Effect of using various doses of Bromocriptine in estrus induction and subsequent fertility in lactating anestrus Iraqi Ewes

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Summary

Forty eight (48) anestrus lactating Iraqi ewes aged between 2-4 years were undertaken 40 days postpartum in Babylon province (Technical institute in Al-Mussaib). Ewes were randomly divided into 4 equal groups according to type of treatment implemented. Group 1 (G1) were treated with vaginal sponges impregnated with 60 mg Medroxy Progesterone acetate for 10 days. Immediately after sponge removal, each ewe was injected IM. with 500 IU. Equine choriogonadotropines. Ewes of G2 were treated with Medroxy Progesterone acetate and Equine choriogonadotropines as mentioned above in addition n to 10 mg bromocriptine/day orally for 10 successive days at the same time of sponges insertion. Animals of G3 were treated with Medroxy Progesterone acetate and Equine choriogonadotropines in addition to 20 mg bromocriptine/day orally for 10 days. Ewes of G4 were treated with Medroxy Progesterone acetate and Equine choriogonadotropines in addition to 30 mg bromocriptine /day orally for 10 days. All ewes were mixed free with 5 fertile rams for 7 days after hormonal treatment to detect estrus and natural mating. Results showed that the duration of response to treatment was significantly longer $P<0.05$ in G1 (3.42±0.17) days than that recorded in G4 (1.14±0.12), G3 (1.20±0.21) and G2 (2.16±0.14) days. Consequently, the number of ewes which showed estrus was significantly high $P<0.05$ in G4 (100%) compared to G3 (75%), G1 (83.3%) and G2 (91.6%). The percentage of pregnancy was significantly higher $P<0.05$ in G3 (100%) versus 70%, 83.3% and 90.9% in G1, G4 and G2, respectively. Serum estrogen values were gradually increased with the increased doses of bromocriptine in all groups while progesterone value was decreased at the last days before sponges removal in all ewes.

Keywords: Bromocriptine doses, Estrous induction, Lactating ewes, Estrogen, Progesterone.

Introduction

Ewes are usually reared for their reproductivity represented by multiple lambing and to a lesser degree for their production of milk, hide, wool and manure (1 and 2). Reproduction in postpartum ewes is usually influenced by several factors, including duration of lightening, nutrition, breed, age, diseases, ambient temperature, body weight and presence of the male in the flock (3 and 4). Estrus induction and synchronization with subsequent fertility have been successfully achieved in anestrus ewes either by using progesterone with eCG (5-7) or Melatonin (8-10). Rodway (11) who tried to apply bromocriptine for improving the reproductive efficiency in anestrus lactating ewes. However Range (12) had reported that bromocriptine has no effect on uterine contraction in human being while (13 and 14) suggested that suppression of prolactin by bromocriptine during lactation had an effect on plasma FSH, LH, Estrogen, ovulation and luteal function in ewes. Also they suggested that there was a greater likelihood of an earlier resumption of breeding activity in the ewe and might also depend on the day length period. Since there is a shortage in the knowledge of using bromocriptine in the veterinary practice, particularly farm animals. The aim of this study was focused on the effect of using progesterone, eCG and various doses of bromocriptine on estrus induction and fertility rate in lactating anestrus Iraqi ewes and serum levels of estrogen and progesterone hormones.

Materials and Methods

Forty eight (48) of anestrus lactating Iraqi ewes aged between 2-4 years were undertaken after 40 days postpartum in Babylon province in the south west of Iraq. The animals were divided randomly and equally into 4 groups (12 ewe/ group) according to the type of treatment implemented. The control group (G1) treated with vaginal sponges impregnated 60 mg of Medroxy acetate progesterone, MAP,

(Upjohn LTD, Fleming way, Grawly, Sussex; England) for 10 days. Immediately after sponges removal each ewe was injected with a single dose of 500 I.U eCG (Folligon Intervet international B. Holland). The 2nd group (G2) was treated with MAP + eCG in the same procedure applied in (G1) I + 100 mg of Bromocriptine (Parlodine ASIA Pharmaceutical industries; Syria), (10 mg orally for the same 10 successive days of sponges insertion). The 3rd group (G3) was treated with MAP + eCG + Bromocriptine 200 mg (20 mg orally for the same 10 days of sponge insertion). While 4th group (G4) was treated with MAP + eCG + Bromocriptine 300 mg (30 mg orally for the same 10 days of sponge insertion).

Treated ewes were mixed free with 5 fertile rams for 7 days after hormonal treatment to detect estrus and for natural mating. Blood samples were collected from the jugular vein by disposable syringes in days 0, 3, 6 and 10 of hormonal treatment. Hormonal assay has been conducted according to (15) using radioimmunoassay (RIA) to estimate the levels of estrogen and progesterone. The kits were provided by Immunotech, A Bechman Coulter Company, de Latter de Tassigny, France. The intra assay and inter assay coefficient of variation were 5.8 – 9, respectively. Mean, Standard error, Chi-Square, F. test and Anova two ways statistical analyses were used.

