

قسم : الولادة والتلقيح الصناعي .
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تقييم العلاج ببعض قواض الرأحم كوسيلة للوقاية من احتباس المشيمة

في الأبقار الحلابة

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أجريت ثلاث محاولات كطرق وقائيه لتقييم حقن البروستاجلاندين والأوكسيتوسين والإرجومترين بعد الولاده مباشرة وتأثيرها على فترة نزول المشيمه عقب الولاده الطبيعيه وغير الطبيعيه ، وقد أجريت التجربه على ١١٦ بقره من الأبقار الفريزيان والخليط وقسمت الى أربعة مجاميع كالتالى :

المجموعه الأولى : أشتملت على ٣٢ حيوان ٩١ عسر ولاده ، ٢٢ ولاده طبيعيه) تركت بدون علاج واستعملت كضوابط لمقارنة النتائج .

المجموعه الثانيه : أحتوت على ٢٢ بقره (٤ عسر ولاده ، ١٨ ولاده طبيعيه) حقن كل حيوان منها عضليا بواسطة ٢٥ مجم من البروستاجلاندين (اليوتاليز)

المجموعه الثالثه : أشتملت على ٤٠ بقره (٥١ عسر ولاده ، ٢٥ ولاده طبيعيه) حقنت كل بقره منها عضليا بواسطة ٦٠ وحده دوليه اوكسيتوسين .

المجموعه الرابعه : أحتوت على ٢٢ بقره (٤ عسر ولاده ، ١٨ ولاده طبيعيه) حقنت كل واحده منها بواسطة ١٤ مجم ميشيل إرجومترين . وقد كان معدل إحتباس المشيمه فى المجموعه الضابطه ٢٤ر٤٪

مقارنة بنظيرتها فى مجموعه البروستاجلاندين (٢٢ر٧٪) ومجموعه الأوكسيتوسين (١٥٪) ومجموعه الإرجومترين (٢١ر٨٪) . كما أظهرت النتائج ايضا أن الأوكسيتوسين اختزل بطريقه معنويه من معدل إحتباس المشيمه بينما كان البروستاجلاندين من أسرع العلاجات فى طرد المشيمه من حيث الوقت بعد العلاج ، كما كان معدل حدوث التهاب الرحم أقل فى المجموعه المعالجه (٢٢ر١٪) عنها فى المجموعه الضابطه (٢٤ر٤٪) بالإضافة الى أن نسبة الإخصاب كانت مرتفعه فى المجموعه المعالجه عنها فى المجموعه الضابطه .

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**EVALUATION OF VARIOUS UTEROTONIC SINGLE TREATMENTS
FOR PROPHYLAXIS OF RETAINED PLACENTA IN DAIRY COWS**
(With 2 Tables)

By

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SUMMARY

Triple blind randomized clinical trials were performed to assess the efficacy of immediate postpartum (pp) injection of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), Oxytocin and ergometrine on the duration of placental expulsion following both normal and abnormal parturitions. One hundred and sixteen Holstein Friesian and crossbred cows were assigned randomly following calving to one of four treatment groups. Group I, 32 animals [9 had dystocia (D) and 23 had normal birth (NB)] received saline and used as control. Group II, 22 cows [4 D and 8 NB], each animal received 25mg $PGF_{2\alpha}$ [Lutalyse^(R)], Group III, 40 cows (5 D and 35 NB), each cow was administered 60 i.u. oxytocin and Group IV, 22 cows (4 D and 18 NB), each cow was given 1.4 mg methylergometrine. The time until fetal membranes released was calculated. The placenta was considered retained, when the fetal membranes were not released 12 hours PP. The rate of placental retention was 34.4% for controls compared to 22.7%, 15% and 31.8% for $PGF_{2\alpha}$, oxytocin and methylergometrine-treated cows respectively. Oxytocin reduced significantly the occurrence of retained placenta, while $PGF_{2\alpha}$ caused only rapid release of the placenta when injected immediately after calving. Moreover, the incidence of PP metritis was less in the treated groups (23.1% vs 34.4% in the controls). In addition, the percentage of animals having optimum service period was significantly greater ($X^2=23.81$, $P/0.01$) in treated groups than in the non treated control group.

