INDUCTION OF PARTURITION IN EWES

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ABSTRACT

With the advent of controlled breeding techniques in sheep , it is possible to mate ewes at most time of the year . Our investigation was carried out on 100 healthy ewes showing normal cyclic changes . They were treated with two i.m. injections, 4 hours apart , of $PGF_2\alpha$ at 10^{th} day of estrus to synchronize estrus . They were observed for the next estrus and served by a fertile ram . The day of service was recorded and considered as day 0 of pregnancy . Ewes failed to show estrus were excluded from the experiment. After 17-23 days from mating, fertile ram was re-introduced twice daily for at least one hour each time for detection of ewes that may come in heat again to be served . Pregnancy was diagnosed ultrasonographically using a real-time B-mode ultrasound unit equipped with a 7.5/5MHz transrectal transducer. Scanning of ewes was conducted weekly from 4^{th} to 8^{th} week after mating . Eighty ewes only were diagnosed to be pregnant and actually used in this study and followed up.

At day 140 of gestation , pregnant ewes were divided into 4 groups each of 20 ewes . Group I was injected i.m. with 15 mg $PGF_2\alpha$, group II was injected with 16 mg dexamethasone, group III was injected with 16 mg dexamethasone plus 15 mg $PGF_2\alpha$ given at separate locations and group IV was injected with 4 ml of 0.9 % sterile saline.

There were significant ($P< 0.01$) differences in the mean interval from treatment to lambing. It was 167.85 ± 21.48 , 45.16 ± 4.42, 52.36 ± 6.21 and 177.70 ± 13.39 hours for $PGF_2\alpha$, dexamethasone, dexamethasone plus $PGF_2\alpha$ injected group and control group , respectively.

No ewes were lambed within 72 hours from injection in both control and $PGF_2\alpha$ injected groups , whereas 65% (13 ewes) was lambed within 48 hours from injection in dexamethasone group vs.25% (5 ewes) was lambed within 48 hours from injection of dexamethasone plus $PGF_2\alpha$. All ewes were lambed within 72 hours from injection of either dexamethasone alone or dexamethasone plus $PGF_2\alpha$..

There was no significant difference between the four groups in the placental deliv-

ery time in hours (3.18 ± 4.79 , 1.65 ± 0.49, 3.84 ± 4.89 and 3.48 ± 4.85 hours for PGF_2a,dexemethasone, dexamethasone plus $PGF_2\alpha$ and control groups , respectively). Few cases of placental retention were observed in all groups except dexamethasone group. No cases of dystocia were recorded . All born lambs were viable except 4 (one in $PGF_2\alpha$ group, one in dexamethasone plus $PGF_2\alpha$ group and two in control group).. There was no difference in the number of lambs born in the 4 groups .

It could be concluded that , injection of dexamethasone alone in ewes near term leads to delivery of viable and healthy lambs within a predictable period from injection of drug without dystocia or placental retention .

INTRODUCTION

With the advent of controlled breeding techniques in sheep . It is possible to mate ewes at most times of the year **(Boland and Gordon, 1979)**. Many factors such as season of mating , breed of sire , number of lambs born and sex of the foetus have been indicated as affecting the duration of gestation in ewes **(Amir et al., 1980)**.

Induction of lambing can be a useful managemental tool to concentrate labor , synchronize the time of lambing for increasing surveillance and providing assistance of this critical time and more effective use of available facilities and labor, as well as to control pregnancy toxemia . However aceurate breeding records are essential if such program is to be successful, as efficacy decreases when treatment is given too early in gestation , and the viability of lambs born more than a few days prior to term is likely to be poor **(Kastelic et al., 1996)**.

Many theories as to what initiates parturition have been proposed. The fetal pituitary-adrenal axis seems to determine the moment of birth and artificial stimulation of this mechanism might enable the induction of parturition in sheep at a pre-determined moment **(Rommerein and Slyter, 1981)**.

It was found that glucocortieoids, estrogens and prostaglandin are all involved in the normal process of parturition **(Thorburn, 1979)**. Corticosteroids have been used to induee lambing in ewes when given late in gestation. Different forms of eorticosteroids such as dexamethasone **(Bosc, 1972, Joyce, 1974 & Shevah, 1974)**, flumethasone **(Emadi and Noakes, 1973, Emadi, 1974 & Harman and Slyter, 1980)** or betamethasone **(Lucas, and Notman, 1974)** have been used with varying levels of success . Prostaglandin F2α or many of its analogues are highly effective in the induction of farrowing in pigs **(Buckrell, 1988)**. **Day and Southwell (1979)** had shown that pregnancy has been terminated in a high proportion of goats within 50 hours of in-

jection of 125 or 250 ug cloprostenol. However , a poorer response has been observed following the use of 15 mg $PGF_2\alpha$ in sheep nearer term (**Harman and Slyter , 1980**). While, induction of lambing with cloprostenol in addition to dexamethasone was ineffective to reduce the interval from treatment to lambing than using dexamethasone alone (**Kastelic et al., 1996**) . It is apparent that, there are conflicting reports on the use of different agents for induction of lambing in ewes .

