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**EVALUATION OF THE EFFECTS OF TWO
PROTOCOLS USING PROSTAGLANDIN F_{2α} AS A
TREATMENT OF RETAINED PLACENTA IN DAIRY
COWS IN ALGERIA**
(With 2 Tables)

By

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**تقييم عدة طرق لمعالجة إحتباس المشيمة عند الأبقار بإستعمال هرمون
البروستاجلاندين ف_{2α} ألفا، في الجزائر**

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هدف هذه الدراسة هو تسليط الضوء على أهمية إستعمال هرمون البروستاجلاندين عند الأبقار التي تعاني من مشكلة إحتباس المشيمة. شملت هذه الدراسة ٤٠ بقرة من سلالة الفريزيان، قسمت إلى أربعة مجاميع متساوية (ن=١٠). المجموعة الأولى استعملت كشاهد. المجموعة الثانية حقنت بالماء المقطر فقط. المجموعة الثالثة حقنت بهرمون البروستاجلاندين، في اليوم الذي لوحظ فيه إحتباس المشيمة. المجموعة الرابعة حقنت بنفس هرمون البروستاجلاندين، لكن بواسطة جرعتين: الجرعة الأولى في بداية العلاج والثانية في اليوم الخامس عشر بعد الحقن الأولى. كل الأبقار تم الكشف عن مدى تراجع الرحم فيها، في اليوم الثلاثين من الولادة، بطريقة جس المستقيم باليد. تقييم الكفاءة التناسلية في الأبقار المعالجة كانت تهدف إلى دراسة الوقت الخاص للشيوع ابتداء من يوم الولادة، الأيام المفتوحة في هذه الأبقار، نسبة التلقيح في التسفيد الأول، ونسبة التلقيح الكلية. لم نلاحظ إختلاف نسبي بين أبقار المجموعة الثالثة والرابعة، لكن كانت النسبة متباينة بين المجموعة الأولى والثانية والآخرين. أهمية حقن الهرمون تمثلت في تقليص الفترة ما بين الولادة وعودة الشيوع في الأبقار، وتقليص الفترة ما بين الولادة والتلقيح، وكذلك تقليص عدد التلقيحات للحصول على الحمل عند هذه الأبقار.

SUMMARY

The aim of this study was to prove the interest of injection of a synthetic analogue of PGF_{2α}(Cloprostenol), in cows with retained placenta and

whose are subject to manual deliverance. The study included 40 friesian cows breed, distributed on to 4 groups: (1) The first group, without treatment, (2) The 2nd group has been injected by saline (4 ml), the day of the delivery, (3) The 3rd group has been injected by PGF2 α (4 ml, IM) the day of the delivery, (4) The 4th group has been injected twice by PGF2 α (4 ml, IM): the day of the delivery and 15 days after. All cows were examined for uterine involution by rectal palpation on day 30 post-partum. Afterwards they were re-examined 2-4 weeks later. The parameters used to measure subsequent reproductive performance were days to first service, days open, first service conception rate and conception rate. The history of each animal was observed up to next pregnancy when possible. Treatment of retained placenta with a single or two intramuscular injections of 500 mg Cloprostenol have a significant effect on reproductive performance in treated group 3 and 4, than in control groups (1 and 2). This significant effect was noted in reducing the interval from birth to first mating, the interval from birth to conception and the number of service by conception. However, we have observed no significant effect between the group 3 and 4, for the same parameters of evaluation. However, a single injection of Cloprostenol at the moment of deliverance had a positive repercussion on the ulterior fertility and it's not necessary to repeat the treatment 15 days later.

Key words: Retained placenta, late uterine involution, PGF2 α , dairy cows.

INTRODUCTION

Estimates of the annual incidence of uterine infections in postpartum animals in herds range from 10 to 50% of the dairy cattle (Arthur *et al*, 1992 and Lewis, 1997). Early identification and diagnosis of reproductive problems through a herd health program are an essential part of successful dairy management. A cow must be pregnant by 85 day post partum to achieve a 12-month calving interval. This is the backbone of sound reproductive management in an economical dairy business (Greaves and Mc Lean, 2002; Mateus *et al*, 2002).