INTRODUCTION

The role of prostaglandin upon the physiological mechanism of placental separation in the cow has been stated by HORTA (1981), where it was shown that cyclooxygenase (enzyme responsible for synthesis of $PGF_{2\alpha}$) inhibition early after calving leads to a retention of the afterbirth. Moreover, the pharmacological effects of PGE_2 and $PGF_{2\alpha}$ was studied in relation to the time needed for placental separation and expulsion and to the strength of uterine contractions (HORTA, 1984). The results obtained suggested that PGE_2 inhibits the normal placental separation process, while $PGF_{2\alpha}$ seems to stimulate this mechanism, consequently it was postulated that an imbalance in $PGE_2/PGF_{2\alpha}$ synthesis early in PP could be associated with placental retention. $PGF_{2\alpha}$ seems to be synthesized in the maternal caruncle because

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the high 15-hydroxyprostaglandin dehydrogenase concentration is supposed to be associated with a high synthetic activity (KEIRSE, et al. 1976, 1977).

It has been known that oxytocin simulates the final myometrial activity and the expulsion of the foetus after the Ferguson's reflex is induced during parturition. Oxytocin release must be sustained thereafter to expell the after birth (RUESSE, 1980). Therefore, exogenous oxytocin has been suggested for prevention of a retained placenta immediately postpartum (ROBERTS, 1971; CURTIS, 1973 and MILLER and LODGE, 1984).

Concomitantly, ergometrine maleate has been demonstrated that has a powerful oxytocic and vasoconstrictor effect (SLOSS and DUFTY, 1980), which is thought to make it valuable in uterine atony.

Although there are good deal of circumstantial recent experimental evidences that PCF₂ oxytocin and ergometrine are uterotonic in early postpartum uterus (SLOSS and DUFTY, 1980; BRETZLAFF and OTT, 1981; ARMSTRONG-BACKUS, et al. 1983; KO, et al. 1985), little is known of their clinical applications for prevention of retained placenta. Therefore, triple blind randomized clinical trials were performed to assess the efficacy of immediate PP injection of PCF₂ oxytocin and ergometrine on the duration of placental expulsion following both normal and abnormal parturations as well as on subsequent fertility.

MATERIAL and METHODS

One hundred and sixteen Friesian Holstein and crossbred cows calved from January 1986 to March 1987 were used in this investigation. In the analysis of the herd over about one year period there was a recorded average of 17.5% retained placentas (39/227). Immediately following calving, all cows were assigned randomly to one of four treatment groups (Table 1). In group I, 32 animals (9 cows had dystocia and 23 had normal birth) received saline and used as control. Group II consisted of 22 cows (4 cows had dystocia and 18 calved normally), each animal received a single injection of 5ml of PCF₂ (25 mg. Lutalyse^(R), Ubjon Co., Kalamazoo MI), immediately following calving. In group III, 40 cows (5 cows had dystocia and 35 calved normally) were given 6ml of oxytocin (60 IU, oxytocin synth. Giba - Geigy Limited, Basle, Switzerland). In group IV, 22 cows (4 cows had dystocia and 18 cows had calved normally) were administered 7ml. of methergin (1.4mg, Methylergometrine hydrogen maleate, Swiss pharma S.A.E. Cairo). The time of calving, time of injection, time of placental release, incidence of calving difficulty (dystocia) and incidence of twins were recorded for all animals. The hours until fetal membranes released were calculated as the time (hours) from calving until spontaneous placental expulsion. Animals were considered to have retained placenta if the foetal membranes were not released within 12 hours PP.

Data were statistically analysed by using t-test and χ^2 according to SNEDECOR and COCHRAN (1976).