Results and Discussion

Table (1) the number of ewes in G1 responded to treatment with 60 mg MAP*+ 500 I.U eCG, signs of estrus were detected in10 ewes out of 12 (83.3%) and the duration of response after sponge removal was 3.42±0.17 days, 7 of them (70%) became pregnant. In G2, 11 ewes out of 12 (91.6%) responded to treatment and showed signs of estrus 2.16 ±0.14 days after sponges removal. Ten ewes out of the 11 responded (90.9%) became pregnant. In G3 nine ewes out of 12 (75%) responded to treatment and showed signs of estrus 1.20±0.21 days after sponges removal. All responded ewes (100%) became pregnant.

In G4, 12 ewes out of 12 (100%) responded to treatment and showed signs of estrus within 1.14±0.12 days. 10 ewes out of the 12 responded (83.3%) became pregnant. In (Table, 1). the number of ewes responded to various doses of bromocriptine with MAP and eCG hormones was increasing with the increase in bromocriptine doses except the ewes of G3 in which 9/12 (75%) response was registered which could be attributed to the body condition and individual variations in response to hormones or to the inadequate time for estrus detection (16).

Table, 1: Types of treatments and results of estrus response, duration and subsequent pregnancy rates in ewes.

Group No.	Type of treatment	No. of animals	No. of ewes showed estrus	Duration of response M±S.E day	No. of ewes became pregnant
1	Vaginal sponges 60 mg + eCG 500 I.U.	12	10 (83.3%) C	3.42 ±0.17 a	7 (70%) d
2	V.S. 60 mg + eCG 500 I.U. + 100 mg Bromocriptine	12	11 (91.6%) B	2.16 ±0.14 b	10 (90.9%) B
3	V.S. 60 mg + eCG 500 I.U. + 200 mg Bromocriptine	12	9 (75%) D	1.20 ±0.21 c	9 (100%) A
4	V.S. 60 mg + eCG 500 I.U. + 300 mg Bromocriptine	12	12 (100%) A	1.14 ±0.12 c	10 (83.3%) C

Different small letters means significant differences at P<0.05 within groups

The duration of response was significantly shorter (P<0.05) in the 3rd and 4th groups compared to those of the 1st and 2nd groups, nevertheless the females in the 2nd group showed signs of estrus in a period significantly (P<0.05) shorter than the 1st group. These results are correlated to the gradual increase in bromocriptine doses in concomitant with the groups of ewes (11). In the 3rd group of ewes, although there was a lower percentage of response to treatment but the subsequent fertility of ewes which became pregnant later was significantly (P<0.05) higher than other groups (100%). It could be therefore assumed that the lower percentage of estrus detection in G3 is ascribed either to prolonged lactation or to other environmental factors (10 and 17).

As the target of any reproductive performance is to get a better quantity and quality of off spring, the percentage of ewes in G2, G3 and G4 which became pregnant were

significantly higher (P<0.05) than the control G1 (Table, 1) which could indicate that bromocriptine had an influence in either promoting follicular growth and maturation or increasing estradiol positive feedback for preovulatory LH peak by decreasing prolactin release from the anterior pituitary gland (18-20). However a significant difference (P<0.05) in pregnancy rate was also recorded between ewes groups which means that the higher doses of bromocriptine do not steadily or always induce fertile estrus (11).

Results of (Table, 2) shows that 7 out of 10 ewes in G1 became pregnant, their delivery was normal, one of the ewes delivered twins, 4 of the lambs were males and 4 were females and all of them were alive. In G2 10 out of the 11 ewes became pregnant, two of them suffered from dystocia and also two of them delivered twins, 6 of the lambs were males and 6 were females, one of the lambs died soon after birth. In G3 9 out of the 9 ewes became pregnant, one of them showed difficult birth, 4 of them had twins, 9 of the lambs were males and 4 were females, 2 of the lambs died later. In G4 10 out of 12 ewes became pregnant, one of them needed assistant at birth, 4 of them had twins, 8 of the lambs were males and 6 were females, one of the twins died soon after delivery.

In (Table, 2) dystocia or assisted delivery was recorded in groups of ewes treated with bromocriptine in addition to MAP and eCG, however it is unfair to accuse bromocriptine as a main factor for such conditions but it could be referred to the number of twins delivered in groups of ewes which received bromocriptine. In this context twins were relatively higher and may be consider as a factor for difficult birth and neonatal death. The number of dead fetuses (4/47) is considered as an acceptable average of fetal loss post partum (17).

