 hours after the onset of oestrus and again at 12-hour intervals for as long as they remained in oestrus. After 10 days the ewes were again tested with vasectomized rams to identify those ewes returning to service. This procedure was performed for two cycles following the induced oestrous period.

All data were analysed statistically according to Snedecor & Cochran (1967).

Results

The oestrous response, interval from device withdrawal to onset of oestrus and the length of the induced oestrous period for the different treatment groups are presented in Table 1. Figure 1 illustrates the oestrous response for the two treatment groups.

Although there was no significant difference in the oestrous response between the intravaginal CIDR dispenser and intravaginal sponge-treated groups, the time from device withdrawal to onset of oestrus was significantly ($P<0,01$) shorter (31,2 h vs 62,5 h) for ewes

Table 1 The oestrous response, interval to oestrus and duration of oestrus in ewes following synchronization with intravaginal CIDR dispensers or intravaginal sponges

Item	CIDR dispensers	Intravaginal sponges
Number of ewes	37	30
Oestrous response %	97,3	96,7
Interval (\pm SD) from cessation of treatment to onset of oestrus (h)	31,2 \pm 14,3	62,5 \pm 18,7
Range (h)	2 - 66	36 - 102
Duration (\pm SD) of oestrus (h)	32,7 \pm 12,2	47,4 \pm 19,4

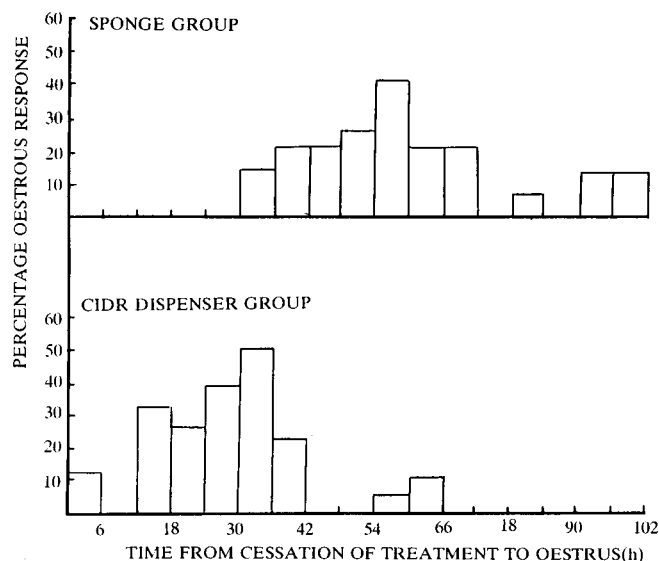


Figure 1 The distribution of the occurrence of oestrus in Karakul ewes following progestagen treatment

treated with the CIDR dispenser. The duration of the induced oestrous period was significantly ($P<0,01$) shorter in the CIDR dispenser group (32,7 h vs 47,4 h) when compared to the intravaginal sponge group. Of the intravaginal sponge-treated ewes 6,7% (two ewes) lost sponges and 80% had a foul-smelling mucus discharge on withdrawal, while in the case of the intravaginal CIDR dispensers 13,5% (five ewes) lost dispensers and only 12,5% had a vaginal discharge on withdrawal.

Of the group receiving dispensers, two of the five ewes that lost dispensers during the treatment period, exhibited oestrus during the observation period and were mated.

No significant difference in the serum progesterone

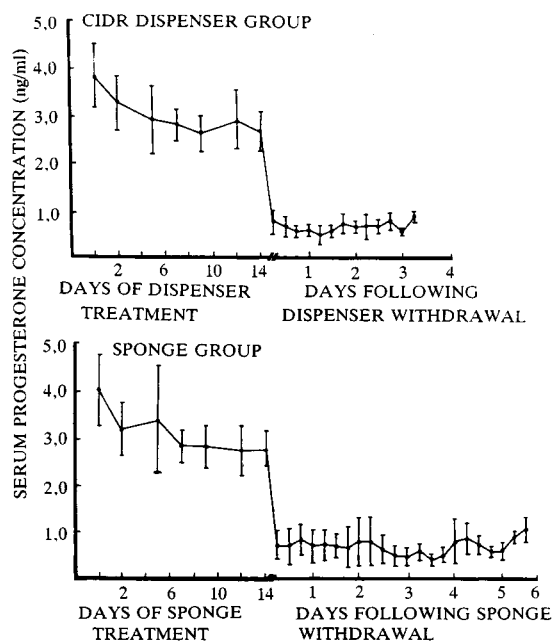


Figure 2 The mean (\pm SD) serum progesterone concentrations for the two intravaginal progestagen treatment groups during and after withdrawal

concentrations at the onset of the induced oestrous period or during the entire blood sampling period (Figure 2) was noted for the two respective treatment groups. Following progestagen treatment, the serum progesterone concentration decreased by 75,0% and 71,2% within 6 hours following sponge and dispenser withdrawal respectively. The mean serum LH concentrations (being indicative of ovulation) and position relative to the onset of oestrus are presented in Figure 3. The mean serum progesterone at the onset of oestrus and the mean times of the peak LH values relative to the termination of treatment and the oestrous period are shown in Table 2.