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Table (1)
Distribution of experimental animals

| Animals | Control | Treatment | | |
|--------------------------------|---------|--------------------|----------|-----------|
| | | PGF ₂ α | Oxytocin | Methergin |
| No. of cows had dystocia | 9 | 4 | 5 | 4 |
| No. of cows had normal calving | 23 | 18 | 35 | 18 |
| Total No. of animals | 32 | 22 | 40 | 22 |

RESULTS

It is clear from the data (Table 2) that the incidence of placental retention differs between the treated groups. The rate of placental retention was 34.4% for control cows as compared to 22.7%, 15% and 31.8% for the PGF₂α oxytocin and methergin-treated cows respectively.

The mean length of time from parturition to placental release was 5.3±0.23 for the control and 4.4±0.29, 4.8±0.21 and 5.5±0.26 for the PGF₂α oxytocin and methergin-treated animals respectively (Table 2). Moreover, the incidence of postpartum metritis was less in the treated than control group (23.1% vs 34.4%).

The percentage of animals having optimum service period was significantly greater ($X^2 = 23.81$, $P < 0.01$) in treated groups than in the non treated control group (Table 2).

DISCUSSION

Retained placenta has been reviewed and discussed in veterinary literature (ROBERTS, 1971 and SQUIRES, 1980). The normal incidence of retention is 8% in dairy herds but rises from 25 to 70% following dystocia. Treatment of retained placenta has always been controversial issue (PALMER, 1932 and ROBERTS, 1971), however, the prevention of the condition has not been as thoroughly discussed. Methods of prevention have included both the minerals selenium (JULIEN, *et al.* 1976) and iodine (MOBERG, 1959) and Vitamines A, D and E (ISHAK, *et al.* 1983) supplementation of the prepartum cow. Additionally oxytocin and PGF₂α have been suggested for prevention of a retained placenta (ROBERTS, 1971; GURTIS, 1973; MILLER and LODGE, 1984 and GROSS, *et al.* 1986).

Under the condition of these trials a single [M injection of oxytocin (60 IU), PGF₂α (25mg) decreased the percentage of cows with placental retention. This reduction was only significant in animals injected with oxytocin ($X^2 = 3.96$) but failed to show significance in animals injected with PGF₂α. On the other hand, methergin (1.4 mg) failed to show improvement

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in the incidence of retained placenta had seemed to be comparable to control group (31.8% vs 34.4%). These results are partially parallel to the findings of GROSS, et al. (1986) regarding $\text{PGF}_2\alpha$ administration, where they demonstrated that application of $\text{PGF}_2\alpha$ (Lutalyse) within 1 hour PP is effective in reducing the incidence of placental retention for at least induced calving model. Also our results support previous findings of HORTA (1984), GROSS, et al. (1985) and HORTA, et al. (1986) who propose action for $\text{PGF}_2\alpha$ to stimulate placental separation in the cow, as well as they deduced that a deficiency of $\text{PGF}_2\alpha$ or a lack of the conversion of PGE to $\text{PGF}_2\alpha$ is responsible for placental retention. Moreover, this effect was also observed by HERSCHLER and LAWRENCE (1984) after clinical application of fenprostalene (a long acting $\text{PGF}_2\alpha$ analogue) for treatment of cows had retained placenta. Since $\text{PGF}_2\alpha$ had a direct effect on mouse macrophages, increasing their phagocytosis, whether this phenomenon occurs in cattle is unknown (RAZIN, et al. 1978). However, chemotaxis and leucocytes presence in the placentomes are required for normal loosening of the placenta and when both were absent the incidence of retained placenta approached 100% (GUNNINK, 1984 a). Also unidentified leucocyte chemotaxis inhibiting factor (LCIF) was demonstrated in the bovine cotyledons with retained placentas (GUNNINK, 1984 b) and this could be a causative factor for an insufficient loosening process. Moreover, Polish workers (ROMANIUKOWA, 1984) reported that phagocytosis was impaired in cows with retained foetal membranes and metritis.

