Acta vet. scand. 1983, 24, 269—274.

From the Department of Obstetrics and Gynaecology, Faculty of Veterinary Medicine, Swedish University of Agricultural Sciences, Uppsala, Sweden.

EXOGENOUS PROSTAGLANDIN $F_{2\alpha}$ PROMOTES UTERINE INVOLUTION IN THE COW

By

Jan-Otto Lindell and *Hans Kindahl*

LINDELL, J.-O. and H. KINDAHL: *Exogenous prostaglandin $F_{2\alpha}$ promotes uterine involution in the cow.* Acta vet. scand. 1983, 24, 269—274. — Three newly delivered dairy cows were given prostaglandin $F_{2\alpha}$ during the immediate postpartum period. $PGF_{2\alpha}$ was administered from day 3—13 post partum in doses of 25 mg twice daily. Endogenous release of $PGF_{2\alpha}$ and progesterone was studied in blood plasma during the experimental period. Rectal examination of the uterus was performed every second day in order to establish the end of uterine involution. Uterine involution in the three cows was completed days 16, 23 and 20, respectively. These figures are to be compared with earlier investigations of uterine involution times, which show about 27 days. It was concluded that $PGF_{2\alpha}$ had a positive effect on the uterine muscular tone.

uterine involution; prostaglandin $F_{2\alpha}$; bovine.

Recent studies in the cow have demonstrated a massive postpartum release of prostaglandin $F_{2\alpha}$ continuing for 2—3 weeks (*Lindell et al.* 1982). It was further demonstrated that a significant correlation between uterine involution and the duration of the postpartum prostaglandin release exists, e.g. cows with long duration of this postpartum prostaglandin release had a comparatively shorter involutionary period. Furthermore, a positive correlation has been found between time for completed uterine involution and the first ovulation (*Madej et al.* 1983).

The aim of the present investigation was to study whether massive exogenous doses of prostaglandin $F_{2\alpha}$ to newly delivered cows could shorten the period for uterine involution.

---

* This study was supported by grants from Upjohn Company, Kalamazoo, Michigan, U.S.A.

MATERIALS AND METHODS

Three pregnant primiparous dairy cows (crossbreeds of Swedish Friesian Breed, SLB, and Swedish Red and White Breed, SRB) were used in the present study. The animals were stabled at the clinic from about the eighth month of pregnancy. Blood was collected from the jugular vein once daily prior to expected parturition and then twice daily. Blood plasma was removed and stored at —18°C until analysed. The animals were followed during the same period in order to facilitate blood sampling. The endogenously produced $PGF_{2\alpha}$ was determined as the main blood plasma metabolite 15-keto-13,14-dihydro-$PGF_{2\alpha}$. Progesterone was determined as an indicator of corpus luteum function. The hormones were determined by means of radioimmunoassays (*Kindahl et al.* 1976). No attempts were made to determine levels of 15-keto-13,14-dihydro-$PGF_{2\alpha}$ exceeding 3 nmol/l.

Following delivery, rectal examination was performed every second day in order to establish the day when uterine involution was completed. Uterine size, location, tone and symmetry were used as indicators. Complete uterine involution was established when the uterus had returned to its normal location in the pelvic cavity and the consistency and tone of the uterine wall were normal and the uterine horns had become almost equal in size (*Morrow et al.* 1969). The ovaries were palpated in order to follow follicular development.

From day 3—13 after parturition, prostaglandin $F_{2\alpha}$ (Dinolytic, Upjohn Company, U.S.A.) was administered twice daily at 7 a.m. and 5 p.m. The drug was administered intramuscularily in doses of 25 mg each time. The blood samples were collected immediately before the injections of $PGF_{2\alpha}$ thus reflecting the endogenous prostaglandin release.

RESULTS

All 3 cows calved normally at the expected time. The fetal membranes were expelled spontaneously within hours following parturition. As can be seen from Fig. 1, all cows had high levels of the PG-metabolite from the day of delivery and for 10—15 days thereafter. No side effects could be attributed to the massive doses of prostaglandin $F_{2\alpha}$.