Regarding the mean time interval from device withdrawal to the pre-ovulatory LH peak value and the interval from the onset of oestrus to the pre-ovulatory LH peak, the time in the CIDR dispenser group was significantly ($P < 0,01$) earlier (28,0 vs 78,0 h and 5,3 vs 17,3 h respectively). No significant difference in the interval between the pre-ovulatory LH peak and the end of the induced oestrous period was found.

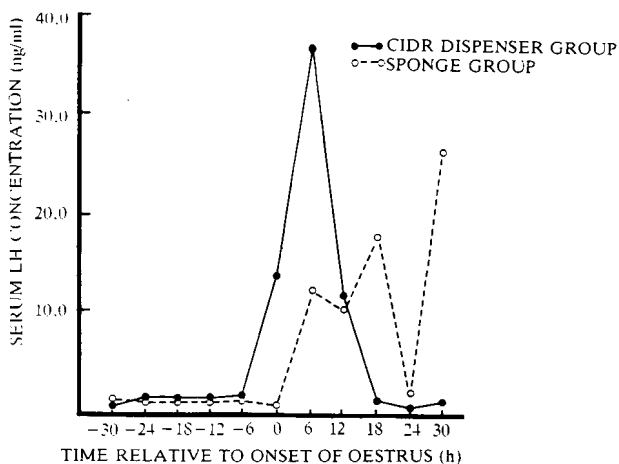


Figure 3 Mean serum LH levels relative to onset of oestrus in Karakul ewes receiving two intravaginal progestagen treatments

Table 2 Serum progesterone concentration at oestrus and the time of serum LH peak values (mean \pm SD) relative to the termination of treatment and the induced oestrous period of animals sampled.

Item	CIDR dispensers	Intravaginal sponges
Serum progesterone concentrations at onset of oestrus (ng/ml)	0,51 \pm 0,11	0,48 \pm 0,21
Serum LH peak concentrations (ng/ml)	51,0 \pm 22,2	57,6 \pm 3,18
Interval from device withdrawal to LH peak (h)	28,0 \pm 15,3	78,0 \pm 18,4
Interval from oestrus onset to LH peak (h)	5,3 \pm 4,7	17,3 \pm 9,9
Interval from LH peak to end of oestrus (h)	24,0 \pm 6,7	23,5 \pm 6,2

Table 3 The nonreturn-, conception- and lambing rates following synchronization with progestagen devices

Item	Intravaginal	
	CIDR dispensers	Intravaginal sponges
No ewes mated	36	29
Nonreturn rate (%)	83,3	93,1
Ewes lambing/ewes mated (%)	72,2	79,3
Lambs born/ewes mated (%)	75,0	89,7
Lambs born/ewes lambing (%)	103,8	113,0

The reproductive data for the two regimes of progestagen administration are presented in Table 3.

From Table 3 it is evident that there was no significant difference in the reproductive performance in the respective device groups.

Discussion

In this experiment the use of both MAP intravaginal sponges and CIDR dispensers during the breeding season proved highly efficient as progestagen-synchronizing agents — especially when it is taken into account that no PMSG was used during these synchronization programmes. PMSG in conjunction with a progestagen has been demonstrated to increase the number of ewes responding and concentrating the occurrence of oestrus (van der Westhuysen, 1980).

A minor disadvantage experienced with the CIDR dispenser was the ease of insertion when compared to sponges and the rate of loss. This could be due to ignorance regarding the use of the dispensers. It does seem, however, that practical problems will be encountered when applying this device to maiden ewes. The trend of abnormal patterns of cervical mucus excretion on progestagen withdrawal (especially the sponge) is a factor that warrants investigation — there have been reports of detrimental effects on both sperm transport and survival (Hawk, 1971) with the sponge. Although the oestrous response was almost identical following the sponge and dispenser treatment, the time from device withdrawal to the onset of the induced oestrous period was significantly ($P < 0,01$) shorter in the case of the CIDR dispenser.