With this end in view, we selected a synthetic corticosteroid, dexamethasone, PGF2α analogue, lutalyse and a combination of both whose injected towards the end of gestation for induction of lambing in ewes.

MATERIAL AND METHODS

Animal and breeding :

This experiment was conducted on a private farm in Dakhlia province during the breeding season of ewes , The ewes were fed on Alfa alfa and 400 g / head / day of a commercial concentrate (14% crude protein). Mineral salt and water were offered ad libitum .

One hundred apparently healthy ewes ranging 2-4 years old and showing normal cyclic changes were selected for this investigation. Two weeks before the experiment, ewes were dewormed and submitted to general physical examination.

Experimentation:

The selected ewes were treated with two intra-muscular (i.m.) injections, 4 hours apart of PGF2α (lutalyse, Upjohn, Kalamazoo, U.S.A.) at day 10 of estrus (**Ott et al., 1980**) to synchronize estrus. They were observed for the next estrus and served by a fertile ram. The day of service was recorded and considered as day 0 of pregnancy. Ewes that failed to show estrus were excluded from the experiment. After 17-23 days from mating, fertile ram was re-introduced twice daily for at least one hour each time (at 07.00 and 19.00) for detection of ewes that may come in heat again in order to be served. Pregnancy was diagnosed ultrasonographically using a real-time B-mode ultrasound unit equipped with a 7.5/5 MHz transrectal transducer (Ultrascan 50, Mitsubishi, Japan) according to **Buckrell (1988)**. Carboxy methyle cellulose was used as an ultrasonic coupling gel (Medico-Scan, Chester labs Inc., U.S.A.). scanning of ewes was conducted weekly from fourth to eight week after mating. Out of 100 ewes, only 80 were diagnosed pregnant and actually used in this study and followed up until parturition.

At day 140 of pregnancy, pregnant ewes were allocated among four groups each of 20 ewes:

Group I : was injected i.m. with 15 mg $PGF_2\alpha$ (3ml Lutalyse).

Group II : was injeeted i.m. with 4 ml Fortecortine (each ml contain 4mg dexamethasone, 21-dihydrogen phosphate in the organic solvent benzyl alcohol as a preservative) (GlaxoWellcome, Egypt).

Group III : was injectcd with 16mg of dexamethasone plus 15mg $PGF_2\alpha$ given at separate locations.

Group IV : was injected with 4ml of 0.9% sterile saline.

Ewes in all groups were observed after treatment and the induction time in hours, placental delivery time in hours, lambs survival and number of dystocial cases were recorded.

Statistical analysis :

The relationship between the four groups concerning the data recorded was statistieally analyzed using one-way analysis of variance **(Snedecor and Cochran, 1980)** whenever needed.

RESULTS

The obtained results (table 1) revealed that, there was significant ($p< 0.01$) difference in the mean interval in hours from treatment to lambing, while, there was no significant variation in the placental delivery time in hours between the four groups.

The retention of placenta was met only in three ewes (one in $PGF_2\alpha$ group, one in dexamethasone pulse $PGF_2\alpha$ group and the 3rd one was met in the control group). There were no cases of dystocia were observed in all groups. All born lambs were viable except four (one in $PGF_2\alpha$, one in dexamethasone pulse $PGF_2\alpha$ group and two in the control group) were dead. There was no difference in the number of lambs born between the four groups.

Distribution of lambing following treatment (table 2) showed that in both control and $PGF_2\alpha$ groups, there was no ewes lambed within 72 hours post injection, whereas, 65% of ewes in dexamesathone treated group and 25% in dexamethasone plus $PGF_2\alpha$ group were lambed within 48 hours from injection. All ewes in dexamethasone and dexamethasone plus $PGF_2\alpha$ groups were lambed within 72 hours.

DISCUSSION

Parturition is believed to be initiated when adrenocorticotropic hormone (ACTH) from the fetal pituitary gland causes a release of cortisol from the fetal adrenal cortex. The fetal eortisol reduc-

es placental progesterone production and increases placental estrogen production, resulting in release of $PGF_2\alpha$ from the uterus. Consequently, uterine activity increases, the corpus luteum undergoes luteolysis, and parturition is initiated **(Barth, 1988)**. Dexamethasone and other synthetic glucocorticoids mimic fetal cortisol and have been successfully used to induce parturition in the ewe **(Rommercin and Slyter, 1981)**.