Some authors have been attempted to minimize the incidence of retained placenta in dairy herds by routinely injection of oxytocin PP in cows with and without difficult parturations (CURTIS, 1973; RUSSE, 1980 and MILLER and LODGE, 1984). Our clinical findings are partially consistent with the previous findings of RUSSE (1980). Advantageously, the results of oxytocin injection PP was superior than the other clinical trials used. Concomitantly RUSSE (1982) demonstrated that exogenous oxytocin given immediately after dystocia or caesarean section reduced considerably the incidence of retained placenta. In contrast, MILLER and LODGE (1984) have observed no significant difference in retained placenta between control and oxytocin treated cows following calving.

Regarding the results of methergin, less encouraging results were observed after administration and had no advantageous effect on placental expulsion in comparison with the control and other treated groups. There was no circumstantial clinical evidence could be obtained from available literature, however, most of the usage of ergonovine (ergot compound) is based on empirical results rather than controlled experiments. In addition, it is considered to produce a prolonged series of uterine contractions which is thought to make it valuable in uterine atony (GUSTAFSSON, 1984). However, in the PP cow (1 to 14 days after parturation), ZEROBIN (1980) failed to demonstrate increased uterine activity immediately or within several hours of the administration of ergometrine maleate.

The data presented here would suggest that both oxytocin and $\text{PGF}_2\alpha$ play a facilitatory role in the dropping of placenta, through enhancing uterine contraction and/or may have a stimulatory effect on phagocytosis by uterine leucocytes (RAZIN, et al. 1978 and VANDEPLASSCHE and BOUTERS, 1983), where the later factor is proved to be required for normal loosening of the placenta (GUNNIUK, 1984).

Regarding service period, advantageous results were noticed in treated cows as compared to control ones. These results are in partial accord with findings of KUCHARSKI, et al. (1980) and BOB, et al. (1984). Contradictorily, RICHEL, et al. (1984) and KUMMER, et al. (1984) did not find any significant difference in the average service period after application of carbetocin (long acting oxytocin). However, they reported that shortest service period was found in cows treated with both oxytocin and $\text{PGF}_2\alpha$. It is difficult to interpret the effect of oxytocin,

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PGF₂ and ergometrine on the interval from calving to conception since the results in individual groups are very different and the differences were caused by a quite number of factors. However, results of several studies indicate that cows with retained placenta have an increased incidence of metritis and that metritis require further treatment and does significantly affect subsequent fertility (SANDALS, *et al.* 1979; RICHEL, *et al.* 1984 and DOHOO and MARTIN, 1984). Consequently, it is conceivable that in herds that have a relatively high incidence of retained placenta administration of oxytocin or PGF₂ immediately following normal or abnormal parturition may would have a beneficial and economic effects to minimize the problem and reduce the costs of further treatment.

Table (2)
Effect of PGF₂ oxytocin and Methergin on placental expulsion in dairy cows.

| Group | Retained placenta | | | Dropped placenta | | | Total No. of Animals | % R.P | Time from treatment to expulsion (hours) | | % of animals with optimum S.P |
|------------------|-------------------|----|-------|------------------|---|-----------------|----------------------|-------|--|-------|-------------------------------|
| | N.B | D | Total | N.B | D | Total | | | Mean | Range | |
| Control saline | 2 | 9 | 11 | 21 | - | 21 ^a | 32 | 34.4 | 5.3±0.23 ^c | 2-8 | 28.1 |
| PGF ₂ | 1 | 4 | 5 | 17 | - | 17 | 22 | 22.7 | 4.4±0.29 ^d | 2-6 | 41 |
| Oxytocin | 3 | 3 | 6 | 32 | 2 | 34 ^b | 40 | 15.0 | 4.8±0.21 | 1-7 | 62.5 |
| Methergin | 3 | 4 | 7 | 15 | - | 15 | 22 | 31.8 | 5.5±0.26 | 3-8 | 41 |
| Total | 9 | 20 | 29 | 85 | 2 | 87 | 116 | | | | |

a and b significantly different from each other 5% level ($X^2 = 3.96$)

c and d significantly different from each other 5% level.