The level of estradiol in the serum of different groups of ewes was estimated in Nmol/L on days 0, 3, 6 and 10 of sponge insertion (Table, 3 and Fig. 1). In G1 estradiol was recorded as 78.17±18.81, 89.37±26.13, 135.24±16.56 and 212.43±32.17 on days 0, 3, 6 and 10, respectively. In G2 estradiol was 87.12±16.34, 141.11±30.25, 236.14±41.62 and 295.42±52.34, respectively. In G3 estradiol was 91.26±20.11,134.16±31.12, 256.23±40.33 and 311.06±42.20, respectively. In G4 estradiol was 108.22±17.13, 156.07±30.61, 278.12±40.21 and 346.42±51.38, respectively.

Estradiol in (Table, 3) has a significant (P<0.05) gradual increase with the sustainable increase in the bromocriptine doses among the sequence groups of ewes which indicates a relative remarkable effect of bromocriptine dose with the concomitant elevated level of estradiol in blood which agreed with the findings of (16 and 21). Significant effect (P<0.05) was also recorded within the same groups since the level of estradiol was increased with the period of daily bromocriptine administration which might support the results of estrus detection and short duration of response to treatment.

Table, 2: Represents information concerning parturition and off spring of local ewes.

Group No. of ewes	Pregnancy records	Nature of parturition Nor. Dyst.	Type of parturition Sing. Twin.	Sex of lambs M F	Viability A D
1	7/10	7 -	6 1	4 4	8 -
2	10/11	8 2	8 2	6 6	11 1
3	9/9	8 1	5 4	9 4	11 2
4	10/12	9 1	6 4	8 6	13 1
Total	36/42	32/36 4/36	25/36 11/36	27/47 20/47	43/47 4/47
	85.7%	88.8% and 11.2%	69.4% and 30.6%	57.7% and 42.6%	91.4% and 8.6%

Table, 3: Serum level of estrogen (N mol/L) in different treated groups.

Days of blood collection	G1 (control)	G2	G3	G4
0	78.17 ±18.81 Ad	87.12 ±16.34 Bd	91.25 ±20.11 Cd	108.22 ±17.13 Dd
3	89.37 ±26.13 Ac	141.11 ±30.25 Bc	134.16 ±31.12 Cc	156.07 ±30.61 Dc
6	135.24 ±16.56 Ab	236.14 ±41.62 Bb	256.23 ±40.33 Cb	278.12 ±40.21 Db
10	212.43 ±32.17 Aa	295.42 ±52.34 Ba	311.06 ±46.20 Ca	346.42 ±51.38 Da

In (Table, 4 and Fig. 2) level of progesterone in the serum of different groups of ewes was estimated in Nmol/L on days 0, 3, 6 and 10 of sponge insertion. In the G1, the level of progesterone was recorded as 2.11±0.02, 1.03±0.03, 1.01±0.02 and 0.93±0.02, respectively. In G2 the level of progesterone was 2.36±0.11, 0.72±0.10, 0.68±0.03 and 0.40±0.02 Nmol/L, respectively. In G3 the level of progesterone was recorded as 2.58±0.21, 0.86±0.03, 0.56±0.04 and 0.34±0.01, respectively. In G4 the level of progesterone was recorded as 3.01±0.36, 1.06±0.21, 0.58±0.14 and 0.28±0.02, respectively.

Results of progesterone (Table, 4) showed variable and inconsistent levels among the sequential groups of ewes within the first two collections of blood (day 0 and day 3) but later in day 6 and day 10 a steady significant decline ($P<0.05$) was manifested in concomitant with the elevated levels of bromocriptine which could be attributed to the decline in progesterone release from the sponges at the few days before withdrawal and bolstered by the significant decline ($P<0.05$) of progesterone and prolactin within the same groups of ewes (21 and 22).

Table, 4: Serum level of progesterone (N mol/L) in different treated groups.

Days of blood collection	G1 (control)	G2	G3	G4
0	2.11 ±0.02 Aa	2.36 ±0.11 Aa	2.58 ±0.21 Aa	3.01 ±0.36 Ba
3	1.03 ±0.03 Ab	0.72 ±0.10 Bb	0.86 ±0.03 Bb	1.06 ±0.21 Ab
6	1.01 ±0.02 Ab	0.68 ±0.03 Bb	0.56 ±0.04 Cc	0.58 ±0.14 Cc
10	0.93 ±0.02 Ac	0.40 ±0.02 Bc	0.34 ±0.01 Bd	0.28 ±0.02 Cd

Different small letters means significant differences at $P<0.05$ within groups. Different capital letters means significant differences at $P<0.05$ between groups.

In conclusion, bromocriptine, which has not been implicated before in manipulating estrus and fertility in anestrus Iraqi ewes, showed improvement in estrus and pregnancy rates in concomitant with the higher recommended daily oral dose of 30 mg for 10 days.