Many factors during late gestation, parturition and early lactation can lower reproduction efficiency. These include mastitis, cystic ovaries, lack of body condition, retained placenta and anestrus. Also, certains disorders occur together. For example, a cow with milk fever will frequently have a retained placenta. These post partum problems lengthen calving intervals and affect reproductive efficiency (Roberts, 1986).

In most herds, 10% or more of the cows will still have their placenta attached at 24 or more hours after calving. Most animals or cows will normally expel their placentae within 12 hours. Retained placentas are more frequent in cases of dystocia, toxins, abortions and certain infectious diseases (brucellosis, chlamydiosis and Q-fever. Cows with a history of not expelling the placenta will probably continue to have problems (Bekane *et al*, 1994 and Frederiksson *et al*, 1985).

Selenium appears to play an important role to placental release. Selenium appears to be involved in the release of prostaglandin. Prostaglandin may induce the release of the placenta by stimulating collagenase activity. Collagenase breaks down collagen, the material that cements the cells of the uterus and placenta together. Vitamins A and D are also involved (Abo-Shusha, 1990; Osman and Shehata, 1992 and Hemmingway, 2003).

Cows should also be provided with a clean, comfortable calving area. Sanitation is essential to prevent uterine infections as well as getting the calf off to a good healthy start (Laven and Peters, 1996 and Sabry *et al*, 1997).

If treatment of retained placenta is necessary, it is desirable to use drugs that do not cause residue problems in milk, such as oxytocin and prostaglandin. These drugs increase uterine motility.

Intramuscular injections of $\text{PGF}_2\alpha$ have become the preferred treatment for retained placenta in cattle, in many countries (Lewis, 2003; Scott *et al*, 2005). Exogenous $\text{PGF}_2\alpha$ is used to induce luteolysis and clear uterine infections. In fact, $\text{PGF}_2\alpha$ seems to have effects that are independent of its effects on corpus luteum function. Even though exogenous $\text{PGF}_2\alpha$ has become the preferred treatment, intrauterine and systemic antibiotic treatments are common in many countries (Chenault, 2001). General concerns about the relationship between antibiotic used in livestock and the potential for accelerating the evolution of antibiotic-resistant strains of bacteria have aimed our research at determining whether nonantibiotic, native compounds can be used to enhance host immunity and prevent or resolve uterine infections (Roberts, 1986; Laven and Peters, 1996; Koningsson, 2001 and Lewis, 2003).

$\text{PGF}_2\alpha$ is a proinflammatory molecule that stimulates the production of various proinflammatory cytokines, and it may enhance uterine production of leukotriene B_4 . Proinflammatory cytokines and leukotriene B_4 enhance phagocytosis and lymphocyte functions. Even though, there are clear associations among prostaglandin $\text{F}_2\alpha$, leukotriene B_4 , proinflammatory cytokines, phagocytosis, and

lymphocyte functions. The mechanism of action of exogenous PGF₂α in overriding the down-regulatory effects of progesterone and resolving uterine infections has not been elucidated. Defining this mechanism should yield new prevention and treatment strategies for uterine infections that do not rely on antibiotic and antimicrobial compounds (Roberts, 1986 and Guilbault *et al.* 1989 and Dhaliwal *et al.* 2001).

MATERIALS and METHODS

In a field trial Cloprostenol (Estrumate®), a synthetic analogue of prostaglandin F₂α was used therapeutically, after diagnosis of retained placenta (fetal membranes were considered retained if not expelled within twelve hours after parturition). The trial was conducted from January to December 2005 on several commercial dairy herds in Tiaret, Algeria. A total of 40 Friesian cows, were enrolled in the study. Animals were allotted in 4 groups of 10 cows.