± Standard error.

N.B = Normal birth

D = Dystocia

R.P = Retained Placenta

S.P = Service period

REFERENCES

- Armstrong-Bachus, C.S.; Hopkins, F.M. and Eiler, H. (1983): The uterotonic effect of prostaglandin F₂ and oxytocin on the postpartum cow. Proc. 4th Ann. Meet. Conf. Res. Workers, Chicago, Abstract, 93.
- Bob, O.; Klimes, V.; Reichel, F. Kohouf, L.; Cep, K. and Slegr, J. (1984): Our experience in the application of Depotocin inj. Spofa in the postpartum period. Biol. Chem. Vet. (Praha) XX (XXVI), 3: 197-200.

- Bretzlaff, K.N. and Ott, R.S. (1981): Postpartum reproductive problems in a large dairy herd. *Bovine Clinics* 1, 4: 4-5.
- Curtis, R.A. (1973): Prevention of retained foetal membranes in cattle. *Vet. Rec.* 92: 292-293.
- Dohoo, J.R. and Martin, S.W. (1984): Disease, production and culling in Holstein-Friesian cows. IV. Effects of disease on production. *Prev. Vet. Med.* 2: 75-770.
- Gross, T.S.; Williams, W.F. and Manspeaker, J.E. (1985): In vitro placental prostaglandin synthesis in the late pregnant and peripartum cow. *Biol. Reprod.* 32 (1): 154.
- Gross, T.S.; Williams, W.F. and Moreland, T.W. (1986): Prevention of the retained fetal membrane syndrome (retained placenta) during induced calving in dairy cattle. *Theriogenology*, 26 (3): 365-370.
- Gunnink, J.W. (1984 a): Retained placenta and leucocytic activity. *Vet. Q.*, 6: 49-51.
- Gunnink, J.W. (1984 b): Prepartum leucocytic activity and retained placenta. *Vet. Q.*, 6: 52-54.
- Gustafsson, B.K. (1984): Therapeutic strategies involving antimicrobial treatment of the uterus in large animals. *JAVMA*, Vol. 185, No. 10: 1194-1198.
- Herschler, R.C. and Lawrence, J.R. (1984): A prostaglandin analogue for therapy of retained placentae. *Vet. Med.* June 1984, 822-826.
- Horta, A.E.M. (1981): Accao do acetil salicilato de lisina sobre a expulsao da placenta em bovinos. *Rev. Port. Cien. Vet.* 76: 207-212.
- Horta, A.E.M. (1984): Efeitos das prostaglandinas E₂ e F₂ alpha sobre a retencao placentaria induzida pelo acetilsalicilato de lisina em vacas leiteiras; estudo da motilidade uterina. *zootecnia*, 33: 39-47.
- Horta, A.E.M.; Chassagne, M. and Brochart, M. (1986): Prostaglandin F₂ alpha and prostacyclin imbalance in cows with placental retention: new findings. *Ann. Rech. Vet.* 17, 4: 395-399.
- Ishak, M.A.; Larson, I.I.; Owen, F.C.; Lowry, S.R. and Erickson, E.D. (1983): *Journal of dairy science* 66, 99 [cited after Hickey et al. (1984): Effects of oxytocin on placental retention following dystocia. *Vet. Record*. February 25, 1984 PP. 189-190.
- Julien, W.E.; Conrad, H.R.; Jones, J.E. and Moron, A.L. (1976): Selenium and Vitamin E and incidence of retained placenta in parturient dairy cows. *J. Dairy Sci.* 59: 1954-1959.
- Keirse, J.J.C.; Mitchell, M.D. and Flint, A.P.F. (1977): Changes in myometrial and placental 15 hydroxy prostaglandin dehydrogenase with ovine parturition: production of prostaglandin metabolites in vitro and in vivo. *J. Reprod. Fert.* 51, 409-412.
- Keirse, M.J.C.; Hicks, B.R. and Turnbull, A.C. (1976): Metabolism of prostaglandin F₂ alpha in fetal and maternal cotyledons of sheep. *J. Reprod. Fert.* 46: 417-420.
- Ko, C.H.; Chen, Z.Y.; Whitmore, H.L. McKenna, D.J.; Brodie, B.O. and Gustafsson, B.K. (1985): The effect of prostaglandin on myometrial activity in postpartum cows. The 66th conference of research workers in animals disease, Nov. 11-12, 1985, Chicago, U.S.A.
- Kucharski, J.; Janowski, T.; Chmiel, J. and Glazer, T. (1980): Prophylactic treatment with some uterus contractions performing drugs in cows post-partum. 9th Int. Cong. on Animal reproduction & AI, 16-20 June 1980 Spain-MADRID Vol. IV, 663-665.
- Kummer, V.; Zraly, Z.; Holcak, V.; Hruska, K. Svecova, D.; Veznik, Z. and Canderle, J. (1984): Regulation of puerperium in cows by depotocin and oestrophan. *Biol. Chem. Vet. (Praha)* XX (XXVI), 2: 141-149.
- Miller, B.J. and Lodge, J.R. (1984): Postpartum oxytocin treatment for prevention of retained placenta. *Theriogenology*, 22, 4: 385-389.
- Moberg, K. (1959): Abstract of papers from 3rd world congress on fertility and sterility Amsterdam. P. 914.
- Palmer, C.C. (1932): Clinical studies on retained placenta in the cow. *JAVMA*, 80, 59.
- Razin, B.; Bauminger, S. and Globerson, A. (1978): Effect of prostaglandins on phagocytosis of sheep erythrocytes by mouse peritoneal macrophages. *J. Ret. End. Soc.* 23: 237-242.