This may relate to a more consistent drug release from the CIDR dispenser compared to the sponge. Moreover, the squeezing of the sponge at the time of withdrawal, may give a final burst of progestagen, whereas the solid matrix of the CIDR dispenser would not. This better synchrony achieved would suggest that when thinking of fixed-time insemination, the time of artificial insemination requires adjustment.

The period from intravaginal sponge withdrawal to oestrus obtained is similar to the time interval quoted by Faure, Boshoff & Burger (1983) of 64,0 \pm 12,24 hours in Karakul ewes. Regarding the duration of the induced oestrous period, here the group treated with the CIDR dispensers had a significantly ($P < 0,01$) shorter oestrous period, compared to the group treated with intravaginal

sponges (32,7 vs 47,4 h). Both gonadotrophic insufficiency and poor ovarian response and a disturbance of the endocrine balance at the induced oestrus could contribute to this phenomena in the sponge-treated group.

The serum progesterone profiles obtained with both progestagen treatments followed a similar pattern and within 6 hours following device withdrawal, the mean serum progesterone concentration was well below 1 ng/ml. Serum progesterone concentrations at the onset of oestrus (0,51 vs 0,46 ng/ml for dispensers and sponges respectively) compare well to values obtained by Yuthasastrakosol, Palmer & Howland (1975) and Thorburn, Basset & Smith (1969) in sheep.

The pattern of LH secretion, with a slight increase in the basal concentrations approximately 2 days prior to the pre-ovulatory LH surge and a decrease afterwards, agrees with other reports (Niswender, Roche, Foster & Midgley, 1968; Baird & McNeilly, 1981). This pre-ovulatory peak in LH concentration being indicative of ovulation. The increased LH secretion (pre-ovulatory surge) starts between 0 and 10 hours following the onset of oestrus (Hopkinson & Pant, 1973) in sheep, however this surge could occur significantly earlier in relation to the onset of oestrus and this LH release often occurs prior to the onset of oestrus (Cumming, Blockey, Brown, Catt, Goding & Kaltenbach, 1970; Lishman, 1972). This did in fact occur in one of the ewes from which blood was sampled in the dispenser group — showing a LH peak value 6 hours prior to the onset of oestrus. In the sponge-treated group and for sheep exhibiting oestrus, the position of the LH peak varied from 6 to 30 hours following the onset of oestrus — in contrast to the dispenser group where the position of the LH peak varied from 6 hours prior to the onset of oestrus to 12 hours following the onset of oestrus — suggesting a higher degree of control of ovulation.

A significant difference ($P < 0,01$) in the time from device withdrawal to the LH peak and from the onset of oestrus to the LH peak was observed — with the CIDR dispenser responding earlier in both cases. This is attributed to the longer delay in oestrous response by the sponge group, but the reason for the difference in the position of the LH peak relative to the onset of oestrus between the two progestagen administrations remains obscure. Cumming, *et al.* (1970) found that in Cronolone-treated ewes, the onset of the LH peak occurred earlier in relation to the onset of oestrus than in untreated ewes. The effect of exogenous progestagen on endogenous oestrogen production results in a pattern of production of oestradiol which differs from that of untreated ewes (Smith & Robinson, 1970). It has been suggested that due to an inadequate suppression of the release of pituitary gonadotrophin, particularly FSH, a steroid imbalance at oestrus results in a slightly abnormal endocrine state at the ensuing oestrus (Robinson, 1968). In ewes cycling naturally, ovulation is quoted as occurring between 19 and 35 hours following the onset of oestrus (Cumming, Buckmaster, Blockey, Goding, Winfield & Baxter, 1973), with the time relationship of the LH peak and ovulation of 21 – 26 hours being constant, suggesting that it is the gonadotrophin triggering

the ovulation mechanism. According to Thimonier & Pelletier (1971) the longer interval between oestrus and the pre-ovulatory LH surge could be related to the number of ovulations *per se*. This was supported by Wheaton, Raabe & Burrill (1977) who found that ewes, within a breed, with multiple ovulations have a longer interval than ewes which had a single ovulation, possibly due to a difference in follicular secretion rates. It is interesting to note that in both groups the interval from the peak LH surge and the end of oestrus were very similar, suggesting that even here a time relationship exists.

Regarding the fertility results achieved in this study, the conception-, lambing- and fecundity rates were not significantly different for the two progestagen regimes. These results obtained are acceptable, especially when it is considered that no PMSG was used in either treatment groups.

In a synchronization programme it is the fertility obtained which could eventually determine the feasibility of such a programme. Results obtained in this experiment indicate the CIDR dispenser to be a highly efficient synchronizing agent and warrants further research on different breeds of sheep, in various seasons and the use in conjunction with PMSG.

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