It was found that between 6 and 10 days before normal term is a safe period for induction of labour in sheep **(Silver, 1992)**. The author added that, at this stage the fetal pituitary-adrenal axis is fully competent, the feedback mechanism ensures that a short pre-partum surge of cortisol occurs.

Our results indicated that injection of dexamethasone alone resulted in the shortest and least variable interval from injection to parturition. Similarly, previous study found that, injection of 16mg dexamethasone resulted in the shortest and least variable interval from treatment to lambing **(Kastelic et al., 1996)**. The failure of $PGF_2\alpha$, when injected with dexamethasone to reduce the interval from treatment to lambing in the present study might be attributed to that addition of $PGF_2\alpha$ dissociates luteolysis from suppression of placental progesterone production and, hence, makes the interval from treatment to parturition more variable **(Boland, 1982 &Kastelic et al., 1998)**. On the other hand, previous study found that $PGF_2\alpha$ alone shorten the interval from injection to lambing **(Harman and Slyter, 1980)**. This disagreed with our results as when $PGF_2\alpha$ was injected alone it did not affect the interval from injection to lambing. This variation may be attributed to difference of day of gestation at which the inducing agent was injected, as well as the different breeds. However, the present results agreed with those obtained by **Boland et al. (1982)** who stated that induction time in $PGF_2\alpha$ group nearly equal to control group. This agreed also with the fact that the corpus luteum in ewes has normal luteal function until parturition although it was not necessary for maintenance of pregnancy except only during the first 50 days and after that, the placenta is responsible for the major part of progesterone secretion **(Jaimes et al., 1985)**.

As regard to the placental delivery time, the obtained results revealed that, there was no significant difference in the placental delivery time, which showed a great variability expressed as a standard deviation. The few observed cases of retained placenta were not associated with any treatment. A high incidence of complete or partial placental retention was reported following induced parturition using either $PGF_2\alpha$ **(Kask et al., 2000a)** or dexamethasone **(Kask et al., 2000a& Kask et al., 2000b)** around two weeks before expected calving time. This was attributed to the too early injection of the parturition-inducing agent. The loss of placental adherence in cows is thought to occur after the placentome has undergone a process of maturation, with maturity usually being reached 3-5 days before parturition **(Grunert et al., 1989)**. Actually, placen-

tal retention must be strongly linked to stress, as suggested by the highly increased cortisol levels during the 12 and 24 hours before calving. This increase was thought to be a decisive of PGE metabolite (PGEM) increase 24, 48 and 72 hr before calving **(Wiebkal et al., 2001)**. Probably, PGE2 is converted into $PGF_2\alpha$ in placenta during the pre partum period of cows without placental retention **(Hoedemaker et al., 1990)**. No cases of dystocia were observed in all groups. Dystocia observed in some studies to be coincidental but not due to $PGF_2\alpha$ injected for induction of parturition **(Bretzlaff and Ott, 1983, Haibel and Hull, 1988& Romano et al., 2001)**.The viability of lambs born was not affected by the inducing agent and the mortality was sporadic. These results agree with those of previous researchers **(Rommereiu and Slyter, 1981; Boland, 1982 & Kastelic et al., 1996)**. The high survival rate in our study indicates that the timing of injection of lambing-inducing agent did not affect normal lung maturation or surfactant production **(Silver, 1992 & Romano et al., 2001)**. This is strengthened by the postulation that induction of premature calving often leads to loss of the calf and retention of placenta **(Refsdal, 2000)**.

In conclusion, injection of dexamethasone alone in ewes near term leads to delivery of viable healthy lambs within a predictable period from the time of injection of the drug without dystocia or retained placenta.

Table (1): Effect of different treatments on induction time, placental delivery time, incidence of placental retention, dystocia, number of lambs born and mortality rate of lambs. (Mean ±SD).

Group	Induction time (hr)	Placental delivery time (hr)	Mortality rate of lambs	Incidence of retained placenta	Incidence of dystocia	Number of lambs born
Group I (n=20)	167.85^{a} ±21.48	3.18^{a} ±4.79	1	1	0	34
Group II (n=20)	45.16^{b} ±4.42	1.65^{a} ±0.49	-	0	0	33
Group III (n=20)	52.36^{c} ±6.21	3.84^{a} ±4.89	1	1	0	34
Group IV (n=20)	177.70^{d} ±13.39	3.84^{a} ±4.85	2	2	0	32

Data within columns with different superscript differ significantly (P <0.01).
n= number of ewes.