In cow No. 1, uterine involution as judged from rectal palpation was completed on day 16. Elevated PG-metabolite levels

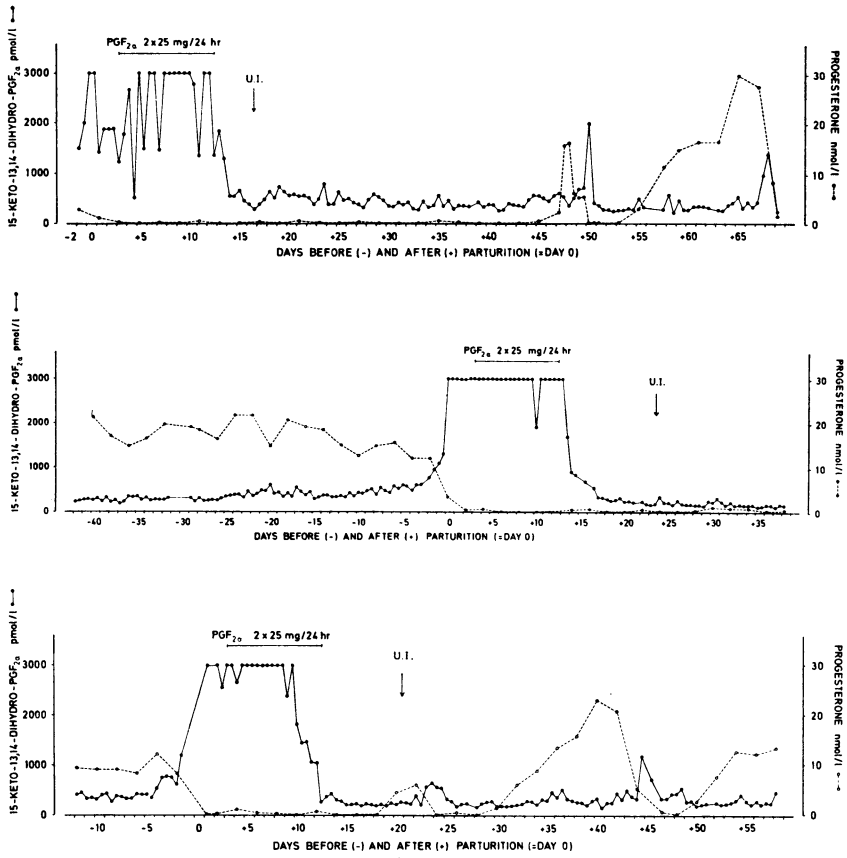

Figure 1. Blood levels of 15-keto-13,14-dihydro-$PGF_{2\alpha}$ (●——●) and progesterone (○---○) in cow No. 1 (upper panel), cow No. 2 (middle panel) and cow No. 3 (lower panel). Horizontal bar indicates days for administration of 25 mg $PGF_{2\alpha}$ twice daily. Arrow and U.I. indicate day for completed uterine involution.

were recorded until day 12 post partum. Follicular growth could not be registered until about day 42 post partum, followed by an increase in progesterone levels. This luteal phase lasted for 4—5 days and ended with a concomitant rise in the PG-metabolite level on day 50 post partum. A new ovulation occurred on day 53 followed by a normal length of cycle.

Cow No. 2 had completed uterine involution on day 23 post partum. The endogenous prostaglandin production was maintained for up to 15 days. No ovarian activity as judged by rectal

palpation and blood progesterone levels could be registered during the observation period of 38 days.

Cow No. 3 had a completed uterine involution on day 20 and an elevated PG-metabolite level was maintained for up to 11 days. This cow had a growing follicle on day 15 followed by a 5—6 days luteal phase which ended in conjunction with an elevation in the PG-metabolite level. A second ovulation occurred on day 27 and this ovulation was followed by a normal length of luteal phase. This luteal phase ended with a release of $PGF_{2\alpha}$. A third ovulation was recorded on day 48.

DISCUSSION

Apart from its effect as a luteolysin in the cow, $PGF_{2\alpha}$ has the physiological effect of stimulating smooth muscle contractility. The effect might be of importance in the role of regulating uterine motility. It has been shown that a relationship exists between the duration of postpartum $PGF_{2\alpha}$ release and the time for uterine involution (*Lindell et al.* 1982). It is reasonable to assume that the uterine synthesis of $PGF_{2\alpha}$ increases uterine muscle tone and thus promotes uterine involution.

The results of this study show that the period for completion of uterine involution after massive exogenous doses of $PGF_{2\alpha}$ is about 20 days, viz. for the 3 cows, 16, 23 and 20 days, respectively. These figures are to be compared with those of earlier investigations in untreated cows which show 26.2 days (*Casida & Wenzke* 1936), 29.4 days (*Casida & Wisnicky* 1959), 29.6 days (*Lindell et al.* 1982), 27.0 days (*Larsson et al.* 1982) and 24.7 days (*Madej et al.* 1983). Thus, it is very likely that high doses of exogenous administration of $PGF_{2\alpha}$ might speed up the uterine involution.