In each group, an attempt was made to remove carefully the fetal membranes. After the manipulation, an intrauterine antibiotic treatment was administered. Cows of the 4 experimental groups have received the following treatments:

Control group 1: received no treatment.

Control group 2: received only an intramuscular injection of 4 ml of saline.

Group 3: received a single intramuscular injection of 500 mg Cloprostenol (4 ml Estrumate®) at the day of delivery.

Group 4: received two intramuscular injection of 500 mg Cloprostenol (4 ml Estrumate®). The first injection at the beginning of the treatment, within the 5 days after birth, and the second injection, 15 days after the first injection.

All cows were examined for uterine involution control by rectal palpation on day 30 post-partum.

Afterwards they were re-examined two to four weeks later. The parameters used to measure subsequent reproductive performance included days to first service, days open, first service conception rate, and conception rate. The history of each animal was observed up to next pregnancy when possible.

RESULTS

A/ Uterine involution:

Uterine involution has been studied and quantified by mean of rectal palpation of internal genital tract and results are presented on Table 1:

Table 1: Relationship between Cloprostenol (PGF2 α) injection, and uterine involution in treated versus not treated cows.

Uterine involution control at day 30	Group I : Total %	Group II : Total %	Group III : Total %	Group IV : Total %
Normal uterine Involution	30 % (n = 3)	40 % (n = 4)	60 % (n = 6)	70 % (n = 7)
Sub involution	20 % (n = 2)	10 % (n = 1)	20 % (n = 2)	20 % (n = 2)
Delayed uterine involution (metritis)	50 % (n = 5)	50 % (n = 5)	20 % (n = 2)	10 % (n = 1)
Total	100 % (n = 10)	100 % (n = 10)	100 % (n = 10)	100 % (n = 10)

In the absence of treatment, only 30 % of the cows in group 1 and 2 have presented a normal uterine involution. With a single intramuscular injection of 500 mg Cloprostenol (PGF2 α) at the day of delivery, the results were better, and uterine involution was done within the deadlines in 60 % of the cases (n = 6), and that among this group, two cows had a delay of uterine involution.

For group 4, cows having received a double injection of PGF2 α , one the day of delivery and the second 15 days after, the percentage of the subjects having had a normal involution was 70 % of the cases (n=7), appreciably higher compared to those which underwent a single injection. In this group, only one cow underwent a delay of uterine involution.

B) Fertility:

Table 2: Relationship between Cloprostenol (PGF2 α) injection and fertility parameters, in treated versus not treated cows.

	Number of cows	Interval Birth – First Mating [Mean]	Interval Birth – Conception [Mean]	Number of services [Mean]	% of non return in heats
Group 1	10	86,7	116,7	2,2	50 %
Group 2	10	72,9	112,3	2	60 %
Group 3	10	61,7	80,7	1,5	80 %
Group 4	10	59,5	70	1,4	90 %

Fertility parameters of each cow of the fourth studied groups were evaluated, starting from the number of services (here, number of natural mating), interval birth to first mating, interval birth to conception, and finally the percentage of non return in heat.

In the absence of treatment for groups 1 and 2, the animals underwent an average of 2 to 2,2 mating by conception, against 1,5 to 1,4 for the animals of groups 3 and 4 having respectively received 1 and 2 injections of Cloprostenol. With regard to the interval birth to conception, the results confirm the really influence of PGF2 α treatments. Thus, cows treated with 1 or 2 injections of Cloprostenol were respectively fertilized 36 and 46,7 days earlier than not treated cows.

DISCUSSION

For uterine involution control, each cow of the fourth groups was submitted to a transrectal examination, practised on day 30 post partum. The criteria selected were the degree of opening and the position of the cervix, the nature and the volume of the flows, the diameter of the uterine horns as well as the presence of an ovarian activity.