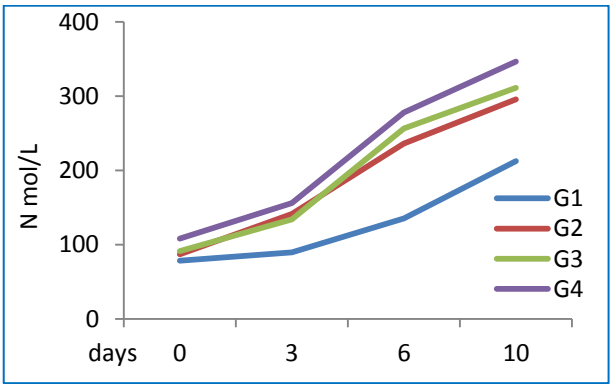

Figure 1: Serum level of estrogen (N mol/L) in different groups

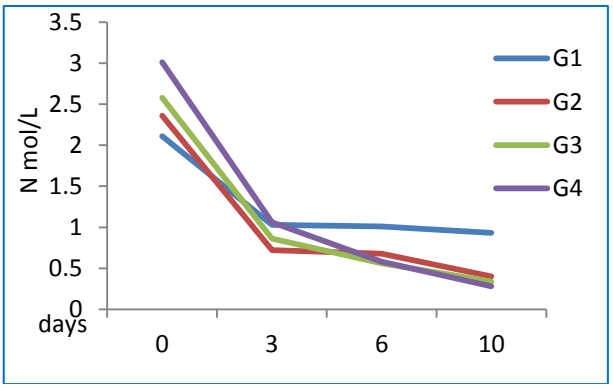

Figure 2: Serum level of progesterone (N mol/L) in different groups.

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تاثير استعمال جرع مختلفة من البروموكربتين في استحداث الشبق والخصوبة المستقبلية في النعاج العراقية في أثناء مرحلة انعدام الشبق الرضاعي

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الخلاصة

استعملت في هذا البحث 48 نعجة عراقية بعمر 2-4 سنه بعد الولادة بنحو 40 يوماً في محافظة بابل . قسمت هذه النعاج عشوائيا إلى اربع مجاميع متساوية اعتماداً على نوع العلاج المستعمل. المجموعة الأولى (G1) عولجت بوضع اسفنجات مهبلية مشبعة بـ60 ملغم من مِيذْروكْسي بروجستيرون أسيتات لمدة 10 ايام وبعد رفع الاسفنجات زرقت عضليا بـ 500 وحدة دولية من هرمون الفرس المشيمي. المجموعة الثانية (G2) عولجت بنفس العلاجات السابقة فضلاً عن 10 ملغم من البروموكربتين عن طريق الفم يوميا لمدة عشرة أيام متتابعة في أثناء وضع الاسفنجات المهبلية (مجموع الكمية 100ملغم). المجموعة الثالثة (G3)

عولجت كسابقها لكنها جرعت 20 ملغم من البروموكربتين يومياً. أما المجموعة الرابعة (G4) فقد عولجت بنفس العلاجات السابقة فضلاً عن 30 ملغم من البروموكربتين جرعت لمدة عشرة أيام متتابعة (المجموع 300 ملغم). في اليوم العاشر أطلقت المجاميع الأربعة للنعاج مع خمسة أكباش خصبة لمدة 7أيام لغرض كشف الشبق وضمان التلقيح. أظهرت النتائج بان مدة الشبق بعد اليوم العاشر كانت أطول معنويا ($P<0.05$) في المجموعة الاولى (3.42±0.17) يوم قياسا بالمجموعة الرابعة (1.14±0.12) والثالثة (1.20±0.21) والثانية (2.16±0.14) يوم. ان عدد النعاج التي اظهرت الشبق كانت أكثر معنوياً في المجموعة الرابعة (100%) بالمقارنة مع الثالثة (75%) والأولى (83.3%) والثانية (91.6%). اما نسبة الحمل فكانت الأعلى معنوياً ($P<0.05$) في المجموعة الثالثة (100%) بالمقارنة مع الأولى (70%) والرابعة (83.3%) والثانية (90.9%). لقد لوحظ ارتفاع تدريجي لمستوى هرمون الاستروجين في الدم بزيادة جرعة البروموكربتين في جميع المجاميع، في حين سجل البروجسترون انخفاضا في الأيام الاخيرة قبل إزالة الاسفنجات المهبلية في جميع مجاميع التجربة. الاستنتاج مركب البروموكربتين يزيد الخصوبة والحمل في النعاج العراقية بعد الولادة.

الكلمات المفتاحية: بروموكربتين، استحداث الشبق، نعاج المرضعة، هرمون الأستروجين، هرمون البروجسترون.