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- Reichel, F.; Seveikova, E.; Rajchard, J.; Caslavka, J.; Mojzís, J. and Svab, I. (1984): Testing of carbetocin (Depotocin inj.) on cattle in the field. *Biol. Chem. Vet. (Praha)* XX (XXVI), 2: 153-164.
- Roberts, S.J. (1971): *Veterinary Obstetrics and Genital Diseases (Theriogenology)*. Edward Bros., Ann. Arbor, Mich, 1971, PP. 321-324.
- Romaniukowa, K. (1984): Phagocytosis in the uterus. *Proc. Xth Int. Cong. Anim.* XI 30-33.
- Russe, M. (1982): Myometrial activity postpartum in: Karg H, Schall enberger, E.: *Factors influencing fertility in the postpartum cow*, Boston, Martinus Nijhoff publishing, PP. 55-60.
- Sandals, W.C.D.; Curtis, R.A. Cote, J.F. and Martin, S.W. (1979): The effects of retained placenta and metritis complex on reproductive performance in dairy cattle- A case control study *Can. Vet. J.* 20: 131-135.
- Sloss, V. and Dufty, J.H. (1980): *Handbook of bovine obstetrics*. Williams & Wilkins, Baltimore/London PP. 156. Chapter 10, General Therapy.
- Snedecor, G.W. and Cochran, W.G. (1976): *Statistical methods*, Iowa State College Press, Ames.
- Squires, A.G. (1980): *Current Therapy in Theriogenology I*. Ed. D.A. Morrow, Philadelphia, W.B. Saunders, P. 186.
- Vandeplassche, M. and Bouters, R. (1983): Phagocytosis in the blood and uterine exudate of mares, cows and cows. *Proc. IIIrd Int. Sympos. World Assu. Vet. Lab. Diag.* Ames. IA, 1: 83-89.
- Zerobin, K. (1980): Die uterus motorischen ablaufe während Geburt und Buerperium beim Rind und deren Beeinflussbarkeit, in *proceedings, 11th Int. Congr. Diseases of cattle*, 2: 1127-1163.