During present experiments, 30 % only of cows presented a normal uterine involution in the absence of PGF2 α treatment (group 1 and 2), against 50 and 60 % for the animals treated respectively by a single injection (group 3) or two injections (group 4). These results are lower than those published by authors having used "étiproston", another synthetic analogue of PGF2 α , in cows whose delivery was spontaneous. Tainturier (1991) has found the following averages: 36 %, 70, 1 % and 80, 2 % respectively for control group, group 2 (having received a single injection of PGF2 α) and group 3 (having received a double injection of PGF2 α).

Cardin (2000), obtained 50 % of normal uterine involution in the control group against 80 % for the treated groups. Concerning the rates of metritis (delay of uterine involution) observed in this present work, they were 30 %, 20% and 10% respectively for groups I, III and IV. Present results are similar to those published by Mami (1997), who has followed the same protocol by using étiproston and by delivering the cows manually. The rates observed by Ilari (1998) are also close as our results, and found 40 %, 15, 8 % and 10 % respectively for groups 1, 2 and 3.

We have observed an average of 2, 2 to 2, 0 respectively for control groups (1 and 2), against 1,5 and 1,4 respectively for group 3

(having received a single injection) and group 4 (having received a double injection of PGF2 α , at 15 days interval). These results are comparable with those found by Ilari and Cardin.

	Control Group	Group 1: Single injection of PGF2 α	Group 2: Double injection of PGF2 α
Ilari (1998)	1,8	1,6	1,3
Cardin (2000)	1,8	1,5	1,3

In addition, Tainturier (1991) brought back an average of 1, 37 in cows which received a single injection of étiproston.

Mami (1997) by using étiproston and by delivering the cows manually, has found 153 days, 98 days and 67 days respectively for control groups (1 and 2), and group 4 (having received a double injection of PGF2 α , at 15 days interval). These averages are very close as of our results: 116 \pm 28,9 day, 80,7 \pm 12,27 days and 70 \pm 17,36 days, respectively for groups 1, 2 and 4. Ilari (1998) and Cardin (2000) have also observed comparable results:

	Control Group	Group 1 : Single injection of PGF2 α	Group 2: Double injection of PGF2 α
Ilari (1998)	114,4 \pm 51	101,7 \pm 32,7	98,4 \pm 44
Cardin (2000)	114,4 \pm 51	98,5 \pm 45,3	98,4 \pm 44

However, it should be noted that the standard deviations of the average values are more significant at Ilari and Cardin compared to our results. That marks a great individual variability inside the two batches.

CONCLUSION

The good course of the postpartum is essential for the reproductive future of the milk cow. The placental retention, current affection after births, involves a fall of cow's reproductive performances: Delayed uterine involution, lengthening of birth conception intervals. Taking into account the specific role of PGF2 α and its synthesis analogues of synthesis on the genital tract (uterotonicity and luteolysis), the experimentation of a double injection of PGF2 α (Cloprostenol), the day of birth, and 15 days after was tried. The uterotonic effect of Cloprostenol seems to be beneficial, and which results in a faster involution uterine (cervix positioned in the pelvic area within 30 days) in the treated compared to non treated cows. Likewise,

the rate of delayed uterine involution (metritis) passes from 30 and 40 % respectively for group's 1 and 2 (untreated animals) to 20 and 10 % respectively for group's 3 and 4 (treated animals). The direct consequence of these changes is an improvement of the fruitfulness of the treated animals, resulting in a significant reduction (31,5 days) of birth conception interval, between group 2 (having received saline injection) and group 3 (having received a single injection of Cloprostenol). In the same way, the number of services by conception which falls of from $2 \pm 0, 66$ for group 2 to $1, 5 \pm 0, 52$ for group 3. In addition to that, the non return to estrus rate observes to him also a clear improvement with 80 and 90 % respectively for the treated groups 3 and 4 against 50 and 60 % respectively for the untreated groups 1 and 2.

We can also concluded from present results that saline injection for control group 2, does not induce any significant difference on the parameters studied compared to control group 1. Finally, a double injection of Cloprostenol (at 15 days interval) gives more favourable results than a single injection.

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