Table (2): Distribution of lambing following treatment.

Group	Ewes lambed within 48hr		Ewes lambed within 72hr		Ewes lambed after 72hr	
	No	%	No	%	No	%
Group I (n=20)	0	0	0	0	20	100
Group II (n=20)	13	65	20	100	0	0
Group III (n=20)	5	25	20	100	0	0
Group IV (n=20)	0	0	0	0	20	100

n= number of ewes.

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الملخص العربى

إحـــداث الولادة إصطناعيـــاً فى النعـــــاج

المشتركون فى البحث

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مع قدوم التقنيات الحديثة للتحكم فى تناسل الأغنام بات من الممكن تلقيح النعاج فى معظم أوقات العام. وقد أجريت دراستنا على ١٠٠ نعجة بصحة جيدة وتظهر التغيرت دورة الشبق الطبيعية، وقد تم حقنها بحقنتين فى العضل تفصلها أربع ساعات، من البروستاجلاندين إف ٢ ألفا فى اليوم العاشر من دورة الشبق حتى يتم تزامن الشبق فى وقت واحد، وقد تم ملاحظتها لظهور أعراض الشبق عليها وتم تلقيحها بواسطة كبش خصب، وقد أعتبر آخر يوم فى التلقيح هو اليوم صفر من الحمل، وقد تم إستبعاد النعاج التى لم تظهر عليها علامات الشبق من التجربة، وبعد ١٧-٢٣ يوماً من التلقيح تم إدخال كبش خصب مره أخرى (مرتين يومياً) فى كل مرة لمدة ساعة على الأقل للكشف عن النعاج التى من الممكن أن تأتى فى الشبق مرة أخرى حتى يتم تلقيحها.

وقد تم تشخيص الحمل باستخدام جهاز فحص الموجات فوق الصرتية حيث تم فحص النعاج بالموجات فوق الصرتية إسبوعياً إبتداءاً من الإسبوع الرابع وحتى الإسبوع الثامن من التلقيح، وقد تم تشخيص الحمل فى ٨٠ نعجة فقط وهى بالتالى التى أستخدمت فعلياً فى هذه الدراسة وتم تتبعها.

وفى اليوم ١٤٠ من الحمل، تم تقسيم النعاج العشار لأربع مجموعات كل منها يتكون من ٢٠ نعجة وتم حقن المجموعة الأولى عضلياً بـ ١٥ مجم من البروستاجلاندين إف ٢ ألفا، والمجموعة الثانية بـ١٦ مجم من الديكساميثازون، والمجموعة الثالثة بـ ١٦ مجم ديكساميثازون بالإضافة إلى ١٥مجم من البروستاجلاندين إف، والمجموعة الرابعة بـ ٤ مللى من ٩ر.٪ محلول ملح معقم. وقد كانت هناك فروق معنوية فى متوسط الزمن من العلاج حتى حدوث الولادة.

ولم تلد نعاج خلال ٧٢ ساعة من الحقن سواءاً فى المجموعة الحاكمة أو المجموعة المحقونة بالبروستاجلاندين إف ٢ ألفا، بينما ولدت ١٣ نعجة (٦٥٪) خلال ٤٨ ساعة من حقن الديكساميثازون مقابل ٥ نعاج فقط (٢٥٪) ولدت فى المجموعة المحقونة ديكساميثازون وبروستاجلاندين إف ٢ ألفا معاً. كما أن كل النعاج قد ولدت خلال ٧٢ ساعة من حقن الديكساميثازون مفرداً أو الديكساميثازون مع البروستاجلاندين إف٢ ألفا.

ولم يكن هناك أى فروق معنوية بين الأربع مجموعات فى زمن نزول المشيمة بالساعات، وقد تم ملاحظة إحتباس مشيمى فى حالات قليلة موزعة على كل المجموعات فيما عدا مجموعة الديكساميثازون، ولم تسجل حالات عسر ولادة فى كل المجموعات، كما أن كل الحملان قد ولدت حية فيما عدا أربع حملان، ولم يكن هناك فروق تذكر فى عدد الحملان المولودة فى الأربع مجموعات.

ومن الممكن إذاً إستنتاج أن حقن الديكساميثازون مفرداً فى النعاج بالقرب من زمن الولادة الطبيعى يؤدى إلى ولادة حملان حية وسليمة صحياً وذلك خلال فترة زمنية صغيرة ومعقولة من حقن العقار بدون حدوث حالات عسر ولادة أو إحتباس مشيمى.