The present study comprised only 3 animals but they all showed a shorter period for uterine involution than the normal.

To further investigate the positive influence of exogenous $PGF_{2\alpha}$, more animals must be treated and especially animals with impaired uterine involution, e.g. due to retained fetal membranes or puerperal uterine infections.

The very high doses of $PGF_{2\alpha}$, 25 mg twice daily, were chosen because of the fact that the uterus itself produces large amounts of prostaglandin, that injected $PGF_{2\alpha}$ is rapidly metabolized and that only minor amounts will reach the uterus. Exactly how much $PGF_{2\alpha}$ will reach the uterus is impossible to calculate, but

taking into account that 25 mg is enough to induce luteolysis and that this treatment had a positive influence on the uterus, the amount should be in the right order of magnitude.

No side effects could so far be attributed to these high doses of $PGF_{2\alpha}$. *Eiler et al.* (1981) found that high repeated doses of $PGF_{2\alpha}$ caused a refractoriness of the uterine musculature. However, from the present study it can be shown that administration of 25 mg $PGF_{2\alpha}$ twice daily did not cause such effects. On the contrary, exogenous $PGF_{2\alpha}$ had a positive effect on the tone of the uterine musculature and involution time.

REFERENCES

Casida, L. E. & W. G. Wenzke: Observations on reproductive processes in dairy cattle and their relation to breeding efficiency. Proc. Amer. Soc. Animal Prod. 1936, *29*, 221—223.

Casida, L. E. & W. Wisnicky: Effects of diethylstilbestrol dipropionate upon postpartum changes in the cow. J. Animal Sci. 1959, *9*, 238—242.

Eiler, H., J. Oden, R. Schaub & M. Sims: Refractoriness of both uterus and mammary gland of the cow to prostaglandin $F_{2\alpha}$ administration; Clinical implication. Amer. J. vet. Res. 1981, *42*, 314—317.

Kindahl, H., L.-E. Edqvist, E. Granström & A. Bane: The release of prostaglandin $F_{2\alpha}$ as reflected by 15-keto-13,14-dihydro-$PGF_{2\alpha}$ in the peripheral circulation during normal luteolysis in heifers. Prostaglandins 1976, *11*, 871—878.

Larsson, K., H. Kindahl, Å. Malmqvist, L.-E. Edqvist & L. Jansson: Post partumperiodens förlopp hos förstakalvande mjölkkor. (The post partum period in primiparous dairy cows). Proc. 14:th Nordic Veterinary Congr., Copenhagen 1982, 327—331.

Lindell, J.-O., H. Kindahl, L. Jansson & L.-E. Edqvist: Postpartum release of prostaglandin $F_{2\alpha}$ and uterine involution in the cow. Theriogenology 1982, *17*, 237—245.

Madej, A., H. Kindahl, W. Woyno, L.-E. Edqvist & R. Stupnicki: Blood levels of 15-keto-13,14-dihydro-$PGF_{2\alpha}$ during the postpartum period in primiparous cows. 1983 (submitted for publication).

Morrow, D. A., S. J. Roberts & K. McEntee: A review of postpartum ovarian activity and involution of the uterus and cervix in cattle. Cornell Vet. 1969, *59*, 134—154.

SAMMANFATTNING

Exogent prostaglandin $F_{2\alpha}$ förkortar tiden för livmoderinvolutionen hos ko.

Under senare år har visats att livmodern hos ko producerar stora mängder prostaglandin $F_{2\alpha}$ under förlossningen samt under en

period på mellan 2 till 3 veckor därefter. Vidare har visats ett samband mellan durationen av denna prostaglandinfrisättning och tiden för livmoderns involution. Ju längre tid efter förlossningen som prostaglandin frisättes ju snabbare sker involutionen. I föreliggande undersökning har 3 nykalvade kvigor behandlats med $PGF_{2\alpha}$ under tiden 3—13 dagar efter förlossningen. Dosen har varit 25 mg och djuren har behandlats med denna dos två gånger dagligen. Rektalundersökning har utförts var annan dag för fastställande av tidpunkten när livmoderinvolutionen är avslutad. Resultaten visade att livmodern hos de 3 kvigorna var helt återbildad efter respektive 16, 23 och 20 dagar. Detta är en förkortning av tiden jämfört med tidigare undersökningar vilka visar i genomsnitt ca 27 dagar.

(Received August 4, 1983).

Reprints may be requested from: Jan-Otto Lindell, the Department of Obstetrics and Gynaecology, Faculty of Veterinary Medicine, Swedish University of Agricultural Sciences, S-750 07 Uppsala, Sweden.